Application of automated MRI volumetric measurement techniques to the ventricular system in schizophrenics and normal controls*

Martha E. Shenton¹, Ron Kikinis², Robert W. McCarley¹, David Metcalf², James Tieman² and Ferenc A. Jolesz²

Harvard Medical School, ¹Department of Psychiatry (Brockton VAMC and Massachusetts Mental Health Center) and ²Department of Radiology (Brigham and Women’s Hospital), Brockton, MA, U.S.A.

(Received 4 September 1990, revised received 13 December 1990, accepted 20 December 1990)

As an initial approach to computer-automated segmentation of cerebral spinal fluid (CSF) vs. brain parenchyma in MR scans, and the transformation of these data sets into volumetric information and 3D display, we examined the ventricular system in a sample of ten chronic schizophrenics with primarily positive symptoms and 12 normal subjects. While no significant differences were noted between groups on volumetric measures of ventricular brain ratio or lateral ventricle size, normals showed a pattern of left > right lateral ventricular volume asymmetry not present in the schizophrenics. Within the schizophrenic group, departure from the normal left > right pattern was highly correlated with thought disorder.

Key words: Magnetic resonance imaging; Ventricular volume; Magnetic resonance imaging volumetric measurement

INTRODUCTION

With the advent of new in vivo brain imaging techniques such as computed axial tomography (CT) and magnetic resonance imaging (MRI), it has now become possible to test longstanding hypotheses of abnormal morphometric features in the schizophrenic brain (e.g., Bleuler 1911/1950; Kraepelin, 1919). Many CT studies in schizophrenia have reported enlargement of the lateral and third ventricles and of the sulci, findings which, though nonspecific, may indicate tissue loss or failure of development (e.g., Johnstone et al., 1976; Weinberger et al., 1979; Nasrallah et al., 1982; see also discussion in McCarley et al., 1989, and review in Shelton and Weinberger, 1986). Similar CSF space abnormalities have been reported in MRI studies in schizophrenia (e.g., Besson et al., 1987; Kelsoe et al., 1988; Andreasen et al., 1990; Suddath et al., 1990). That negative findings have also been reported (e.g., Smith et al., 1984, 1987; Mathew et al., 1985; Rossi et al., 1990) suggests that particular features of abnormal brain morphology may be present in only a subgroup(s) of schizophrenic patients and/or may reflect methodological differences.

A clear desiderata in MRI ventricular studies would be to have automated segmentation techniques that fully exploit volumetric information, thus maximizing sensitivity and reducing potential inconsistencies inherent in manually performed linear/area measurements. We here summarize the methodology, and present initial results, of what is to our knowledge the first use of automated.
computerized MR image processing techniques to make volumetric measurements and three-dimensional displays of brain and CSF spaces in a sample of chronic schizophrenics and normal controls. Our goals were thus two-fold: (1) to describe specific methodological advances in extracting and displaying information from MR scans, and (2) to illustrate the application of these new image processing techniques in a small subject sample.

METHODS

Subjects
The schizophrenic group was comprised of ten chronic, male, right-handed, neuroleptic medicated schizophrenics (median daily dose equivalent to 860 mg of chlorpromazine), recruited from in-patient wards at the Brockton Veterans Administration Medical Center. Information from the Schedule for Affective Disorders and Schizophrenia (SADS) (Spitzer et al., 1978) and from chart reviews was used to make DSM-III-R (APA, 1987) diagnoses. Further criteria for subject selection were: between the ages of 20 and 55, right-handed, no history of ECT (electroconvulsive shock treatment), no neurological illness, no significant alcohol or drug abuse in the last 5 years (using DSM-III-R criteria and determined from a series of interview questions regarding the amount of alcohol consumption over various time periods), and no medications with known effects on brain MRI. The descriptive data for this sample are presented in Table 1 which shows that the patients were chronic and had a preponderance of positive symptoms.

12 normal control subjects, carefully screened for disease factors that could affect brain function, including alcohol abuse, were recruited from among hospital staff and were matched for sex, handedness and age. They were receiving no medication, and had no history of psychiatric or neurological illness in themselves or in their first degree relatives. There were no significant differences between the two groups in height, weight, head circumference, or social-economic status of family of origin (see Table 1). Differences were present in education ($p < 0.002$) and there was a non-significant trend for normal controls to have a higher estimated verbal IQ (based on Information Subscale; $p \leq 0.058$) (see Table 1). All subjects gave informed consent.

MR imaging protocol

Instrumentation. The MRI data were acquired using conventional long repetition rate double echo spin echo sequences on a GE Signa 1.5 Tesla MRI System (General Electric Co., Milwaukee, WI) with a standard 30 cm head coil. Multi-axial, long TR, double echo series were performed with either TR = 2800 TE 30/80 ms, slice thickness 5 mm, and 2.5 mm gap (50%), for the patient group, or TR = 2000 TE 30/80 ms, interleaving 5 mm, no gap, for the normal control group. In these double echo images the second echo provides high contrast for CSF while the combination of first and second echoes provides the best contrast between gray and white matter. The protocols were different because of upgrades in the hardware and software of the MR scanner which followed the data collection on the schizophrenic patients. This upgrade allowed the acquisition of more data, and hence better spatial resolution, without sacrificing signal-to-noise ratio. Careful visual examination of the images from the two protocols revealed no visually apparent differences in the contrast between CSF and brain in the two sets of images. However, since the two protocols were different, we thought it important to test for any measurable effect of parameters by comparing them in the same subject. Thus for control purposes we acquired both protocols in one subject and then followed the same procedure of segmenting the images into tissue classes (e.g., brain, CSF, connective tissue/vessel – see below) for both acquisitions. The differences between these two protocols on all of the absolute and relative volumetric measures (i.e., % of intracranial volume), for all tissue classes, were less than 1%. Further independent data showing the comparability of the two protocols is presented in Kikinis et al. (1990). We emphasize nevertheless that these differences were taken into account in making calculations regarding the number of slices needed to obtain the 120 mm slab that contained the ventricular system. For the no gap protocol, the distance between slice centers was 5 mm and we used 24 slices to comprise the 120 mm slab ($5 \times 24 = 120$); for the 2.5 mm gap protocol, the distance between slice centers was 7.5 mm so we used 16 slices to comprise the 120 mm slab.
<table>
<thead>
<tr>
<th></th>
<th>Schizophrenics</th>
<th>Normal controls</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n</strong></td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>40.90 ± 0.1615</td>
<td>40.30 ± 0.27</td>
</tr>
<tr>
<td><strong>Height (inches)</strong></td>
<td>70.50 ± 0.73</td>
<td>70.21 ± 0.32</td>
</tr>
<tr>
<td><strong>Weight (lbs.)</strong></td>
<td>179.40 ± 30.90</td>
<td>180.60 ± 26.76</td>
</tr>
<tr>
<td><strong>Head circumference</strong></td>
<td>58.75 ± 0.59</td>
<td>57.79 ± 0.23</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td>11.75 ± 0.18</td>
<td>16.58 ± 0.14</td>
</tr>
<tr>
<td><strong>Social class family of origin</strong></td>
<td>3.20 ± 0.103</td>
<td>2.82 ± 0.133 (n = 11)</td>
</tr>
<tr>
<td><strong>Wais-Verbal IQ</strong></td>
<td>100.60 ± 18.14</td>
<td>119.70 ± 22.76 (n = 10)</td>
</tr>
<tr>
<td><strong>Age of onset (years)</strong></td>
<td>20.10 ± 0.38</td>
<td></td>
</tr>
<tr>
<td><strong>Duration of illness (months)</strong></td>
<td>231.00 ± 74.26</td>
<td></td>
</tr>
<tr>
<td><strong>% time in hospital</strong></td>
<td>63.10 ± 0.26</td>
<td></td>
</tr>
<tr>
<td><strong>Mostly positive symptoms</strong></td>
<td>7</td>
<td></td>
</tr>
<tr>
<td><strong>Mostly mixed symptoms</strong></td>
<td>3</td>
<td></td>
</tr>
<tr>
<td><strong>Mostly negative symptoms</strong></td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Total thought disorder</strong></td>
<td>90.02 ± 64.25</td>
<td></td>
</tr>
</tbody>
</table>

*a* = Head circumference assessed using nasion, inion, and preauricular landmarks.

*b* = 3.56, df = 20, p < 0.002.

*c* = 0.73, df = 19, p < 0.474 (SES-based on the Hollingshead Index (Hollingshead, 1965) where 1 = business/professional, 2 = medium business, 3 = skilled, 4 = semiskilled, and 5 = unskilled.

*d* = 2.02, df = 18, p < 0.058.

*e* = Actual time in months spent in the hospital divided by duration of illness defined by the time span between first hospitalization and the present.

*f* = Ratings done using the Scale for Assessment of Positive Symptoms (SAPS, Andreasen, 1984).

*g* = Ratings done using the Scale for the Assessment of Negative Symptoms (SANS, Andreasen, 1981).

*h* = Assessment of total thought disorder using the Thought Disorder Index (TDI) (Solovay et al., 1986).

(7.5 × 16 = 120; interpolations were made for data between slices). We emphasize also that all volumes computed on the gap protocol were adjusted by extrapolation to reflect true brain volume of the tissue class under consideration, as is standard using a single pass Spin Echo technique (Pavlicek et al., 1984). The no gap is simply a spin echo sequence with two passes, with the second pass covering the area not included in the first. In a single pass spin echo, the values in the gap are based on interpolations from information from the slice below and above the gap. The start and end point for the 120 mm used the same landmarks, as described below.

**Landmarks and normalization.** As an initial approach to brain volumetric analyses we focused on a brain slab selected to include the entire ventricular system, including the third and fourth ventricles. This slab was defined as beginning 15 mm below the internal acoustic canal (IAC), a convenient and objective reference point, and extending 120 mm rostrally. Measurements were made on all intracranial contents within this slab and all were corrected for head size.* For convenience in reference we will henceforth refer to this 120 mm slab as the intracranial cavity (ICC).

**Computer assisted volumetric measures.** Axial images were processed on a DEC Micro Vax (Digital Equipment Corporation, Westborough, MA) and in some cases on a 386 PC with a 16-bit image processing system. For the sake of brevity we present only the normalized data.

*The formula for normalization for head size was: \[a/(3-a)/a(3-a)^2\]; where \(a\) is the length of the structure (from the IAC to the top of the 120 mm mark) divided by the radius of the sphere (from IAC to vertex) for each subject. The mean was then derived for all \(a\)'s (there were no differences between normal controls and schizophrenics and so the numbers were pooled, \(n=22\)). The mean for all subjects was then used as the term in the denominator. All anatomical measures for each subject were then multiplied by this individually specific scale factor. When calculations were performed for the non-normalized data, the results were virtually the same, i.e., the same measures discriminated between groups. Further, when volume was calculated using relative volume, i.e., % of intracranial volume, again, the same measures discriminated between groups. For the sake of brevity we present only the normalized data.
MA) with ITEX image processing hardware using: (1) a semi-automated algorithm to identify the intracranial cavity (ICC), (2) a fully automated separation of its contents into brain, CSF, and vessels/tissues, and (3) a semi-automated separation of the CSF into subarachnoidal space and ventricular space (entire system contained in 120 mm slab). The 3D representation of the ventricular system was carried out using a connectivity program (see below) in conjunction with a TAAC board on a SUN workstation for visual display and operator interaction.

STEP 1 An automated edge detection algorithm was used to identify the intracranial cavity (ICC) for each subject. This generated short line segments which were connected automatically under the assumption that the ICC has a curvilinear shape. The outline of the ICC was then used as a mask for the remaining steps.

STEP 2 The contents of the ICC were divided into brain, CSF, and connective tissue/vessels based on a multivariate look-up table (Udupa et al., 1982). This procedure uses information from both the first echo of the spin echo sequence (see Fig. 1B, column 1) and the second echo of the spin echo sequence (see Fig. 1B, column 2) in making tissue characterizations. For example, part of the algorithm used the rule that what is bright on both the first and second echo is initially classified as CSF. Then, in addition, a local histogram technique was used to compensate for fluctuations in signal intensity (see Sandor et al., 1988). The absolute volumes of each pixel (voxels) were then used to calculate volumes, automatically, for all slices and for each tissue class (for more details see Kikinis et al., 1990; Sandor et al., 1990). Thus at the end of the analysis, a tabulation of absolute and relative volumes was provided for all tissue classes and this information was available for every slice and also for specified 3D brain tissue/structures.

STEP 3 CSF was further differentiated into subarachnoidal and intraventricular regions by placing the cursor manually on intraventricular spaces and using a 2D region growing algorithm to change all of the contiguous CSF labeled pixels in these regions into a different label and color code on the display (see Fig. 1A). This process was completely automated. The only manual steps performed involved placing the cursor on the left and right lateral ventricles (manually separated by a midline division), and on the subarachnoidal space. The automation of the region growing algorithm is desirable because it is: (1) repeatable, and (2) the computer is ‘blind’ to subject group and to left vs. right lateral ventricles. The color coded segmentation of tissue can be seen in Fig. 1B (see column 3), where the final tissue characterization for three different axial slices is presented. This figure serves as an illustrative example only since the final product is the volume measures based on all slices that comprise the ventricular system, as well as the 3D display of the ventricular system (see below; see also Fig. 1A). Ventricular brain ratio (VBR) was computed by dividing the volume of the lateral ventricles by the volume of the ICC contained in the 120 mm slab. Brain/CSF ratio was also computed (atrophy measure).

STEP 4 3D reconstructions were generated from the labeled maps that were used for volumetric analysis; this step involved using a connectivity program that marked the surface voxels and used the dividing cubes algorithm of Cline et al. (1987, 1988) to then generate a model of the surface. This procedure is very different from previous techniques for extracting information from MR data sets in that it is able to use data from an arbitrary number of 2D slices to create a 3D representation. The process, and its end result, is analogous to tightly fitting a rubber sheet over the surface of a structure. To correlate the extent of agreement of results from this new approach with previous measures, we also calculated area measurements for the lateral ventricles using the axial slice which showed the largest body of the lateral ventricles, as done for our CT work (McCarley et al., 1989). The outline of the intracranial cavity, and the body of the lateral ventricle, was then traced and digitized (wire-grid electromagnetic digitizer, SPD-Series Graphics Tablet Scriptel Corporation, 1985). Interrater reliability for this procedure for two raters was r = 0.929 (n = 20, p < 0.001). All MR images were evaluated by a clinical neuroradiologist who reported no gross abnormalities for any of the subjects.

RESULTS

Fig. 1A illustrates the results of the image processing and three-dimensional ventricular system re-
construction possible with this technique. The three different perspectives on the ventricular system illustrate the capability for rotations in 3-space. Of note is the detail of the rendering of the island in the third ventricle produced by the thalamic massa intermedia and the relatively modest in vivo size of the temporal horn portion of the lateral ventricle. Fig. 1B illustrates the information gleaned from T2 weighted and proton density images when they are segmented using the specialized image processing hardware and software that we described in the Methods section.

As shown in Table 2, there were no significant differences between schizophrenic and control groups for: (1) CSF volume (total, subarachnoidal or ventricular CSF), (2) brain volume, or (3) volume of connective tissue/vessels. There were also no significant differences noted for brain/CSF ratio or VBR (ventricles/ICC x 100). Similarly, the manual linear VBR measurements showed no group differences and there was a high correlation between values obtained using the automated volumetric and the manual linear measurements (r = 0.91, p < 0.001).

A comparison of left vs. right lateral ventricle volumes did however reveal that the normal subjects showed a left > right asymmetry (11/12 subjects, p ≤ 0.05, Mann Whitney U test; and r = -4.40, df = 11, p ≤ 0.001), whereas the schizophrenics did not show a statistically significant left > right asymmetry and, in fact, 3/10 schizophrenics showed a right > left pattern (see Table 3). The schizophrenics also showed a statistically significantly larger variance on the left-right measure of asymmetry (\(F_{max} = 7.08, df = 9, 11, p ≤ 0.01\)).

Our previous CT study in schizophrenia (McCarley et al., 1989) found a significant association within the schizophrenic group between abnormalities of left temporal lobe CSF spaces and the Thought Disorder Index (TDI) (Solovay et al., 1986). We therefore thought it important in the present study to examine the relationship, within the schizophrenic group, between the trend toward an abnormal left-right lateral ventricular system asymmetry and TDI scores. These two variables were highly and statistically significantly correlated (see Fig. 2; Spearman’s rho = -0.93, p ≤ 0.01, two-tailed test); schizophrenics who showed more left > right asymmetry (the pattern shown by normals) had lower thought disorder while those with right > left asymmetry (a pattern unlike the normals) showed higher thought disorder.

**DISCUSSION**

The goals of this study were two-fold: (1) to present automated brain-CSF voxel segmentation techniques and their use in volumetric measurements and 3D reconstructions of MR images, and (2) to present illustrative, initial data from the application of these techniques to a small sample of schizophrenic patients and normal control subjects. We believe that these techniques represent an important new approach to quantifying information from MR images, while three dimensional reconstruction allows the visual depiction of complex structures. Previously applied to patients with neurological disorders (Kikinis et al., 1990), these new techniques also appear to be useful in studies of schizophrenics and, as an initial illustrative application, we have examined the ventricular sys-
Level of: 4th Ventricle

Level of: Temporal & Occipital Horns of Lateral Ventricles

Level of: Slice Showing Largest Area of Lateral Ventricle
TABLE 2

**Absolute volume (cm³) and relative volume of brain and CSF spaces in schizophrenics and normal control subjects (120 mm)**

<table>
<thead>
<tr>
<th>Group</th>
<th>Anatomical region</th>
<th>Absolute volume* mean (SD)</th>
<th>p value</th>
<th>Relative volume (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCL</td>
<td>Total ICC−120 mm slab</td>
<td>1,505.03 ± 119.82</td>
<td>0.383</td>
<td>100.00</td>
</tr>
<tr>
<td>SZ</td>
<td>(Intracranial cavity)</td>
<td>1,545.35 ± 84.88</td>
<td></td>
<td>100.00</td>
</tr>
<tr>
<td>NCL</td>
<td>Brain</td>
<td>1,212.23 ± 092.49</td>
<td>0.148</td>
<td>80.62</td>
</tr>
<tr>
<td>SZ</td>
<td></td>
<td>1,267.95 ± 078.53</td>
<td></td>
<td>82.05</td>
</tr>
<tr>
<td>NCL</td>
<td>CSF</td>
<td>237.02 ± 041.38</td>
<td>0.665</td>
<td>15.72</td>
</tr>
<tr>
<td>SZ</td>
<td>(Subarachnoidal)</td>
<td>229.98 ± 031.69</td>
<td></td>
<td>14.88</td>
</tr>
<tr>
<td>NCL</td>
<td>CSF</td>
<td>30.06 ± 014.98</td>
<td>0.147</td>
<td>1.96</td>
</tr>
<tr>
<td>SZ</td>
<td>(Intraventricular)</td>
<td>22.26 ± 007.12</td>
<td></td>
<td>1.44</td>
</tr>
<tr>
<td></td>
<td><strong>Subcomponents of intraventricular CSF (CSFVENT)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(a) Lateral ventricles</td>
<td>24.21 ± 012.72</td>
<td>0.123</td>
<td>[1.58]</td>
</tr>
<tr>
<td></td>
<td>(b) Left ventricle</td>
<td>17.06 ± 006.42</td>
<td></td>
<td>[1.11]</td>
</tr>
<tr>
<td></td>
<td>(c) Right ventricle</td>
<td>13.02 ± 006.85</td>
<td>0.114</td>
<td>[0.85]</td>
</tr>
<tr>
<td></td>
<td>(d) 3rd and 4th ventricles</td>
<td>11.19 ± 005.92</td>
<td>0.146</td>
<td>[0.73]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8.03 ± 003.17</td>
<td></td>
<td>[0.52]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.76 ± 002.29</td>
<td>0.486</td>
<td>[0.38]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.20 ± 001.05</td>
<td></td>
<td>[0.34]</td>
</tr>
<tr>
<td>NCL</td>
<td>Connective tissue/</td>
<td>25.72 ± 006.24</td>
<td>0.813</td>
<td>1.71</td>
</tr>
<tr>
<td>SZ</td>
<td>vessels</td>
<td>25.16 ± 004.40</td>
<td></td>
<td>1.63</td>
</tr>
</tbody>
</table>

*Note that the values here are larger than in many other studies although our VBR measure is similar to that noted in a previous CT study done in our laboratory (McCarley et al., 1989) and these values are within the range of 9-35 cm³ for lateral ventricles reported in the literature (e.g., Grant et al., 1988 (13.7±5.2 ml); Wyper et al., 1979 (37 ml)).

TABLE 3

**Comparison between left and right lateral ventricles for schizophrenics and normal control subjects**

<table>
<thead>
<tr>
<th>Anatomic region</th>
<th>Group</th>
<th>Mean (SD)</th>
<th>Paired t test</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left lateral ventricle</td>
<td>Schizophrenic</td>
<td>9.03 ± 3.64</td>
<td>-1.35</td>
<td>9</td>
<td>0.210</td>
</tr>
<tr>
<td>Right lateral ventricle</td>
<td></td>
<td>8.03 ± 3.17</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left lateral ventricle</td>
<td>Controls</td>
<td>13.02 ± 6.85</td>
<td>-4.40</td>
<td>11</td>
<td>0.001</td>
</tr>
<tr>
<td>Right lateral ventricle</td>
<td></td>
<td>11.19 ± 5.92</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

In a sample of schizophrenics and normal control subjects.

In this initial small sample, no differences between groups were noted on several over-all volumetric measurements: (1) CSF volume (total, intraventricular, or subarachnoidal), (2) brain volume, (3) brain/CSF ratio (atrophy measure), (4) connective tissue/vessels, (5) VBR, or (6) third and fourth ventricle volume. This lack of schizophrenic-normal differences on the CSF measure is in contrast to many previous reports (reviewed in Shelton and Weinberger, 1986) although there have also been reports of negative MR findings (e.g., Smith et al., 1984, 1987; Mathew et al., 1985; Rossi et al., 1990). While it is difficult to interpret negative findings, which are not unexpected using small sample sizes, we think it equally important to point out some possible differences in our subject populations which may also contribute to the lack of CSF differences.
First, although both schizophrenics and normals were within the CSF volume ranges reported in the literature (e.g., Wyper et al., 1979; Grant et al., 1987, 1988), both were in the upper range, suggesting possible sample variation. Second, the schizophrenic patients studied by us had predominantly positive symptoms (7/10, with the remaining three being of mixed symptom type), and, third, all were right-handed. These sample characteristics may represent an important departure from those samples where large ventricular volumes were found in schizophrenics, i.e., the strongest correlations in the CT literature has been between negative symptoms and enlarged lateral ventricles (see Shelton and Weinberger, 1986). In addition, Andreasen and co-workers (1982, 1985) reported that 31% of patients characterized by negative symptoms were left-handed, and in a recent MRI report by this group, schizophrenics with negative symptoms had significantly larger lateral ventricles than those with mixed or positive symptoms (Andreasen et al., 1990). It is also known that right handedness reduces variations in known asymmetries of brain morphology (LeMay, 1984).

Our negative findings, therefore, may reflect a different subgroup of patients, possibly indicating very different pathology, who, though clearly chronic, were right-handed and showed a preponderance of positive symptoms. This line of reasoning is compatible with current concepts of heterogeneity of schizophrenia and multiple subgroups (Tsuang and Simpson, 1988). We think it unlikely that our findings are due to differences between our computerized vs. previous manual measurements (see Jack et al., 1988), since our manual area measurements were highly correlated with computerized measurements of the lateral ventricles and neither method showed a statistically significant difference between groups.

A positive finding of interest in the current study was that normal control subjects showed a left > right asymmetry in lateral ventricle size. This finding is consistent with the literature using manual measurements (LeMay, 1984). The schizophrenic patients in our sample did not show a statistically significant left > right asymmetry; in fact 3 out of 10 showed the reverse asymmetry, right > left. The absence of asymmetry in the schizophrenic group is consonant with recent MRI reports. For example, Suddath et al. (1990) reported bilateral lateral ventricular enlargement in the ‘ill’ member of identical twins discordant for schizophrenia but found no asymmetry. A lack of asymmetry was also present in the schizophrenic samples of Rossi et al. (1990) and Stratta et al. (1989). Heckers et al. (1990) found no left-right asymmetry in their schizophrenic group as a whole compared to normal controls although a paranoid subgroup did show left > right asymmetry compared with normals. Kelsoe et al. (1988) reported no asymmetry for the schizophrenic group, although a posterior > anterior enlargement was present. Crow’s (1990) study of post-mortem brains of schizophrenics found that the left temporal horn was larger than the right in schizophrenic patients.

That the absence of asymmetry in the current study has clinical and functional significance is suggested by the high correlation of thought disorder with the degree of departure from the normal L > R asymmetry (rho = -0.93). We caution that the small size of the present sample makes uncertain the extent of generalizability of the finding to the entire population and makes important a replication in a larger sample. Finally we note the departure of schizophrenics from the symmetry or asymmetry pattern shown by normals on a variety of other biological variables, including P300 electrophysiological measures (McCarley et al., 1991), post-mortem morphometric measures (Brown et al., 1986; Jakob and Beckman, 1989), in vivo MRI

---

**Fig. 2.** Relationship between left minus right lateral ventricle volume (in cm³) and Total Thought Disorder Index score within the schizophrenic group (n=8 had both measures; Spearman’s rho = -0.93, p<0.01, two-tailed).
ACKNOWLEDGMENTS

The authors gratefully acknowledge the technical and administrative support provided by Brian Chiango, Maureen Ainslie, Eve Chiango, Mary Ellen Korvec, Mary Egan, and Susan Johnson; and the editorial comments and suggestions provided by Steven Faux, Paul Nestor, Brian O’Donnell, Seth Pollak, and Scott Smith.

REFERENCES

Mathew, R.J. and Partain, C.L. (1985) Midsagittal sections of
the cerebellar vermis and fourth ventricle obtained with magnetic resonance imaging of schizophrenic patients. Am. J. Psychiatry 142, 970–971.


