SURGICAL PRODUCTION OF COLLATERAL INTRACRANIAL CIRCULATION

AN EXPERIMENTAL STUDY*

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During the past decade a considerable body of work has accumulated upon methods of augmenting deficient local circulation. The approach has been chiefly along two different lines: (1) Procedures directed at the autonomic nervous system to relieve local vasoconstriction; (2) Surgical production of accessory circulation to the involved part. The autonomic approach has been followed extensively in certain forms of peripheral vascular disease, especially those in which vasoconstriction is an important factor. The second method has been utilized for the heart (Beck^{2, 3, 13} and O'Shaughnessy^{14, 15, 16}) and for the kidneys^{7, 11, 12} in the form of pedicled muscle or omental grafts. The possibility of favorably influencing circulation by a third, or hormonal, approach must be admitted, but evidence is almost entirely lacking on this phase at present.

Applying the general problem to the specific case of intracranial circulation, one is forced to the conclusion that vasoconstriction plays a minor rôle in causing or maintaining a circulatory deficit (Cobb⁴). Both vasodilator and vasoconstrictor nerve fibers have been demonstrated on cerebral vessels, but Forbes and Cobb⁹ have estimated that these vasoconstrictor nerves are only about one-tenth as effective as are those to the cutaneous vessels. While the possibilities of the autonomic attack upon the problem of intracranial circulation have not yet been fully explored, clinical observations in recurrent gliomata and convexity meningiomata influenced the choice of the accessory circulation method for the present study.

The cranial circulation is unique in having two parallel arterial systems: intracranial and extracranial, the latter usually abundant even when the former is defective. The temporal muscles afford a means of grafting a considerable extracranial blood supply to a large

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area of the cerebral convexities. The well-vascularized suboccipital muscles are similarly available to augment the cerebellar circulation.¹⁰

Monkeys (*Macaca mulatta*) were used as experimental animals. After either preliminary or concomitant ligation of one or more of the main arteries to the brain, the superior border of the temporal muscle was separated from its origin and reflected to expose most of the underlying squamous portion of the temporal bone. The insertion, and blood and nerve supply of the muscle were not disturbed. A large defect was made in the temporal bone, the exposed dura

was excised, and the underlying arachnoid peeled gently away from the cerebral convolutions. The periosteal surface of the temporal muscle was scarified and applied directly to the denuded brain. The superior border of the muscle was sutured to the remaining free edge of the dura at the margin of the bony defect (Fig. 1). In

FIG. 1. Diagrammatic illustration of temporal muscle grafts and accessory vascular channels. The approximate sites of arterial ligations in the neck are indicated.

some of the animals suboccipital muscle grafts were also applied to the denuded cerebellar cortex. Control animals had serial ligations of the internal carotid and vertebral arteries in the neck or intracranially without the application of muscle grafts. The accessory circulation was studied by arterial injection methods, by specimens cleared according to the Spalteholz technic, and by histological sections.

The first group of experiments¹⁰ was designed to test the functional efficiency of the artificially produced collateral blood supply. Two animals had bilateral temporal muscle grafts, and three controls had vascular ligations without grafts. The serial ligations of the four major arteries were all performed in the neck at two- to four-week intervals. Since the ligation of both internal carotids and both

vertebral arteries in this manner was well tolerated by the control animals, no definite conclusions could be drawn concerning the functional efficiency of the accessory extracranial vascular communications in the grafted animals. However, definite collateral vascular channels joining the brain and the adherent temporal muscle were demonstrated both in the histological sections (Figs. 2 and 3) and by the injection technic (Figs. 4 and 5). The connecting zone between the muscle and brain was composed of vascular granulation tissue through which communicating vessels containing injected particles of dye could be identified joining the muscle to the pial vessels (Fig. 6).

In an effort to exclude as much as possible the naturally existing collateral arterial channels, proximal to the circle of Willis, the arterial occlusions were performed intracranially in the second group of experiments.¹⁰

In two monkeys, after previous ligation of the four major vessels in the neck and the application of bilateral temporal and suboccipital grafts, both vertebral arteries were clipped intracranially. The animals survived the procedures and at autopsy India ink was injected into the common carotid arteries (Fig. 7). Cleared thin sections demonstrated abundant vascular channels between the brain and all the muscle grafts.

Two animals with unilateral temporal grafts failed to survive the second carotid clipping at intervals of three and twelve weeks, respectively, after the initial graft.

Monkey No. 57.

April 27, 1939: Right internal carotid artery occluded intracranially with silver clip; right temporal muscle graft applied.

May 17, 1939: Left internal carotid artery occluded intracranially with silver clip; left temporal muscle graft applied. Following this operation the animal became unresponsive, and appeared as though decerebrate. There was a complete paralysis of the third cranial nerve on the left side. Death occurred on May 19, 1939.

At autopsy, after intracranial clipping of both vertebral arteries, a trypan blue solution was injected into each common carotid artery. With the calvarium removed and the dura reflected it was possible to observe the injection material as it appeared in the cortical vessels. On the right side (3-week-old graft) the dye slowly entered the common carotid artery and gradually spread to the exposed temporal muscle. It then appeared in the larger pial vessels directly adjacent

to the muscle graft and spread in a fan-like fashion over the surface of the brain. The dye was then observed in the areas supplied by both anterior cerebral arteries along the sagittal sulcus, indicating free communication through the middle cerebral artery to the circle of Willis, which was later found to be well injected when the brain was removed. On the left side (2-day-old graft) none of the dye crossed from the left temporal muscle directly to the brain.

Monkey No. 66.

May 3, 1939: Right internal carotid artery occluded intracranially with silver clip; right temporal muscle graft applied.

July 27, 1939: Left internal carotid artery occluded intracranially with silver clip; left temporal muscle graft applied. Postoperative course same as that of Monkey No. 57. Death occurred on August 1, 1939.

Both vertebral arteries were clipped intracranially and a gelatin and India ink mixture was injected into the common carotid arteries. The vessels in the circle of Willis and in both sides of the brain were well outlined with the pigment. The left graft was only loosely adherent and was easily detached.

On histological examination the connecting zone between the brain and the right temporal graft was composed of a thin layer of well-differentiated fibroblasts which closely resembled adult connective tissue cells. This layer was intimately adherent to the surface of the brain, and in places projected for a short distance into the substance of the cortex, resembling minute fibroglial scars. The cortical architecture was otherwise unchanged. Small islands of pia and arachnoid cells were present between the connecting zone and the brain but there was no evidence of extensive regeneration of these membranes. Connecting blood channels filled with India ink were observed in cleared sections.

One grafted animal tolerated bilateral carotid and vertebral clipping.

Monkey No. 67.

May 4, 1939: Right internal carotid artery occluded intracranially with silver clip; right temporal muscle graft applied.

July 26, 1939: Left internal carotid artery occluded intracranially with silver clip; left temporal muscle graft applied.

January 4, 1940: Left vertebral artery clipped intracranially; suboccipital muscle graft applied.

April 17, 1940: Right vertebral artery clipped intracranially.

This animal suffered no ill effects from the procedures and is alive and without symptoms (January 1, 1941).

Two grafted monkeys survived the intracranial clipping of one carotid and both vertebral arteries and cervical ligation of the remaining internal carotid artery. The corresponding control animals tolerated the intracranial occlusion of three of the major vessels, but died shortly after the cervical ligation of the fourth.

Monkey No. 200.

September 27, 1939: Right temporal muscle graft applied.

October 25, 1939: Both vertebral arteries clipped intracranially; suboccipital muscle graft applied.

January 5, 1940: Left internal carotid artery occluded intracranially with silver clip; left temporal muscle graft applied.

April 15, 1940: Cervical ligation of right internal carotid artery. Normal recovery. Animal alive and well (January 1, 1941).

Monkey No. 337. Control.

November 2, 1939: Both vertebral arteries clipped intracranially.

January 12, 1940: Left internal carotid artery clipped intracranially.

April 22, 1940: Cervical ligation of right internal carotid artery. On the following day a left-sided paresis was noted. On April 26, there was a complete left-sided hemiplegia. On April 27, the animal was found dead in his cage. Common carotid arteries injected with India ink and gelatin mixture.

At autopsy the presence of the clips on the left internal carotid and on both vertebral arteries was verified. The cervical portion of the right internal carotid artery was found to be completely ligated. The brain was pale and stained poorly. There appeared to be a greater accumulation of the ink in the cerebellum, the midbrain, and the occipital lobes. This was true on the surface of the brain as well as on cross section. In many places the ink was seen to be definitely in the veins. The arteries were for the most part unstained.

Monkey No. 246.

October 4, 1939: Right internal carotid artery occluded intracranially with silver clip; right temporal muscle graft applied.

January 9, 1940: Left temporal muscle graft applied.

February 2, 1940: Both vertebral arteries clipped intracranially; suboccipital muscle graft applied.

April 16, 1940: Cervical ligation of left internal carotid artery. Normal recovery. Animal alive and well (January 1, 1941).

Monkey No. 237. Control.

October 4, 1939: Right internal carotid artery clipped intracranially.

February 2, 1940: Both vertebral arteries clipped intracranially.

April 16, 1940: Cervical ligation of left internal carotid artery.

April 17, 1940: Animal found dead in cage. Common carotid arteries injected with India ink and gelatin mixture.

At autopsy the sites of occlusion of the four major vessels were verified. The findings in the brain were almost identical with those of Monkey No. 337.

In this group both of the grafted monkeys tolerated the total vascular occlusion and are symptom free. The two controls died following the ligation of the fourth vessel. This suggests that the grafts may have effectively served as the medium for an adequate and protective blood supply to the brain.

Finally, an experiment was carried out to determine if accessory vascular channels would develop between the brain and muscle grafts when the major intracranial vessels were *not* interrupted at any point.

Monkey No. 179.

August 21, 1939: Right temporal muscle graft applied.

August 29, 1939: Suboccipital muscle graft applied.

October 20, 1939: Left temporal muscle graft applied.

The animal was sacrificed on November 20, 1939, and a gelatin and India ink mixture was injected into the common carotid arteries. In the cleared sections many communicating vessels were found between the brain and both temporal muscle grafts (right side, 12 weeks old; left, 4 weeks old). In the course of removing the brain from the cranium the suboccipital muscles were dislodged from the cerebellum to which they did not appear to be firmly adherent. The vessels in this area could, therefore, not be studied.

Monkey No. 952.

August 18, 1939: Right temporal muscle graft applied.

August 28, 1939: Suboccipital muscle graft applied.

February 19, 1940: Left temporal muscle graft applied.

The animal was quite listless following the last operation. On February 23, 1940, a series of convulsions began which involved the right face and neck and the right upper arm. The seizures lasted

from five to fifteen minutes. The soft tissues at the site of the left subtemporal decompression were never tense or bulging. On March 11, 1940, the animal was found dead in his cage.

At autopsy no cause for the convulsions was apparent on gross examination. The seizures were thought to be due to excessive trauma inflicted at the time of the last operation rather than to the formation of a fibroglial scar. The grafts were firmly in place. The observations after injection with gelatin and India ink were essentially the same as those noted in Monkey No. 179.

Surgical augmentation of blood supply to an organ is dependent first upon an abundant circulation in the donor area. This requirement is readily fulfilled in the distribution of the external carotid artery with its rich anastomoses, high degree of vascularity, and relative freedom from serious occlusive vascular disease. This "parallel" circulation often appears ample even in the presence of a grave vascular deficit only a centimeter distant within the cranium. The temporal and suboccipital muscles afford an excellent opportunity for joining the extracranial with the intracranial circulation.

A second requisite for the successful application of this method is the presence of sufficient anastomoses in the vessels of the recipient part to allow satisfactory distribution of the accessory supply of blood. Contrary to the contention of Cohnheim,⁵ published in 1872, that the arteries of the brain are end-arteries, there has been in recent years a gradual acceptance of the view that rather numerous anastomoses occur within the cerebral circulation. The work of Craigie⁶ on the rat and of Alexander and Putnam¹ in man yields definite evidence of frequent arterial anastomoses in the pial vessels, some in the pre-capillaries, and free communications in the capillary bed. Evans and McEachern⁸ injected radiopaque material into the common carotid artery in monkeys and were able to establish its presence distal to silver clips previously applied to branches of the middle cerebral artery. It would appear, therefore, that a suitable vascular bed is present on the surface of the cortex to receive the grafted blood supply.

The present work has demonstrated that an accessory arterial blood supply for the brain can be produced in monkeys by means of temporal and suboccipital muscle grafts. The new anastomotic channels are patent as early as three weeks following the application of the graft and develop even in the absence of arterial occlusions. After intracranial ligation of the four major arteries, satisfactory

injection of the cerebral and cerebellar vessels was obtained through the collateral pathways.

In only one animal were convulsive seizures noted. These occurred four days after the application of a temporal muscle graft and involved the contralateral face, neck, and arm. In all the remaining animals no unusual symptoms were noted over periods up to twenty months.

Experiments concerning the functional efficiency of these vascular communications were, for the most part, difficult to evaluate, since the abundant naturally existing collateral channels permitted the control animals to survive multiple intracranial as well as cervical arterial ligations. However, in one small group of four animals, the two experimental monkeys survived the intracranial clipping of one internal carotid and both vertebral arteries as well as the cervical ligation of the remaining internal carotid artery. The controls both died shortly after ligation of the latter vessels. This seemed to indicate that the grafts were efficient sources of collateral blood supply.

The grafts were solidly attached to the underlying brain by a vascular layer of fibroblasts which gradually assumed the characteristics of adult connective tissue cells.

The clinical application of this method for supplementing intracranial circulation should be preceded by further experimental observations, including long-term studies, which are now in progress. Cerebral arteriosclerosis, recurrent cerebral thromboses, and intracranial aneurysms requiring internal carotid ligation suggest themselves as possible examples where augmentation of the intracranial circulation would be desirable.

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FIG. 2. Monkey No. 8. Right temporal graft (6 weeks old), H. & E., x 125. Vascular communication (V) between granulation tissue (G) and brain (B). (See reference 10 for details concerning this animal and the others here illustrated.)

FIG. 3. Monkey No. 8. Right temporal graft (6 weeks old), H. & E., x 200. Vascular communication (V) between granulation tissue (G) and brain (B).

FIG. 4. Monkey No. 72. Left temporal graft (16 weeks old), cleared section, 300 μ , trypan blue injection, x 20. Vascular communications between muscle (M) and brain (B).
 FIG. 5. Monkey No. 72. Right temporal graft (12 weeks old), cleared section, 300 μ , trypan blue injection, x 55. Vascular communication (V) between muscle (M) and brain (B).

FIG. 6. Monkey No. 72. Right temporal graft (12 weeks old), H. & E., 100μ , $\times 50$. Connecting zone of vascular granulation tissue (G) between muscle (M) and brain (B).

FIG. 7. Monkey No. 90. Bilateral grafts of temporal and suboccipital muscles (M), India ink and gelatin injection.