Brain elasticity changes with ventriculomegaly

FREDERICK H. SKLAR, M.D., JAN T. DIEHL, M.D., CHESTER W. BEYER, JR., M.D., AND W. KEMP CLARK, M.D.

Divisions of Neurological Surgery and Neuroradiology, and Department of Anesthesiology, University of Texas Health Science Center at Dallas, Dallas, Texas

The pressure-volume relationship of brain elasticity was determined in 32 patients during servo-controlled variable-rate lumbar infusions to measure net cerebrospinal fluid (CSF) absorptive capacity. Several indices were used to estimate ventricular size from computerized tomography scans. The results show a linear relationship between ventricular size and the elasticity slope which relates the natural logarithm of pressure to volume. It follows that a hydrocephalic patient should show a greater intracranial pulse amplitude at a given pressure than does a patient with normal-sized ventricles. Although these elasticity changes may simply be the result of the ventriculomegaly, it seems possible that the pressure-volume elasticity relationship may be of etiological importance in disorders of the CSF system.

KEY WORDS: pressure-volume relationship, brain elasticity, intracranial pressure, cerebrospinal fluid, hydrocephalus, pseudotumor cerebri
prone with their heads turned to one side; the larger patients were studied on their sides. A single lumbar puncture was made with a large-bore Touhy needle through which a small catheter was introduced to measure pressure. A special adapter permitted the infusion and withdrawal of fluid through the needle around the pressure-recording catheter.

The servo-controlled variable-rate lumbar infusion technique involved measuring the rate at which lactated Ringer's solution had to be infused into the lumbar subarachnoid space in order to maintain intracranial pressure (ICP) constant at a desired level. Multiple constant-pressure plateaus were studied, and the infusion rate at a particular pressure plateau was considered equivalent to the arithmetic difference between the rates of CSF absorption (A) and formation (F). The net CSF absorptive capacity was calculated as the slope of the (A-F) versus ICP curve. Pressure-volume elasticity measurements were made as ICP was abruptly changed from one constant-pressure plateau to another by the rapid infusion or withdrawal of fluid. A Harvard pump with reciprocally arranged syringes and a solenoid valve system made it unnecessary to interrupt the infusion protocol to refill the syringes. Radial artery pressure was monitored continuously to avoid unsafe reductions of cerebral perfusion pressure. Mean ICP, blood pressure, and infusion-volume data were sampled at 1-second intervals by a PDP 11/34 computer. The ICP and volume data were displayed on a Tektronix 4010 graphics terminal.

The pressure-volume data from the rapid-rate infusions or withdrawals of fluid were subjected to linear regression analysis with the least-squares technique to calculate the elasticity slope, defined as the slope relating the natural logarithm of pressure to the volume infused. For each patient, elasticity slope values from the rapid-rate fluid infusions and withdrawals were averaged to give a mean elasticity slope.

Each patient was evaluated with CT scanning. Several indices were used to estimate ventricular size quantitatively on the basis of the CT scan. A frontal horn index (FHI) and a trigone index (TI) were calculated. These indices are defined graphically in Fig. 1, and represent ratios between the maximal ventricular width and the total brain width at the levels of the frontal horns and the trigones, respectively. The FHI of this study corresponds to the "first cerebroventricular index of the frontal horns" as described by Hahn and Rim. The TI was calculated from measurements of the CT image which best showed the ventricular trigones at their widest point. This CT plane of section was usually at or just above the level of the posterior aspect of the tentorial in-

*Harvard pump with syringes and valve system manufactured by Harvard Apparatus Co., Millis, Massachusetts.
Brain elasticity changes

Regardless of the method used to estimate ventricular volume, the results of the regression analysis indicate a statistically significant relationship between the elasticity slope and the size of the ventricles. Some patients showed focal areas of ventricular enlargement; occasionally the ventricular trigones were disproportionately enlarged compared to the frontal horns. Accordingly, the elasticity slope correlated best with the ventricular index (p < 0.01), slightly better than either the frontal horn index (p < 0.02) or trigone index (p < 0.05). It is recalled that the VI was calculated as the sum of the FHI and the TII.

Figure 5 summarizes the ventricular sizes, CSF absorptive capacities, and elasticity slopes for the hydrocephalic and adult pseudotumor patients. The two children with so-called "infantile pseudotumor cerebri" are not included in this illustration because of uncertainty associated with their diagnoses. These children had large heads, signs and symptoms of intracranial hypertension, CSF absorptive defects, and small ventricles with generous subarachnoid spaces on CT scan. However, because they may represent an entirely different disease entity, their data have been excluded from these summary figures. One child had a very low mean elasticity slope value of 0.033; the other, a very high value of 0.23.

Nine patients had adult pseudotumor cerebri, seven of whom had CSF absorptive defects as measured by the variable-rate servo-controlled lumbar infusion technique. These data have been reported previously;20 net CSF absorptive capacities of 0.13 ml/min/mm Hg and below were considered to be abnormal. On the other hand, there were 11 patients with active communicating hydrocephalus, and these patients had similar CSF absorptive defects (Fig. 5B). The

Fig. 2. Clinical diagnoses of 32 patients studied with the servo-controlled lumbar infusion technique.

The hydrocephalic group not only had larger ventricles (Fig. 5A, p < 0.002), but showed significantly greater elasticity slope measurements (Fig. 5C, p < 0.05).

The serial elasticity measurements of a single 21-year-old female patient with pseudotumor cerebri are of particular interest. This patient was studied four times over a 7-month period, and these data are summarized in Fig. 6. Elasticity slope measurements of the first three studies were not significantly different, although the patient had resolved her symptomatology with adjustment of her medications (Fig. 6A–C). However, when the test was repeated 3 months after the medications had been discontinued, the elasticity slope measurements were significantly greater than those of the previous studies (p < 0.001). It is likely that this final elasticity slope value represented the patient's pressure-volume relationship once the disease had become inactive.

Discussion

In the present study, the data strongly suggest that patients with ventriculomegaly have greater elasticity slopes than do patients with small ventricles, and the elasticity slope-ventricular size relationship appears to be linear. We have defined the term "elasticity slope"
Brain elasticity changes

TABLE 1
Pressure-volume elasticity function in normal and hydrocephalic dogs from data in the literature

<table>
<thead>
<tr>
<th>Animal</th>
<th>Experimental Model of Lim, et al.</th>
<th>Hyperbolic Model*</th>
<th>Elasticity Slope</th>
</tr>
</thead>
<tbody>
<tr>
<td>normal dogs</td>
<td>$dV/dP = 0.47e^{-0.02P}$</td>
<td>$(dV/dP)(P) = 1.8$</td>
<td>0.56</td>
</tr>
<tr>
<td>hydrocephalic dogs</td>
<td>$dV/dP = 0.25e^{-0.001P}$</td>
<td>$(dV/dP)(P) = 1.1$</td>
<td>0.91</td>
</tr>
</tbody>
</table>

*Data from Lim, et al., fit by Sklar and Elashvili to hyperbolic mathematical model relating compliance and pressure.

as the regression slope relating the natural logarithm of pressure to infusion volume. It follows from the mathematics of the exponential pressure-volume function that elastance ($dP/dV$) is linearly related to ICP with a slope equivalent to the elasticity slope. Furthermore, there is a linear relationship between intracranial pressure and ICP, and the resulting slope value should provide an estimate of brain elasticity. This ICP-monitoring technique measures the pressure response to the intracranial volume changes occurring with each cardiac cycle ($dV$). Such an approach assumes that these physiological volume changes are relatively constant. Thus, a patient with a high elasticity slope value would be predicted to show greater intracranial pulse amplitudes at a given ICP than does another patient with a low elasticity slope value. Adult patients with so-called “normal-pressure” hydrocephalus have been noted in the literature to have unusually large pulse amplitudes. These observations of increased pressure pulsations at normal levels of ICP are consistent with the thesis that patients with communicating hydrocephalus have increased elasticity slope values. The results of the present study predict that patients with enlarged ventricles should show greater intracranial pulse amplitudes than do other patients with normal or small-sized ventricles, and this pulse difference should be accentuated at graded levels of intracranial hypertension.

Others have made elasticity measurements in hydrocephalic patients. Shulman and Marmarou demonstrated the classical exponential pressure-volume curve in children with hydrocephalus, but Miller, et al., could not show such a relationship in hydrocephalic patients with their VPR technique (volume-pressure response to a 1-ml change in intraventricular volume). Data from their patients did not appear to follow the classical linear elastance-pressure model. However, ICP variability is linearly related to the level of ICP, and the slope of this relationship varies directly with the elasticity slope. Hydrocephalic patients would therefore be expected to show greater pressure fluctuations over a spectrum of pressures. Thus, increased measurement variations with a small-aliquot technique such as the VPR could possibly obscure the classic pressure-volume response. Certainly, there is no doubt that the data from the patients with hydrocephalus in the present study showed an exponential relationship between pressure and volume.

Lim, et al., measured differences in ventricular compliance ($dV/dP$) between normal dogs and hydrocephalic dogs with aqueductal stenosis. Although they concluded that compliance is an exponential function of pressure, their data also fit a hyperbolic mathematical model relating compliance and pressure as would be predicted from the following linear elastance-pressure function:

\[
\frac{dP}{dV} = \beta P + \alpha \\
\frac{1}{(dP/dV)} = 1/((\beta P + \alpha) \\
(dV/dP)(\beta P + \alpha) = 1,
\]

where $\beta$ is the elasticity slope. Table 1 summarizes the various pressure-volume elasticity curves reported to fit the data of Lim, et al., for normal and hydrocephalic dogs. It is of particular interest that the predicted elasticity slope for the hydrocephalic animals is nearly twice the calculated value for the normal dogs.

Are these elasticity changes the cause or the result of the ventricular enlargement in some forms of
hydrocephalus? Bering removed the choroid plexus from one lateral ventricle in dogs. The side from which the plexus had been removed failed to enlarge when these animals were made hydrocephalic with intracisternal kaolin. Similarly, Wilson and Bertan sectioned an anterior choroidal artery in dogs and showed that the ipsilateral ventricle remained consistently smaller when the animals were treated with intracisternal lampblack to induce hydrocephalus. Moreover, they were able to measure pulse amplitude differences between the two lateral ventricles and exaggerate these pulse asymmetries by raising the ICP. Such data suggest that in a single animal, there were different elasticity pressure-volume functions for each of the two cerebral hemispheres. Moreover, Pettorossi, et al., could create hydrocephalus in animals by synchronizing a pulsating intraventricular balloon to the cardiac cycle in order to accentuate the intracranial pulse pressure without changing mean ICP. The brains showed pathological features typical of obstructive hydrocephalus. Sato, et al., demonstrated increasing pulse pressure amplitudes without concurrent ICP increases in serial recordings from patients developing communicating hydrocephalus after subarachnoid hemorrhage and trauma. It is, therefore, apparent that changes in the pressure-volume elasticity function can alter the course of developing hydrocephalus. Moreover, the cited study of Pettorossi, et al., suggests that these elasticity changes may actually cause the ventricular enlargement. The elasticity data from the present series are entirely consistent with these observations.

On the other hand, patients with pseudotumor cerebri appear to have significantly lower elasticity slopes. In a previous report, we presented in detail the results of servo-controlled variable-rate lumbar infusions in patients with benign intracranial hypertension. Most of the patients had CSF absorptive defects. However, there has been considerable controversy as to why these patients with alleged CSF absorptive defects should have small ventricles. The results of the present study suggest that these patients are protected from developing hydrocephalus as a result of their anatomic and physiological characteristics that determine the pressure-volume elasticity function. On the one hand, the elasticity slopes of pseudotumor patients may be lower than those of hydrocephalic patients because the ventricles are smaller. On the other hand, perhaps patients with pseudotumor cerebri do not contract hydrocephalus because their elasticity slopes are low. The serial elasticity slope measurements from a patient with pseudotumor cerebri studied four times over 7 months are interesting in this regard (Fig. 6). This patient showed a significant increase in the elasticity slope measurements once she had become entirely asymptomatic off all medications. Presumably the disease had become arrested. These data suggest that in pseudotumor cerebri, a low elasticity slope is associated with disease activity and may account for the paradoxical occurrence of small ventricles in the face of a CSF absorptive defect.

It is, therefore, concluded that the pressure-volume relationship of brain elasticity may indeed be an important parameter to study in health and disease. Changes in the elasticity function may play important roles in the pathophysiology of common diseases involving the CSF compartment.

Acknowledgments

The authors wish to thank Ms. Jena Simmons for her secretarial assistance in the preparation of this manuscript.

References

Brain elasticity changes


_address reprint requests to: Frederick H. Sklar, M.D., Division of Neurological Surgery, The University of Texas Health Science Center, 5323 Harry Hines Boulevard, Dallas, Texas 75235._