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AUGMENTATION OF REGIONAL CEREBRAL BLOOD FLOW BY MICROVASCULAR ANASTOMOSIS

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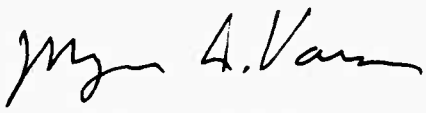

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TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

ABSTRACT

Intracranial surgical procedures for cerebrovascular occlusive disease have become feasible with the development of microvascular surgical techniques. This study assessed the ability of microanastomosis of the superficial temporal cortical artery to augment cerebral blood flow after clip occlusion of the middle cerebral artery in the dog. A variable degree of flow depression and consistent disruption of the blood-brain barrier occurred after occlusion. Augmentation of cerebral blood flow after anastomosis was associated with widening of the hysteresis loop obtained on autoregulatory testing but was unrelated to the degree of clinical recovery.

I. INTRODUCTION

Recent advances in stroke therapy have been highlighted by 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 procedures available,[10,15] 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 accomplished in 115 selected cases.[3] While the clinical and radiographic indications for these procedures are currently under investigation, the assumption that these grafting procedures 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 but anatomic continuity has not necessarily been associated with functional benefit. Crowell and Olsson[1] noted in 10 dogs that neurologic function was related to the interval between occlusion and anastomosis but was unrelated to 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 is to determine the effect of superficial temporal cortical artery microanastomosis on cerebral blood flow and its autoregulation. Such information may allow critical evaluation of the benefits to be expected from utilizing such therapy in man.

II. MATERIALS AND METHODS

Adult foxhounds weighing 20-24 kg were anesthetized with 25 mg/kg pentobarbital and intubated. The femoral artery and vein were cannulated to monitor arterial blood gases and to administer drugs and fluids. Using a curvilinear scalp incision, the superficial temporal artery was isolated, the bulky temporalis muscle was sharply excised, and a large hemicraniectomy was performed. Using the operating microscope at 25-40 x magnification, a 1.5- to 2.0-cm segment of the superficial temporal artery was dissected free from its bed so as not to traumatize branches of the carotid nerve along the adventitia. A Statham 1- or 2-mm electromagnetic flow probe was then placed around the exposed vessel. After blood flow readings were obtained at normal blood pressure, constancy of flow was measured at hypertensive and hypotensive levels (Table I). The animals were placed in padded cages and allowed to recover. Approximately 1 week later flow in the superficial temporal artery was again measured following which the dura was opened widely, and 4 ml/kg of 2 percent Evans blue solution was injected intravenously. If hyperemia, swelling or leakage of Evans blue solution was noted 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 PE 50 Teflon catheter. The catheter was inserted to the region of the carotid bifurcation, and bolus injection of 3 to 4 mCi of ^{133}Xe was performed. The washout of ^{133}Xe was monitored with the gamma camera (Pho/Gamma III) using a modified crystal head for laboratory animals and the 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 Nuclear Data Med II 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 Neo-Synephrine or oligemic hypotension to effect changes in cerebral perfusion pressure. Vasoreactivity to hypercapnia was tested using a 5 percent CO_2 gas mixture with controlled ventilation.

Using the operating microscope, a microaneurysm clip was applied to the main branch of the middle cerebral artery at the level of the 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 x 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 cutdown 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.

III. RESULTS

Complete data were obtained in 13 of 22 healthy and 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 anastomosis could not be performed after satisfactory base-line and post-occlusion studies in three animals. In two of the animals included in the final tabulation, the PO_2 dropped transiently during control studies to 53 and 49 mm Hg respectively, but in both cases these blood gases returned to normal prior to occlusion of the middle cerebral artery. In no case was there a significant pH drop (< 7.34) throughout the course of the experiment, although in three animals arterial pH values achieved alkalotic levels.

Control animals.

A. Blood flow values (normotension, eucapnia, normoxia). Blood flow in the main branch of the superficial temporal artery varied between 5 and 18 ml/min in different animals, with a mean value of 9.5 ml/min at a mean perfusion pressure of 132 mm Hg (Table I). Post-TAA and post-PAA indicate values after microanastomosis to temporal cortical and parietal cortical arteries respectively.

Table I. Superficial Temporal Artery Blood Flow (13 dogs)

	Control	Post-TAA	Post-PAA
Normotension	9.5 (5-18)	8.2 (4-16.3)	6.8 (2.6-11.6)
Hypertension (< 240 mm Hg)	+27% (21-35)	+31% (22-36)	+29% (21-33)
Hypotension (> 55 mm Hg)	-60% (40-100)	-42% (20-52)	-48% (31-59)

A mean regional cerebral blood flow of 36.5 ml/100 g per min was noted in the frontal region, 31.1 ml/100 g per min in the temporal region and 30.5 ml/100 g per min in the parietal region. Compartmental values for these same regions agreed closely, and flow rates in fast and slow components as well as those derived by Zierler's stochastic equation are given in Table II.

Table II. Augmentation of Regional Cerebral Blood Flow in the Adult Foxhound after Middle Cerebral Root Occlusion

		Frontal	Temporal	Parietal
Control (n = 13)	λ H/A*	36.5 ± 6.2	31.1 ± 4.7	30.5 ± 6.6
	Fg	50.2 ± 11.1	46.5 ± 7.2	61.1 ± 9.0
	Fw	18.6 ± 7.2	13.6 ± 6.7	13.0 ± 5.1
Occlusion (n = 13)	λ H/A	21.0 ± 8.5§	11.1 ± 5.7§	25.2 ± 9.5
	Fg	37.6 ± 6.1	31.2 ± 6.2±	57.1 ± 6.0
	Fw	12.7 ± 6.5†	8.3 ± 2.5±	9.6 ± 2.0†
Postocclusion (n = 3)	λ H/A	22.2 ± 6.7	10.1 ± 4.5	23.6 ± 8.9
	Fg	34.5 ± 4.0	31.8 ± 5.8	53.1 ± 6.2
	Fw	11.5 ± 4.2	9.2 ± 3.6	10.5 ± 3.1
Post-TAA (n = 7)	λ H/A	28.98 ± 6.7†	15.32 ± 4.1±	34.78 ± 4.1†
	Fg	51.89 ± 6.3±	43.06 ± 5.0±	78.80 ± 7.2±
	Fw	17.53 ± 4.2	11.45 ± 3.2†	13.25 ± 3.1±
Post-PAA (n = 3)	λ H/A	20.5 ± 9.1	12.7 ± 7.7	23.4 ± 11.0
	Fg	39.1 ± 8.5	33.1 ± 2.0	52.5 ± 9.3
	Fw	9.6 ± 3.1	6.2 ± 1.6	8.0 ± 1.5

* λ H/A = Zierler's mean flow equation, Fg = flow in gray matter, Fw = flow in white matter

† Significant to the < .05 level

± Significant to the < .01 level

§ Significant to the < .001 level

B. Constancy of flow. Moderate augmentation of flow within the main branch of the superficial temporal artery was seen in 13 animals. A maximal flow increase of 35 percent was noted after which flow remained constant despite further elevations of perfusion pressure. All animals displayed constancy of intracerebral flow ($F = K \cdot p < 1$) despite a change in mean blood pressure of up to 70 mm Hg (Figure 1). A small degree of hysteresis or lag between pressure and intracerebral flow was noted between mean blood pressures of 60 and 140 mm Hg in all control animals. Graded hypercapnia was associated with a progressive rise in mean cerebral blood flow although at the higher PCO_2 values the rate of rise was greater. This is illustrated in Figure 2.

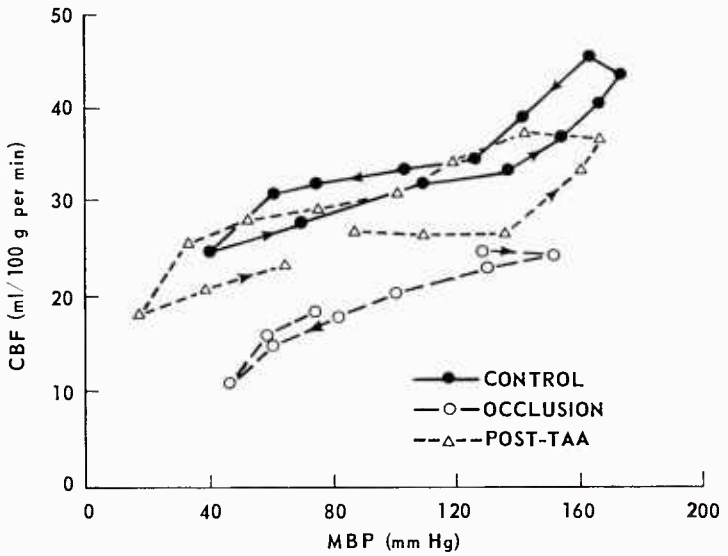

Figure 1. Relationship of mean cerebral blood flow to mean blood pressure in experiment No. 7. Control studies indicate constancy of flow ($\Delta < 12$ percent) despite a change of mean blood pressure of 70 mm Hg. After occlusion the ischemic bed is passively dependent on blood pressure. After temporal cortical artery anastomosis, a wide hysteresis loop is described at the extremes of blood pressure ranges with some return of autoregulation at intermediate levels of perfusion.

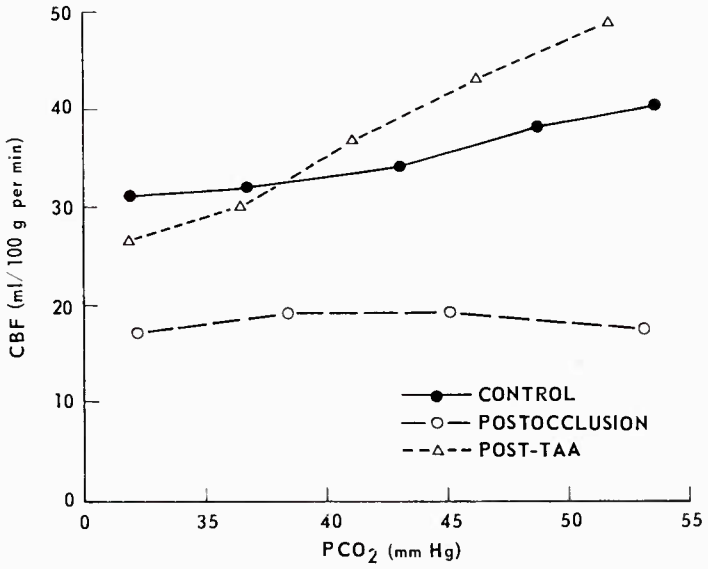

Figure 2. Relationship of mean cerebral blood flow to arterial PCO_2 levels in experiment No. 7. Control studies demonstrate the greater vasoactivity at 40-55 mm Hg than at 30-40 mm Hg. After occlusion mean hemispheric flow responses showed a decrease with hypercapnia. After temporal cortical artery anastomosis there was an earlier hyperemia with hypercapnia which achieved absolutely greater levels than the controls.

Middle cerebral artery occlusion. Postocclusion blood flow studies in 10 animals required a minimum of 1 hour and 10 minutes 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, 2-1/2, 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 mean and white matter flow values in the frontal region, a significant reduction in the white matter flow in the parietal region, and a very highly significant reduction in mean, gray and white matter flow in the temporal region after occlusion

(Table II). 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-minute 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 (Figure 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 Figure 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 minutes to 3-3/4 hours. The period of complete stasis in the cortical artery during which time tourniquets were fastened without the T-tube never exceeded 5 minutes and 20 seconds. Severe vasospasm was present in the cortical artery segment in two experiments with a further reduction of 15 percent and 22 percent 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 percent was noted in the graft segment. In the other two animals no significant change in flow was noted in

graft segments (Table I). Cerebral blood flow was augmented within the ischemic hemisphere after this procedure in all five animals. As noted in Table II, 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 within 2-1/2 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 (Figure 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 PCO_2 values (Figure 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 II).

Functional evaluation. Because of the anesthetic requirements, serial neurologic evaluation could not be performed just prior to grafting. In three animals undergoing clip occlusion only, all had severe postoperative deficits including circling and anorexia in one and coma in two. Two of the three animals with parietal cortical artery grafts, as well as two animals in whom temporal cortical grafts were followed by spasm, showed poor neurologic function progressing to death. One animal with a parietal cortical graft experienced anorexia and circled but survived. Of the five animals with successful

proximal temporal artery anastomosis, neurologic 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 anorexic for 5 days after surgery. Thereafter no deficit was detectable.

IV. 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. The value of this technique is limited to short-term studies; however, 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. Pathologic studies by Olsson et al.[11] 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 reconstituted after grafting. Improvement in flow was noted after more proximal anastomosis and no benefit was derived from grafting to distal 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 the difference in results. The proximal graft subserved those regions most affected by the occlusion and this may have been reflected in the overall improvement noted in other regions in the hemisphere. While the functional results could not be correlated with specific degrees of improvement in cerebral blood 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,[14] dog,[12] monkey[2] and man[8] and was present in all base-line 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.[14] 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.[5,6] 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[13] and Gotoh et al.[4] 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.[9] This was noted after middle cerebral artery occlusion in two of five animals but after temporal cortical grafts hypercapnia augmented mean CBF. James et al.[7] noted that the decremental effect of sympathetic stimulation on cerebral blood flow is more obvious at a high PCO_2. The increase in blood flow which we noted after temporal cortical anastomosis was relatively and absolutely greater at higher PCO_2 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.

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13. ABSTRACT

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