Many attempts have been made to measure the volume of the various intracranial compartments in humans. Most investigators have used traditional volumetric methods (casts) to make such measurements, which generally have been limited to measurement of the brain and/or ventricular size. The use of fresh or fixed autopsy material has led to the introduction of various artifacts attributable to post mortem swelling and/or shrinkage due to fixation. Extraventricular cerebrospinal fluid (CSF) volume has been difficult to assess by these methods, including computerized tomography (CT), because of the unavoidable introduction of artifacts, insufficient resolution to depict the entire sulcus system, and the inadequate contrast between the brain and CSF. Many of these artifacts are avoided or minimized with the use of magnetic resonance (MR) imaging, which provides enhanced contrast discrimination and resolution of the various cranial compartments. In the present study we have used MR image-based segmentation to measure the brain, ventricular, and extraventricular CSF volumes of normal volunteers.

Clinical Material and Methods

Population Studied

This study was reviewed and approved by the institutional human research committee and all individuals studied provided informed consent prior to participation. A total of 26 male (54 ± 16 years of age, range 24–80) and 23 female (58 ± 16 years of age, range 29–79) volunteers underwent MR imaging of the head between March 1988 and November 1991. Twenty-three men 38 to 80 years old were selected from the database of the Normative Aging Study at the Boston Veterans Administration Outpatient Clinic, details of which have been provided previously. The other 26 participants were selected from our own database, and although they did not undergo laboratory or neuropsychological testing as did those from the normative aging study, they were deemed to be free of any severe cardiovascular, neurological, or psychiatric disorder, including drug abuse and alcoholism.
Magnetic Resonance Imaging Procedures

Magnetic resonance images of the brain were obtained on a 1.5-tesla imaging system (Signa; General Electric Corp., Milwaukee, WI) using double-echo (echo times 30 and 80 msec), long-repetition time (TR) 2000–4000 msec), multislice (interleaved 3- or 5-mm slice thickness), spin-echo data and 256 × 192 matrix, with a half Fourier technique. The images covered the entire brain from the vertex to the foramen magnum. The data were processed on a Sun Microsystems (Mountain View, CA). Initially, the double-echo long TR images were filtered to improve the signal/noise ratio. Figure 1a and b shows paired proton density and T2-weighted images that were obtained from one of our volunteers. A scatterplot (Fig. 1c) was derived by plotting the pixel signal intensities from the proton and T2-weighted images in which the operator identified standard sampling points for each tissue category. Proton density images were used to identify air and bone for background and extracranial tissue. Because the CSF appears isointense on the proton density image and bright on the T2-weighted image, the latter images were used to identify brain and CSF. The selected loci for brain were the frontal cortex, cerebellar cortex, dentate nucleus, head of the caudate nucleus, red nucleus, globus pallidus, internal capsule, cerebral peduncle, splenium, and genu of the corpus callosum, and for CSF the cerebellomedullary and preoptic cisterns, and both of the anterior horns and trigone of the lateral ventricles. Each selected locus appears on the scatterplot, and computer interpolation was used to calculate the nearest neighbor and to create a feature map (Fig. 1d). The latter was then used to derive the segmented images (Fig. 1e) from which the computer automatically extracted the signal for extracranial tissues. Correction for ventricular CSF was made semiautomatically with a connectivity program that generated the final segmented image (Fig. 1f). The areas in square centimeters were then calculated from the final segmented image.
by counting pixels, and the volume in cubic centimeters was generated by multiplying by the slice thickness. All image processing was done on an MR console with programs developed by General Electric and the Surgical Planning Laboratory of this institution. Segmentation and volumetric analysis were performed using methods that have been previously tested for accuracy and reliability. Intracranial, brain, ventricular, and extraventricular CSF volumes were examined separately. Intracranial volume in cubic centimeters was calculated as the sum of the brain, ventricular, and extraventricular CSF volumes.

Values for the absolute or relative volume of the various intracranial compartments in men and women are reported either as sample means ± sample standard deviations (SDs) or as percentages of the intracranial volumes, respectively. The latter, referred to as regular values, do not require correction for the long-term increase in brain weight postulated to affect the population as a whole during the last century because it can be assumed that such increases, which generally are attributed to such factors as improved nutrition and increased body stature, would affect brain and intracranial volume similarly. To determine the influence of age on these parameters, values for both women and men were sorted according to age into three 20-year age-span groups or plotted as a function of age (Fig. 2), the values for both sexes decreased with age, although less distinctly for women.

Assessment of Error

To assess the error (SD/mean) of these measurements, segmentation and volumetric determinations were repeated three times on each of four men and four women ranging in age from 37 to 77 years who were selected randomly. To reduce bias, repeat measurements on each participant were separated by more than 1-month intervals. The repeat segmentation and volumetric determination of the eight selected cases indicated the errors to be 1.0%, 1.9%, 4.6%, and 7.7% for the respective intracranial, brain, ventricular, and extraventricular CSF volumes.

Statistical Methods

Analysis of variance was used for determination of statistical significance between the absolute intracranial compartment volumes and the relative values of the two sexes and the three age groups. Computer programs were used for statistical analysis and to derive best fitting curves (Figure-P; Biosoft, Ferguson, MO).

Results

Total Intracranial Volume

All subjects were sorted into three age groups, each covering two decades (Table 1). The absolute and relative mean values for the intracranial and brain volumes and the various CSF volumes for men and women are shown in Table 2, whereas the p values for comparisons between volumes are listed in Table 3. The average total intracranial volume was significantly greater (p < 0.0001) in men (1469 ± 102 cm³) than in women (1289 ± 111 cm³) and reached 1384 ± 139 cm³ in all 49 subjects. With increasing age the total intracranial volumes of both men and women remained fairly constant, even though there was a tendency for the women’s intracranial volume to increase when plotted against age (not shown). However, in all three age groups the men’s intracranial volume remained significantly higher than that of the women.

Brain Volume

The mean brain volume in all participants was 1227 ± 135 cm³ and was significantly larger (p < 0.0001) in men (1302 ± 112 cm³) than in women (1143 ± 106 cm³), as shown in Table 2. This difference between sexes decreased with age when the absolute brain volumes were compared, because the values for men decreased significantly faster (−4.7 cm³/year; p < 0.05) than those for women (−0.6 cm³/year), which remained almost stable. From the middle to the oldest age group the absolute brain volume declined significantly (p < 0.001) in the men, by 12% and was not significantly different from the value for women in the oldest age group. Interestingly, and in contrast to the absolute values, the relative brain volumes for both sexes were 89% overall. Likewise, when the individuals were divided by age, there was no difference between the sexes in relative brain volume (Table 2). When the relative brain volumes were plotted as a function of age (Fig. 2), the values for both sexes decreased with age, although less distinctly for women.

Cranial CSF Volume

The total cranial CSF volume averaged 157 ± 59 cm³ in all subjects, 167 ± 67 cm³ in men, and 146 ± 47 cm³ in women and accounted for 11.4% of the intracranial volume in each case (Table 2). In both men and women the cranial CSF volume expanded with age, more markedly between the middle and old age group (men 63%, p < 0.01; women 53%, p < 0.001) than between the young and middle age group (men 28%, p < 0.05; women 26%, not significant). In each of the three respective age groups...
and in the groups as a whole the cranial CSF volume was consistently larger in men and in women, but the difference was statistically significant only for the oldest age group (p < 0.05). A continuous increase over the entire adult age span was observed when the relative cranial CSF volume was plotted as a function of age (Fig. 3), in which the rate tended to be greater in men (0.24%/year) than in women (0.18%/year).

**Ventricular Volume**

As shown in Table 2, the respective overall mean ventricular volumes for men and women were similar (25 cm³). There was a significant difference between the sexes in the mean ventricular volumes for the youngest age group only (p < 0.05). On comparing ventricular volumes between the youngest and middle age groups, little or no change was found for either sex. However, a marked and significant increase in ventricular volume of men (94%, p < 0.001) and women (60%, p < 0.05) was noted between the middle and oldest age groups. When the relative ventricular volumes were plotted as a function of age (Fig. 4 left), it was apparent that the ventricular volume of men and women increased continuously, and at the same rate, with age. However, this was no longer evident when the

### TABLE 2

*Average values of absolute and relative brain compartment volumes in normal adults assessed by magnetic resonance imaging*

<table>
<thead>
<tr>
<th>Volume (cm³)</th>
<th>Sex &amp; Age Group</th>
<th>Intracranial Absolute</th>
<th>Brain Absolute</th>
<th>Brain Relative</th>
<th>CSF Absolute</th>
<th>CSF Relative</th>
<th>Ventricular Absolute</th>
<th>Ventricular Relative</th>
<th>Extra-ventricular Absolute</th>
<th>Extra-ventricular Relative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>both sexes</td>
<td>1384 ± 139</td>
<td>1227 ± 135</td>
<td>89 ± 4</td>
<td>157 ± 59</td>
<td>11 ± 4</td>
<td>25 ± 11</td>
<td>1.8 ± 0.8</td>
<td>133 ± 52</td>
<td>10 ± 3</td>
</tr>
<tr>
<td></td>
<td>I</td>
<td>1357 ± 133</td>
<td>1255 ± 126</td>
<td>93 ± 1</td>
<td>102 ± 21</td>
<td>8 ± 1</td>
<td>17 ± 5</td>
<td>1.3 ± 0.3</td>
<td>85 ± 21</td>
<td>6 ± 1</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>1427 ± 151</td>
<td>1293 ± 145</td>
<td>91 ± 2</td>
<td>134 ± 25</td>
<td>9 ± 2</td>
<td>19 ± 6</td>
<td>1.3 ± 0.5</td>
<td>115 ± 24</td>
<td>8 ± 2</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>1370 ± 133</td>
<td>1167 ± 108</td>
<td>85 ± 3</td>
<td>204 ± 54</td>
<td>15 ± 3</td>
<td>33 ± 10</td>
<td>2.4 ± 0.6</td>
<td>171 ± 49</td>
<td>12 ± 3</td>
</tr>
<tr>
<td></td>
<td>all men</td>
<td>1289 ± 111</td>
<td>1143 ± 106</td>
<td>89 ± 4</td>
<td>146 ± 47</td>
<td>11 ± 4</td>
<td>25 ± 11</td>
<td>1.9 ± 0.8</td>
<td>121 ± 40</td>
<td>9 ± 3</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>1257 ± 88</td>
<td>1162 ± 78</td>
<td>93 ± 1</td>
<td>95 ± 21</td>
<td>8 ± 1</td>
<td>15 ± 3</td>
<td>1.2 ± 0.2</td>
<td>80 ± 21</td>
<td>6 ± 1</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td>1254 ± 98</td>
<td>1134 ± 110</td>
<td>90 ± 2</td>
<td>120 ± 15</td>
<td>10 ± 2</td>
<td>20 ± 6</td>
<td>1.6 ± 0.5</td>
<td>100 ± 17</td>
<td>8 ± 2</td>
</tr>
<tr>
<td></td>
<td>all women</td>
<td>1320 ± 125</td>
<td>1137 ± 122</td>
<td>86 ± 2</td>
<td>183 ± 31</td>
<td>14 ± 2</td>
<td>32 ± 10</td>
<td>2.4 ± 0.7</td>
<td>151 ± 27</td>
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<tr>
<td></td>
<td>I</td>
<td>1469 ± 102</td>
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<td>89 ± 4</td>
<td>167 ± 67</td>
<td>11 ± 4</td>
<td>25 ± 11</td>
<td>1.7 ± 0.7</td>
<td>142 ± 59</td>
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<tr>
<td></td>
<td>II</td>
<td>1458 ± 82</td>
<td>1349 ± 89</td>
<td>93 ± 2</td>
<td>109 ± 21</td>
<td>8 ± 2</td>
<td>20 ± 4</td>
<td>1.4 ± 0.4</td>
<td>90 ± 22</td>
<td>6 ± 2</td>
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<tr>
<td></td>
<td>III</td>
<td>1513 ± 81</td>
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<td>91 ± 2</td>
<td>140 ± 27</td>
<td>9 ± 2</td>
<td>18 ± 6</td>
<td>1.2 ± 0.4</td>
<td>123 ± 24</td>
<td>8 ± 2</td>
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<tr>
<td></td>
<td>all</td>
<td>1431 ± 122</td>
<td>1203 ± 80</td>
<td>84 ± 4</td>
<td>228 ± 66</td>
<td>16 ± 4</td>
<td>35 ± 10</td>
<td>2.4 ± 0.6</td>
<td>194 ± 60</td>
<td>13 ± 3</td>
</tr>
</tbody>
</table>

* Relative volumes are calculated as compartment volume/intracranial volume × 100% ± standard deviation. CSF = cerebrospinal fluid.

**TABLE 3**

*Comparison of brain compartment volumes in different age groups and between the sexes in normal adult volunteers*

<table>
<thead>
<tr>
<th>p Value</th>
<th>Sex &amp; Age Group</th>
<th>Intracranial Absolute</th>
<th>Brain Absolute</th>
<th>Brain Relative</th>
<th>CSF Absolute</th>
<th>CSF Relative</th>
<th>Ventricular Absolute</th>
<th>Ventricular Relative</th>
<th>Extra-ventricular Absolute</th>
<th>Extra-ventricular Relative</th>
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<td>I vs. II</td>
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<td>II vs. III</td>
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<tr>
<td>female</td>
<td>I vs. II</td>
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<td>I vs. II</td>
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</table>

* Statistical significances of differences were calculated by analysis of variance. Age groups are defined in Table 1. CSF = cerebrospinal fluid; — = no significant difference detected.

* J. Neurosurg. / Volume 84 / June, 1996
relative ventricular volumes were plotted as a function of brain volume (Fig. 4 right). The relative ventricular volume of the men was significantly and inversely correlated with total brain volume (brain volume = $-0.004$, p $< 0.001$), whereas for women no such correlation was observed. This may be partially explained by the fact that the relative ventricular volume of the women may have been underestimated because of skull volume, which tended to increase with age. Additionally no age correlation was observed for brain volume in the women, so that one would not expect a correlation between the clearly age dependent relative ventricular volume and the brain volume.

Extraventricular CSF Volume

The overall average extraventricular CSF volume tended to be larger in men (149 ± 59 cm$^3$) than in women (121 ± 40 cm$^3$) (Table 2). Similarly, the mean extraventricular CSF values for each respective age group tended to be higher in men than in women, but were significantly different only for the oldest age group (p $< 0.05$). However, the extraventricular CSF volume of men as well as women increased with age, almost doubling over the 56-year age span of the participants; the most striking increase in extraventricular CSF volume was observed in both sexes between the middle and the oldest age group (male, 58%, female, 51%; p $< 0.01$ for both). Comparing the relative extraventricular volumes of the various age groups, no statistically significant differences were detected between the two sexes. But when the relative extraventricular CSF volumes were plotted as a function of age and as a function of brain volume, both men (p $< 0.01$) and women (p $< 0.05$) showed a significantly inverse correlation (Fig. 5 left and right).

Discussion

Various studies have shown that as the brain ages its weight and volume decrease and conversely the volume of the cranial CSF increases. This relationship of the brain and cranial CSF to aging is based primarily on studies made on autopsy material. Some studies have shown that values derived from such material are prone to errors attributable either to brain swelling after death or to shrinkage during fixation. The introduction of pneumoencephalography made possible in vivo measurements of these compartments and consequently the circumvention of post mortem and fixation artifacts. However, such studies were mostly limited to measurement of linear dimensions and the calculation of various ratios used as indices of ventricular enlargement or brain atrophy. Moreover, this approach had its own limitations, such as expansion of CSF compartments following introduction of air, and because of its invasive nature, its restriction to patients with neurological disorders. Computerized tomography offers a much less invasive in vivo procedure to study brain structure and ventricular architecture, and many reports have appeared on the use of CT to measure ventricle volume. Unfortunately, because of the difficulty in distinguishing true extraventricular CSF from brain, due to artifacts produced by calvarial bone and to inadequate contrast and poor resolution on CT images, only a few attempts have been made to measure the cranial extraventricular CSF volume. Such image artifacts are minimized with MR imaging, which allows for better contrast and resolution, and thus a more accurate measurement of the extraventricular CSF space.

Intracranial and Brain Volume

Age-related decrease in the weight of adult brains has often been noted in cross-sectional studies. Some investigators have questioned whether such decreases are due to aging, because it is known that the stature of humans, as well as the size of the head and brain, has increased during the last century. Thus, it is argued that the decrease in brain weight or volume observed in cross-sectional studies may reflect this trend; those born earlier in the century would have on average smaller heads and brains than those born later. However, in a study of 130 cadavers of normal men and women, Miller and Corsellis found that even after correction for the effects of fixation and long-term increase in brain size, the volume of the cerebellar
Age-related changes in compartmental brain volumes

hemispheres of both men and women over the age of 50 declined approximately 2% per decade.

Davis and Wright\(^\text{11}\) used autopsy material obtained from 87 normal brains in persons ranging from 22 to 94 years of age and measured brain and intracranial volume. They noted that the brain/intracranial volume ratio, which remained constant from 22 to 55 years of age, decreased significantly thereafter. The authors reasoned that, because the long-term changes should have affected brain and intracranial volume similarly, the decrease in the ratio must be attributable to brain atrophy. This disparity between the change in cranial capacity and brain volume with age, which was noted by Rudolph\(^\text{51}\) as early as 1914, also is apparent in our study, in which the intracranial volume either does not change (men) or has a tendency to increase (women) with age even though in both sexes brain volume decreases significantly. It is not clear from these cross-sectional studies why this discrepancy exists, because the observed increase in stature of humans over the last century has been noted in most populations. The most likely explanation is that the head size of humans, and consequently the intracranial volume, increases with age and that such changes mask the long-term trend that affects the population as a whole. This supposition is supported by the longitudinal studies of Finby and Kraft\(^\text{16}\) and of Israel,\(^\text{31}\) in which skull radiographs obtained in individuals spanning a 20-year period were compared and significant increases in head size were detected. However, Tallgren,\(^\text{54}\) in a study of 32 women aged 20 to 73 years, in which lateral cranial films spanning intervals of 15 years were compared, found no change in the cranial vault or skull thickness with increasing age. In a more comprehensive study of normal aging, Friedlaender, \textit{et al.},\(^\text{17}\) measured the head circumference, length, and breadth of more than 1800 veterans ranging in age from 22 to 80 years and found that in all decades of life the head size of individuals determined at two separate time intervals over a 5-year span increased significantly. Such cyclic and age-related trends act to confound the interpretation of results of cross-sectional studies because, although it is clear that the average brain volume of individuals is larger in the younger than in the older age groups, it is not possible to determine to what extent such changes are due to an aging process.

![Fig. 4. Scatterplots showing relative ventricular volume plotted against age (left) and brain volume (right).](image)

![Fig. 5. Scatterplots showing relative extraventricular volume plotted against age (left) or as a function of brain volume (right).](image)
There is also some uncertainty as to when adult brain volume or weight begins to decrease. Some have reported that it starts as early as 25 years of age \(^2,13\) but others suggest that its onset is much later in life \(^{11,30,43,52}\). In their study of normal adult cerebellar hemispheres Miller, et al. \(^44\) noted that the hemispheres decreased at a linear rate beginning at age 20 and that the rate was significantly greater in men than in women. However, when these values were corrected for the incremental increase reported in their earlier study, an age-related shrinkage of approximately 2% per decade was detected only after the age of 50 years. Moreover, in contrast to the studies of others who had reported brain shrinkage in men to be either faster \(^53\) or slower \(^30\) than in women, the corrected values indicated that the rate of decline was similar for both sexes. \(^43\)

Use of autopsy material in some of these studies may have contributed to these disparate results because ionic shifts occurring post mortem are known to alter the volume of the CSF as well as that of the intra- and extracellular compartments of the brain. \(^2\) Furthermore, changes in brain weight, ranging from 1.4% to 8.5%, are known to occur during formalin fixation. \(^28,30,53\) Obviously, these post mortem and fixation artifacts are avoided in in vivo, noninvasive techniques such as CT or MR imaging are used.

In our study only the average brain volume of men in the oldest age group is significantly smaller than that of the younger groups. However, when brain volumes of men and women are normalized to the intracranial volume, which in both sexes does not change significantly between the young and middle age groups, it appears that brain volume begins to decline after 60 years, which coincides with the onset of the gradual widening of the third ventricle as reported by LeMay. \(^38\) The decline rate of the relative brain volume in the oldest age group accelerates more in men (0.53%/year) than in women (0.26%/year), this compared with the overall decline rate of men (0.24%/year) and women (0.18%/year). This is in line with the divergence and decline rates in total fresh hemispheric volumes noted by Miller, et al. \(^44\) for 47 men (0.28%/year) and 44 women (0.15%/year) ranging from 20 to 98 years of age, and the decline rate of approximately 0.23% per year for the brain/intracranial volume ratio observed after 55 years of age in 87 normal adults. \(^11\) This is also consistent with the observations of Yamaura, et al. \(^29\) who showed that the brain volume index decreased with age, but more dramatically after the age of 50 years. It is tempting to suggest that the long-term trend noted by Miller and Corsellis \(^44\) is the predisposing factor in this divergence but it should be stated that all our volunteers were born after 1900 when, as noted by these investigators, the increase in brain weight for males and females was similar. Menopause may be a factor, as indicated by the studies of Grant, et al. \(^22\) which show that cranial CSF volume in women is significantly altered during the menstrual cycle.

It has long been held that because the brain and cranial CSF are contained within a rigid bony enclosure, changes in brain volume will be reflected by changes in the cranial CSF volume. The results of our study support this supposition although head size and intracranial volume are known to expand with age. For instance, as shown in Fig. 5 right, there is a significant correlation between brain volume and relative extraventricular CSF volume, and it becomes apparent that small changes in the volume of the much larger brain compartment will result in marked changes in the volume of the cranial CSF compartment. This indicates that analysis of changes in the relative cranial or ventricular and extraventricular CSF volumes as a function of age may provide good indicators of brain shrinkage.

### Cranial CSF Volume

Cranial CSF volume averaged 167 ± 67 cm\(^3\) in men and 146 ± 47 cm\(^3\) in women and in both sexes accounted for 11.4% of the intracranial volume. These values are larger than those reported by Lups and Haan, \(^41\) Weston, \(^58\) Condon, et al., \(^8\) and others (Table 3). Gado, et al., \(^18\) did not provide actual volumes but reported the cranial CSF volume to be 11.4% of the total intracranial volume, a value identical to our relative intracranial CSF volume given above. In our study intracranial CSF volume increased at an average yearly rate of 3.4 cm\(^3\) (2.8%) for men and 2.5 cm\(^3\) (2.5%) for women. These values are slightly greater than those reported by Grant, et al., \(^22\) for a somewhat younger group of normal men (1.9%/year) and women (1.6%/year) whose age ranged from 18 to 64 years.

### Ventricular Volume

In the present study the mean ventricular volume (25 ± 11 cm\(^3\)) is similar to the average ventricular volume (22.4 cm\(^3\)) reported by Last and Tompsett. \(^37\) The later derived their volumetric measurements from ventricular casts made from brains of 24 normal individuals ranging in age from 29 to 73 years. Like us, they observed no difference between the ventricular volumes of men and women. However, in contrast to our results they reported no increase in this volume with age. Participants in our study showed no ventricular expansion between the youngest and middle age group, but between the middle and oldest age group there was a significant enlargement in ventricular volume. Although this observation is consistent with results from others, \(^28,32,47,49\) it is not clear from such comparisons whether expansion of ventricular volume with age differs between men and women. Other groups using casting methods and autopsy material have reported smaller \(^1 (-20 \text{ cm}^3)\) and larger \(^56 (30 \pm 19 \text{ cm}^3)\) mean ventricular volumes than ours. Unfortunately, many of these studies fail to provide the age range of their material and/or the cause of death. The range in ventricular volumes (12–31 cm\(^3\)) obtained with CT scanning \(^2,10,49\) is comparable to the range of volumes (7–30 cm\(^3\)) reported in MR studies. \(^9,10,15,34,36,55,56\)

### Extraventricular CSF Volume

Many investigators have attempted to measure the CSF volume. One of the first was Weston, \(^29\) who aspired the CSF immediately after death from the cadavers of patients who died from dementia praecox (age range 19–51 years) or paresis (age range 31–54 years) and estimated the cranial CSF volumes to be 110 and 135 cm\(^3\), respectively. Unfortunately, no values for neurologically intact subjects were reported. Davis and Wright \(^9\) used a different method to measure the cranial CSF volume of cadavers. These investigators used a lubricated balloon filled with water to...
occupy the entire cranial cavity from which the brain, dura, falx, and tentorium had been removed previously. The difference between the volume of the water contained in the balloon and that of the fresh brain, as determined by the direct measurement of extraventricular CSF space on CT scans are surmised to account for this disparity. Because the direct measurement of extraventricular CSF volume; an observation consistent with that of Teasdale, al.,56 but not of others,47,60 who have suggested a biexponential increase accelerating with advancing ages.

Although a statistical comparison of the mean extraventricular CSF volumes of men and women in our study did not always prove to be significant, it is apparent that the cranial extraventricular CSF space is consistently larger in men than in women. Others have reported similar findings.21,23 Moreover, as brain volume decreases with

end of text

TABLE 4

Summary of brain volumes and cranial, ventricular, and extraventricular CSF volumes as determined by various methodologies*

<table>
<thead>
<tr>
<th>Method</th>
<th>Volume</th>
<th>Cranial CSF (cm³)</th>
<th>Ventricular CSF (cm³)</th>
<th>Extraventricular CSF (cm³)</th>
<th>Authors, Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>postmortem studies</td>
<td>M, 1370 g; F, 1277 g</td>
<td>123</td>
<td>30</td>
<td></td>
<td>Harvey, 1911</td>
</tr>
<tr>
<td></td>
<td>M, 1397 g; F, 1261 g</td>
<td></td>
<td></td>
<td></td>
<td>Weston, 1921</td>
</tr>
<tr>
<td></td>
<td>M, 1354 g; F, 1218 g</td>
<td></td>
<td></td>
<td></td>
<td>Shibata, 1936</td>
</tr>
<tr>
<td></td>
<td>M, 1375 g; F, 1235 g</td>
<td></td>
<td></td>
<td></td>
<td>Last &amp; Tompsett, 1953</td>
</tr>
<tr>
<td></td>
<td>M, 1444 g; F, 1257 g</td>
<td></td>
<td></td>
<td></td>
<td>Davis &amp; Wright, 1977</td>
</tr>
<tr>
<td></td>
<td>M, 1371 cm³</td>
<td></td>
<td></td>
<td></td>
<td>Dekaban &amp; Sadowsky, 1978</td>
</tr>
<tr>
<td></td>
<td>M, 1346 g; F, 1181 g</td>
<td></td>
<td></td>
<td></td>
<td>Ho, et al., 1980</td>
</tr>
<tr>
<td>uncertain CT studies</td>
<td>60</td>
<td>35</td>
<td>25</td>
<td></td>
<td>Hubbard &amp; Anderson, 1981</td>
</tr>
<tr>
<td></td>
<td>M, 1343 cm³</td>
<td></td>
<td></td>
<td></td>
<td>Hubbard &amp; Anderson, 1983</td>
</tr>
<tr>
<td></td>
<td>M, 1349 cm³</td>
<td></td>
<td></td>
<td></td>
<td>Harper &amp; Kri, 1985</td>
</tr>
<tr>
<td>MR imaging studies</td>
<td>123</td>
<td>25</td>
<td>98</td>
<td></td>
<td>Lups &amp; Haan, 1954</td>
</tr>
<tr>
<td></td>
<td>M, 146; F, 115</td>
<td></td>
<td></td>
<td></td>
<td>Brassow &amp; Baumann, 1978</td>
</tr>
<tr>
<td></td>
<td>M, 189 (11.7%†); F, 146 (10.7%‡)</td>
<td>116</td>
<td>21</td>
<td>116</td>
<td>Cramer, et al., 1990</td>
</tr>
<tr>
<td></td>
<td>F, 146 (10.7%‡)</td>
<td></td>
<td></td>
<td></td>
<td>Kohn, et al., 1991</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Malko, et al., 1991</td>
</tr>
</tbody>
</table>

* Abbreviations: CSF = cerebrospinal fluid; CT = computerized tomography; MR = magnetic resonance.
† Relative value of the cranial cavity.
‡ Relative value of the cranial cavity.

Age-related changes in compartmental brain volumes
age, the shrinkage is best reflected by measuring increases in the relative extraventricular rather than the relative ventricular CSF volumes. In both sexes the increase of ventricular volume with age represented only a small fraction of the overall increase in cranial CSF volume. Indeed, most of the cranial CSF volume expansion occurring with age was attributable to the increase observed in the extraventricular CSF volume. Teasdale, et al.,56 arrived at the same conclusion, stating that the increase in cortical sulcal volume was predominantly responsible for expansion of the total cranial CSF volume with age.

Finally, as illustrated in Table 4, the extraventricular CSF volumes determined by various MR imaging sequences are considerably larger than those determined by the more traditional methods. Indeed, MR image–generated cranial CSF volumes are on average larger than the combined cranial and spinal CSF volumes (140 cm$^3$) cited in the literature.12,41 It may be argued that use of autopsy material in many of the previous studies contributes to this discrepancy, because it is known that brain swelling after death encroaches on the cranial CSF compartments. However, if this were the case it may be anticipated that similar discrepancies exist between the MR image and traditionally generated ventricular and brain volumes as well. This appears not to be the case, because ventricular and brain volumes determined by MR imaging are, in most cases, quite similar to those generated by the more traditional techniques. Multiplying the average brain volumes reported herein by the specific gravity of human brain (1.037)$^57$ converts these values to brain weights (male, 1350 g; female, 1186 g).

Furthermore, the MR image–generated volumes also are considerably larger than the combined cranial and spinal CSF volumes (127 ± 25 cm$^3$) determined from ventriculolumbar perfusion studies of three patients (age 63 ± 3 years) with normal or slightly enlarged ventricles.49 In our studies the volume occupied by arachnoid trabecular and small blood vessels normally found within the cranial subarachnoid space is not discriminated from CSF by MR image segmentation. Consequently, this volume is included in the extraventricular CSF volume determination. The age-dependent expansion of the extraventricular CSF volume could therefore be due to an increase of the cranial subarachnoid space and the extraventricular CSF space. We are not aware of any study in which the volume occupied by these structures has been determined or whether this volume changes with age. If such structures do occupy a significant fraction of this space, the disparity between the MR image and more traditionally generated values may be explained. However, if they do not, MR imaging segmentation may be identifying an extraventricular CSF compartment that heretofore was unrecognized.

Computerized MR image processing segmentation provides a noninvasive in vivo technique to measure intracranial, brain, and ventricular and extraventricular CSF volumes that avoids many of the artifacts associated with traditional methods. This technique can be expected to improve our knowledge of physiological and biochemical processes that affect these cranial compartments throughout life. In addition, it should provide a powerful tool to better understand and manage clinical problems associated with the various types of ventricular enlargement.

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