Influence of Superficial Temporal Artery to Middle Cerebral Artery Bypass on Cerebral Blood Flow in Dogs with Middle Cerebral Artery Occlusion

P. W. Hitchon, M.D., N. F. Kassell, M.D., C. E. Gross, M.D.,
H. P. Adams, M.D., and T. R. Hill, M.S.

SUMMARY Eight dogs had a superficial temporal artery to middle cerebral artery (STA-MCA) anastomosis, followed immediately by ligation of the ipsilateral middle cerebral artery. Subsequently, utilizing the radioactive microsphere technique, regional cerebral blood flow determinations were made both before and after ligation of the superficial temporal artery. A significant reduction in blood flow of 20-35% was noted in both cerebral hemispheres, caudate and thalamic nuclei, brain stem and cerebellum following occlusion of the bypass. It is our impression that this generalized reduction in flow is due to a redistribution of blood from normal areas to areas previously supplied by the bypass. This implies that the newly created extracranial to intracranial arterial anastomosis reduces the shunting of blood from zones of higher to zones of lower flow through the circle of Willis and leptomeningeal collaterals. It also suggests a mechanism for the improvement in neurological function referable to areas of the brain remote from the bypass which is detected in some patients after STA-MCA anastomosis.

THE ROLE of superficial temporal artery to middle cerebral artery bypass (STA-MCA) in the treatment of patients with cerebrovascular insufficiency remains controversial. In specific instances this procedure is believed to improve ipsilateral cerebral hemisphere blood flow and function previously compromised by occlusive vascular disease.1-4 Under certain circumstances, functional neurologic improvement has been observed in the contralateral hemisphere, posterior fossa and on neuropsychological testing.5-7 It has been suggested that the mechanism for functional improvement is based on enhancement of cerebral blood flow (CBF) in perfusion fields at a distance from the bypass through reversal of a pre-existing "steal" made possible by the newly-created collateral supply.1,3-6

The purpose of this study is to document the influence of cerebral revascularization on both the ipsilateral and contralateral cerebral hemispheres, basal ganglia, cerebellar and brain stem flow in dogs subjected to middle cerebral artery occlusion and ipsilateral superficial temporal to middle cerebral artery anastomosis.

Materials and Methods

Experiments were performed on 13 adult mongrel dogs of both sexes weighing approximately 25 kg each. Under pentobarbital anesthesia (25 to 30 mg/kg i.v.) unilateral end-to-side anastomosis of the superficial temporal artery to middle cerebral artery was carried out.8,10 Immediately following completion of the bypass, the proximal middle cerebral artery was occluded with a small clip placed at the internal carotid-middle cerebral artery junction.

Three hundred thousand units of procaine and 300,000 units of benzathine penicillin G were given intramuscularly at the time of surgery and continued for 3 days postoperatively. The animals were examined daily for neurological deficit. Between the tenth and fourteenth postoperative days, the dogs were again anesthetized with intravenous pentobarbital and a lateral carotid angiogram was performed via the transfemoral route using Renografin 60.10 Of the 13 dogs that had the bypass operation, 8 were ultimately included in the analysis. Five animals were excluded for the following reasons: one developed a wound infection, one had to be excluded for technical reasons, one died from dehydration secondary to intractable diarrhea, one died of complications incurred during angiography, and one died of hypoxia secondary to malposition of the endotracheal tube.

Two weeks following bypass surgery, cerebral blood flow determinations were made utilizing the radioactive microsphere technique.11-14 Anesthesia was induced in the dogs, using chloralose (50 mg/kg) and urethane (500 mg/kg) i.v., and the animals were maintained on a 2 to 1 mixture of nitrous oxide and oxygen supplemented with intravenous morphine sulfate (1 mg/kg). The animals were intubated, paralyzed with Pancuronium (0.1 mg/kg) and ventilated to maintain an arterial Pco2 of 40 mm Hg. End tidal CO2, O2 and N2O were monitored with a Medispect mass spectrometer.1 Catheters were inserted into one brachial and one femoral artery for withdrawal of blood samples and monitoring of mean arterial pressure (MAP). A catheter was placed into the superior vena cava

*E. R. Squibb & Sons, Inc., Princeton, NJ.
†Chemetron, 1801 Lilly Avenue, St. Louis, MO.
through a femoral vein for measuring central venous pressure (CVP) and administration of drugs. A #7 French pigtail catheter was introduced through the femoral artery into the left ventricle for injection of microspheres. Esophageal temperature (Temp) and heart rate (HR) were continuously monitored. All physiological parameters were continuously recorded on a Hewlett-Packard eight channel monitor.* Arterial blood gases, serum electrolytes, blood urea nitrogen, serum creatinine, serum osmolality, and hematocrit (Hct) were determined at intervals throughout each experiment.

The operative site of the STA-MCA bypass was re-explored and the superficial temporal artery identified and isolated. Two cerebral blood flow determinations were made, the superficial temporal artery supplying the anastomosis was ligated, and 30 minutes allowed to elapse before performing 3 additional blood flow measurements. These results were compared and averaged and will hereafter be referred to as "patent" and "ligated" CBF’s. The brain, heart, and kidneys were then removed for blood flow analysis. The brain was sectioned in the midline and each half divided into the following anatomical subdivisions: 1) frontal lobe, 2) parietal lobe, 3) temporal lobe, 4) occipital lobe, 5) caudate, 6) thalamus, 7) brain stem, 8) cerebellum. Unless otherwise stated the CBF values presented hereafter are the means for the eight dogs in ml/100 g of brain tissue/min ± standard error of the mean (SEM). Data were analyzed on the basis of the paired t-test, and a one-tailed confidence level of $p < 0.05$ was considered significant.

**Results**

The eight dogs analyzed were all neurologically intact so far as concerned their level of consciousness, appetite, gait, and response to stimulation after the STA-MCA anastomosis and MCA ligation had been performed. In each of these dogs, angiography demonstrated the bypass to be patent. The vital signs remained stable throughout the entire study (table 1), with the exception of an increase in heart rate from 126 ± 14 to 136 ± 13 per min, associated with a slight drop in hematocrit from 43 ± 3 to 41 ± 3 Vol %. There were also no significant changes noted in electrolytes, blood urea nitrogen, creatinine or serum osmolality.

Ligation of the STA reduced total brain CBF by approximately 29% from 84 to 60 ± 6 ml/100 g/min. A decrement of the same order of magnitude occurred in the cerebral hemispheres, caudate, thalamus and posterior fossa (table 2). Regional CBFs were significantly different only between the temporal and parietal lobes of either hemisphere (fig.), although the mean hemispheral flow on the operated side remained significantly lower than its counterpart, 58 ± 6 vs 65 ± 7 ml/100 g/min.

*Hewlett-Packard, Andover, MA.*

<table>
<thead>
<tr>
<th>Parameter</th>
<th>STA patent</th>
<th>STA ligated</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{PCO}_2$</td>
<td>$41.1 \pm 0.53$ mm Hg</td>
<td>$41.3 \pm 0.51$ mm Hg</td>
</tr>
<tr>
<td>$\text{PO}_2$</td>
<td>$145 \pm 6$ mm Hg</td>
<td>$136 \pm 8.5$ mm Hg</td>
</tr>
<tr>
<td>pH</td>
<td>$7.32 \pm 0.01$</td>
<td>$7.34 \pm 0.01$</td>
</tr>
<tr>
<td>MAP</td>
<td>$119 \pm 6.5$ mm Hg</td>
<td>$115 \pm 7.1$ mm Hg</td>
</tr>
<tr>
<td>CVP</td>
<td>$8 \pm 0.7$ mm Hg</td>
<td>$8 \pm 0.8$ mm Hg</td>
</tr>
<tr>
<td>TEMP</td>
<td>$36.9 \pm 0.3^\circ \text{C}$</td>
<td>$36.7 \pm 0.4^\circ \text{C}$</td>
</tr>
<tr>
<td>HR</td>
<td>$126 \pm 14$/min</td>
<td>$136 \pm 13$/min</td>
</tr>
<tr>
<td>HCT</td>
<td>$43 \pm 3$ Vol. %</td>
<td>$41 \pm 3$ Vol. %</td>
</tr>
</tbody>
</table>

Mean ± sem. No significant changes noted between "patent" and "ligated" values.

**Figure.** Ipsilateral and contralateral rCBF (ml/100 g/min) are represented before and after STA ligation. F = frontal, T = temporal, P = parietal, O = occipital, Cd = caudate, Th = thalamus, CBL = cerebellum, BS = brain stem. Asterisks indicate statistically significant differences between structures of either hemisphere. Vertical bars represent SEM.
Middle cerebral artery occlusion has been shown experimentally to augment flow through an STA-MCA bypass as well as increase the bypass patency rate. Radioactive microspheres offer a reliable and reproducible method of measuring organ blood flow. Values for CBF obtained with microspheres are consistent over time, comparable to measurements obtained by other techniques, and are not subject to problems of "see through" and extracranial superimposition.

With the STA patent, the CBF in the hemisphere ipsilateral to the MCA occlusion was lower than the flow in the opposite hemisphere, but was not reduced to ischemic levels. This suggests that the bypass was capable of providing adequate circulation to the bed previously nourished by the MCA. This is consistent with the observations of Crowell et al. and Levinthal et al., who found STA-MCA anastomoses decreased the incidence of infarction in dogs following MCA occlusion. In our experiments the lowest flows were noted in the frontal, temporal, and parietal lobes ipsilateral to the MCA ligation, while the flow in the caudate nucleus was no different from the contralateral. In the dog and cat, the caudate is most susceptible to infarction after MCA occlusion, the reason being that the caudate, unlike the cerebral cortex, is not endowed with a rich collateral network and is thus more prone to suffer from a reduction in blood flow. One possible explanation for these discrepant observations is that the STA-MCA bypass is capable of carrying sufficient blood to maintain normal flow in the MCA distribution, including the caudate nucleus. The decreased CBF in the frontal, temporal, and parietal lobes may be an epiphenomenon related to surgical manipulation and retraction rather than reflect compromised circulation.

The generalized reduction in CBF noted in all structures examined bilaterally following STA ligation (table 2) may be explained on the basis of a redistribution of blood or shunting. The sudden cessation of flow through the STA may cause redistribution of blood flow via the circle of Willis and the

### Table 2: Mean Regional Cerebral Blood Flow (rCBF) ± SEM ml/100 g/min Before and After STA Ligation

<table>
<thead>
<tr>
<th>Structure</th>
<th>Ipsilateral to Bypass</th>
<th>Contralateral to Bypass</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>STA Patent</td>
<td>STA Ligated</td>
</tr>
<tr>
<td>Frontal Gray</td>
<td>94 ± 12</td>
<td>62 ± 6</td>
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<tr>
<td>White</td>
<td>57 ± 3</td>
<td>44 ± 3</td>
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<tr>
<td>Parietal Gray</td>
<td>77 ± 8</td>
<td>57 ± 6</td>
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<tr>
<td>White</td>
<td>46 ± 3</td>
<td>33 ± 3</td>
</tr>
<tr>
<td>Temporal Gray</td>
<td>69 ± 5</td>
<td>49 ± 5</td>
</tr>
<tr>
<td>White</td>
<td>57 ± 4</td>
<td>42 ± 6</td>
</tr>
<tr>
<td>Occipital Gray</td>
<td>96 ± 10</td>
<td>71 ± 9</td>
</tr>
<tr>
<td>White</td>
<td>59 ± 5</td>
<td>43 ± 4</td>
</tr>
<tr>
<td>Caudate</td>
<td>142 ± 22</td>
<td>107 ± 13</td>
</tr>
<tr>
<td>Thalamus</td>
<td>96 ± 15</td>
<td>70 ± 10</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>77 ± 7</td>
<td>57 ± 5</td>
</tr>
<tr>
<td>Brainstem</td>
<td>69 ± 6</td>
<td>51 ± 6</td>
</tr>
</tbody>
</table>

The % drop is the difference between "patent" and "ligated" flows expressed as a percentage of the "patent" rCBF. All rCBFs were significantly reduced by the ligation at the p < 0.05 confidence level.

### Table 3: Total Weighted Brain CBF - Before and After STA Ligation

<table>
<thead>
<tr>
<th>Dog</th>
<th>Total brain ml/100 g/ml</th>
<th>Bypass Flow (ml/min)</th>
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<tr>
<td></td>
<td>Patient</td>
<td>Occluded</td>
</tr>
<tr>
<td>3</td>
<td>92</td>
<td>87</td>
</tr>
<tr>
<td>4</td>
<td>65</td>
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<td>9</td>
<td>72</td>
<td>59</td>
</tr>
<tr>
<td>12</td>
<td>127</td>
<td>66</td>
</tr>
<tr>
<td>13</td>
<td>54</td>
<td>54</td>
</tr>
</tbody>
</table>

M ± SEM 84 ± 8 60 ± 6 20 ± 7

The reduction in CBF following ligation is significant.
leptomeningeal collaterals. Through these collateral channels blood is distributed to the MCA field from the contralateral carotid artery via the anterior cerebral artery and from the vertebrobasilar circulation via the posterior cerebral artery.

The bilateral reduction in CBF which occurred after occlusion of the STA is reminiscent of diaschisis described in humans and experimental animals. In certain situations following ligation of major cerebral arteries, metabolism and flow in the contralateral hemisphere decrease, presumably from transneuronal depression of function. For diaschisis to occur, the flow in the ipsilateral hemisphere must be reduced to levels that result in infarction. In our experiments flow was determined in fragments of tissue weighing between 2 and 4 g, and in only one instance was flow reduced below 30 ml/100 g/min by STA ligation. It is, therefore, unlikely that diaschisis played a role in the generalized reduction of CBF after STA ligation.

We believe that the patent STA-MCA bypass prevented shunting or "steal" of blood to the deprived zone, i.e. the MCA bed. Conversely, creating a new collateral to an ischemic zone by an STA-MCA bypass has the potential of reversing a pre-existing steal. This has been suspected to occur in humans, revealed not only an increase in the CBF of the ipsilateral hemisphere, but also of the contralateral frontal lobe.

It is our impression from this study that the STA-MCA bypass may, in certain circumstances, improve CBF of both adjacent and distant structures by the restoration of CBF to normal levels in areas which may have been reduced to critical levels by "steal."

Acknowledgment

The authors would like to thank Dr. Melvin Marcus for his invaluable advice and support and Mary Kay Gerk and Leonard Brooks for their perseverance and assistance.

References

Embolic Distal to Stenosis of the Middle Cerebral Artery

HAROLD P. ADAMS, JR., M.D., AND CORDELL E. GROSS, M.D.

SUMMARY  Fibrin-platelet microembolism in cortical branches distal to stenosis of the middle cerebral artery was directly visualized in a patient with transient ischemic attacks (TIA) and was histopathologically confirmed. Cerebral microembolism may produce TIA in patients with stenosis of the middle cerebral artery and may influence the success of the extracranial-intracranial bypass operation in treatment of these patients. Stroke, Vol 12, No 2, 1981

INTEREST in stenosis of the middle cerebral artery has been stimulated by development of the microsurgical extracranial-intracranial bypass operation. Most transient ischemic attacks (TIA) secondary to stenosis of the middle cerebral artery are believed to occur on a hemodynamic basis. We report a patient with stenosis of the middle cerebral artery and TIA, who had fibrin-platelet microembolism distal to the stenosis confirmed.

Patient Report

The patient was a 52-year-old, right-handed, insulin-dependent diabetic woman who was in her usual state of health when she spontaneously developed approximately 10 attacks of lightheadedness and difficulty speaking, each lasting a few minutes. Three days later she had a severe temporal-occipital headache. Following a nap, her headache resolved but she had difficulty finding words when trying to speak. She was admitted to a community hospital for treatment of a small stroke and she gradually improved. Eight days following the initial TIA, she developed transient increased difficulty in speaking associated with numbness of the right lower extremity. She was then transferred to the University of Iowa Hospitals.

Her neurological examination was normal except for a slow, deliberate type of speech. She did not have errors in naming, repeating or understanding commands. The remainder of her examination was normal. Complete blood count, platelet count, prothrombin time, partial thromboplastin time, serum cholesterol, blood urea nitrogen, electrocardiogram, echocardiogram, chest roentgenograph and nuclide brain scan were normal. Her blood sugar was 434 mg/dL. Angiography demonstrated a 50% segmental stenosis of the left middle cerebral artery 5 mm distal to its origin (fig. 1). The left internal carotid artery and other cerebral arteries were normal.

She agreed to participate in the Cooperative Study of Extracranial/Intracranial Arterial Anastomosis and was randomized to surgical therapy. On day after randomization, she had several transient attacks of numbness of the right foot and difficulty finding words. Intravenous heparin therapy was begun. Two weeks after her initial TIA, a superficial temporal artery-middle cerebral artery anastomosis (STA-MCA bypass) was performed. During her operation, after the cortical artery had been dissected free from the arachnoid, blood flow in the artery appeared to slow and then stop. Almost simultaneously, a 3 mm long white embolus emerged from the depths of the Sylvian fissure in the isolated artery. The embolus proceeded distally in a staccato fashion with each beat of the heart. Temporary clips were placed on the artery, trapping the embolus in the area of the planned recipient site, and an embolectomy was performed. Microscopic examination of the embolus demonstrated an unorganized fibrin-platelet clot (fig. 2). Immediately after operation, her neurological ex-
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