Experimental augmentation of regional cerebral blood flow by microvascular anastomosis

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Intracranial surgical procedures for cerebrovascular occlusive disease have become feasible with the development of microvascular surgical techniques. This study assesses the ability of microanastomoses of the superficial temporal and cortical arteries to augment cerebral blood flow after clip occlusion of the middle cerebral artery in the dog. The ischemic insult was marked by a variable degree of regional flow depression but consistent disruption of the blood-brain barrier. Significant augmentation of cerebral blood flow was noted after anastomosis to cortical arteries in proximity to the occlusion and was associated with a characteristic widening of the pressure flow hysteresis loop obtained on autoregulatory testing. Survival was noted only in those animals demonstrating a measurable flow increase, although the latter could not be correlated with specific degrees of neurological improvement.

KEY WORDS □ cerebral blood flow □ infarction □ microvascular anastomosis □ autoregulation

RECENT advances in stroke therapy have included the development of direct intracranial surgical approaches to ameliorate focal occlusive lesions. Microvascular techniques now allow the construction of collateral channels to cortical vessels less than 1 mm in diameter to improve the blood supply of the ischemic brain. Among the various types of procedure available, superficial temporal-to-middle cerebral cortical anastomosis has the widest application. The procedure is clinically feasible in middle cerebral root or intracranial internal carotid occlusion and has been reported in 115 selected cases. While the clinical and radiographic indications for this procedure are currently under investigation, the assumption that such grafting techniques will augment cerebral blood flow has not been established.

The canine experimental model has been useful in developing the technique of superficial temporal-to-cortical artery anastomosis because of the size of the middle cerebral vessels. Angiographic evaluation postoperatively has been of particular value in documenting patency which, however, is not necessarily associated with functional benefit. Crowell and Olsson noted in 10 dogs that neurological function was related to the interval between occlusion and anastomosis but was unrelated to long-term patency of the graft.

The need for objective hemodynamic data.
describing the function of these new collaterals is becoming obvious. The purpose of this study was to determine the effect of superficial temporocortical artery microanastomosis on cerebral blood flow and its autoregulation. This information may allow critical evaluation of the benefits to be expected from a comparable therapy in man.

**Materials and Methods**

Adult foxhounds weighing 20 to 24 kg were anesthetized with 25 mg/kg of phenobarbital and intubated. The femoral artery and vein were cannulated to monitor arterial blood gases and to administer drugs and fluids. After a curvilinear scalp incision was made, the superficial temporal artery was isolated, the bulky temporalis muscle sharply excised, and a large hemicraniectomy performed. A 2.0 to 4.0 cm segment of the superficial temporal artery was dissected free from its bed, and a 1 or 2 mm Statham electromagnetic flow probe* was then placed around the exposed vessel. Blood flow readings were obtained at normal blood pressure, and constancy of flow was measured at hypertensive and hypotensive levels (Table 1). Approximately 1 week later flow in the superficial temporal artery was again measured, after which the dura was opened widely and 4 cc/kg of 2% Evans blue solution was injected intravenously. If hyperemia, swelling, or leakage of Evans blue solution were noted as a result of the hemicraniectomy or postoperative trauma, the experiment was terminated.

Regional cerebral blood flow studies were facilitated by retrograde catheterization of the sternomastoid branch of the common carotid artery with a PE50 Teflon catheter. The catheter was inserted to the region of the carotid bifurcation, and a bolus injection of 3 to 4 mCi of 185Xe was performed. The washout of 185Xe was monitored with the gamma camera† using a modified crystal head for laboratory animals and a high-sensitivity collimator. The anatomical marker, in conjunction with the persistence oscilloscope, eliminated extracerebral radioactivity and allowed for the definition of three irregularly shaped areas of interest which we have labeled frontal, temporal, and parietal. The computer‡ provided individual values for mean flow and compartmental flow, as well as flow in the fast and slow components. Control cerebral blood flow measurements were made, and autoregulation of flow was tested using neosynephrine or oligemic hypotension to effect changes in cerebral perfusion pressure. Vasoreactivity to hypercapnia was tested using a 5% CO2 gas mixture with controlled ventilation.

With the use of the operating microscope, a microaneurysm clip was applied to the main branch of the middle cerebral artery at the level of the lateral lenticulostriate perforators. At intervals thereafter, postocclusion cerebral blood flow, autoregulation, and vasoreactivity studies were performed. A 1-cm segment of the cortical artery either adjacent to the clip site in the temporal region or more distally over the parietal region was mobilized by stripping the arachnoid and dividing one or two small underlying branches. The superficial temporal artery was then brought into the operative field, and microanastomosis was performed over a T-tube in the cortical artery with 10-0 suture at 40× magnification.

Patency was evaluated by noting visible pulsations or the presence of discoloration or visible stasis. Photographs of the external surface of the anastomosis were taken following which postoperative regional cerebral blood flow and graft flow studies were performed as described previously. Angiographic visualization of the anastomosis site required a separate cut down on the superficial temporal artery; and, since our main interest was in a study of flow characteristics, this was performed at the conclusion of selected experiments only.

**Results**

Complete data were obtained in 13 of 22 healthy, neurologically normal dogs. Technical failures as a result of occlusion at the anastomosis site occurred in four animals. Severe postoperative vasospasm of the cortical artery was noted in two animals. The

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*Electromagnetic flow probe made by Statham Instruments, Inc., Oxnard, California 93030.
†Pho-Gamma III camera made by Nuclear Chicago, Chicago, Illinois.
‡Nuclear Data Med II computer made by Nuclear Chicago, Chicago, Illinois.
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TABLE 1

Superficial temporal artery blood flow (13 dogs)*

<table>
<thead>
<tr>
<th>Blood Pressure</th>
<th>Control</th>
<th>Post TAA</th>
<th>Post PAA</th>
</tr>
</thead>
<tbody>
<tr>
<td>normotension</td>
<td>9.5 (5-18)</td>
<td>8.2 (4-16.3)</td>
<td>6.8 (2.6-11.6)</td>
</tr>
<tr>
<td>hypertension</td>
<td>+27% (21-35)</td>
<td>+31% (22-36)</td>
<td>+29% (21-33)</td>
</tr>
<tr>
<td>(&lt;240 mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hypotension</td>
<td>-60% (40-100)</td>
<td>-42% (20-52)</td>
<td>-48% (31-59)</td>
</tr>
<tr>
<td>(&gt;55 mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Blood flow during normotension expressed in cc/min. Values at altered blood pressure expressed as percentage change of normotensive flow values. TAA = temporal artery anastomosis, PAA = parietal artery anastomosis.

anastomosis could not be performed after satisfactory baseline and postocclusion studies in three animals.

Control Studies

Blood Flow Values (Normotension, Eucapnia, Normoxia). Blood flow in the main branch of the superficial temporal artery varied between 5 and 18 cc/min in different animals, with a mean value of 9.5 cc/min at a mean perfusion pressure of 132 mm Hg (Table 1). A mean regional cerebral blood flow of 36.5 cc/100 gm/min was noted in the frontal region, 31.1 cc/100 gm/min in the temporal region, and 30.5 cc/100 gm/min in the parietal region. Compartmental values for these same regions agree closely, and flow rates in fast and slow components as well as those derived by Zierler's stochastic equation are given in Table 2.

Constancy of Flow. Augmentation of superficial temporal artery blood flow was seen in 13 animals, although constancy of intracerebral flow (F = K \cdot P < I) was present (Fig. 1). A small degree of hysteresis or lag between pressure and intracerebral flow was noted between a mean blood pressure of 60 to

TABLE 2

Augmentation of regional cerebral blood flow in the adult foxhound after middle cerebral root occlusion

<table>
<thead>
<tr>
<th>Flow*</th>
<th>Frontal</th>
<th>Temporal</th>
<th>Parietal</th>
</tr>
</thead>
<tbody>
<tr>
<td>control</td>
<td>( \lambda ) H/A</td>
<td>36.5 ± 6.2</td>
<td>31.1 ± 4.7</td>
</tr>
<tr>
<td>n=13</td>
<td>Fg</td>
<td>50.2 ± 11.1</td>
<td>46.5 ± 7.2</td>
</tr>
<tr>
<td>Fw</td>
<td>18.6 ± 7.2</td>
<td>13.6 ± 6.7</td>
<td>13.0 ± 5.1</td>
</tr>
<tr>
<td>post-occlusion</td>
<td>( \lambda ) H/A</td>
<td>21.0 ± 8.5†</td>
<td>11.1 ± 5.7§</td>
</tr>
<tr>
<td>n=13</td>
<td>Fg</td>
<td>37.6 ± 6.1</td>
<td>31.2 ± 6.2‡</td>
</tr>
<tr>
<td>Fw</td>
<td>12.7 ± 6.5†</td>
<td>8.3 ± 2.5‡</td>
<td>9.6 ± 2.0†</td>
</tr>
<tr>
<td>( &lt;3 hrs)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>post-occlusion</td>
<td>( \lambda ) H/A</td>
<td>22.2 ± 6.7</td>
<td>10.1 ± 4.5</td>
</tr>
<tr>
<td>n=13</td>
<td>Fg</td>
<td>34.5 ± 4.0</td>
<td>31.8 ± 5.8</td>
</tr>
<tr>
<td>Fw</td>
<td>11.5 ± 4.2</td>
<td>9.2 ± 3.6</td>
<td>10.5 ± 3.1</td>
</tr>
<tr>
<td>post-TAA</td>
<td>( \lambda ) H/A</td>
<td>28.98 ± 6.7*</td>
<td>15.32 ± 4.1†</td>
</tr>
<tr>
<td>n=7</td>
<td>Fg</td>
<td>51.89 ± 6.3†</td>
<td>43.06 ± 5.0‡</td>
</tr>
<tr>
<td>Fw</td>
<td>17.53 ± 4.2</td>
<td>11.45 ± 3.2‡</td>
<td>13.25 ± 3.1†</td>
</tr>
<tr>
<td>post-PAA</td>
<td>( \lambda ) H/A</td>
<td>20.5 ± 9.1</td>
<td>12.7 ± 7.7</td>
</tr>
<tr>
<td>n=3</td>
<td>Fg</td>
<td>39.1 ± 8.5</td>
<td>33.1 ± 2.0</td>
</tr>
<tr>
<td>Fw</td>
<td>9.6 ± 3.1</td>
<td>6.2 ± 1.6</td>
<td>8.0 ± 1.5</td>
</tr>
</tbody>
</table>

\( \lambda \) H/A = Zierler's mean flow equation; Fg = flow in gray matter; Fw = flow in white matter.

\( \ddagger p < .05. \)

\( \ddagger \ddagger p < .01. \)

\( \ddagger \ddagger \ddagger p < .001. \)

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140 mm Hg in all control animals. Graded hypercapnia was associated with a progressive rise in mean cerebral blood flow although at the higher pCO₂ values the rate of rise was greater (Fig. 2).

**Middle Cerebral Artery Occlusion**

Postocclusion blood flow studies in 13 animals required a minimum of 1 hour 10 min; and, in some animals, were extended over a 3-hour period after application of a clip to the middle cerebral root. In three of these animals studies were also obtained over the course of 2, 2½, and 5 days postocclusion. Evans blue staining of the cortical surface was present after occlusion and before completion of the anastomosis in all animals. There was a significant reduction in the mean gray and white matter flow in the temporal region after occlusion (Table 2). The mean time required for flow to reach its nadir after occlusion was approximated to the beginning of each washout study, which was performed over a 15-min period. These were achieved between 22 and 35 minutes, and interregional differences were not significant.

Seven animals in this group underwent changes in perfusion pressure during conditions of normoxia and normocapnia. All demonstrated varying degrees of intolerance to induced moderate hypotension, and hypertensive stimuli did not effectively augment flow (Fig. 1). Graded hypercapnia was associated with a decrease in flow in two animals and no significant change in three others. The latter is illustrated in Fig. 2.

**Temporal Cortical Branch Microanastomosis**

The time between application of the clip to the middle cerebral artery to completion of the anastomosis ranged from 90 min to 3¼ hours. The period of complete stasis in the cortical artery during which time tourniquets were fastened without the T-tube never exceeded 5½ min. Severe vasospasm was present in the cortical artery segment in two experiments, with a further reduction of 15% and 22% in mean flow values compared to postocclusion values. Recovery of flow values did not occur when measured 2 days later. At the latter examination, extremely severe cerebral edema precluded further use of these animals.

In five temporal cortical anastomoses, there was no grossly visible spasm, although in one, some kinking of the cortical artery segment was noted. In three of the five animals a reduction in flow values of 15%, 22%, and 26% was noted in the graft segment. In the other two animals no significant change in flow was noted in graft segments (Table 1). Cerebral blood flow was augmented within the ischemic hemisphere after this procedure in all five animals. As

![Fig. 1. Experiment 7.](image)

![Fig. 2. Experiment 7.](image)
Experimental augmentation of regional cerebral blood flow

noted in Table 2, there was some improvement in mean flow in all regions after temporal artery anastomosis, but the increase in flow in the temporal region was most marked. Four of the five animals in this group demonstrated a peculiarity of autoregulation 2½ hours after microanastomosis. Although constancy of flow was present between mean blood pressures of 90 and 140 mm Hg, a very wide degree of hysteresis was obtained during sequential alterations in blood pressure. Wide residual hysteresis loops were present in all four animals for as long as 10 days after anastomosis (Fig. 1). Hypercapnia produced a progressive increase of blood flow in all four animals, and in three of the four the relative augmentation of flow was most marked at the higher pCO₂ values (Fig. 2).

Parietal Cortical Artery Anastomosis

In three animals there was no overall improvement in either mean flow, gray matter or white matter flow. The postoperative values in the parietal regions themselves were not significantly improved over the postocclusion values (Table 2).

Functional Evaluation

Because of the anesthetic requirements, serial neurological evaluation could not be performed just prior to grafting. The three animals undergoing clip occlusion only had severe postoperative deficits, including circling and poor feeding in one and coma in two. Two of the three animals in whom temporocortical grafts were followed by spasm, showed poor function progressing to death. One animal with a parietal cortical graft ate poorly and circled but survived. Of the five animals with successful proximal temporal artery anastomosis, neurological function was unrelated to the degree of recovery of blood flow. All animals survived, although the one with the largest percentage increase in flow remained stuporous and ate poorly for 5 days after surgery. Thereafter no deficit was detectable.

Discussion

Consideration must be given to the obvious problems inherent in a study of cerebral blood flow in the dog, whose rich extracerebral circulation ordinarily leads to significant overlap of radioactivity. This was circumvented by recording from an open hemicraniectomy flap; however, the use of these animals was thus restricted to 10 days postoperatively. Cerebral trauma was unavoidable after longer intervals despite the protected cage environments. This limits the value of such animal experiments, since it would be of great interest to study the longer term effects of grafting procedures. The usefulness of chronically implanted platinum electrodes for polarographic recording of regional cerebral blood flow is currently being investigated.

Our data, however, do support the impression that significant increases in cerebral blood flow may be achieved by extracranial to intracranial grafting after experimentally induced middle cerebral occlusion in the dog. This was true despite consistent breakdown in the blood-brain barrier after clip occlusion. Pathological studies by Olsson and others suggest that prompt bypass grafting can arrest damage to the barrier resulting from middle cerebral artery occlusion, but we have no specific information on whether the barrier was influenced by grafting. Improvement in flow was noted after more proximal temporal anastomosis, and no benefit was derived from grafting to distal parietal vessels. There was no consistent difference in the size of the recipient vessels or the duration between occlusion and completion of the anastomosis to account for this difference. Ischemic changes after occlusion were reflected in the markedly low regional flow values adjacent to the clip site. The proximal graft subserved those regions most significantly, although an overall improvement in flow was noted in other regions of the hemisphere. While the functional results could not be correlated with specific degrees of improvement in cerebral flow, a more general correlation between the areas to which grafts were placed was noted. Thus, when cerebral blood flow was augmented after occlusion, a higher degree of survival was noted than when there was no improvement in blood flow. If one can extrapolate to the clinical situation it might then be judicious to perform cortical anastomoses as close to the site of obstruction as possible.

Autoregulation of a constant cerebral blood flow is a normal characteristic of the cat, dog, monkey, and man and was present in all baseline studies. A relative inconstancy of flow was noted in the superficial temporal artery. After clip occlusion, as well
as after parietal artery anastomosis, regional cerebral blood flow passively followed changes in blood pressure at hypotensive levels. This pattern has also been noted after cerebral infarction in the cat by Waltz. Autoregulation of blood flow was seen after temporal artery anastomosis despite the presence of an extracerebral arterial graft. The wide hysteresis curves described may bespeak an unstable pressure-sensing and volume-adjusting mechanism. Harper, et al., hypothesized that extraparenchymal resistance changes are under autonomic control while the intraparenchymal arterioles are controlled by chemical or metabolic factors. Recent work by Shinohara and Gotoh and Gotoh, et al., suggests that responses to changes in perfusion pressure are specifically under neurogenic influence. It is possible that our findings are a reflection of the surgical trauma sustained by the periadventitial sympathetic innervation.

The paradoxical response to hypercapnia after focal ischemic lesions has been explained in terms of an "intracerebral steal" effect by Lassen. hypercapnia augmented mean CBF. James, et al., noted that the decremental effect of sympathetic stimulation on cerebral blood flow is more obvious at high pCO2. The increase in blood flow which we noted after temporocortical anastomosis was relatively and absolutely greater at higher pCO2 values compared to control studies. These data may therefore also bespeak a sympathectomy effect at the anastomosis site, and may be exploited when increased perfusion is important.

References

This paper was presented in part at the First International Symposium on Microneurosurgical Anastomoses for Cerebral Ischemia, Loma Linda, California, June, 1973.

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