On measurement of brain elastic response in vivo

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Walsh, E. K., W. W. Furniss, and A. Schettini. On measurement of brain elastic response in vivo. Am. J. Physiol. 232(1): R27-R30, 1977 or Am. J. Physiol.: Regulatory Integrative Comp. Physiol. 1(1): R27-R30, 1977.—The elastic response behavior of brain tissue in vivo has been shown to be sensitive to the physiological environment of the brain and thus represents a useful parameter for identifying effects of controlled changes on the system. Here we describe a method for measuring brain elastic response using an epidural pressure-depth transducer and a minimum number of insertions. The method also serves to identify the nonlinear response of brain tissue.

In a recent study, Walsh and Schettini (7) discussed a method of measuring the elastic response behavior of brain tissue in vivo. That study was motivated by the hypothesis that this characteristic material property would be sensitive to the physiological environment and thus could be used to identify, both qualitatively and quantitatively, the effects of controlled changes on the system, e.g., variation in arterial CO₂ tension, the use of anesthetic agents.

In our studies, brain elastic response is measured by means of a pressure-displacement transducer which permits simultaneous measurements of pressure and displacement, where displacement here refers to the depth of insertion of the transducer radially into the cranial vault. In (7) the elastic response was obtained in terms of an initial pressure-depth ratio determined on the basis of from six to eight subpial insertions. Because numerous insertions might alter the system, we have devised a technique that determines the initial elastic response with fewer insertions and, as will be shown, with somewhat greater accuracy.

Elastic response of brain tissue in vivo. Brain tissue, like most soft biological tissues, is known to exhibit viscoelastic response behavior (2, 4). That is (in the context of our measurements of pressure and subpial insertion depth) the tissue exhibits pressure relaxation at fixed insertion depth, creep insertion at fixed pressure, and instantaneous elastic response. This latter response parameter reflects the ability of the material to exhibit a behavior similar to that of an elastic solid for periods of time short as compared to some characteristic relaxation time of the material.

With the experimental configuration that has been developed (6), the elastic response is obtained by making simultaneous pressure and insertion-depth measurements as the pressure-sensing end of the transducer is inserted a small distance (less than 1 mm) into the subpial region. The incremental change in pressure resulting from the incremental change in insertion into the brain tissue, given in terms of a pressure-depth ratio, is a measure of the elastic response of the subpial material and can be shown to be directly related to the actual elastic modulus of the brain tissue (7). The technique to be described here involves a continual measurement of the pressure and depth and thus a continual evaluation of the slope of the pressure-depth response. This yields two important results. First, the pressure-depth ratio can be determined as a result of a single pressure-depth insertion, whereas earlier methods involved several insertions (7). Second, any deviation from linearity in the pressure-depth response is readily discernible. This will be discussed further in a later section.

METHODS AND PROCEDURE

Measurement of brain elastic response. The tests to date have been made in vivo on mongrel dogs weighing approximately 21 kg. The method of preparation of the animals prior to the elastic response tests has been described elsewhere (e.g., (7)). The measurements are made with a newly developed displacement transducer described at length in (6). Briefly, this transducer consists of a diaphragm-type pressure sensor mounted collinear with a displacement transducer of the differential-transformer type. Thus, as the transducer shaft is inserted into the subpial region the base of the transducer shaft compresses the brain tissue resulting in an increase in pressure. The ratio of the initial change in pressure to the corresponding change in insertion depth, i.e., the pressure-depth ratio, is a measure of the elastic response of the brain tissue.

In (7) the elastic response of brain tissue, in terms of a pressure-depth ratio, was determined as follows. For each of approximately six insertions the maximum pressure pᵣ and corresponding maximum insertion depth δᵣ were recorded. These values were then plotted on graph paper with pressure as the vertical scale and insertion depth as the horizontal scale. An example of the results of one test are shown in Fig. 1 with the circles representing the experimental values and the connecting lines graphical approximations. The intersection of these lines, i.e., the change in slope of the response, is an indication of a sudden change in the region traversed by
FIG. 1. Original method for determining elastic response in terms of the pressure-depth ratio (dog 819). Circles represent values of peak pressure and peak insertion depth. Connecting lines represent graphical approximations to experimental data. Vertical broken line indicates depth \( \delta \), which represents position of subpial region.

To determine the elastic response, it is necessary to carry out the individual pressure-depth insertion in a time short compared to the relaxation time of the material. In a number of tests involved in the study of the in vivo pressure relaxation of brain tissue (4), the minimum relaxation times measured were of the order of 10 s. Thus, it was determined to carry out the elastic response insertions in approximately 1 s. Although this rapid insertion is close to the response time of the graphic recorder, the fact that the shaft is held at the maximum insertion position for 2 s assures that the actual maximum pressure value is recorded.

However, because our main objective was to obtain the pressure-depth ratio with fewer insertions (ultimately, with a single insertion) it was determined to monitor the complete insertion, i.e., the pressure response during the complete insertion. Since this required a recording system with a rapid response time, the graphic recorder was replaced by an oscilloscope (Tektronix, model 551). During the insertion then, the pressure signal was recorded as the vertical (Y) signal and the insertion depth as the horizontal (X) signal. The trace was photographed for subsequent analysis.

RESULTS

Elastic response test. Figure 2 shows an elastic response insertion for the test on dog 950. The pressure-depth ratio was obtained from the trace as follows. In our context, the elastic response is the tangent to the pressure-depth trace just within the subpial region, i.e., just beyond \( \delta \). Thus, the position \( \delta \) was determined from a pressure test carried out just prior to the elastic response test. The use of the pressure test to determine the subarachnoid and subpial positions within the intracranial system has been described earlier (5, 6). In Fig. 3 we show the pressure-depth trace of Fig. 2 along with two others from the same elastic response test but with slightly varying insertion depths. Also shown is the value of \( \delta \) for this test, again, determined from a prior pressure test. Figure 3A shows the actual insertions while in Fig. 3B the traces have been shifted vertically so the pressures \( p_s \) at \( \delta \) are aligned. The justification for this is that each elastic response insertion is carried out in a time short compared to other pressure fluctuations which may occur within the intracranial system during the overall test; in particular, those due to respiration and due to changes in the CSF compartment pressure. Since we are interested in the slope of the pressure-depth response, a vertical shift will not change the results. Note that Fig. 3 exhibits this fact and, indeed, this is what makes the pressure-depth ratio an important parameter; changes in the CSF pressure and arterial and respiratory pressures do not change the pressure-depth ratio. However, changes in the physiological...
values of pressure-depth ratio ranged from 17 to 26 mmHg/mm. Vertical broken line indicates depth \( \delta \), which represents position of subpial region as determined by a prior pressure test (see text).

The tangent to the pressure-depth trace, shown in Fig. 3B, is the measure of the elastic response. The value in this case is 21 mmHg/mm. It seems important to remark at this point that this value is not presented as an actual material parameter, e.g., as the elastic tangent modulus of brain tissue. That is, the value of the measured pressure-depth ratio reflects the experimental configuration as well as the material response. Still, for a given configuration the pressure-depth ratio is a meaningful parameter for identifying changes in the material response.

Additional mechanical response tests. As mentioned earlier, brain tissue in vivo exhibits the viscoelastic properties of pressure relaxation and creep displacement. It is of interest here that both of these tests, which are used to determine the relaxation and creep behavior,² provide additional information regarding the elastic response. For example, for the pressure relaxation test the transducer is rapidly inserted a small distance into the subpial region then held fixed while the pressure-time response is monitored. The pressure rises rapidly during insertion then decays monotonically at fixed insertion depth (4). Characterizing this decay in terms of a relaxation parameter and a characteristic relaxation time provides useful information about the viscoelastic properties of the in vivo tissue. For our present purposes we note that the insertion phase of the relaxation test is identical to that associated with the elastic response test and thus can be used to supplement the elastic response insertions. Likewise, the creep displacement test in which the insertion-depth time response is monitored while a constant weight is applied to the shaft (4) simulates the elastic response test during the insertion. Thus a single series composed of an elastic response insertion, a pressure relaxation test, and a creep test, at varying initial insertion levels provides three elastic response insertions.

Table 1 shows the results for eight elastic response tests carried out in the manner described above. The values of pressure-depth ratio range from 20 to 35 mmHg/mm. This compares with a range of values of 17-26 mmHg/mm reported in (7).

**DISCUSSION**

The time involved in carrying out an elastic response insertion is small compared with the time associated with induced physiological changes in the system. Because of this, along with the sensitivity of the parameter to system changes, we hope to adapt the technique to clinical use. Indeed, as mentioned earlier, this was a motivating factor in the development of the method described here; in particular, the determination of the pressure-depth ratio from a single insertion. The results for the three insertions shown in Fig. 3 indicate that the values of the initial tangent agree to within 10%. In some cases, however, there does seem to be evidence of fluctuations in the pressure response resulting from arterial pulsations which are evident in intracranial pressure measurements. This seems to account for the perturbation in the pressure response in insertion 3 of Fig. 3. Nevertheless, we feel that with experience these anomalies can be readily detected and accounted for.

Of particular interest in the insertions shown in Fig. 3 is the clear indication of nonlinear elastic response. That is, the response for the three insertions are concave upward so that the tangents to the curve have increasing slopes at increasing insertion depths. Nonlinear response in vitro brain tissue has been reported by Galford and McElhaney (1) while nonlinear in vivo behavior has been reported by Metz, McElhaney, and Ommaya (3). In future studies we will consider identifying the elastic response in terms of an initial tangent modulus (pressure-depth ratio) and an initial curvature (of the pressure-depth ratio) and investigate the influence of controlled physiological changes on the nonlinear elastic behavior.

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**TABLE 1. Elastic response as measured by pressure-depth ratio, \( G_0 \), for eight dogs**

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>( G_0 ), mmHg/mm</th>
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<tbody>
<tr>
<td>69</td>
<td>26</td>
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<tr>
<td>81</td>
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<td>975</td>
<td>28</td>
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¹ In the results of seven elastic response tests reported in (7), the values of pressure-depth ratio ranged from 17 to 26 mmHg/mm.

² These tests are described in (6).
REFERENCES