Prevention of Cerebral Infarction in the Monkey by Omental Transposition to the Brain

HARRY S. GOLDSMITH, M.D., SERGE DUCKETT, M.D., PH.D., AND WEI-FAN CHEN, M.D.

SUMMARY The intact omentum of 13 monkeys was lengthened, placed subcutaneously, and laid on the left cerebral hemisphere prior to occluding the left middle cerebral artery. Two of these 13 monkeys developed left cerebral infarct and a right hemiparesis. Nine other monkeys had their left middle cerebral artery occluded without omental protection. All of these 9 developed a left cerebral infarct and 8 of them a right hemiparesis. Intact omentum may prevent a cerebral infarction when placed on the brain prior to MCA occlusion.

Material and Methods
Twenty-five adult stump-tailed monkeys weighing 8–10 K were used (table 1). Three of the animals (G2, G3, G7) died

Changes in Glucose Consumption

For many years glucose was considered to be the only substrate that the brain was capable of utilizing. This view is now known to be incorrect.9 Since brain glucose consumption falls and oxygen utilization rises following OAKG it would appear that alpha ketoglutarate also passes the blood brain barrier and is utilized. The increase in glucose utilization due to hypoxia is virtually abolished.

Changes in Oxygen Utilization

Despite similar low PO2 values, oxygen consumption was higher on the second occasion. The reasons for this are not clear.

Kobayashi and colleagues11 have recently shown in cats that following cerebral ischemia there is a dramatic decrease in brain glutamate concentration. There is at the same time a small rise in glutamine concentration. As electrical activity increases, glutamate concentration returns toward normal values. These findings are in agreement with observations of Folbergrova who had suggested12 that the decrease in glutamate was associated with the suppression of functional activity. The changes following ischemia described by Kobayashi could be secondary to ammonia detoxification, protein degradation, changes in amino acid transport or to changes in the intermediates associated with the tricarboxylic acid cycle. The fact that replenishment of ketoglutarate is associated with higher oxygen utilization would support the latter hypothesis.

References

TABLE 1 Data on 25 Monkeys

<table>
<thead>
<tr>
<th>Transplant Type</th>
<th>Time lapse between transplant &amp; clipping</th>
<th>Infarct</th>
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<tbody>
<tr>
<td>Intact omental transplants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G1</td>
<td>29 days</td>
<td>No</td>
</tr>
<tr>
<td>G2</td>
<td>Died—</td>
<td>—</td>
</tr>
<tr>
<td>G3</td>
<td>Died—</td>
<td>—</td>
</tr>
<tr>
<td>G4</td>
<td>42 days</td>
<td>No</td>
</tr>
<tr>
<td>G5</td>
<td>34 days</td>
<td>No</td>
</tr>
<tr>
<td>G6</td>
<td>37 days</td>
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</tr>
<tr>
<td>G7</td>
<td>Died—</td>
<td>—</td>
</tr>
<tr>
<td>G8</td>
<td>35 days</td>
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</tr>
<tr>
<td>G9</td>
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</tr>
<tr>
<td>G10</td>
<td>43 days</td>
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</tr>
<tr>
<td>G11</td>
<td>44 days</td>
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</tr>
<tr>
<td>G12</td>
<td>44 days</td>
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<td>G13</td>
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<td>G20</td>
<td>33 days</td>
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</tr>
<tr>
<td>G21</td>
<td>33 days</td>
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</tr>
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</tr>
<tr>
<td>Clip only</td>
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</tr>
<tr>
<td>G14</td>
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</tr>
<tr>
<td>G15</td>
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<td>—</td>
</tr>
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<td>G16</td>
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<td>—</td>
</tr>
<tr>
<td>Muscle transplants</td>
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</tr>
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<td>G17</td>
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</tr>
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<td>G18</td>
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</tr>
<tr>
<td>G19</td>
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</tr>
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</tr>
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<td>G23</td>
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<tr>
<td>G24</td>
<td>31 days</td>
<td>Yes</td>
</tr>
<tr>
<td>G25</td>
<td>31 days</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Anesthetic complications during surgery and were not included in the final evaluation. Of the 22 monkeys who did survive the entire experiment, 9 (G14 to G19, G23 to G25) had MCA occlusion and served as controls. The other 13 (G1 to G13 and G20 to G22) had omental transposition to the brain prior to MCA occlusion.

Omental Transposition

The 13 monkeys in the omental series had general anesthesia — halothane administered through an endotracheal tube. The animals were placed on their right side in a semi-oblique position for laparotomy. The omentum was elongated by the technique previously reported in man (fig. 1). After the omentum had been extensively lengthened, it was brought up through a subcutaneous tunnel along the chest, shoulder, and up to the back of the neck (fig. 2). All incisions were closed without drainage. At this point, the monkeys were placed in a semiprone position and a craniotomy was performed in the left temperoparietal region. This was done by making a U-shaped incision in the left temperoparietal region with the base of the skin flap facing the occipital region (fig. 3) and the base of the underlying soft tissue flap toward the ear. The periosteum overlying the exposed portion of the skull was removed and burr holes made in the cranium. These were connected and a piece of bone measuring approximately 3 × 3 cm was removed. The underlying dura was carefully incised (fig. 4) and the

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**Figure 2.** Subcutaneous tunnel being made along chest toward skull. Forefinger at top of illustration inserted in incision at base of neck through which omentum will be delivered.

**Figure 3.** U-shaped incision on left side of head. Note elongated omentum protruding from neck incision.
pedicled omentum laid on the underlying brain and secured by several sutures to the cut edge of the dura (figs. 5, 6).

Four to 6 weeks after the craniotomy, the monkeys were again given general anesthesia and another U-shaped incision was made down to the skull with the attachment of the flap based over the temporal region. A craniotomy was performed at the base of the skull in front of and below the initial craniotomy in order to reach the proximal portion of the left MCA for occlusion. Part of the zygoma was removed to reach this area of the skull.

After the craniotomy, which measured approximately $3 \times 3$ cm, the dura was opened and the temporal lobe gently lifted to expose the MCA lying in the Sylvian fissure. Two to 4 occluding Hemoclips (Weck, medium sized) were placed on the proximal portion of the MCA between the internal carotid artery and the trifurcation of the MCA. The dura was then approximated with several non-absorbable sutures followed by replacement of the soft tissues overlying the dura. No drains were left in the wound, and the skin was closed with interrupted non-absorbable sutures.

Control Series

The 9 monkeys in the control series had general anesthesia and a left temporoparietal craniotomy in a manner identical to the monkeys who had omental transposition.

Group I (Monkeys G14, G15, G16)

The monkeys in Group I had a craniotomy at which time the left MCA was occluded. This was to verify the results of MCA occlusion.
Group II (Monkeys G17, G18, G19)

After the dura was opened in Group II animals, the overlying temporal muscle was laid directly on the brain. Four to 6 weeks later, the left MCA was occluded in a manner comparable to the monkeys in Group I.

Group III (Monkeys G23, G24, G25)

The monkeys in Group III had general anesthesia and a craniotomy. A 2 x 2 cm piece of omentum, removed from the abdomen, was placed on the underlying brain after the dura was opened and secured to the surrounding area with several interrupted, absorbable sutures. The scalp was then approximated over the free omental graft without drainage and the animal allowed to recover. Four to 6 weeks later, the MCA was occluded in a manner identical to the monkeys in Groups I and II.

All the monkeys in Groups I, II and III and those with omental transposition were killed 7-10 days after MCA occlusion. At sacrifice, they were given 50 mgm of heparin intravenously and 20 ml of Microfil*, a radiopaque plastic material which solidifies in small blood vessels, was injected into the common carotid arteries. The purpose was to visualize the results of MCA occlusion, to observe anomalies in cerebral vascularization (fig. 7), and to evaluate the distribution of blood vessel anastomosis between the omentum and the soft tissue overlying the brain. To allow hardening of the plastic material within the cerebral vascular network, each monkey was placed in an ice box overnight. The following day, the brain was removed, placed in 10% formalin for 2-3 days, and x-rayed (fig. 8).

The brain was fixed in 10% buffered formalin for a month and the entire midsection, from the front of the basal ganglia to the posterior portion of the thalamus, was cut coronally in layers 2-3 cm thick, dehydrated in alcohol, and cleared in methyl salicylate (fig. 9). This method provides transparencies of the brain in which the injected vascular system is visible. In addition, areas of pathology are highlighted and the location of the metal clips on the MCA can be examined.

Representative tissues of the brain and the area of omental cerebral attachment were imbedded in celloidin and paraffin and stained with hematoxylin-eosin, Nissl, Heidenhain stains and phosphotungstic acid-hematoxylin to demonstrate cells, myelin and gliosis.

* Canton Bio-Medical Products, Inc., Boulder, CO.
Results

Controls (Groups I, II, III)

All the control monkeys — except G24 — developed a right hemiparesis with weakness and paralysis of the right extremity (fig. 10). Cerebral infarcts were grossly evident by naked eye examination in the left hemisphere of all 9 monkeys. Histological examination of this area confirmed the destruction of cerebral tissue and the presence of macrophages in the infarct.

Experimental Series

Two of 13 monkeys (G21, G22), which had omental transposition to the brain prior to MCA occlusion, developed a left cerebral infarct and right hemiparesis. The remaining 11 monkeys in this group developed neither a cerebral infarct nor hemiparesis. Examination of methyl salicylate transparencies of serial histological sections of representative areas of the brains of the 11 clinically normal monkeys showed no histological changes; however, the 2 hemiparetic monkeys had grossly evident cerebral infarctions by naked eye examination. Histological examination also showed tissue destruction and macrophages in the basal ganglia and surrounding tissue in the left hemisphere of these 2 brains. One of these specimens (G21) was found to have the omentum unattached to the underlying brain surface. The omentum of the other hemiparetic monkey (G22) was found firmly adherent to its brain but the omentum was attached in the parietal occipital region. This finding raised the question as to whether the posterior positioning of the omentum might have resulted in inadequate secondary vascularization to areas of the brain normally supplied by the MCA.

A comparison between the control and experimental monkeys in this study showed that placing the attached omentum on the brain prior to MCA occlusion yielded a statistically significant difference in preventing cerebral infarction with a P-value of 0.002 using Chi square with Yates correction.

Discussion

Attempts have been made\(^6\) to introduce an extracranial source of blood by placing temporal muscle flaps directly on the brain. Vascular anastomosis developed between these two structures but in humans the amount of blood to the brain was insufficient and the method was abandoned. More recently, microscopic methods have been used to reroute blood flow to small vascular channels of the brain,\(^7\) but these sophisticated techniques required the availability of small patent cerebral blood vessels distal to an intracranial arterial block. Even when there is a suitable vessel for this type of surgery, there always remains the danger that occlusion at the end side vascular shunt can result in even less blood flowing to the brain distal to the anastomosis than before operation.

We decided to use the attached omentum to revascularize the brain because of its ability to vascularize not only intra-peritoneal but extraperitoneal structures.\(^8\) Previous studies reported from our laboratory showed that the transposition of the intact omentum to dog brain did not cause cerebral pathology and the amount of blood delivered to the brain following occlusion of the MCA was sufficient to prevent cerebral infarction.\(^9\) The experimental use of the omentum for treating pathological cerebral conditions was reported by Yasargil and colleagues\(^8\) who used the omentum on dog brain for cerebral spinal fluid absorption in hydrocephalus; the omentum was used in a free fashion with arterial and venous connections made to the superficial temporal artery and vein.

The cerebral infarction developed in our animals was contingent upon the occlusion of the MCA, and examination of the monkey brains revealed that the clips had been placed on either side of the lenticulostriate vessels of the MCA. The visual and histological comparison of the infarcted brains (G14–19, and G21–25) to the normal monkey brain (G1–G13) strongly suggests that placing the intact attached omentum directly upon the brain can improve cerebral vascularization and prevent cerebral infarction produced by MCA occlusion. This operative procedure has been found to
be safe, easily accomplished when one knows the technique, and results in no neuropathological changes at the site of the omental transposition.

Note
(See Letter to the Editor: Omental Transposition To Human Brain, p. 272.)

References

SUMMARY Continuous-wave Doppler sonography is a reliable method for detecting severe subclavian stenosis and occlusion as well as subclavian steal. Intermediate stages leading to subclavian steal can also be detected. These are characterized by a cardiac-phase-dependent alternating flow direction in the vertebral artery. Some cases of proximal subclavian or proximal vertebral artery stenosis produce a systolic deceleration of flow in the vertebral artery. Stenosis and occlusion of the subclavian artery as well as stenosis of the subclavian and vertebral arteries can be distinguished. The pulse curve changes described can be reversed by a vascular by-pass.

REVERSE FLOW in the vertebral artery resulting from occlusion of the proximal subclavian artery (subclavian steal) which was first described in an angiographic study, can be demonstrated by transcutaneous Doppler sonography. Since occlusion of the proximal subclavian artery usually develops slowly with progression of arteriosclerotic stenosis, it is to be expected that intermediate, previously undescribed, flow patterns of forward and reverse flow will be found in flow studies of the vertebral artery. The results presented in this paper show it is possible to demonstrate such intermediate forms (incomplete steal) by means of Doppler sonographic examination of the subclavian and vertebral arteries. Characteristic changes are also described in patients with high-grade proximal stenosis of the vertebral artery, which could not previously be differentiated with certainty from hypoplasia and occlusion.

Material and Methods
The transcutaneous semiquantitative measurement of velocity and direction of blood flow was carried out with a directional continuous wave Doppler device, "Débitmètre Ultrasonique Delalande," at a frequency of 4 MHz. The Doppler pulse curves and the ECG were simultaneously registered on a direct-writing recorder (Cardirex 4-channel, Siemens and Brush 2-channel).

Recordings of flow in the subclavian artery are made in the supraclavicular fossa. Medial or lateral alignment of the probe allows examination of the proximal or distal portion of the vessel. The vertebral artery is examined at the level of the atlas slope, but it is not possible to determine by transcutaneous examination whether the afferent (flow to probe) or efferent (flow away from probe) section of the atlas slope is reached by the ultrasonic beam. The upward or downward direction of the pulse curves in relation to the zero line gives no clear indication of forward or reverse flow in this artery. This can only be determined by functional tests. With reverse (armward) flow, raising peripheral resistance to flow (compression of the upper arm or closure of the fist) causes deceleration of flow followed by raised flow velocity in the vertebral artery (postischemic hyperemia).

With forward flow in the vertebral artery upper arm compression usually causes no significant change in flow velocity. The pulse curves of the vertebral artery for antegrade and retrograde flow, which show distinct differences, are illustrated in figure 1A and 1D, together with the effect caused by upper arm compression. In this study, for the purpose of simplification, the Doppler device was...
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