Experimental Mechanical Arterial Stimulation at the Circle of Willis

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According to various clinical observations, cerebral vessels may develop local spasm in reaction to operative manipulation.1,2,5,7 This clinical experience is supported by a number of laboratory experiments.1,2,5,7

Although mechanical stimulation is obviously only one of several factors that may cause cerebrovascular spasm at operation, it is more subject to control and modification than other factors such as intracerebral chemical irritation4,9 or various extracerebral effects. However, the means whereby gentle mechanical stimuli cause changes in cerebral vessel size are not clearly understood. Except for the closure of an occlusive clip, the forces applied to vessels are kept to a minimum which may be considered fairly consistent when applied by the same operator during the same dissection. Nonetheless, even when the force is minimal, local spasm may occur. We wondered if perhaps the direction in which the force is applied with relation to the vessel wall actually modifies or even determines the nature of the reaction. Specifically, would there be any noticeable difference in resulting spasm if similar minimal forces were applied separately at right angles to and parallel with the long axis of the vessel wall?

With this question in mind, we exposed the circle of Willis in the cat by microdissection. Then, using the micromanipulator, we applied a single gentle stroke to the vessel wall in one of two directions, either at right angles to the long axis or parallel with it. In some cases, any subsequent reactions were tested against topical application of vasoconstrictors or vasodilators. In others, the stimuli were applied after stellate gangliectomy or cervical sympathectomy.

Materials and Methods

Fifty-two healthy cats weighing between 2 and 3 kg were anesthetized with intraperitoneal nembutal (25 mg/kg). After cannulation of the trachea and connection to a respirator, the animal was placed on a warm blanket. The head was fixed to the car bars and mouthpiece of a Horsley-Clarke stereotaxic instrument. Arterial pressure was continuously monitored via femoral catheter, Statham P23AA transducer, and the Sanborn 150 recorder.

Once the preparation was stable, the surface of the skull was widely exposed. Next, a rectangular craniotomy, 2.0×1.0 cm with the long axis in the sagittal plane and its center 1.4 cm anterior to the interaural line, was made to expose the dura. A Zeiss microscope with Robot camera was then oriented to this opening, and dural incision, reflection of the falx, exposure of the corpus callosum, and the particular dissection of the final field were all accomplished by micro technique.

Thus, the anterior part of the corpus callosum was removed and the anterior horn of the right lateral ventricle exposed. Caudate nucleus and adjacent brain substance were also sucked away with a micropipette until the internal carotid and middle cerebral arteries could be seen shining through overlying pia. This translucent covering was carefully incised and peeled away from the circle of Willis. Such slight bleeding as occurred was controlled by gentle application of tiny, moist cotton pledgets, save in rare instances when the coagulation current was used (at low settings) to seal isolated small vessels well away from the principal arteries.

In nine animals, this exposure was extended by removal of anterior commissure and some septal nuclei so as to reveal anterior, middle, and internal carotid arteries on both sides (Fig. 1). If any vasospasm or other change in size, shape, or color of the great vessels occurred during the preparation dissection, that animal was not used in the experiment.

Mechanical stimulation consisted of one gentle stroke with the micromanipulator applied either at right angles to the long axis of the vessel or parallel to it. In some ani-
mals, vasoconstrictors or vasodilators were directly applied to the vessel wall by expelling one drop of solution from a micropipette. Serotonin creatinine sulphate (0.1%) or BaCl₂ (5%) were used as vasoconstrictors, while papaverine hydrochloride (3%), Phenolamine (0.5%), or Xylocaine (2%) were similarly applied to the vessel wall as vasodilators.

In a few animals, the stellate ganglia were exposed and removed following resection of the first rib close to the vertebral column. After this, the cervical chain was also exposed and excised bilaterally.

In each preparation, at the time of sacrifice, the surgical field was fixed (in situ) with 10% formalin. Then the great vessels were subject to final examination (and photography) under the dissecting microscope so that individual specimens could be obtained by postmortem microdissection. These were incised longitudinally and each was fixed, embedded, and stained with hematoxylin and eosin, and phosphotungstic acid hematoxylin.

**Observations**

*Parallel stroking*. When the exposed vessel was stroked in the direction of its long axis, its diameter decreased. This constriction began as a ring-like narrowing with or without accompanying pallor (Fig. 2). Rarely, when the stimulus was repeated (once), the vessel collapsed (Fig. 3). Topical application of the vasodilators uniformly caused a dilatation of each vessel previously constricted by mechanical stimulus. However, there was no consistent reaction to vasoconstrictors. Occasionally, application of serotonin was followed by sudden pallor (or increase of pallor) of the previously constricted vessel, and then by total collapse.

*Right Angle Stroking*. If the exposed vessel was stroked once lightly at right angles to its long axis, its diameter increased. Thereafter, the vessel became pale without further change in size; the pallor began as a small spot that seemed to enlarge into a sleeve-like configuration (Fig. 4). This dilatation could not be reversed by vasoconstrictors nor increased by vasodilators.

*Sequential Stroking*. If a stroke was delivered in the long axis so as to produce ring-like constriction, a subsequent stroke at right angles caused dilatation. These responses, followed under the microscope, presented a sequence of dynamic changes. Thus, a ring-like constriction with pallor seemed to begin at the point of contact and spread proximally and distally for a distance of 2 to 3 mm. Left to itself, this constriction disappeared. But a subsequent stroke at right angles was immediately followed by dilatation for approximately the same distance. This, also, began at the point of contact and spread slowly along the vessel wall until all visible dimensions seemed markedly dilated. Next, this dilated area turned white as a jelly-like clot developed within its lumen. The clot could be easily dislodged by one touch of the micro-manipulator on the overlying wall. However, when left to itself, it remained in situ during a 2-hour observation period (Fig. 5). The appearance of such thrombi is reminiscent of observations described by Florey. After hematoxylin and eosin staining, the thrombi were fenestrated and usually showed endothelial damage.

The responses obtained by similar forces (gentle strokes) applied in various directions other than in parallel or at right angles to the long axis of the great vessel were inconsistent. Occasionally, no reaction occurred; sometimes contraction or dilatation followed. All these responses to the gentle mechanical stimuli were most frequent and striking in middle and anterior cerebral arteries close to their bifurcation from the internal carotid. The latter reacted less frequently and consistently, while middle or anterior cerebral arteries distal to the circle of Willis were least responsive.

These observations were made in 36 animals from a total of 52 used in the experiments. In 10 cases, the preparation was not used for observation because of either a vasospastic reaction in the preparatory dissection or other change which seemed directly relevant to the exposure of the great vessels rather than to their control stimulation. Thus, 42 cats were available for observation. From this subtotal, six provided responses to mechanical stimulation that were indefinite and not reproducible. However, the original responses were reproducible in the other 36 animals. In the average final observation time of 3 hours, these responses to mechanical stimulation were reproduced at least 10 times in each of the 36 animals. Each of the 42 animals actually considered useful for the experiment showed some reaction to stimulation.

**Effects of Sympathectomy**. Neither stellate