The effect of craniectomy on the biomechanics of normal brain

SHIZUO HATASHITA, M.D., AND JULIAN T. HOFF, M.D.
Section of Neurosurgery, University of Michigan, Ann Arbor, Michigan

Does an open skull alter the fundamental biomechanical properties of normal brain tissue? This question was studied in 32 anesthetized cats, 16 of which underwent a standard craniectomy (2.5 x 2.0 cm) in the left frontoparietal region. Brain tissue pressure, regional cerebral blood flow (rCBF), and brain water content were measured from the same area of cortical gray and white matter, and intracranial pressure (ICP) was recorded from the cisterna magna. Brain tissue resistance, tissue compliance, and the pressure-volume index were analyzed in response to a bolus injection of saline into brain tissue or the cisterna magna. Cerebrovascular resistance was also calculated.

In craniectomized animals 2 hours after surgery, ICP had fallen to $3.75 \pm 0.39$ mm Hg, and cortical gray and white matter tissue pressure had fallen to $3.19 \pm 0.47$ and $4.69 \pm 0.54$ mm Hg, respectively (mean $\pm$ standard error of the mean); these variables did not fall further over 4 hours. The pressure-volume index in the same animals increased significantly from $0.67 \pm 0.01$ to $0.86 \pm 0.04$ ml. Tissue compliance rose in the cortical gray matter but tissue resistance fell, approximating that found in subjacent white matter. There was no significant difference between animals with and without craniectomy in rCBF, cerebrovascular resistance, or brain water content in either gray or white matter.

These findings indicate that in the cat craniectomy causes an increase in the compensatory capacity of the intracranial cavity to increased volume. The data also indicate that cortical tissue has high hydraulic conductivity and compliance when the skull is opened.

KEY WORDS • craniectomy • intracranial pressure • pressure-volume index • tissue compliance • cat

SINCE Cushing first described decompressive craniectomy for relief of intracranial pressure (ICP), surgical decompression has been advocated as a treatment for severe brain edema associated with high ICP. Some authors have reported that decompressive craniectomy reduces the risk of mortality in patients with severe cerebral edema after head injury. However, initial optimism regarding the value of hemicraniectomy for severe head injury was not supported in a second study by the same group. While decompressive craniectomy reduced the mortality rate, morbidity was increased in survivors, probably because of the adverse effects of severe cerebral edema and swelling.

Some workers have noted brain swelling when the cortex is exposed to air or surface injury in animals with craniectomy. We recently observed that combined craniectomy and arterial hypertension causes extensive brain edema in cats. The interrelationship of pressure and volume and their effect upon ICP, brain edema, and tissue biomechanics remain unclear, however, despite several studies conducted under normal and pathological conditions.

The present experiment was designed to study the effect of craniectomy on the biomechanics and hemodynamics of normal brain tissue. We investigated the relationship of pressure to volume within the intracranial space and brain tissue in animals with and without craniectomy. In addition, we sought to clarify the relationships between tissue pressure, tissue hydraulic resistance, and tissue compliance within brain when it is exposed by craniectomy.

Materials and Methods

Surgical Protocol

Thirty-two adult cats, each weighing 2.0 to 4.5 kg, were anesthetized with intraperitoneal sodium pentobarbital (30 mg/kg). Cannulas were placed in the femoral artery and vein to measure systemic arterial pressure, to obtain samples for determining arterial blood
gas levels and hematocrit, and to administer drugs as necessary. Each animal was tracheostomized, immobilized with gallamine triethiodide (1.5 mg/kg), and mechanically ventilated with a Harvard respirator.* The animal's head was fixed in a stereotaxic holder. Body temperature and blood gas levels were maintained within physiological limits by a heating pad and ventilator adjustment, respectively. End-tidal CO₂ was continuously monitored and maintained in the physiological range. Two burr holes were made in the left frontoparietal region for the measurement of tissue pressure and regional cerebral blood flow (rCBF): one in the frontal bone (exposing the anterior suprasylvian gyrus) and one in the parietal bone (exposing the lateral gyrus). The exposed regions were closed with oxidized cellulose and dental cement after the monitoring needles were introduced.

In the 16 animals in the craniectomy group, a large craniectomy (2.5 × 2.0 cm) was made in the left frontoparietal bone, leaving the underlying transparent dura mater intact. Care was taken to avoid damaging the brain during the procedure. The 16 control animals did not undergo this procedure.

Measurement of Brain Tissue Pressure, Tissue Resistance, and Tissue Compliance

Brain tissue pressure, tissue resistance, and tissue compliance were measured with our own modification of Marmarou’s method, as previously described. Briefly, a Statham pressure transducer was connected via polyethylene (PE-50) tubing and a three-way stopcock to a 1-cc syringe attached to a Harvard constant-infusion pump and to a No. 23 needle (outer diameter 0.635 mm, inner diameter 0.343 mm). The system was filled with saline that was free of air bubbles. The needles were introduced at an oblique angle into the cortical gray matter of the lateral gyrus and into the topographic bone, leaving the underlying transparent dura mater intact. Hydrogen clearance method. A 250-μm diameter Teflon-coated platinum electrode, with 0.5 mm of the tip exposed, was placed 2 mm posterior to each tissue pressure needle. A silver chloride reference electrode was placed in the temporal muscle. Hydrogen gas (4% to 7%) was administered for about 2 minutes in the inspired air. The desaturation curves were analyzed by the initial-slope method. The regional cerebrovascular resistance was calculated as regional cerebral perfusion pressure (blood pressure – tissue pressure) divided by rCBF.

Experimental Protocol

Systemic arterial pressure, end-tidal CO₂ pressure, ICP, and tissue pressure were recorded continuously on a polygraph. After physiological variables had stabilized, 32 animals were separated into two groups of 16 each: a control group and a craniectomy group. Tissue pressure, rCBF, and ICP were measured, and tissue resistance, tissue compliance, pressure-volume index, and cerebrovascular resistance were calculated in eight animals with and in eight without a craniectomy 2 hours after the operative procedures were completed. Similar measurements and calculations were made in eight animals with and in eight without craniectomy 4 hours later. At the end of each experiment, the cats were sacrificed for macroscopic examination of the brain. If bleeding or tissue damage around the tip of a tissue pressure, with the needle inserted into the cisterna magna. The pressure-volume relationship of the intracranial space was determined using the pressure-volume index technique of Marmarou and colleagues. A bolus of saline (0.20 to 0.23 ml) was injected into the cisterna magna at a rate of 0.051 to 0.057 ml/sec. The pressure-volume index (PVI) was calculated from the peak pressure generated by bolus injection (Pp), using the equation: PVI = V/log(Pp/Po), where V is the volume injected and Pp the baseline ICP preceding the bolus injection.

Measurement of rCBF and Cerebrovascular Resistance

Regional cerebral blood flow was measured by the hydrogen clearance method. A 250-μm diameter Teflon-coated platinum electrode, with 0.5 mm of the tip exposed, was placed 2 mm posterior to each tissue pressure needle. A silver chloride reference electrode was placed in the temporal muscle. Hydrogen gas (4% to 7%) was administered for about 2 minutes in the inspired air. The desaturation curves were analyzed by the initial-slope method. The regional cerebrovascular resistance was calculated as regional cerebral perfusion pressure (blood pressure – tissue pressure) divided by rCBF.

### TABLE 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control 2-Hr Study</th>
<th>Control 4-Hr Study</th>
<th>Craniectomy 2-Hr Study</th>
<th>Craniectomy 4-Hr Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.36 ± 0.01</td>
<td>7.37 ± 0.01</td>
<td>7.34 ± 0.01</td>
<td>7.34 ± 0.01</td>
</tr>
<tr>
<td>PaCO₂</td>
<td>29.9 ± 0.5</td>
<td>28.8 ± 0.5</td>
<td>30.1 ± 0.6</td>
<td>30.3 ± 0.8</td>
</tr>
<tr>
<td>(mm Hg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PaO₂</td>
<td>148.3 ± 2.3</td>
<td>148.1 ± 1.6</td>
<td>147.9 ± 2.1</td>
<td>145.5 ± 2.3</td>
</tr>
<tr>
<td>(mm Hg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hematocrit (%)</td>
<td>36.8 ± 1.2</td>
<td>37.3 ± 1.0</td>
<td>33.8 ± 1.6</td>
<td>34.5 ± 1.6</td>
</tr>
</tbody>
</table>

* Values are means ± standard error of the means for eight animals in each group.
Craniectomy and biomechanics of normal brain

needle was detected, the data from that experiment were discarded.

**Brain Water Content**

After the animals had been sacrificed, the brains were removed. Coronal sections (3.0 mm thick) were immediately cut at the level of the needles and immersed in kerosene. Two 1-cu mm tissue samples were taken from tissue surrounding each needle. All samples were suspended in a kerosene-bromobenzene column for specific gravity determination. Brain water content was calculated and expressed as percentage water.12

**Data Analysis**

Mean pressure values were used from cardiac and respiratory phases of the various pressure waves. Statistical significance of results was determined by paired and unpaired Student's t-test. Values were expressed as mean ± standard error of the mean.

**Results**

**General Physiological Effects**

The arterial blood gas levels, pH, and hematocrit in 32 cats with and without a craniectomy are summarized in Table 1. Arterial blood pH, pCO2, and pO2 were maintained within normal limits throughout the experiments. Mean systemic arterial pressure did not change significantly, remaining at about 120 mm Hg throughout each experiment.

**Intracranial Pressure and Brain Tissue Pressure**

The tissue pressure and ICP levels in 16 control and 16 craniectomized cats sacrificed at 2 and 4 hours after the procedure are shown in Fig. 1. In the control animals, tissue pressures in the cortical gray matter and the white matter were 7.75 ± 0.72 mm Hg and 7.81 ± 0.87 mm Hg, respectively, and the ICP was 6.85 ± 0.23 mm Hg; these values did not change significantly over 4 hours. In the animals subjected to craniectomy, there was a significant fall in ICP and in tissue pressure measured from both the cortical gray and white matter: ICP was 3.75 ± 0.39 mm Hg 2 hours after craniectomy, whereas tissue pressure was 3.19 ± 0.47 mm Hg in the cortical gray matter and 4.69 ± 0.54 mm Hg in the white matter. The reduction of tissue pressure in the cortex was significantly greater than that in the underlying white matter after craniectomy. Neither ICP nor tissue pressure fell further over the subsequent 2 hours.

**Brain Tissue Resistance and Tissue Compliance**

Brain tissue resistance and tissue compliance 2 and 4 hours after the procedure are shown in Figs. 2 and 3 for 32 cats with and without craniectomy. The control values of tissue resistance and tissue compliance in the cortical gray matter differed significantly from those in the white matter. In control animals studied at 2 hours, tissue resistance in the cortical gray matter and the white matter was 10.29 × 10^3 ± 0.75 and 7.38 × 10^3 ± 0.89 mm Hg/ml/min, respectively, whereas tissue compliance in the gray and white matter was 8.77 × 10^-5 ± 0.60 and 13.69 × 10^-5 ± 2.03 ml/mm Hg. Tissue resistance and tissue compliance in both areas were unchanged 4 hours after the procedure.

Craniectomy caused a change of tissue resistance and compliance only in the cortical gray matter when com-
pared with the control group. Tissue resistance in the
cortical gray matter 2 hours after the procedure was
reduced to $7.00 \times 10^3 \pm 0.77$ mm Hg/ml/min, whereas
tissue compliance in the same area increased to $15.28$
$\times 10^{-5} \pm 2.39$ ml/mm Hg. These values approximated
those found in the white matter. In contrast, tissue
resistance and compliance in the white matter of the
craniectomized animals were $7.20 \times 10^3 \pm 0.58$ mm
Hg/ml/min and $13.81 \times 10^{-5} \pm 1.41$ ml/mm Hg,
respectively (values similar to those seen in the control
animals). Tissue resistance and compliance in both
areas 4 hours after the procedures did not differ signifi-
cantly from those values seen at 2 hours. Thus, crani-
extomy did not affect tissue resistance and compliance
in the white matter.

Pressure-Volume Index

Pressure-volume curves, established using stepwise
craniectomy, confirmed the validity of this technique. The PVI's from the
control and craniectomized animals sacrificed 2 and 4
hours after operation are shown in Fig. 4. The mean
PVI for control animals was $0.67 \pm 0.01$ ml 2 hours
after the procedure and $0.62 \pm 0.02$ ml at 4 hours.
Craniectomy caused the pressure-volume index to rise
when compared to values in animals without craniec-
tomy. Pressure-volume indices at 2 and 4 hours were
$0.86 \pm 0.04$ and $0.78 \pm 0.04$ ml, respectively (an insig-
nificant difference).

Cerebral Blood Flow and Cerebrovascular
Resistance

Regional cerebral blood flow and cerebrovascular
resistance are summarized in Table 2. In 16 control
animals the 2-hour values for rCBF in the cortical gray

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**TABLE 2**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control 2-Hr Study</th>
<th>Control 4-Hr Study</th>
<th>Craniectomy 2-Hr Study</th>
<th>Craniectomy 4-Hr Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>cortical gray matter</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rCBF (ml/100 gm/min)</td>
<td>45.94 ± 3.13</td>
<td>44.74 ± 3.13</td>
<td>44.20 ± 3.60</td>
<td>44.05 ± 3.63</td>
</tr>
<tr>
<td>SAP (mm Hg)</td>
<td>126.25 ± 3.75</td>
<td>123.75 ± 4.98</td>
<td>122.50 ± 2.50</td>
<td>121.25 ± 2.95</td>
</tr>
<tr>
<td>TP (mm Hg)</td>
<td>7.75 ± 0.72</td>
<td>7.36 ± 0.51</td>
<td>3.19 ± 0.47</td>
<td>3.25 ± 0.70</td>
</tr>
<tr>
<td>CVR (mm Hg/ml/100 gm/min)</td>
<td>2.67 ± 0.23</td>
<td>2.75 ± 0.21</td>
<td>2.78 ± 0.16</td>
<td>2.77 ± 0.18</td>
</tr>
<tr>
<td>white matter</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>rCBF (ml/100 gm/min)</td>
<td>17.46 ± 1.93</td>
<td>17.53 ± 1.91</td>
<td>15.91 ± 2.09</td>
<td>18.08 ± 2.18</td>
</tr>
<tr>
<td>SAP (mm Hg)</td>
<td>126.25 ± 3.75</td>
<td>123.75 ± 4.98</td>
<td>122.50 ± 2.50</td>
<td>121.25 ± 2.95</td>
</tr>
<tr>
<td>TP (mm Hg)</td>
<td>7.81 ± 0.87</td>
<td>7.44 ± 0.62</td>
<td>4.69 ± 0.54</td>
<td>4.63 ± 0.82</td>
</tr>
<tr>
<td>CVR (mm Hg/ml/100 gm/min)</td>
<td>7.28 ± 0.87</td>
<td>7.28 ± 0.89</td>
<td>7.84 ± 0.82</td>
<td>7.04 ± 0.72</td>
</tr>
</tbody>
</table>

* Values are means ± standard error of the means for eight animals in each group. rCBF = regional cerebral blood flow; SAP = systemic arterial pressure; TP = tissue pressure; CVR = cerebrovascular resistance.
and white matter were 45.94 ± 3.13 and 17.46 ± 1.93
ml/100 gm/min, respectively. There was no significant
difference in rCBF between the control and craniectom-
ized animals and no change over 4 hours.
The control values of cerebrovascular resistance in
cortical gray and white matter were 2.67 ± 0.23 and
7.28 ± 0.87 mm Hg/ml/100 gm/min, respectively. Ce-
rebrovascular resistance in conical gray and white mat-
ter of craniectomized animals at 2 hours was 2.78 ±
0.16 and 7.84 ± 0.82 mm Hg/ml/100 gm/min (an in-
significant difference from control values).

**Brain Tissue Water Content**

Brain water content is presented in Fig. 5. Water
content in the cortical gray and white matter at 2 hours
after craniectomy did not differ from that at 4 hours.
Furthermore, there was no difference in water content
of brain tissue between the craniectomized and control
animals.

**Discussion**

We have demonstrated that a large craniectomy
causes a decrease in pressure in both the cerebrospinal
fluid (CSF) and the parenchyma of normal brain. This
confirms other studies which have shown that decom-
pressive craniectomy effects a reduction in ICP in var-
iouss pathological conditions. 2,6,9 When the cranium is
converted from a so-called “closed” cavity into an
“open” one, however, it is unknown how craniectomy
actually changes the biomechanical properties of the
intracranial compartments during normal and patho-
logical conditions.
The relationship of pressure and volume in the intra-
cranial cavity was assessed with the PVI technique,
using the bolus method. 13 Craniectomy produced an
increase in the PVI, indicating that the CSF space is the
initial compliant part when the cranium is open. Pre-
vious studies have also shown that removal of the
calvaria is associated with an increase in the volume-
buffering capacity of the neural axis. 6,19,21 These find-
ings and our own indicate that a cranial opening in-
creases the volumetric compensatory capacity of the
intracranial cavity.
The relationship of tissue pressure to volume within
brain parenchyma was also evaluated. Craniectomy
produced a dramatic increase of tissue compliance in
the cortical gray matter of normal brain, suggesting that
brain tissue is compliant in the presence of an open
skull. High compliance in brain tissue, in addition to
that of the CSF space, is related to altered pressure-
volume relationships within the intracranial cavity.
The intravascular blood volume must also be consid-
ered in the relationship between ICP and volume. 11 In
our studies craniectomy caused no change in either
cerebral blood flow or cerebrovascular resistance mea-
sured from the same cortical gray matter. Thus, the
compliance of the intravascular blood compartment
was probably not influenced by craniectomy. On the
other hand, Walstra, et al., 23 reported that brain tissue
compliance increases in an infusion model of brain
edema as edema fluid accumulates. We have also dem-
onstrated that tissue pressure and compliance of brain
parenchyma undergo a change in the course of ischemic
brain edema development. 7,8 This accumulation of
fluid within tissue also must affect the pressure-volume
relationship within brain parenchyma. In the present
study, water content of brain tissue did not change
beneath the craniectomy site. These findings together
indicate that brain tissue itself becomes more compliant
when the skull is opened.
The present study demonstrates that a large craniec-
tomy causes a decrease in the pressure of CSF and brain
tissue. Furthermore, craniectomy is associated with an
increase in the volumetric compensatory capacity of
the intracranial space. This change in the volume-
pressure relationship seems to contribute, at least in
part, to the fall in ICP.
Decompressive craniectomy may have adverse effects
on severe cerebral edema and brain swelling in pa-
tients. 22 There is also experimental evidence that cra-
niectomy enhances the formation of brain edema.
Cooper, et al., 2 reported that craniectomy causes an
increase in formation of cold-induced edema. We re-
cently demonstrated that, when arterial hypertension is
combined with a craniectomy, extensive brain edema
develops at the site of craniectomy. 9 We have also
observed that craniectomy enhances the development
of brain edema in experimental cerebral ischemia (un-
published data). An increase in the transmural hydro-
static pressure gradient across the brain capillary bed
produced by craniectomy may be the underlying path-
ogenetic factor.
It is known that the hydraulic conductivity and compliance of tissue influence water movement within the intracranial compartments. In our study, craniectomy caused tissue resistance to fall only in the cortex of normal brain tissue, to a level approximating that in the underlying white matter. This implies that brain tissue has high hydraulic conductivity after craniectomy. In addition, our study of tissue compliance demonstrated that cortical gray matter becomes highly compliant and distensible when a craniectomy is performed. It follows therefore that edema fluid, which originates from blood, can easily accumulate in cortical tissue beneath a craniectomy and spread within gray matter or into adjacent white matter. Consequently, we believe that changes in the mechanical properties of cortical tissue produced by craniectomy (namely, tissue hydraulic conductivity and tissue elastic compliance) play an important part in both the formation of brain edema and its movement within the tissue.

We have demonstrated that craniectomy produces an increase in the volumetric compensatory capacity of the intracranial cavity and that brain tissue develops high hydraulic conductivity and compliance when exposed by bone removal. This implies that ICP falls when the skull is opened and at the same time brain edema formation is facilitated. Therefore, brain edema may actually be enhanced when decompressive craniectomy is used to treat patients with severe head injuries and raised ICP.

References


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