LOCAL SPASM IN CEREBRAL ARTERIES

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INTRODUCTION

This work began as a clinical analysis of patients who suffered unexplained hemipareses following temporal lobectomies. A preliminary survey suggested that the site of disturbance was the internal capsule and that the cause was vascular interference. Further study confirmed this impression and produced strong clinical evidence that the disability was caused by spasm of the capsular arteries in response to mechanical irritation. This evidence is presented here in association with a study of the nature and prevention of local cerebral arterial spasm.

A long-standing controversy exists concerning the role of localized spasm of cerebral arteries in the production of symptoms. Some deny the existence of such spasm altogether. Local arterial spasm has been implicated as the responsible factor in a variety of lesions with vascular insufficiency as a possible basis. These vary from massive cerebral infarcts to the most fleeting symptoms suggestive of transient focal cerebral disturbance.

Local ischemia is variously considered by opponents of vasospasm. Explanations usually involve one or a combination of the following: organic vascular obstruction, insufficiency of collateral circulation, local edema. The question becomes critical in analysis of transient episodes

where indirect evidence must be called upon. Many consider the facile explanation of spasm in cerebral arteries unlikely on the basis of anatomy (relatively less muscle than systemic arteries) and physiology (much less response to autonomic nerve stimulation than systemic arteries).

Pickering (23), a spokesman for the opposition, in a 1948 article stated, concerning vasospasm, "According to this hypothesis a cerebral artery suddenly contracts so fiercely that its lumen is almost or quite obliterated, the corresponding localized sensory or motor paralysis ensues .... the artery opens again .... and the paralysis disappears .... The evidence for it is slight ....The cerebral arteries do not look like arteries that would show intense variations in caliber in response to constrictor stimuli .... constriction of the arteries (to nerve stimulation) is small and insignificant .... Epinephrine directly applied to the cerebral arteries constricts them feebly .... the clear picture of the cerebral arteries that emerges from both anatomic and physiologic investigations is thus of feebly contractile arteries reacting weakly or not at all to vasoconstrictor agents".

The arterial anastamoses between major cerebral arteries have recently been emphasized by Vander Eecken and Adams (26) who hypothesize that when these anastamoses are required to function because of vascular occlusion that

that systemic hypotension or diversion of blood could result in transitory ischemia of portions of the brain. They remark that the most devastating effects of arterial occlusion are in the brain stem and basal ganglia which are supplied by branches of meningeal arteries which have only capillary and arteriolar anastamoses.

Denny-Brown (10) similarly subscribes to the theory that transient symptoms are from episodic failures of collateral circulation and are brought about by falls in blood pressure. He considers that narrowing of lumens, as seen transitorily in retinal vessels, is due to swelling of the vascular intima characteristic of lesions of arterioles in essential hypertension. He states "We submit, however, that in hypertensive encephalopathy the narrowing of vessels is direct evidence of arteriolar obstruction, rather than spasm."

Such hypotheses are not direct refutation of the concept of vasospasm but offer alternative explanations for phenomena often explained on the basis of arterial spasm alone. The ideas of collateral supply and maintenance of pressure head are quite valid but in being so do not invalidate vasospasm.

In favor of vasospasm by the negative evidence of pathology are Hicks and Warren (17) who analyzed 100 cases

of fatal cerebral infarction and found that in 60 of the cases there was no mechanical obstruction of the cerebral vessels by thrombosis, embolism or arteriosclerosis. They theorize "In only a few cases could systemic circulatory failure .... coupled with severe arteriosclerosis be implicated .... It is concluded that apoplexy is an ischemic disease of the brain most often directly caused by cerebral vasospasm ....".

In opthalmoscopic observations of hypertensive retinae reversible local arterial narrowing may be seen to occur in the retinal terminals of the ophthalmic artery which is a branch of the intracranial internal carotid artery. Transient blindness as a neurological symptom is discussed by Fisher (13) who concludes "the intermittent blindness probably depends on interruption of the blood flow to the retina. The mechanism by which this occurs is discussed at some length, with the conclusion that vasospasm or vasoconstriction must be incriminated". His patients had associated contralateral hemiplegias and were suspected of carotid thromboses so that a good case might here be made for transient failures of collateral circulation.

Further clinical evidence is gained from the study of migraine which has been related to vascular activity. Transient hemianopias and tinglings ascribed to vasoconstriction

have been relieved by vasodilators (24).

Basic to the problem is the reactivity of systemic arteries. It is accepted that arteries of the limbs are capable of intense and prolonged spasm upon mechanical stimulation and this has been shown to occur in the absence of autonomic innervation (20). Barnes and Trueta (5) have been able to induce prolonged spasm in limbs of rabbits following tourniquet application.

In 1902 Bayliss (6) noted upon varying intra-arterial tension that "the muscular coat of arteries reacts, like smooth muscle in other situations, to a stretching force by contraction. It also reacts to a diminution of tension by relaxation .... these reactions are independent of the central nervous system, and are of myogenic nature. They are obtained both in the case of vessels in their normal condition in the body, and in excised arteries some hours after death".

Recently, it has been possible to measure total cerebrovascular resistance as related to blood pressure changes. The nitrous oxide method of Kety (18) has shown that there is a marked increase in cerebrovascular resistance in hypertension, that this increased vascular resistance has initial lability and will decrease in response to lowered blood pressure. Kety (19) remarks that cerebral circulation is regulated predominantly "by constriction or dilatation of the flood gates

of cerebral circulation either locally or generally". It would appear that the cerebral arteries are highly reactive to changes in intra-arterial tension.

Arteriography has added more evidence concerning cerebral arterial constriction in man. The outlining by intra-arterial radio-opaque dye of the lumens of cerebral arteries has demonstrated transient focal narrowings, especially adjacent to aneurisms, and Ecker (12) has championed vasospasm as the cause.

Aside from the evidence in the foregoing paragraphs there are a number of direct observations of cerebral arterial spasm.

In 1925 Florey (14), working in Sherrington's laboratory, induced local spasm in cat cerebral arteries by local mechanical and electrical stimulation. He used drawings to illustrate the nature of these constrictions.

This significant observation was elaborated in 1942 by Echlin (11) who photographed such induced constrictions. He was able to show on injection of vital dye into the general circulation that these spasms could produce a true ischemia as evidenced by the restriction of dye peripheral to the focal constrictions. He further demonstrated that spasm appeared to be independent of autonomic nerve supply by induction of spasm in an artery which had been proximally lig-

ated 10 days before. Nerve degeneration was later shown to be present on controlled histological examination of the artery.

Penfield (22) in 1937 illustrated with an artist's drawings local spasm which he had observed in a pial artery during an epileptic seizure of a patient undergoing surgery.

The introduction of solid marble dust emboli into the carotid arteries of dogs was followed by local arterial constrictions which were photographed by Villaret and Cachera (27) in 1939.

In studies of arterial occlusion in monkeys Harvey and Rasmussen (16) noted marked constriction in the proximal middle cerebral artery upon manipulation which preceded clipping and cutting of the artery.

Recently, transient arterial spasm has been photographed in rats through skull windows in a critical work on hypertensive encephalopathy by Byrom (8). The focal constrictions in the cerebral arteries were shown to be associated with focal cerebral edema and correlated with acute cerebral symptoms. Spasm here was attributed to sudden increase in intra-arterial tension from the steep rise in blood pressure caused by renal artery clamping. It was an entirely reversible process.

It must be agreed that these preceding observations do substantiate the existence of cerebral arterial spasm.

However, the transposition of inferences gained from such data to existing clinical cases has always met with warranted argument that it is done on tenuous ground.

The clinical evidence to be presented here strongly favors the occurrence of spasm in the lateral striate branches of the middle cerebral artery as responsible for the incurred hemipareses. The physiological aspect of this study concerns the nature of local cerebral arterial spasm in animals and the results of a search to find by experimentation an agent which when topically applied to cerebral arteries would prevent or relieve local constriction and could be practicably used in human surgery.

MATERIALS AND METHODS

Clinical

Analysis was made of all cases of unexpected post-operative hemiparesis occurring in temporal lobectomies performed by Dr. Wilder Penfield and associates on epileptic patients during the 9 years from 1947-56. Excluded from consideration were all cases with tumors, penetrating wounds, vascular anomalies, pre-operative hemipareses, post-operative hematomas giving immediate symptoms and requiring re-opening and one case which sustained a hemiplegia following a 20 minute period of acute vascular collapse with unobtainable B.P. Openings and removals were generally done under local anesthesia. Closure was done under general anesthesia.

Particular attention in reviewing the patients' records was given to the surgeon's operative report which was customarily dictated immediately following the operation, to the surgeon's drawing which was made during the operation and indicated the extent of removal and to the post-operative clinical course.

MATERIALS AND METHODS

Physiological

Twenty-nine cats, 8 dogs, 2 monkeys and 1 guinea pig were used. Craniotomies were performed under nembutal anesthesia. The cerebral artery concerned was photographed before and at intervals following its local stimulation. Topical application of drugs to arteries was generally made by means of a saturated "cottonoid" compressed cotton pledget for a 5 minute period. Reactivity of treated arteries was compared with that of controls.

Stimulation by mechanical means was usually done by insertion of a nerve hook about the artery with subsequent traction on the vessel or by rubbing and displacing the vessel with a firm, wadded piece of cotton. However, mechanical stimulation of arteries was not generally used since it frequently resulted in slight bleeding which obscured the vessel caliber in photos and a constant stimulus could not be consistently given and compared in different vessels. The most practical method of stimulation was found to be electrical. Bipolar electrodes about 3 mm. apart were applied to the vessel wall usually for 10 seconds. A 60 cycle AC stimulator was used and generally a 6 volt stimulus.

Photography was by an Exacta camera with extension tubes and a 24 mm. lens. An electronic flash was the light

source. Focusing was done by a rack and pinion which had an arm for holding the camera. This entire device was mounted on the animal head holder. Photographs were usually made with Kodak plus X black and white film. In several experiments Kodochrome color film was used. Chronic experiments were done on 2 cats to test drugs for local or systemic toxicity, using one hemisphere as a control.

Exposure of the basilar artery in the dog was by McLean's (21) method in which the approach is made through the palate and pharynx with the mouth widely opened. Sympathectomies were generally performed by mid-cervical section of the sympathetic trunk. The chronic sympathectomy was prepared by Dr. Morrow for another experiment by resection of the superior and inferior cervical sympathetic ganglia.

The following is a list of agents evaluated: pentobarbital, papaverine, papaverine-nicotinamide, caffeine, cocaine, dibucaine, acetyl choline, prostigmine, pilocarpine, epinephrine, levarterenol, isoproterenol, homatropine, pavatrine, HP 164, tolazoline, phentolamine, piperoxan, curare, hexamethonium, histamine, amyl nitrite, reserpine, chlorpromazine, hydralazine, vasopressin, ergotamine tartrate, carbon dioxide, carbonic acid, hyaluronidase, nicotinamide, aminonicotinamide, Avacan and ice cold physiological saline.

RESULTS OF CLINICAL ANALYSIS

A survey was made of 171 cases of temporal lobectomy over a nine year period. Ten (5.8%) were found which had unanticipated and poorly explained post-operative hemipareses. The average age of these patients was 29. There were seven males and three females. Analysis of the records of these 10 patients was made to see if any factors could be found which would elucidate mechanisms responsible for the paresis. Some striking common factors were found in these cases as noted in the following data:

Removals resulting in these deficits were not simple temporal lobectomies but in 9 out of 10 cases included removal of either the insula or adjacent inferior frontal lobe, or both. The general incidence of associated removal of these areas in the temporal lobectomies surveyed was 30%.

Contralateral sensory impairment was present in all cases but less severe in degree than the hemiparesis.

Complete homonomous hemianopia was present immediately post-operatively in all but one of the patients tested. One patient was not tested.

Aphasia was sustained in both cases which had major hemisphere removals.

Slow waves in the EEG were present in all cases post-operatively over a major portion or the whole of the operated hemisphere.

The hemiparesis was noted to have occurred during the course of the operation in half the patients. Testing was done while the patient was under local anesthesia. This does not mean that in the other patients the onset was not during the operation since testing motor function was not routine and general anesthesia was usually begun immediately after or during the final stages of removal.

Reference to the middle cerebral artery was made by the surgeon in half the operative records, and in 3 records manipulation of the artery was described with concern. It is to be noted that removal common to these patients necessitated operating deeply in the fissure of Sylvius and, therefore, about the middle cerebral artery, even though the artery may not have been mentioned in the operative report.

Previous craniotomies on the same side had been performed in half the patients.

Intellectual impairment was present in all of the five patients tested by the Wechsler-Bellevue scale and appeared to roughly parallel the physical disability.

Thus, a syndrome of varying severity might be described in which the patient had a temporal lobectomy and removal in the insula or adjacent inferior frontal lobe which necessitated operating about the proximal middle cerebral artery, and sustained a hemiparesis which may have been noted to have

begun during surgery. This hemiparesis on further testing was found to usually be associated with a homonomous hemianopia, somatic sensory impairment, EEG slow waves over the operated side, a varying degree of intellectual impairment and aphasia if on the dominant hemisphere.

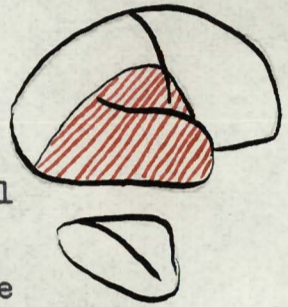
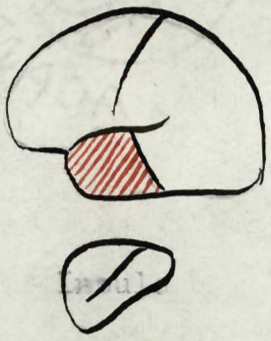
The hemiparesis usually involved face, arm and leg. In half of the patients the arm was more severely affected than the leg, but two of these five also had such serious leg involvement that the aid of a leg brace was required for walking. When the onset was noted during operation it was as either a marked weakness or complete paralysis. Upon arousing from the general anesthesia used in the latter part of the operation complete hemiplegia was present in half the patients, the others had marked hemiparesis. Gradual improvement occurred until by the time of hospital discharge, averaging 40 days after operation, the patients usually had a moderate spastic hemiparesis. Walking was in all cases possible although 3 patients required the assistance of a leg brace and cane. Some patients were stricken less severely. One (J.G.) had only the mildest weakness of leg and arm 1½ years following surgery. Parallel improvement generally occurred in the spheres of sensation, aphasia and intellectual impairment.

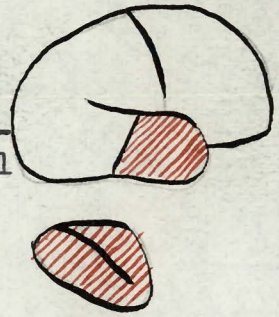
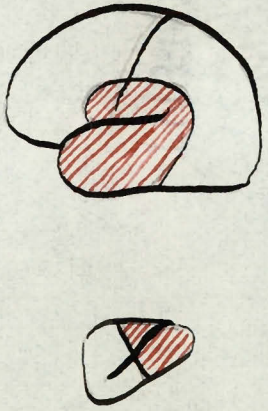
The visual field defect appeared to be permanent, as

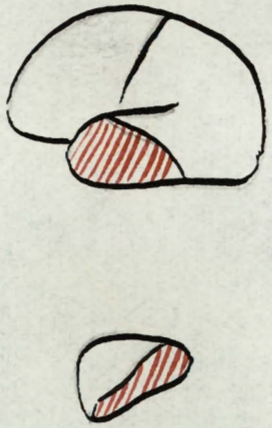
far as noted, in all but one patient whose defect was a complete homonomous hemianopia to confrontation during the early post-operative period but on discharge showed only a homonomous upper quadrantanopia on perimetry. Unfortunately, there is no record on one patient of post-operative visual field examination. The one patient tested who gave no post-operative evidence of hemianopic defect did have an upper homonomous quadrantanopia compatible with the tissue removed.

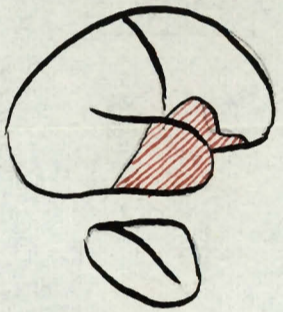
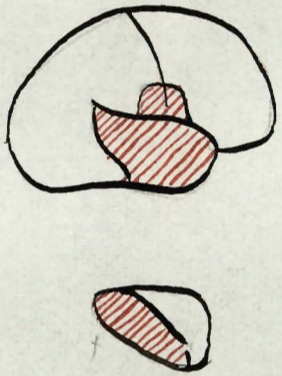
If the hemiparesis was not severe the full scale IQ showed little more than the 5 or 10 point decrease seen in the post-operative hospital course of the usual temporal lobectomy. If the hemiparesis was severe, or, as in one case, the impairment was in the major hemisphere, then the decrease in IQ was much greater. The performance scale deficit was the most marked. In one case (V.L.) this fell from 104 to 56, and in another (J.G.) from 121 to 90. Emotional lability and unstable mood swings were reported in several of these cases.

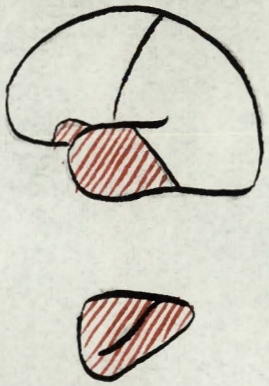
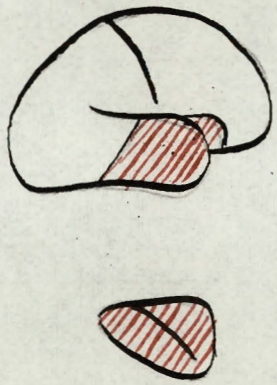
Table 1. lists the 10 patients and the pertinent clinical details. The drawing of the extent of removal is a copy of the surgeon's drawing made at the operation. The insula is enlarged and separately pictured beneath with the same orientation as the hemisphere. The operative notes are direct quotations taken from the notes dictated by surgeons immediately following each operation.

	PRE.OP.STATUS	OPERATION	OPERATIVE NOTE	POST.OP.DISABILITY	EEG
1.	A.B.37 year old woman. No motor or sensory deficits. Left upper homon. quadrantanopia by perimetry. Previous operation 1917 for rt. temporo-parietal abscess. Operated again 1938 with removal of scar tissue in lower end rt. Rolandic & lateral portion temporal lobe.	21 May 1948.  Insula	"At the end of the operation it was observed that there was weakness of the left hand."	3 hours after operation she was fully oriented but had no active movement of left arm and only slight movement of left leg. There was left lower facial weakness. In 2 mos. she was walking with the aid of a foot-drop splint. No note of post-op. visual fields.	4 June 1948. Silent over rt. temp. and slow and sharp waves rt. parieto-occip. Consistent with either a diffuse cortical change or a disturbance arising deep to this and affecting a large cortical surface.
2.	M.T.22 yr. old man. Normal neurolog.examination. Visual fields full by confrontation. Rt. handed.	16 Mar. 1949  Insula	"After a little final removal of white matter the patient did not answer when spoken to. He seemed to have weakness of his rt. hand and was unable to move his foot."	Severe hemiplegia and complete aphasia followed the operation. Recovery was slow. 2 mos. after surgery he was walking but showed marked impairment of motor function and considerable difficulty in speech. He had a rt. homon. hemianopia on confrontation.	2 April 1949. Continuous random delta activity. Maximum voltage over left frontal lobe. No definite alpha rhythm seen.

PRE.OP.STATUS	OPERATION	OPERATIVE NOTE	POST.OP.DISABILITY	EEG
3. A.K.36 yr. old man. Normal neurolog. examination. Visual fields full by perimetry. Previous operation 1949 with removal of rt. temporal tip. Rt. handed.	22 Feb. 1951  Insula	"During the procedure it was discovered that the patient had only partial control of the left hand and foot. This returned within a few moments and it was concluded that traction on the middle cerebral artery during removal of the insula was probably responsible for it."	He sustained a left hemiparesis which improved sufficiently so that he was able to walk alone in about one month. He had a complete left homon. hemianopia by confrontation.	15 March 1951. Continuous random slow delta waves over a large area in the posterior temporal and parietal regions.
4. Y.A.37 yr.old man. Normal neurolog. examination. Visual fields full by perimetry. Left handed.	1 June 1951  Insula	"At the time of sucking out of tissue which was lateral to the large arteries the patient discovered that he could not close his hand although he moves his arm and moves his leg. At this time there was a good deal of handling of the cerebral vessels. ... The procedure was long and tiring because of the great anxiety in handling all of the middle cerebral vessels and removing tissue both above and below them."	Following the operation his rt. arm and leg did not move even on painful stimulation. 7 weeks after operation he had improved so that he could walk with leg brace and cane. He had a complete rt. homon. hemianopia by perimetry.	5 July 1951. Residual delta waves over the left hemisphere with a marked depression of alpha rhythm from the left parieto-occipital area.

PRE.OP.STATUS	OPERATION	OPERATIVE NOTE	POST.OP.DISABILITY	EEG
5. R.D.10 yr. old boy. Normal neurolog. examination. Visual fields full to confrontation. Rt. handed.	25 Jan. 1952  Insula	"...the removal was carried on the surface of the frontal lobe but this removal was carried through the arch made by the middle cerebral artery."	There was post-operative weakness of the left arm and leg which improved so that he was walking about one month later. He had a complete left homon. hemianopia by perimetry.	13 Feb.1952 Constant high voltage delta waves over the rt. hemisphere extending from frontal to central and parietal regions and almost complete absence of normal alpha over rt. hemisphere.
6. J.G.28 yr. old man.No motor or sensory deficits. Complete rt.homon. hemianopia by perimetry. Rt.handed.	29 June 1954  Insula	"The cortex of the insula was removed ...extending a little way underneath the middle cerebral vessels ...The patient became somewhat confused. He used words well and yet would not name pictures. Also right at the end he seemed to be unable to move his rt. arm and hand, and the movement of the face was weak. This evidently came on quite suddenly at about the time the cortex of the insula was being removed."	The morning after operation he was aphasic. He was able to move his rt. arm to painful stimuli but not his leg. 3 weeks later he was walking but had a mild rt. hemiparesis and moderate aphasia. His complete rt. homon. hemianopia was unchanged. Performance IQ had dropped from 121 to 90.	20 July 1954 Slow wave activity from the left frontal region. Background rhythms without any clear alpha and background activity is flatter over the hemisphere than the right.

	PRE.OP.STATUS	OPERATION	OPERATIVE NOTE	POST.OP.DISABILITY	EEG
7.	V.L.25 yr. old man. Neurolog. examination normal. Visual fields full by perimetry. Rt. handed.Operation elsewhere in 1951 with some sub-pial removal of an undetermined amt. of frontal cortex.	19 Jan. 1955  Insula	"The dura was densely adherent...where it had been previously exposed...Hemostasis was obtained with some difficulty ...The frontal operculum has been removed with some of the undersurface of the frontal lobe."	The first post-op. day he was able to move his left leg proximally but not his left arm. He improved until at the time of discharge he walked with a leg brace but had no fine finger movement. Complete left homon. hemianopia by perimetry. Performance IQ had dropped from 104 to 56.	10 Feb. 1955 Continuous random delta waves over entire rt. hemisphere with practical absence of alpha rhythm from rt. occipital.
8.	M.B.21 yr. old woman. Normal neurolog. examination. Visual fields full by perimetry. Rt. handed.	27 Jan. 1955  Insula	"The lower end of the precentral and probably the postcentral gyrus was removed down to the bottom of the fissure of Sylvius... Abnormality was shown in the inferior part of the insula so that cortex ...was completely removed."	She sustained a minimal hemiparesis of left arm, face and leg and a marked left sided sensory loss. She was able to walk alone but dragged her left foot 10 days after operation. Complete left homon. hemianopia by confrontation on several post-op. examinations. Performance IQ had dropped from 77 to 69.	19 Feb. 1955 Persistent delta waves over rt. posterior temporal and occipital areas.

PRE.OP.STATUS	OPERATION	OPERATIVE NOTE	POST.OP.DISABILITY	EEG
9. G.F.33 yr. old man. Normal neurological examination. Visual fields full by perimetry. Left handed. Previous operation 1952 with removal in left inferior parietal lobe.	6 Dec. 1955  Insula	"Following standard temporal lobe removal and the Island of Reil and part of the frontal operculum were then removed...It should be mentioned that papaverine had been placed over the middle cerebral vessels."	The day after operation he had a rt. lower facial weakness and a complete rt. homon. hemianopia by confrontation. Slight flexion of the rt. hip was the only movement on the right. In 6 wks. he could walk without assistance but dragged his rt. foot unless a brace was used. Visual fields 1 month after operation showed a rt. upper homon. quadrant anopia. Performance IQ had dropped from 101 to 89.	21 Jan 1956 Diffuse low voltage slow waves and impairment of regularity of alpha waves from left hemisphere.
10. M.P.38 Yr. old woman. Normal neurological examination. Visual fields full by perimetry. Rt. handed.	13 Dec. 1955  Insula	...removal of the frontal operculum and of the insula was carried out, the vessels were soaked in papaverine and no spasm was seen.However, at the conclusion of this removal there was very definite weakness of the left arm and leg."	The evening of the operation she was unable to move any part of left upper or lower extremity and paralysis of left lower face. In 6 wks. she was able to bear some weight on left foot. Visual fields 10 wks. post-op. by perimetry showed a left sup. quadrant defect in both fields. Performance IQ had dropped from 108 to 82.	1 March 1956 Almost continuous delta activity of maximal amplitude in rt. central region but involving parietal as far as occipital and forward to mid-frontal. Essentially no normal alpha from rt. occipital.

RESULTS IN ANIMAL EXPERIMENTS

Local constriction of cerebral arteries was observed to follow quite reliably upon local irritative stimulation of the vessel either by electrical current or by manipulation and traction. Although mechanical irritation is a stimulus more like that suggested as the factor responsible for vasospasm in the clinical aspect of this study, it was found that electrical stimulation was more easily handled, gave a more constant stimulus value for use in comparing drug effects, did not result in bleeding, and generally gave a more persistent constriction.

Fig. 1 illustrates vasoconstriction from mechanical stimulation in photographs taken before and after manipulation and rubbing of the artery with a firmly wadded piece of cotton. Fig. 2 shows the stimulating electrodes in position and the arterial spasm before and after stimulation with a 6 volt stimulus for 10 seconds. An example of vasoconstriction from an electrical stimulus is shown in Fig. 3 where the contracted state of the artery is seen persisting 10 minutes following stimulation.

Constriction occurred directly upon application of electrodes and intensified gradually until a maximal state of narrowing was achieved. If a maximal stimulus (in these studies 6 volts for 10 seconds) was given the constriction

was maximal usually within 10 seconds after removal of the electrodes, but occasionally constriction would be most marked 40 seconds after stimulation. Stimuli of 2 or 3 volts gave a lesser response. Constrictions varied in persistence from a few seconds to more than 30 minutes. Usually they could be depended upon in the sort of conditions used in most of these experiments to last at least 5 minutes.

Although spasm always spread beyond the span of the bipolar electrodes, it could usually still be regarded as local. Sometimes, however, the narrowing extended as far as ½ cm. along cats' arteries and it was quite common for branches from a main stem to participate in spasm.

At the site where each pole of the bipolar electrode rested on the vessel a maximal indentation usually occurred. This is well seen in Fig. 6. Most often the initial maximal constriction was uniform and intense over the entire length of the artery affected and this double notching was obvious only after some relaxation began to occur with recovery of caliber along the vessel elsewhere than at the points of maximal stimulus delivery. Thus a beaded appearance was often seen.

Variations in intensity of spasm sometimes occurred during the duration of the constriction but usually the degree of narrowing first seen was not surpassed.

The general mode of final caliber recovery was by a gradual resumption of normal diameter with the electrode sites recovering last. At times, however, the points which were initially the most constricted would recover first and initially relaxed segments would proceed to constrict distally as if there were a slowly spreading wave of constriction with a wave of relaxation following. Fig. 3 illustrates this phenomenon in the branch to the right of the main artery. A beaded appearance was often intensified by sharp borders between lengths of narrower and wider diameters. Following mechanical stimulation the factor of sites of maximal stimulus was probably responsible for variations in appearance of spasm.

Shortly after exposure pial arteries were found to be about equally reactive to the same electrical stimuli. Moderate sized arteries appeared to show the most marked constriction. Prolonged exposure or drying of the cortex tended to reduce reactivity. Previous stimulation often made an artery subsequently less responsive.

Dog, cat and guinea pig arteries reacted with equal vigor but monkey (Macaque) arteries over the convexity of the hemisphere were much less reactive than those of the lower mammals. In the monkey a stronger and longer stimulus was required to give somewhat less of a response, although

constriction was definitely present.

Several instances were noted of apparent spontaneous spasm in arteries to which no stimulus had been given. These were chance observations of local narrowings in arteries which were seen shortly after exposure and on serial photographs were shown to later recover uniformity of caliber. Fig. 4 shows such an observation.

Immediately after opening of the dura all the arteries were of slightly smaller diameter than a few minutes subsequently. This was not local constriction. Whether the arteries all slightly dilated from previous intracranial diameter upon exposure to the external environment or whether the initially narrower arteries represented a transient constricted state as a response to the stimulus of dural opening cannot be answered from these observations. An example of such caliber change is seen in Fig. 5. The vessel size tended to be quite constant once this initial change had occurred.

Acute mid-cervical sympathectomy or vago-sympathectomy, either unilateral or bilateral, resulted in a marked Horner's syndrome but did not alter cortical vascular reactivity. Reactivity was similarly unaffected 3 weeks following ipsilateral sympathectomy made in a cat by resecting the superior and inferior cervical sympathetic ganglia and which had produced

a sustained Horner's syndrome. An example of arterial vasoconstriction in this latter preparation is shown in Fig. 6.

Adequate comparison cannot here be made of reactivity between basal and peripheral arteries since a basilar artery study was the only experiment performed on the major vessels connecting to the circle of Willis. The basilar artery of the dog was very reactive in this study (Fig. 7). Over the convexity of the exposed hemisphere in dogs and cats variation in location of equally sized arteries made no apparent difference in reactivity.

A great variety of drugs was tried in an effort to find something suitable for topical application which would prevent or relieve spasm. An attempt was made to select drugs which were known to have an effect on systemic vascular caliber or which might rationally be assumed to have a direct vascular effect by virtue of their known physiological actions, e.g., autonomic drugs.

A method of local application was sought which would retain the agent to the desired restricted area and could be used as a practicable standard method for comparing different drugs. It was found that saturation of a small piece of compressed cotton ("cottonoid") would restrict drug action to the limits of the cotton without spreading to adjacent areas

as did application of drops. An artery of comparable size was stimulated at about the same time as the medicated vessel as a control procedure and reactions compared at like intervals. Photographs were usually taken at 10 seconds, 40 seconds, 2 minutes and 5 minutes following a standard stimulation.

It was found that there were several modes of drug action in relation to spasmogenic stimulus. Some drugs were observed to markedly dilate the artery but not prevent marked spasm on stimulation of the dilated artery. Others gave either the slightest or no dilation and yet adequately prevented the occurrence of subsequent spasm. Another mode of action was that of apparent resistance to induction of spasm immediately following stimulation, but with development of a delayed spasm beginning at an interval of 3, 5, or 10 minutes after stimulation. Drugs which were effective in prevention of spasm following their application did not necessarily relieve constriction if applied to the spastic artery. Other agents were found which were good relievers but only fair preventers of vasospasm.

It was not found that the application of an agent, anesthetic or otherwise, proximally on an artery would prevent spasm upon stimulation of that artery distally.

Papaverine, the most renowned relaxer of vascular spasm, was found to be effective in dilutions to 0.02%. It dilated arteries quite readily, was very good for relief of constriction already present, but gave only moderate or inconstant protection from induction of spasm, even in saturated solutions, and persisted in effectiveness only a minute or two following removal from the vessel. Fig. 8 shows dilation, particularly in background vasculature, following a 5 minute application of 1.8% papaverine. Ten seconds following stimulation there was local constriction at the site of bipolar electrode application. This constriction was gone by 40 seconds, indicating fair protection in this case. However, 10 minutes following the stimulation a delayed spasm was seen. Delayed spasm was not constant following papaverine nor was initial resistance to spasm always as good as shown in this figure.

A combination of effective strengths of papaverine and nicotinamide was tried and appeared to have an additive effect. Relief of spasm already present with papaverine-nicotinamide combination is well shown in Fig. 9 where the drug was effectively applied to relieve spasm on one branch of an equally forked artery. The other branch served as a control with persistence of spasm 15 minutes following an equivalent stimulus. An attempt to achieve greater drug

penetration was tried by later coupling this application with hyaluronidase (Wydase, Wyeth) but without effect.

Carbon dioxide which has been stressed as the most powerful vasodilator in the blood flow studies of Kety (19) was not found in these studies to prevent induction of spasm. Inhalation of 5% CO_2 by tracheotomy tube gave either a definite slight constriction to pial arteries or, occasionally, a slight dilation. Ten per cent CO_2 gave a definite slight dilation and darkening of arteries. Fig. 10 illustrates this effect of 10% CO_2 and the induction of local spasm during its inhalation.

Fig. 11 demonstrates the nature of constriction upon stimulation after caffeine. Caffeine is seen to have given moderate dilation and apparent immediate protection from constriction following stimulation. However, a delayed spasm began to occur 3 minutes after stimulation and became marked at 5 minutes. The constrictions are noted to have given indentations where either pole of the bipolar electrode was applied, and to have involved an adjacent artery which came near the site of application of the upper pole.

The most useful drug was Rogitine (Ciba, also known as Regitine), an adrenergic blocking agent which, in dilutions to 0.05%, gave consistently good protection from induction of spasm and good relief of spasm already present.

Its full effectiveness was present as long as 6 minutes following removal of the drug. Curiously, other adrenergic blocking agents were found to be much less effective. Application of Rogitine was followed by either very slight or no dilation of the arterial system. Fig. 12 shows protection of an artery from induction of spasm and a control vessel with spasm of 6 minutes duration. In Fig. 13 relief of spasm already present is seen to have followed Rogitine application and persistence of spasm is seen in a control artery. Delayed spasm was not noticed with Rogitine.

All the agents evaluated are listed in Table 2. The number of experiments in which the agent was used does not indicate the number of times it was used in one experiment. Each animal was considered a separate experiment. The principle activities of the agents in relation to vasospasm are tabulated.

Agent	No. of exp'ts used in	Effect on artery after 5 minute application	Ability to resist induction of spasm	Ability to relieve spasm already present	Delayed spasm	Comment
Pentobarbital 5% (Nembutal, Abbott)	4	moderate dilation	none			one i.v.injection gave no dilation
Papaverine 1.6%	18	moderate to marked dilation	fair	good	occasional	ineffective 5 min.following application - effective in dilutions to 0.02%
Papaverine-nicotinamide combination	4	moderate to marked dilation	fair to good	good	occasional	ineffective 6 min. following application
Caffeine 25.0% (caffeine sodio benzoate, Hartz)	1	moderate dilation	fair		marked at 3 to 5 min.	
Cocaine 2.0% and 5.0%	7	slight dilation, slight constriction occurred once	none or poor			
Dibucaine 0.067% (Nupercaine, Ciba)	1	slight dilation	none			
Acetylcholine 10% (Hoffman-La Roche)	1	questionable	none			

Agent	No. of exp'ts used in	Effect on artery after 5 minute application	Ability to resist induction of spasm	Ability to relieve spasm already present	Delayed spasm	Comment
Prostigmine 0.05% (Hoffman-La Roche)	1	none	moderate			
Pilocarpine 1.5%	1	moderate to marked dilation	none			
Epinephrine 0.1% (Adrenalin, Parke-Davis)	2	slight dilation once, slight constriction once	poor			
Levarterenol 0.2% (Norepinephrine) (Levophed bitartrate, Winthrop-Stearns)	3	moderate dilation	good	none		
Isoproterenol 0.5% (Isuprel, Winthrop-Stearns)	5	slight dilation	fair to good	fair to good		
Homatropine (Burroughs-Wellcome)	1	moderate dilation	none			small discs dissolved in saline made solution used
Pavatrine (Searle)	1	moderate dilation	none			tablets were dissolved in saline to make solution

Agent	No. of exp'ts used in	Effect on artery after 5 minute application	Ability to resist induction of spasm	Ability to relieve spasm already present	Delayed spasm	Comment
HP 164 0.4% (Parke-Davis)	5	slight dilation	fair to good	none	occurred once	experimental drug not on the market
Tolazoline 2.5% (Priscoline, Ciba)	1	moderate to marked dilation	none			
Phentolamine 0.5% (Rogitine, Ciba)	10	slight dilation	good	good	none	effective in one trial 10 min. following application. Effective in dilution to 0.05% but gave better results with less dilution
Piperoxan 0.2% (Benzodioxane, Poulenc)	2	slight dilation	none or slight	none or slight		
Curare 0.3% (Tubocurarine chloride, Squibb)	1	moderate dilation	none			

Agent	No. of exp'ts used in	Effect on artery after 5 minute application	Ability to resist induction of spasm	Ability to relieve spasm already present	Delayed spasm	Comment
Hexamethonium 2.5% (Vegolysin, Poulenc)	1	slight constriction	none			
Histamine 0.1% (Parke-Davis)	3	may or may not dilate, slight constriction occurred once	poor			
Amyl nitrite (Burroughs-Wellcome)	1	none	none			vapor by inhalation
Reserpine 0.25% (Serpasil, Ciba)	1	questionable	poor			
Chlorpromazine 2.5% (Largactil, Poulenc)	2	moderate to marked dilation	poor to fair	fair		effective in dilution to 0.25%
Hydralazine 2.0% (Apresoline, Ciba)	5	slight dilation	fair	good		effective in dilution to 0.2%

Agent	No. of exp'ts used in	Effect on artery after 5 minute application	Ability to resist induction of spasm	Ability to relieve spasm already present	Delayed spasm	Comment
Vasopressin (Pitressin, Parke-Davis)	1	slight constriction	none			
Ergotamine tartrate 0.05% (Gynergen, Sandoz)	1	slight constriction	fair			
Carbon dioxide 5% Oxygen 95%	4	slight constriction or slight dilation	none			constriction was the more dominant effect
Carbon dioxide 10% Oxygen 90%	1	slight dilation	none			inhalant mixture by tracheotomy
Carbonic acid (H_2CO_3)	1	moderate dilation				made by bubbling 10% CO_2 in saline

Agent	No. of exp'ts used in	Effect on artery after 5 minute application	Ability to resist induction of spasm	Ability to relieve spasm already present	Delayed spasm	Comment
Hyaluronidase 150 TRU (Wydase, Wyeth)	1	no additional effect from Wydase	none			used in conjunction with papaverine-nicotinamide mixture
Nicotinamide 50% (Lilly)	7	moderate to marked dilation	fair		occasional	ineffective 6 min. after application
Aminonicotinamide 0.5% (Horner)	1	slight dilation	fair		marked at 5 min.	experimental drug
Avacan 2.5% (Asta)	1	none				obtained from Frank W.Horner,Ltd.
Ice cold physiological saline	1	none				

DISCUSSION

The extent of deficit in these patients, which in a varying degree included hemiparesis, hemihypesthesia, hemianopia, intellectual impairment and aphasia with major hemisphere involvement, indicates either a widespread damage to most of one cerebral hemisphere, or lesser damage in a critical area where necessary fibers subserving widespread functions are closely situated.

Actual removal of cerebral tissue as was made of the anterior temporal lobe and either insula or adjacent inferior frontal cortex, or both, will not account for such deficit.

Since all these cases did have removals which involved operation about the proximal middle cerebral artery, one would suspect that interference with arterial supply would most properly explain the post operative picture. The portion of the middle cerebral artery operated about lies at the anterior end of the insula, not far from its origin from the internal carotid artery and circle of Willis and just distal to the section from which the lateral striate arteries* spring from the middle cerebral artery to

* The name lateral striate is used here. These arteries were originally called lenticulo-optic by Duret, but it has been shown that they give no significant supply to the optic thalamus. The term lenticulo-striate implies some distinction between the lenticular nucleus and the striate body. Lateral striate was the name used by Abbie for these branches of the middle cerebral artery which tended to enter the anterior perforated space more laterally to distinguish them from the recurrent branch or branches of the anterior cerebral artery which entered medially. Also used are the names strio pallidal, anterior perforating branches, penetrating branches, striate and striato-capsular.

enter the anterior perforated space.

If diminution in the supply of the peripheral middle cerebral artery by proximal vasoconstriction were considered the sole explanation, one could not well account for involvement of the leg which cortically is supplied by the anterior cerebral artery, or of vision which cortical representation is supplied by the posterior cerebral artery.

Removal in the insula was carefully limited to grey matter and none of the substance of the internal capsule is considered to have been physically removed in these operations. Although the internal capsule lies medially it is separated by the lenticular nucleus in all but perhaps the upper reach of the insula, and involvement of the internal capsule here would not account for the deficits sustained.

Just medial to the uncus, which is removed, lies the cerebral peduncle. The leptomeningeal barrier between the two is a guiding medial border which is never transgressed. Interference at the peduncular level by agitation of this border is considered unlikely since the uncus is removed in nearly all temporal lobectomies and yet only those with additional supra-Sylvian removals have had hemiplegia. Neither would peduncular involvement explain the hemianopia.

In these operations no hypotensive episodes occurred which would have unduly taxed blood supply to all of the cerebrum and which might have reduced efficiency of direct

and collateral supply to such a minimum as to make manifest vascular deficits that would not otherwise have been apparent.

Ischemia in the distribution of the lateral striate branches of the middle cerebral artery most adequately explains the disability incurred. Beevor (7) described these deep branches of the middle cerebral as supplying, among other things, the posterior limb of the internal capsule above the upper angle of middle lenticular segment. Abbie (2) (3) in a later extensive work on the anatomy of capsular vascular disease described the lateral striate arteries as supplying the entire internal capsule (anterior limb, genu, posterior limb) and the auditory and visual radiations immediately after leaving the capsule. He places particular significance on the vessel which he calls the deep optic branch of the middle cerebral artery. It is agreed by anatomists that these lateral striate arteries are a major and critical supply to the internal capsule.

Abbie in a further interesting observation on these critical arteries states: "It will be observed that directly after their entrance into the brain the lateral striate arteries are massed together between the putamen and the claustrum, that is, in the base of the external capsule. Thus, for a short time a large number of arteries of different sizes is concentrated within a very small volume of cerebral

substance. This fact provides the explanation for Charcot's observation that the anterior portion of the base of the external capsule is the 'site of election' for cerebral hemorrhage .... The number of arteries crowded within this small space is probably twice as great as that to be found in any other comparable volume of cerebral tissue."

It is generally held, as in Beevor's observation, that the penetrating arteries are essentially end arteries and that there is no connection between the cortical distribution and that of the basal arteries.

Fig. 14 is a drawing I have made from a formalin preserved brain indicating the relationships of the lateral striate arteries. The right temporal lobe is strongly retracted with the tip of retractor on the uncus. The arteries, somewhat diagramatized, are seen to enter the anterior perforated space just medial and anterior to the uncus and just inferior to the limen insulae, the lower limit of the insula. They lie directly between the uncus and the orbital surface of the frontal lobe. Proximal to these vessels the anterior choroidal and posterior communicating arteries arise from the internal carotid artery.

Upon traction or manipulation of the middle cerebral artery lying just superiorly a pulling is probably also exerted at the points where the perforating arteries are

attached. Vasoconstriction as a response to the irritation likely occurs along the main stem of the middle cerebral artery with extension along the perforating branches rendering ischemic their critical distribution. The practical lack of peripheral anastamoses leaves their territory absolutely dependent on the proximal integrity of these vital arteries. The tissue suffering this blood deprivation may include not only the specific fibers of the Rolandic and calcarine areas but also the centrencephalic integrating circuits passing to and from cortex and central brain stem through the area of supply of these anterior perforating arteries.

The anterior choroidal artery which arises from the internal carotid might be considered on the basis of its distribution to account for the described syndrome (1). However, it is adequately supplied with anastamoses arising from the posterior cerebral artery. Since Cooper's (9) series of anterior choroidal artery ligations in man for extrapyramidal disease did not develop subsequent hemiplegia or visual defect, it would suggest that this artery does not have the major responsibility in our cases.

Shellshear (25) states: "I have noticed that the larger the vessel entering the substance of the brain, the more acute is the angle it makes against the direction of the current; and to attain this end both sets from the anterior

and middle cerebral leave the parent trunk at a considerable distance from the place of entry into the anterior perforated spot. It is strange that no reference to this fact, which must have an important clinical bearing can be found in the literature, except in John Hunter's works." Certainly this fact of branching acuity would appear to work against easy maintenance of head of pressure from the parent vessel. Concerning the length of distance traversed it may be pertinent to mention Putnam and Alexander's thesis (4) that the susceptibility of an artery to thrombosis is related to the longer the undivided length (from the last source of blood to the terminal district) and the smaller the diameter. One might modify that idea by using the term vascular insufficiency instead of thrombosis, since vasospasm may be a common precedent event to thrombosis.

That basal arteries may be more susceptible to vasospasm than peripheral arteries is a possibility which cannot here be decided. The observations of Harvey and Rasmussen (16) of marked vasospasm in the proximal middle cerebral artery of the monkey when coupled with the observations made here of poor reactivity of arteries over the convexity of the monkey hemisphere may lead one's thinking in that direction. Certainly the dog basilar artery in these studies proved most reactive.

It may be that the actual insult results from a combination of factors. No doubt several or even all of these penetrating arteries are involved. Thus no chance occurs for interchange of blood at a capillary level or for sustenance of the area due to overlapping of terminal branches. Spasm may also be induced by too deep dissection in the anterior inferior insula thus approaching the arteries as they traverse brain substance. Perhaps the constriction in the middle cerebral artery spreads to involve the anterior choroidal artery and to partially decrease its terminal supply in this area. Providing the constrictive process extended to involve the middle cerebral artery proximal to the lateral striate arteries, the head of pressure to those arteries would be reduced, as it would also by systemic blood pressure falls, further aggravating the condition. Cerebral edema from surgical interference with that hemisphere may add its bit in the area of concern. The existence of adhesions (half the patients had previous craniotomies on the same side) might restrict and bind these vessels which would otherwise have a latitude of movement to withstand some traction. Manipulation and trauma which is extreme and direct may actually sever these vessels. Tearing of the arteries is an extension of the same process which in lesser degree causes spasm. A greater or lesser number of factors might decide the occurrence

of focal anemia and add or detract from the final clinical picture.

As noted in the introduction there is adequate evidence that local constriction of cerebral arteries may occur upon mechanical or electrical stimulation. These studies in search of a local spasm preventive agent have corroborated previous work concerning the nature of such spasm.

These constrictions, it is felt, are not mediated by autonomic fibers but exist as a local arterial reactivity occurring even under local anesthetic or in the sympathectomized or nerve blocked preparation. They are in no sense the weak caliber reductions reported on observations through brain window upon sympathetic nerve stimulation (15).

The endeavor here has been to find a manner in which local cerebral arterial constriction could be absolved. To this end a search has been made for a drug which could be applied locally at the time of surgery on arteries which might undergo irritative manipulation. Various pharmacological categories have been investigated: barbiturates, narcotics, local anesthetics, parasympathomimetic agents, autonomic ganglia blocking agents, histamine, vasodilator and antihypertensive agents, ergot alkaloids, skeletal muscle relaxants, vitamins, CO_2. Few have been without practical drawbacks.

Papaverine was found to be inconstantly helpful. Two of the hemiplegic patients (G.F. and M.P.) actually had local papaverine applied to the proximal middle cerebral arteries, so it would appear that the drug used clinically in this manner is ineffective.

Rogitine (Ciba), an adrenergic blocking compound, was the most effective agent found. It was reliable both in prevention of spasm and in relief of spasm already present. It has been used in dilution of 1:2 at the time of surgery in several cases with no untoward results. One of the hemiplegic patients (J.G.) had his second operation with Rogitine applied locally. At the time of this second operation he had recovered almost fully from his hemiparesis. No gait impairment was apparent. His main difficulty was a moderate aphasia and a permanent homonomous hemianopia, which had been present before the first operation, and continuing seizures for which his second surgical procedure was performed. Following that operation he had no undue deficits and no exacerbation of aphasia, other than during the phase of cerebral edema, even though the frontal operculum and more of the temporal lobe were removed.

There exists a real danger of arterial insufficiency to the vital internal capsule area from local constriction of the lateral striate arteries due to irritative manipulation

of the adjacent proximal middle cerebral artery. The great post-operative deficit occasioned by this ischemia is a surgical tragedy. Although additional proof of the value of topical application as a prophylactic measure is needed, it is considered at present to be the best procedure for avoidance of local arterial spasm when combined with extreme operative care in this region.

SUMMARY

1. An unanticipated post-operative deficit is described which occurred in 10 cases of temporal lobectomy which also had removals of insula or adjacent inferior frontal cortex or both. The deficit consisted of varying degree of hemiparesis, homonomous hemianopia, hemihypesthesia, aphasia (if on major hemisphere) and intellectual impairment.

2. Evidence is presented to support the contention that these post-operative deficits are due to local constrictions of the lateral striate arteries which render their area of distribution ischemic. These constrictions are considered subsequent to mechanical irritation of the proximal middle cerebral artery about which operative removal occurred.

3. The nature of local arterial spasm is described from observations made in animals.

4. Results are reported of a search for an agent which could be used topically for prevention or relief of local arterial spasm. The actions are noted of various drugs on arterial spasm. Rogitine, an adrenergic blocking compound, was the most efficient drug found.

Fig. 1. Spasm Following Mechanical Stimulation

1. Pial artery of cat just before stimulation.
2. Constriction in the same artery 10 seconds following irritative manipulation with a firmly wadded piece of cotton.
3. Scale of 1 cm. used in all figures of vasculature.

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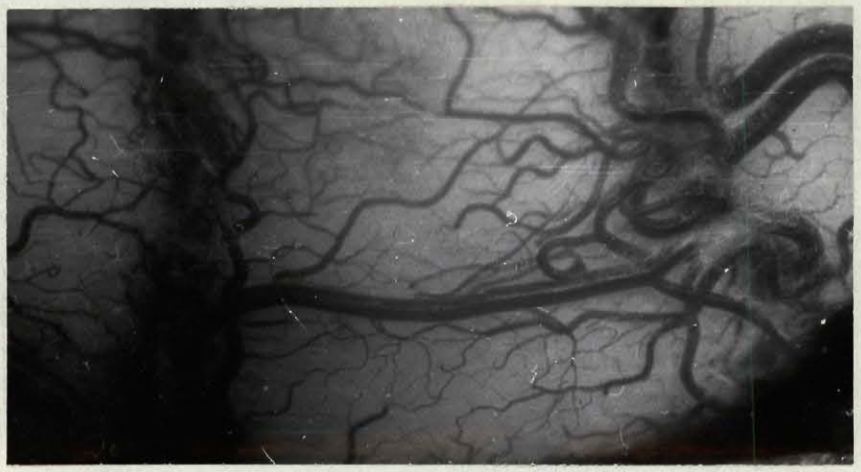

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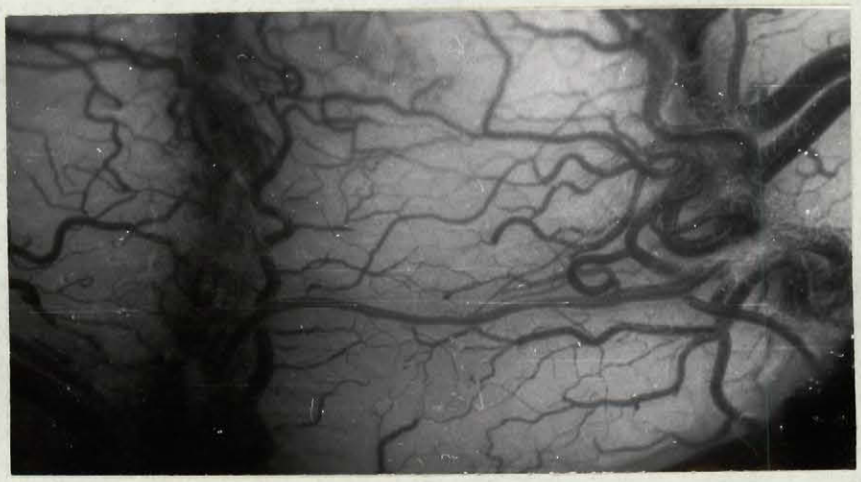

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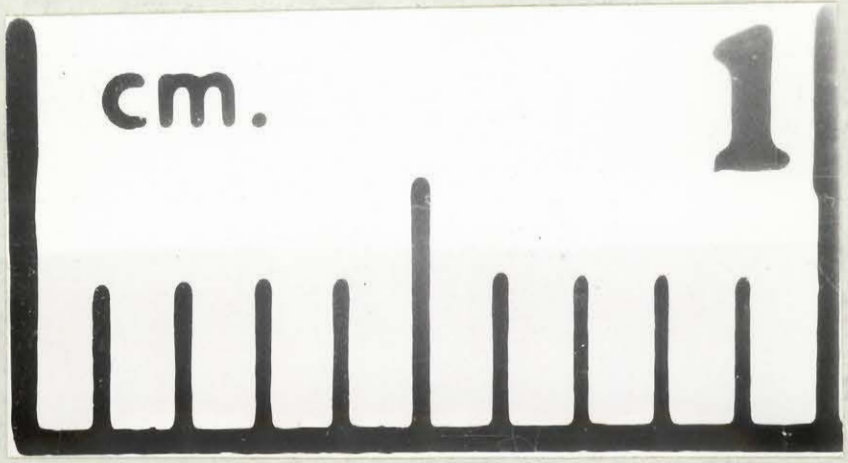

Fig. 1.

Fig. 2. Mode of Electrical Stimulation

1. Cat's artery just before electrical stimulation.
2. Bipolar electrode in position.
3. Constriction immediately following stimulus of 6 volts for 10 seconds.

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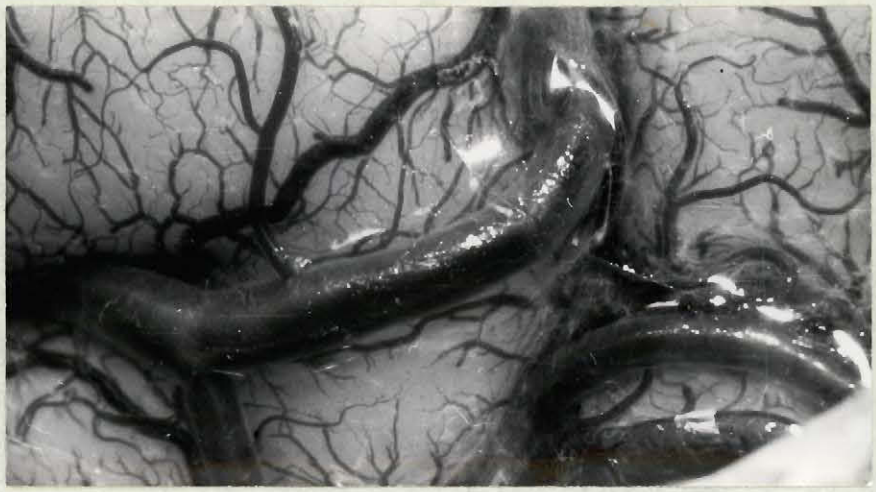

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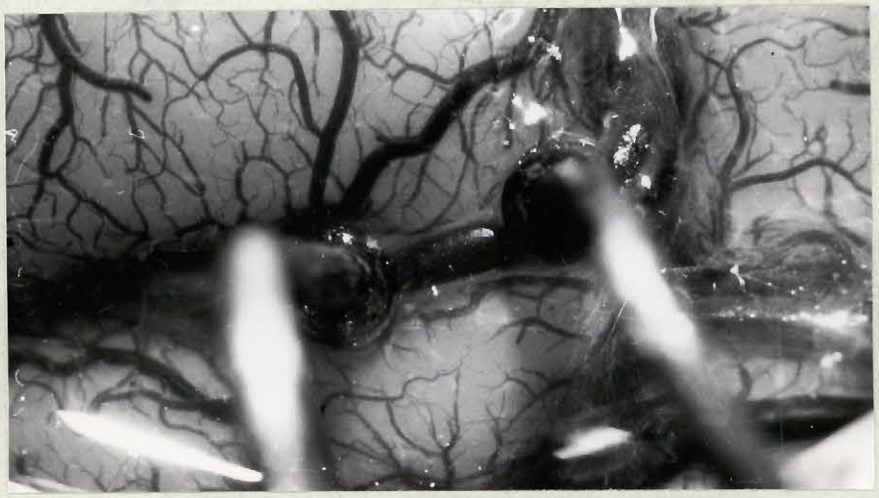

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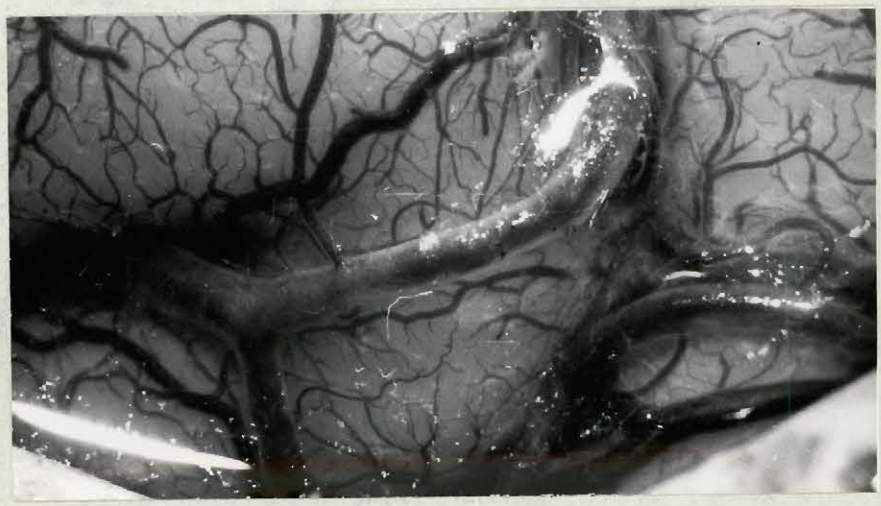
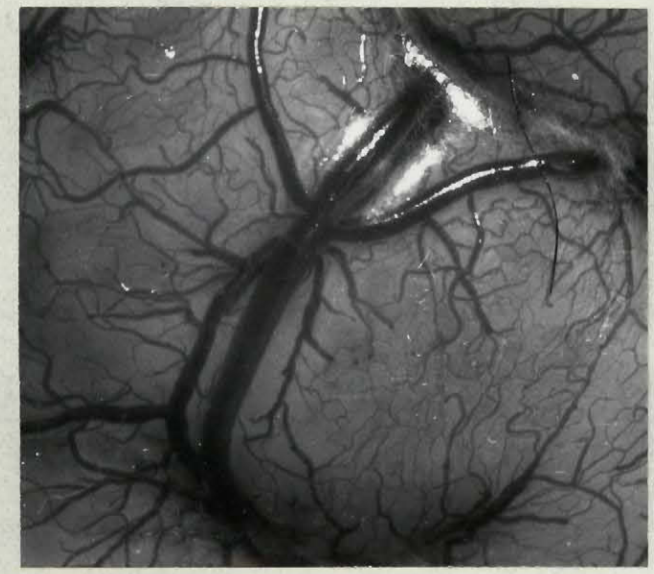


Fig. 2.

Fig. 3. Spasm Following Electrical Stimulation

1. Cat's artery 1 minute before stimulation.
2. Constriction in same artery 10 seconds after stimulus of 6 volts for 10 seconds.
3. 40 seconds after stimulus.
4. Spasm persisting 10 minutes following stimulus. Note mode of caliber recovery.



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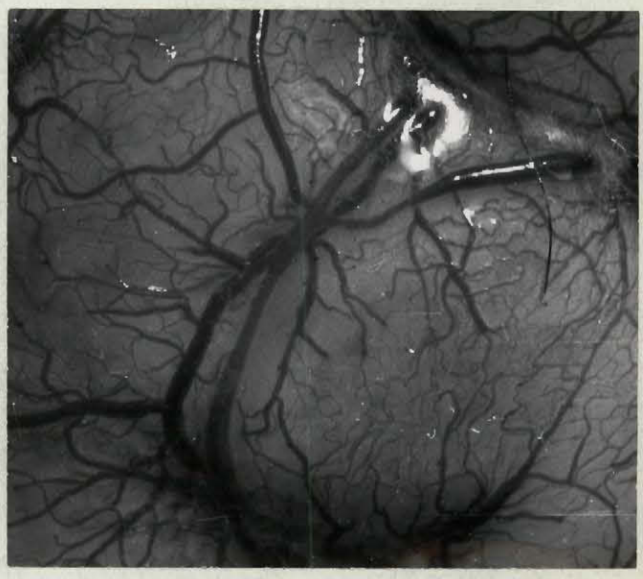

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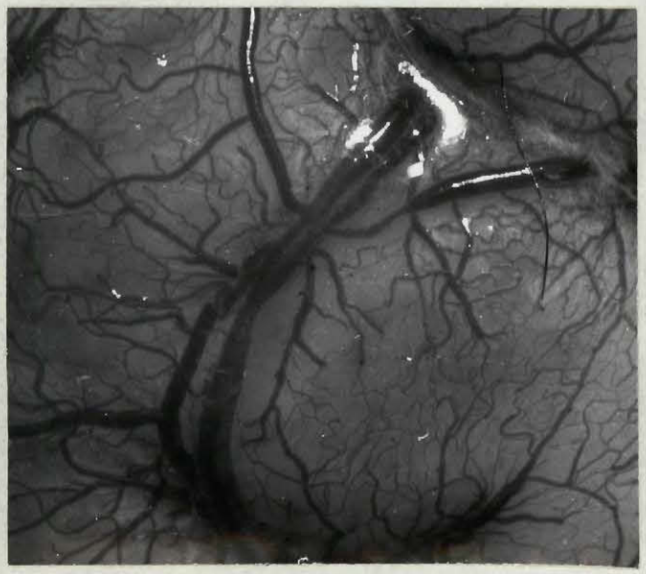

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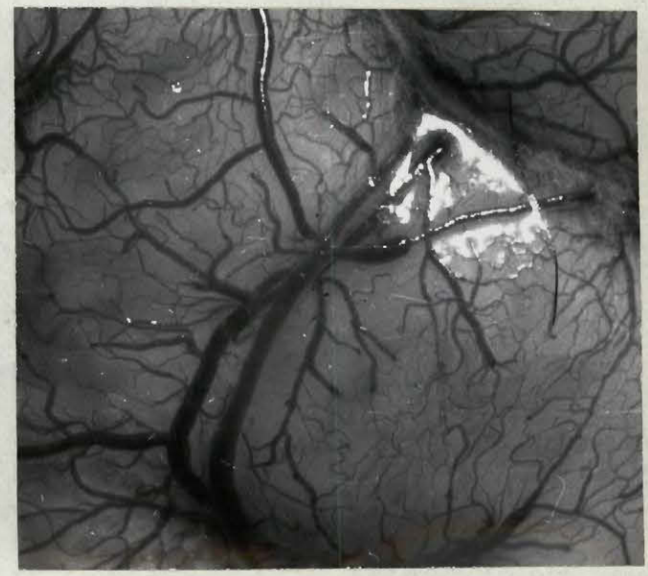

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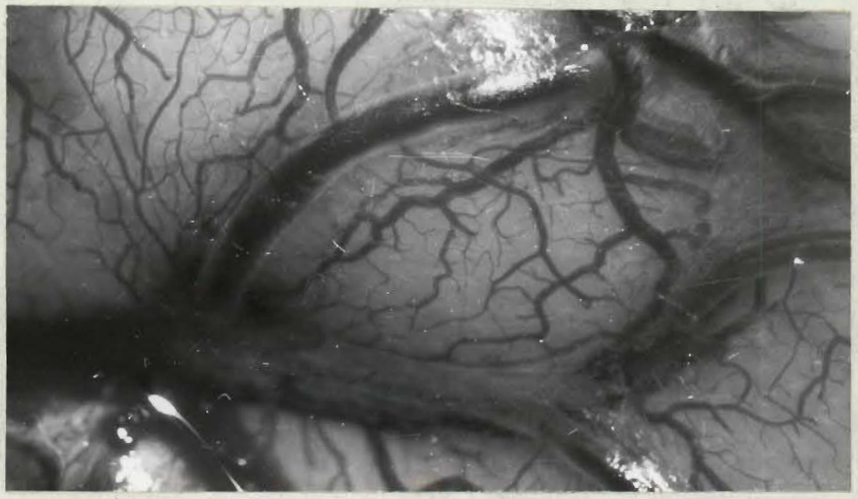
Fig. 3.

Fig. 4. Apparent Spontaneous Spasm

1. Uniform caliber of unstimulated artery which has recovered from the spasm seen below.
2. Apparent spontaneous spasm which occurred 20 minutes after dural opening.



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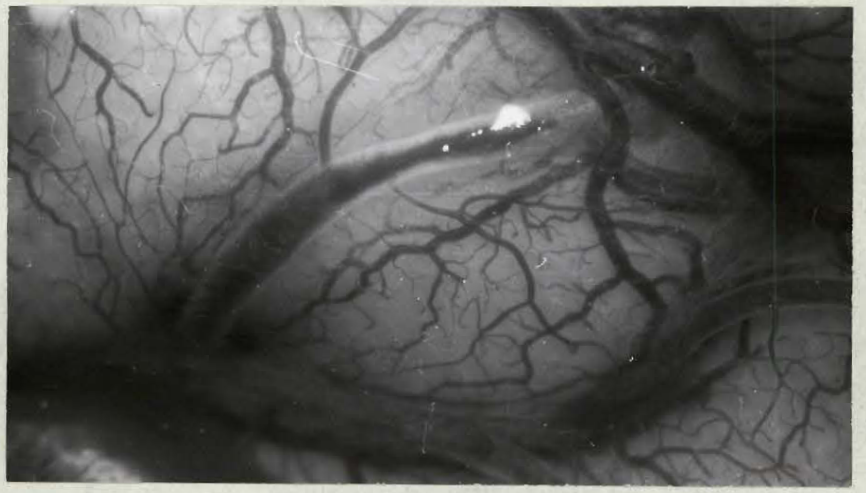

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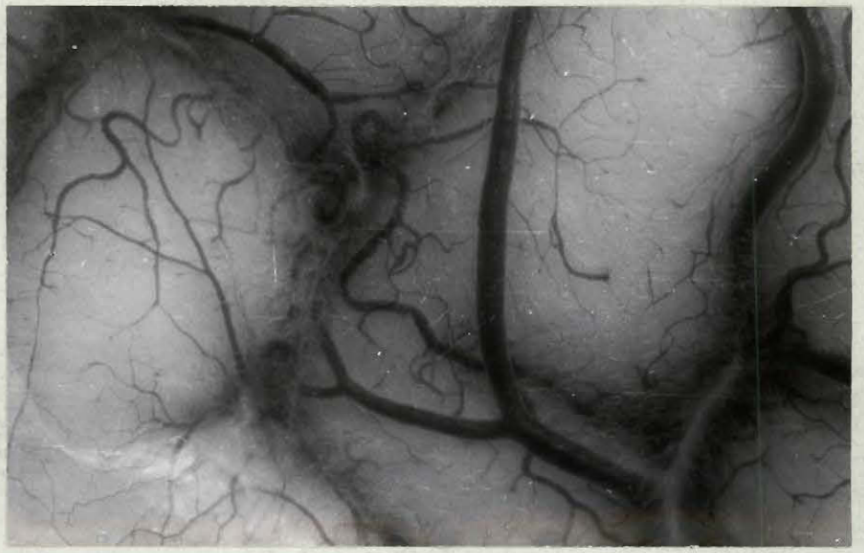
Fig. 4.

Fig. 5. Reaction of Vasculature to Exposure

1. Appearance of vasculature 1 min. after dural opening.
2. 20 minutes later the large artery is typically wider and the pial vasculature slightly flushed. Veins in this case are narrower.



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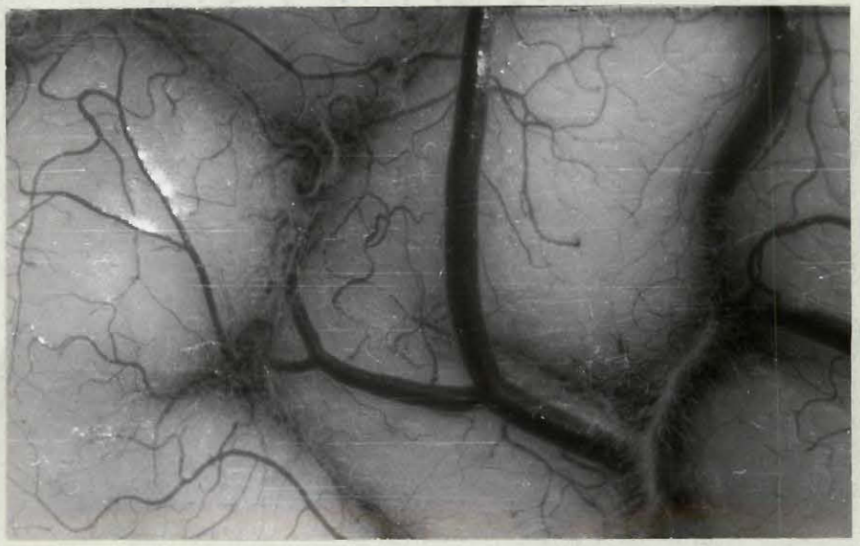

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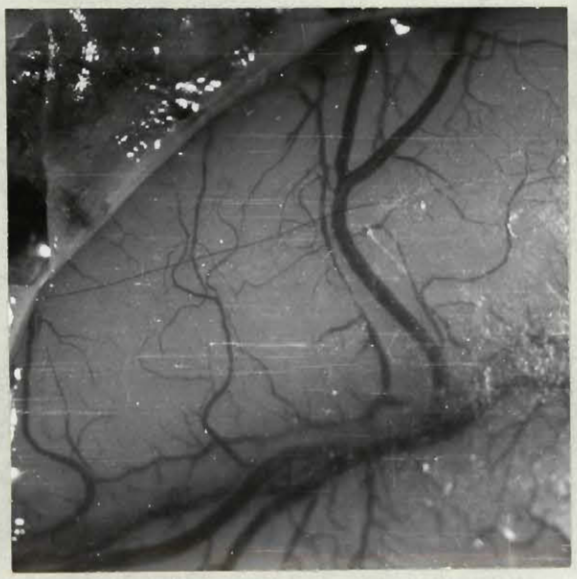
Fig. 5.

Fig. 6. Spasm in Chronic Sympathectomy

1. Unstimulated artery in cat which had an ipsilateral sympathectomy 3 weeks before.
2. Spasm 10 seconds after stimulus of 6 volts for 10 seconds.
3. 40 seconds after stimulus. Note indentations at sites where bipolar electrode touched the vessel.
4. 2 minutes after stimulus.



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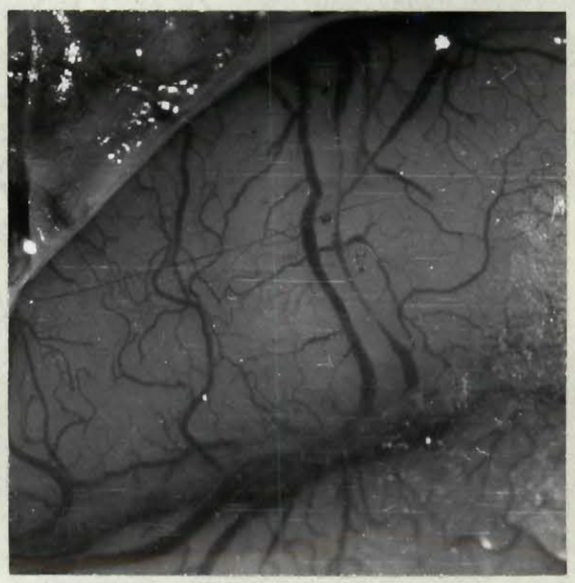

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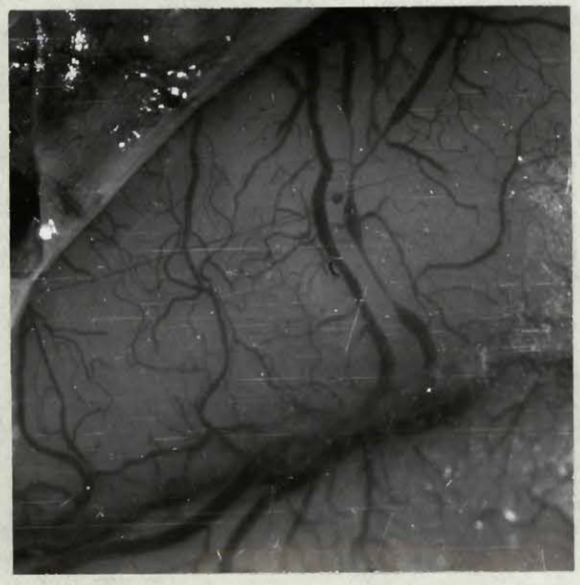

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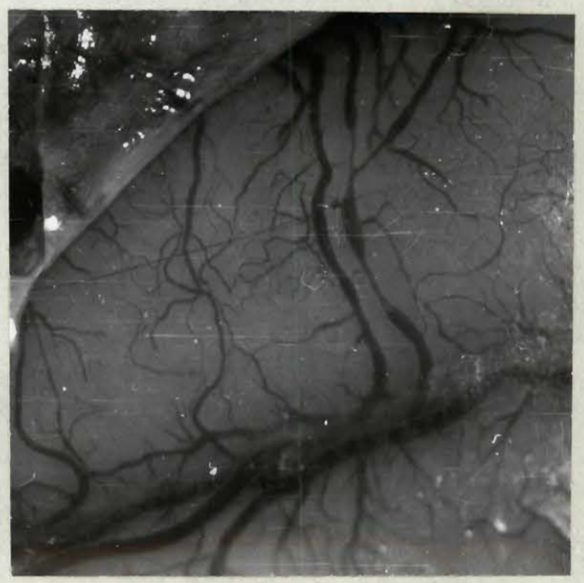
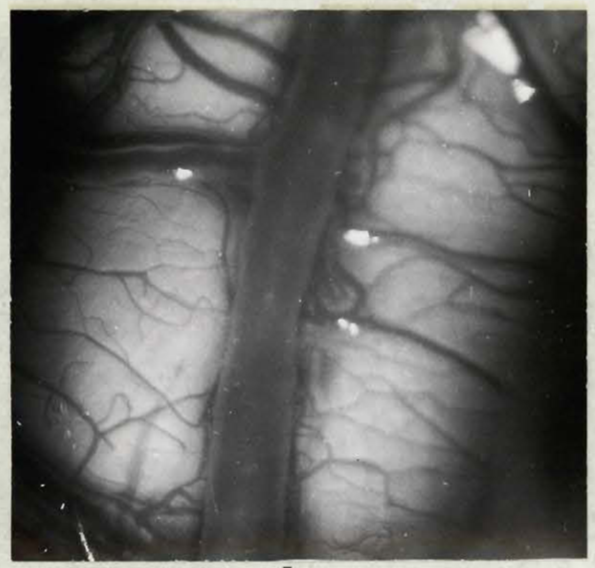


4.

Fig. 6.

Fig. 7. Spasm in Dog's Basilar Artery

1. Artery on ventral surface of pons shortly after the opening.
2. One hour after opening. Little change in caliber.
3. Spasm 10 seconds after stimulus of 6 volts for 10 seconds.
4. Spasm persisting 25 minutes after stimulus.
5. Relief of spasm and dilation of artery after 5 minutes application of a papaverine-nicotinamide mixture.
6. Following re-stimulation the artery remains dilated and is apparently unreactive to stimulus.



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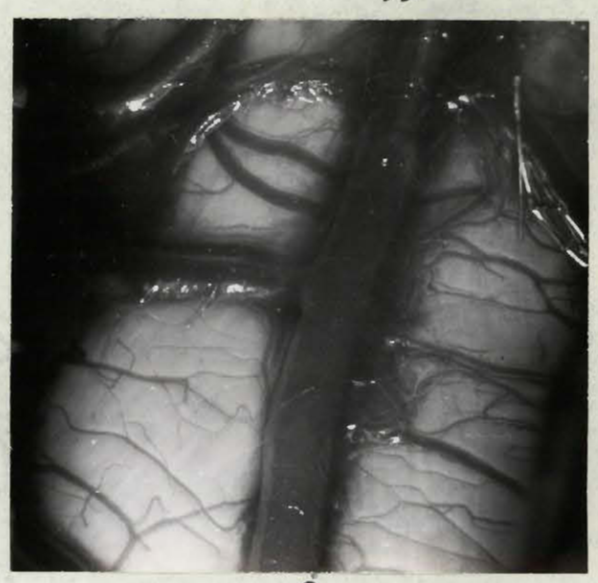

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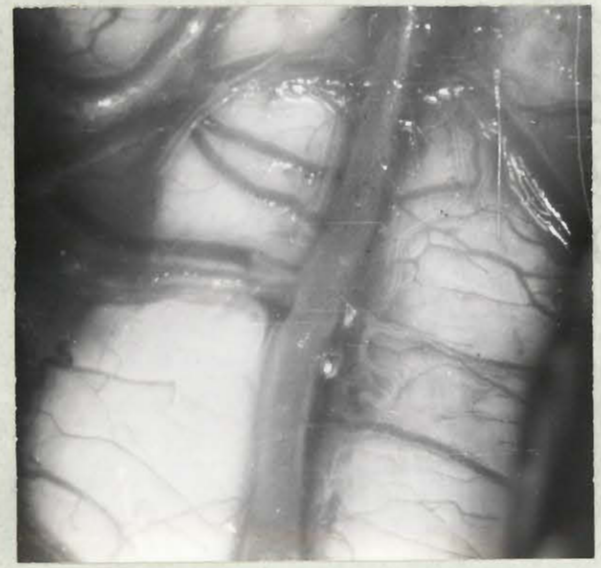

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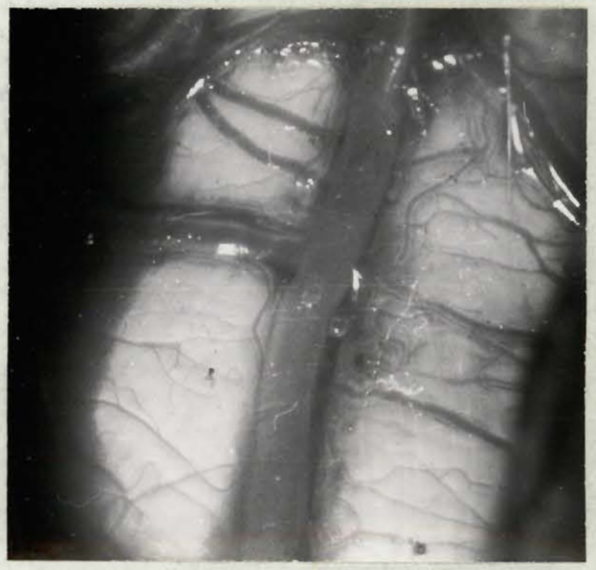

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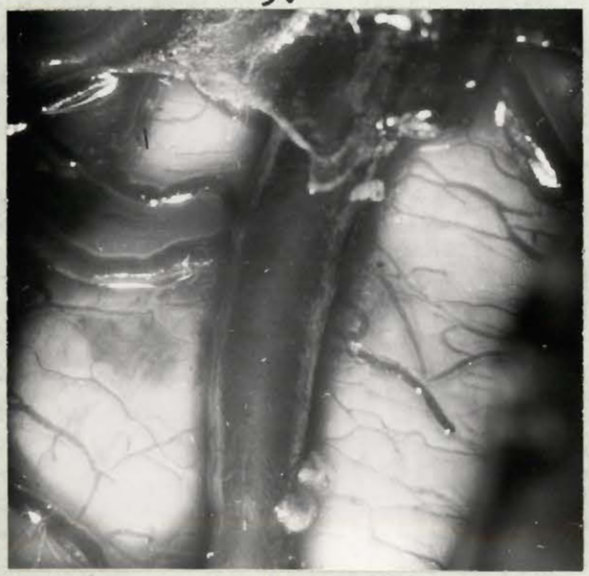

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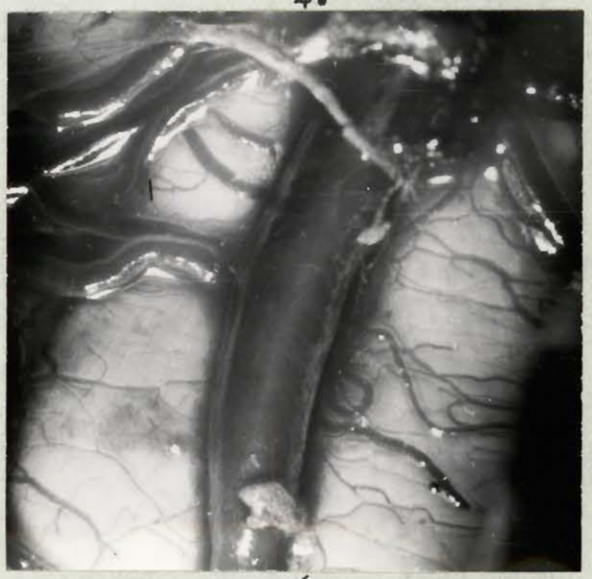

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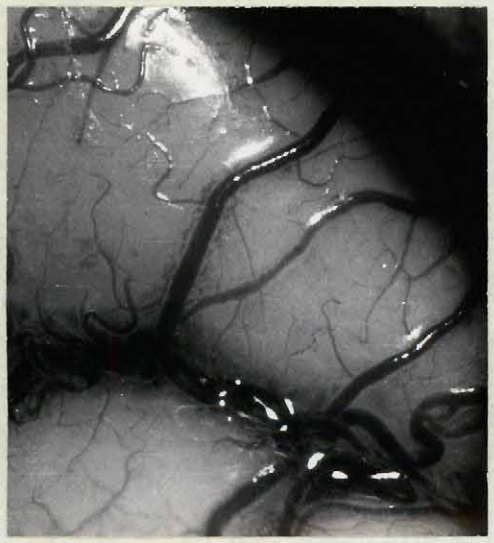
Fig. 7

Fig. 8. Effect of Papaverine

1. Cat's artery before procedure.
2. Same artery after 5 minutes application of 1.8% papaverine. The artery and background vasculature are dilated.
3. Slight spasm 10 seconds after 6 volt stimulus for 10 seconds.
4. 40 seconds after stimulus caliber is recovered. In an untreated vessel spasm would now be marked.
5. 10 minutes after stimulus there is a delayed spasm of the artery. This is not a constant occurrence after stimulation of a papaverine treated vessel.



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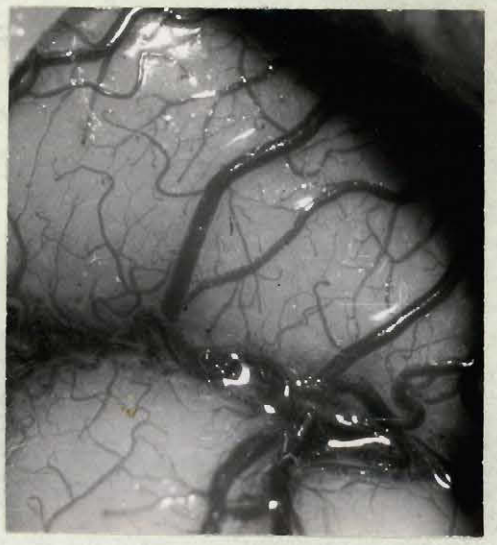

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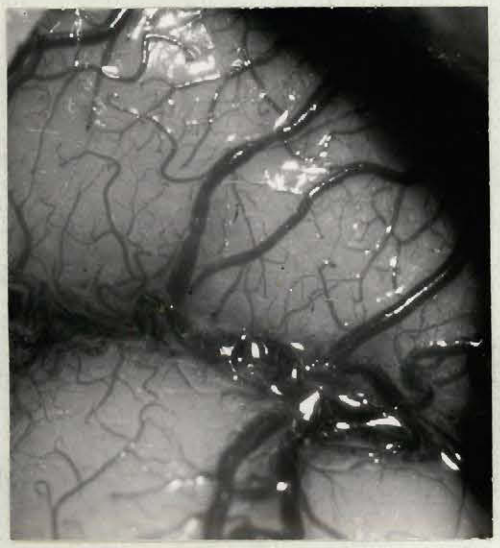

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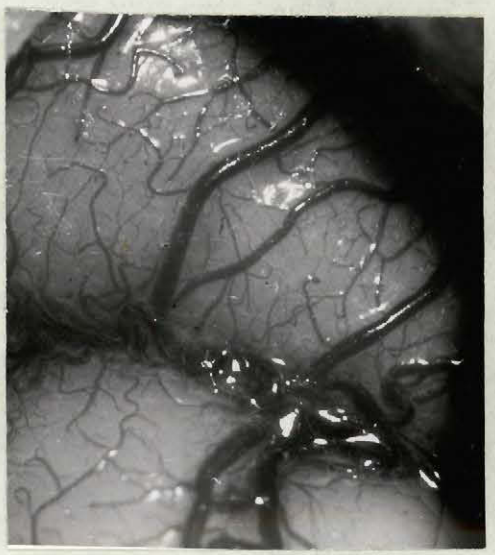

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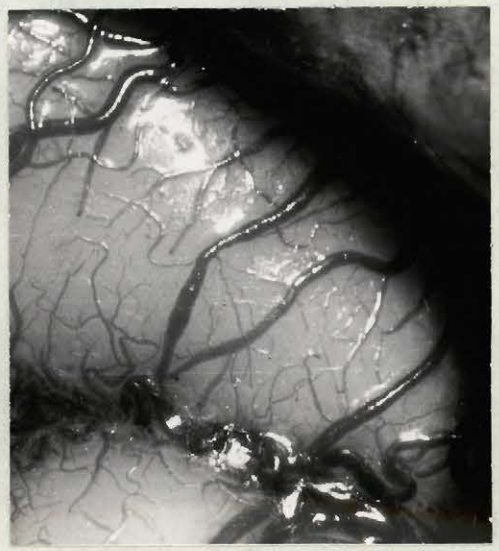

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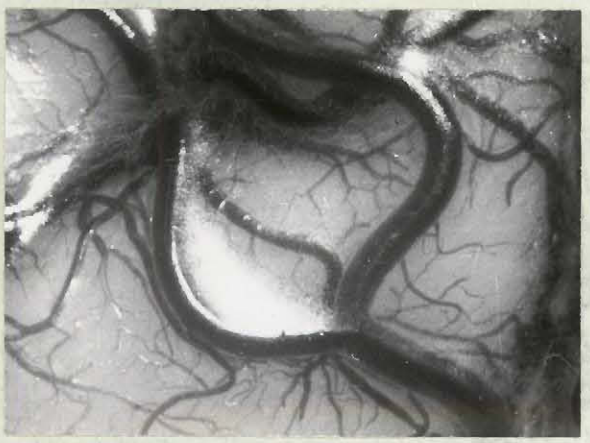
Fig. 8

Fig. 9. Relief of Spasm after Papaverine-nicotinamide Mixture

1. Untreated cat's artery with two approximately equal branches.
2. Spasm in right branch 10 seconds following its stimulation with 6 volts for 10 seconds.
3. Relief of spasm after 1 minute application of papaverine-nicotinamide mixture to the right branch.
4. Similar stimulation of left branch as a control procedure. Spasm 10 seconds later.
5. 2 minutes later.
6. 5 minutes later.
7. 10 minutes later.
8. 15 minutes later the spasm in the left branch persists.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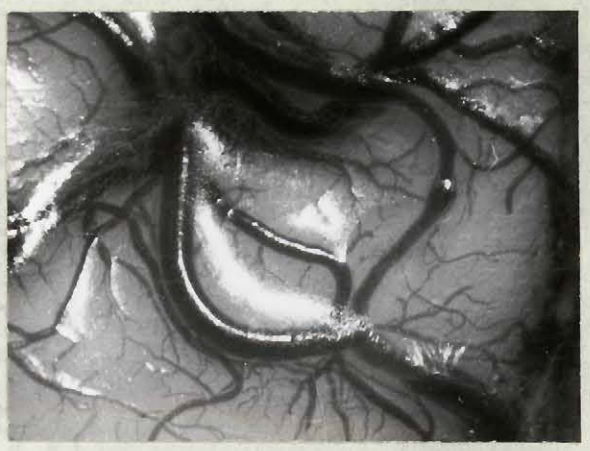
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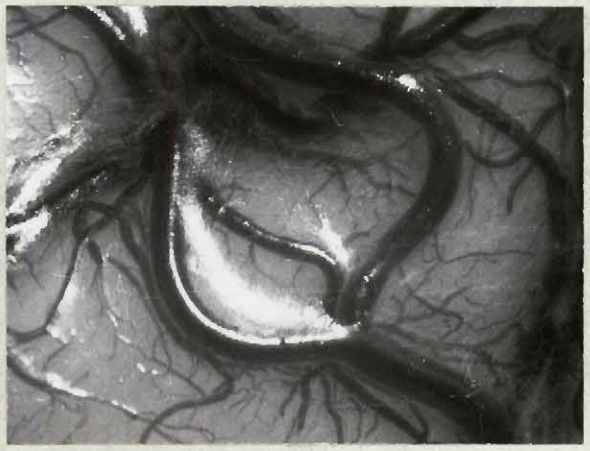
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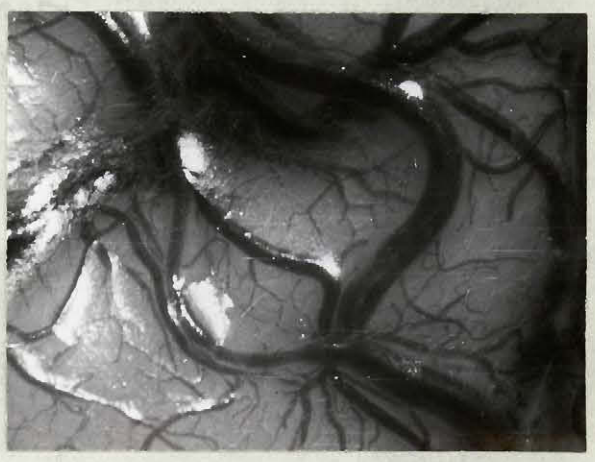
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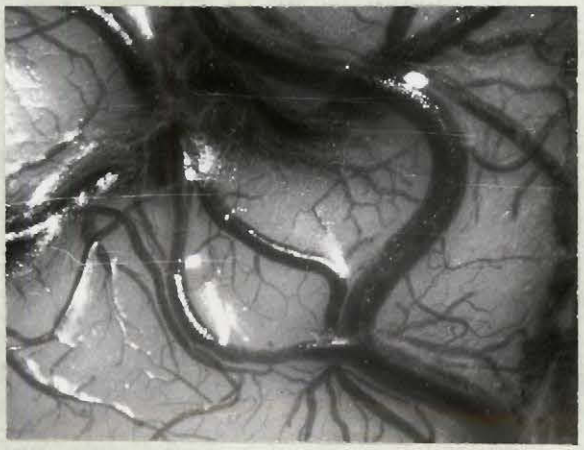
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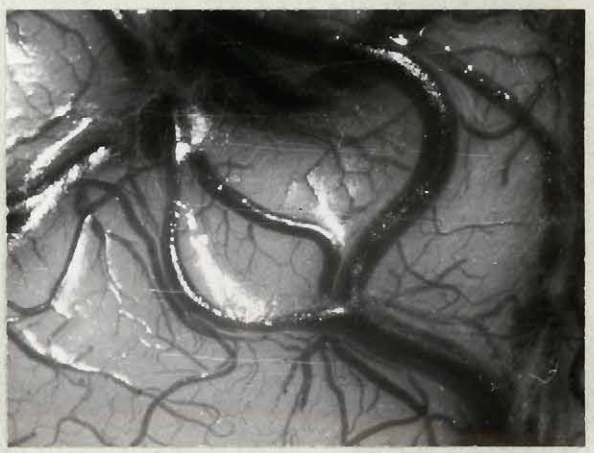
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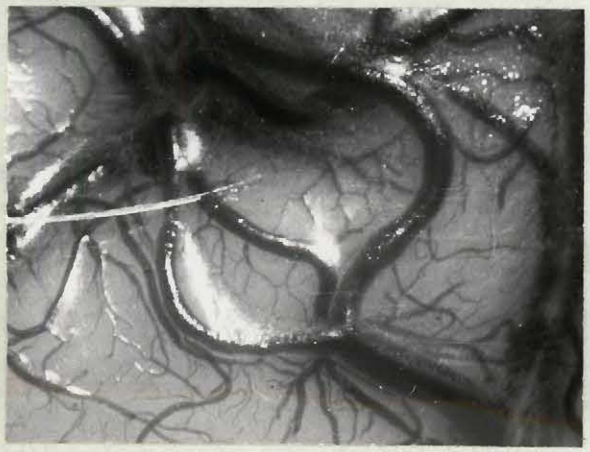
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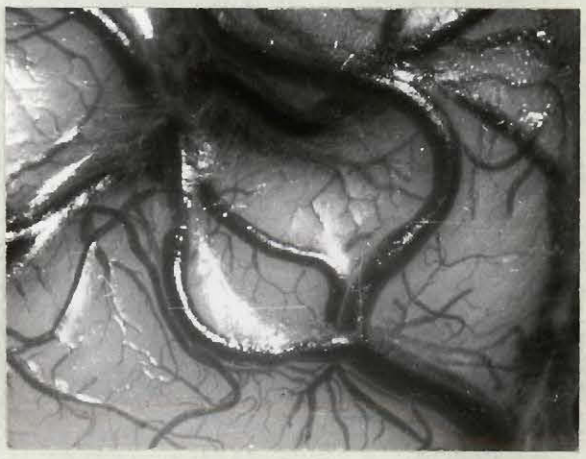
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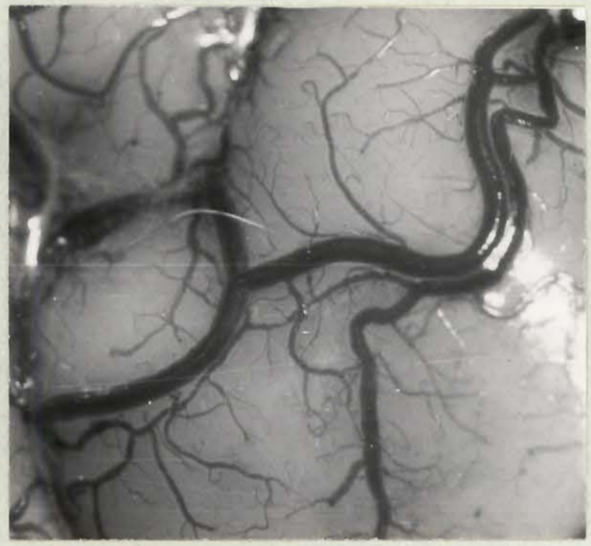
Fig. 9.

Fig. 10. Effect of 10% CO_2

1. Untreated cat's artery.
2. Following tracheotomy inhalation of 10% CO_2-90% O_2 mixture the artery is slightly dilated.
3. Spasm 10 seconds after stimulus of 6 volts for 10 seconds.
4. Spasm 40 seconds after stimulus. The CO_2 had no apparent spasm preventive action.



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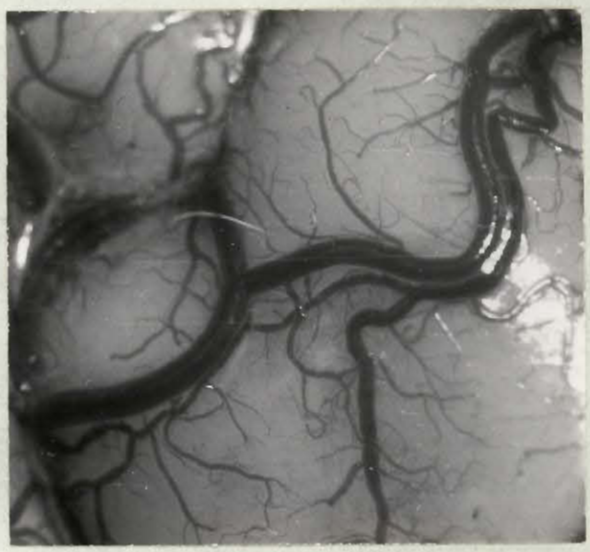

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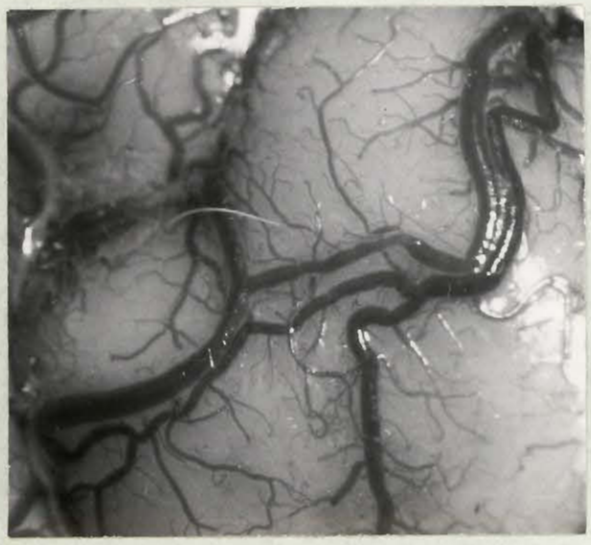

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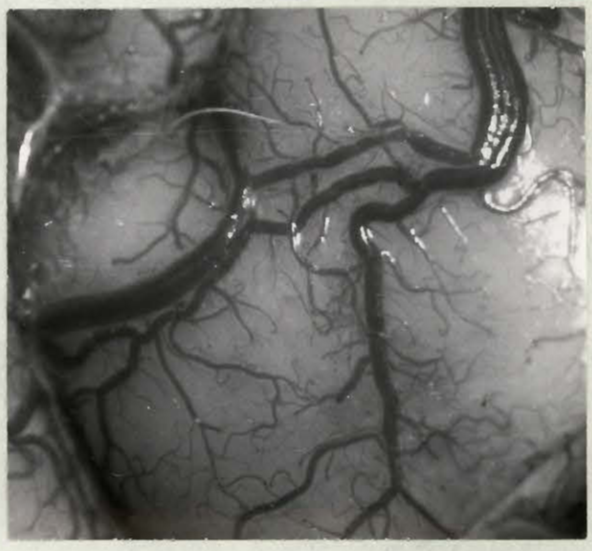

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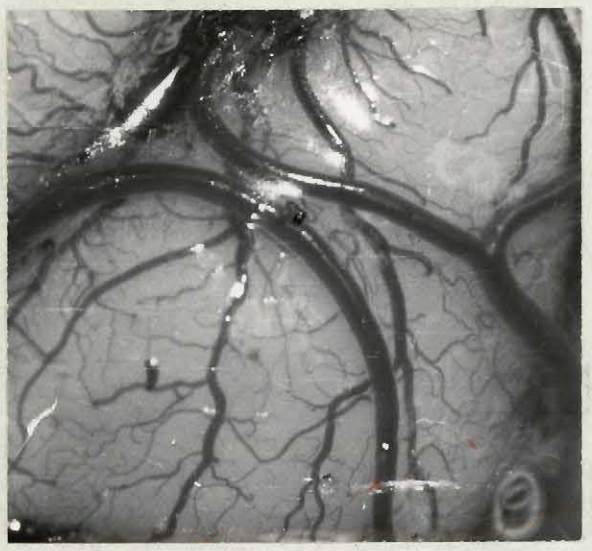
Fig. 10.

Fig. 11. Effect of Caffeine

1. Untreated cat's artery.
2. Dilation of vasculature after 5 minutes application of 25% caffeine sodio benzoate.
3. 40 seconds after stimulus of 6 volts for 10 seconds there is no spasm.
4. Delayed spasm beginning 3 minutes after stimulus.
5. 5 minutes after stimulus the spasm is more intense.



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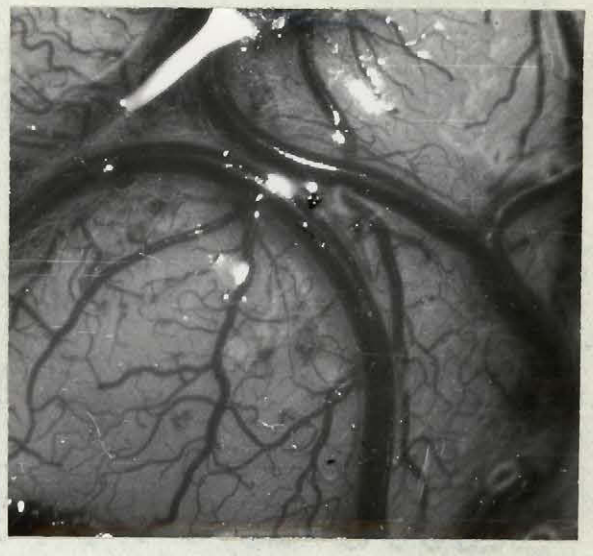

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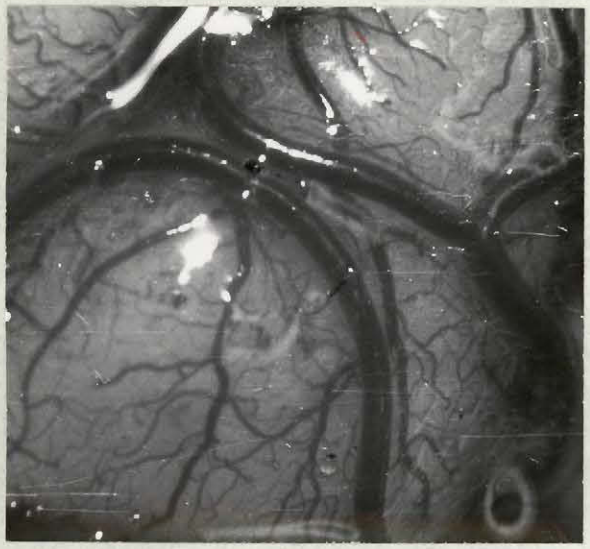

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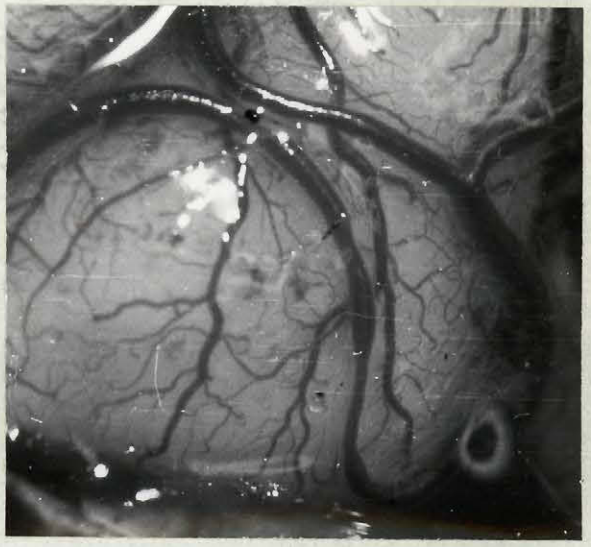

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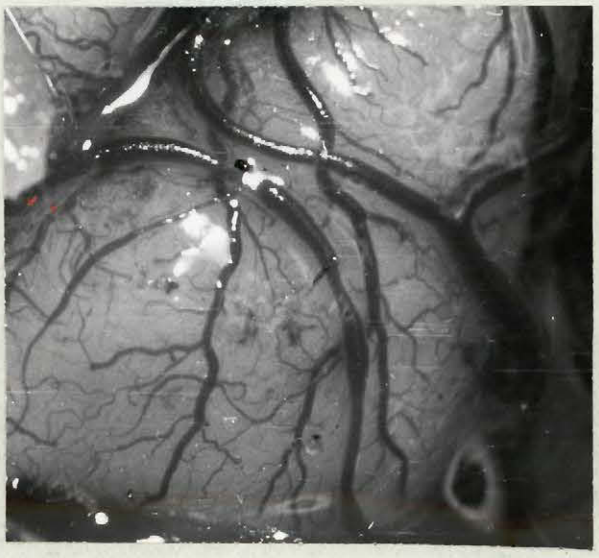

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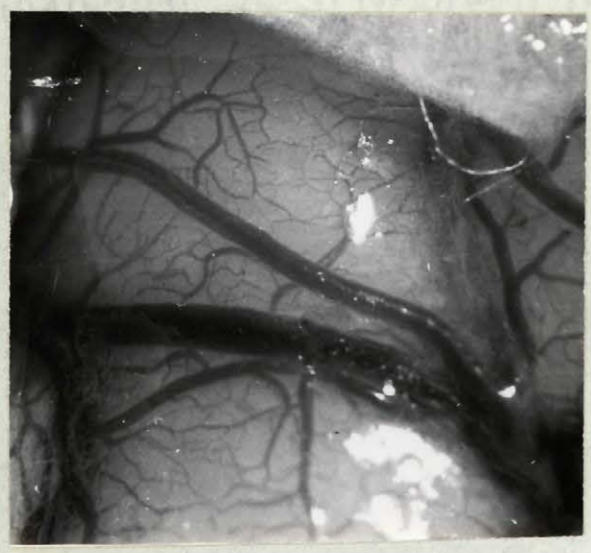
Fig. 11

Fig. 12. Spasm Preventive Effect of Rogitine

1. Untreated cat's artery.
2. Stimulation of the artery after 5 minutes application of Rogitine resulted in no spasm. This photo was taken 6 minutes after stimulus. Interim photos showed the same caliber.
3. Untreated central artery at about the same time in the same cat.
4. Similar stimulation resulted in immediate spasm. This photo taken 6 minutes after stimulus shows persistence of spasm.



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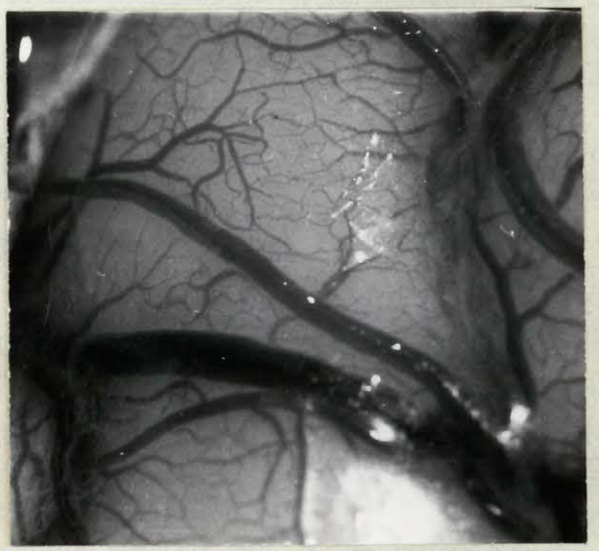

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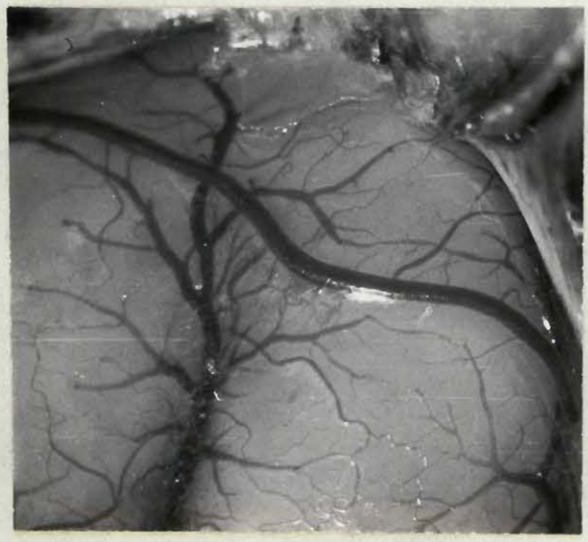

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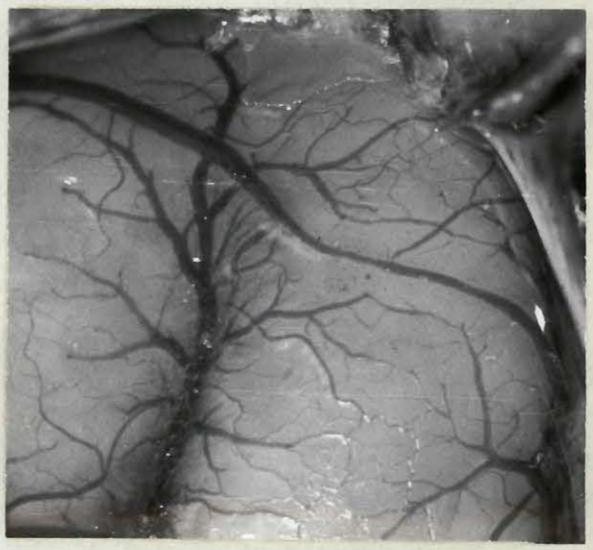

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Fig. 12.

Fig. 13. Spasm Relief by Rogitine

1. Untreated cat's artery.
2. Spasm 15 seconds following stimulus of 6 volts for 10 seconds.
3. Relief of spasm after 1 minute application of Rogitine.
4. 5 minutes after stimulation there is no delayed spasm.
5. Control artery at about the same time in the same cat.
6. Spasm 10 seconds following similar stimulus.
7. 40 seconds later.
8. 5 minutes after stimulation. The spasm persists in the control artery.

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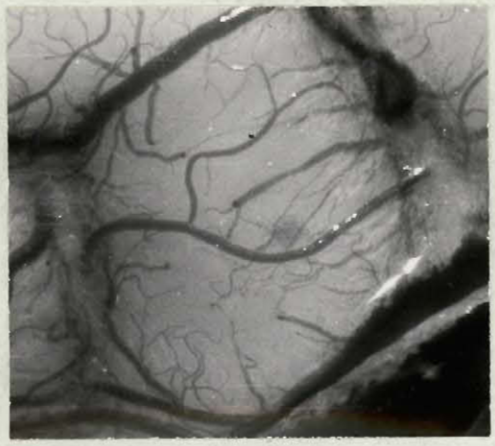

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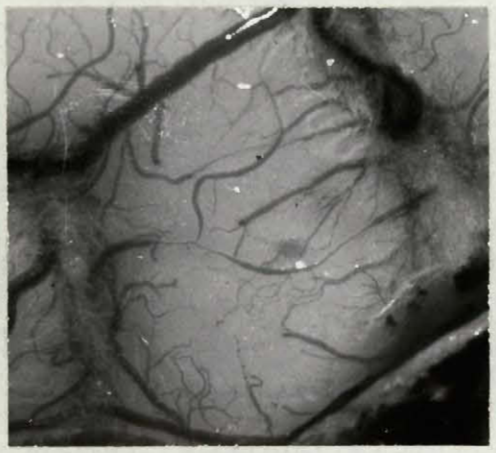

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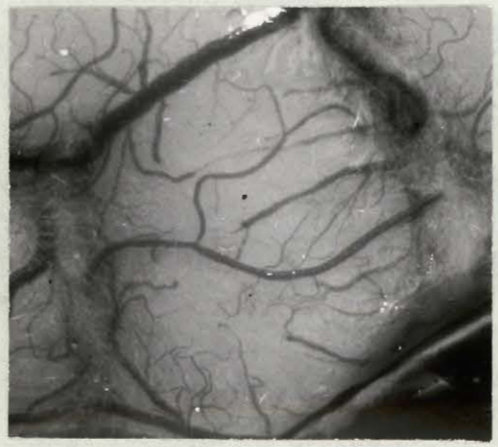

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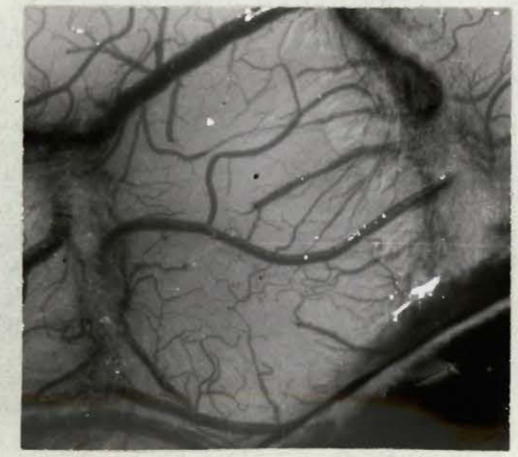

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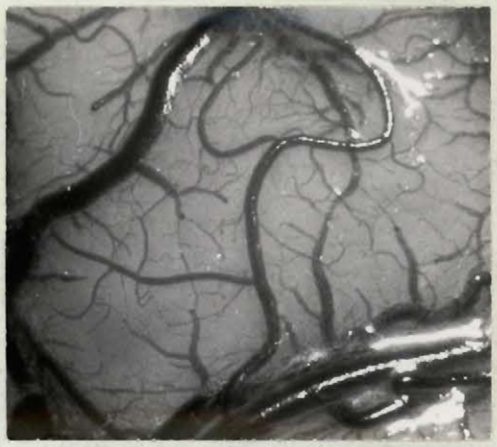

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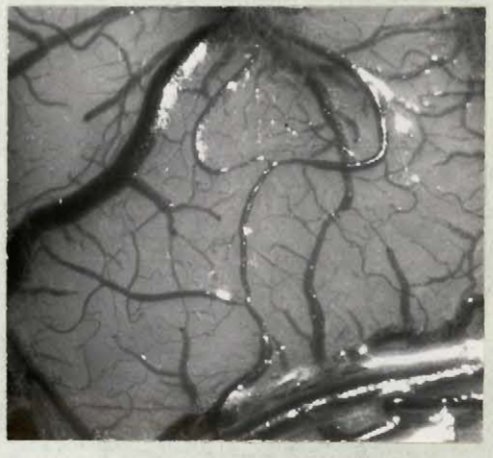

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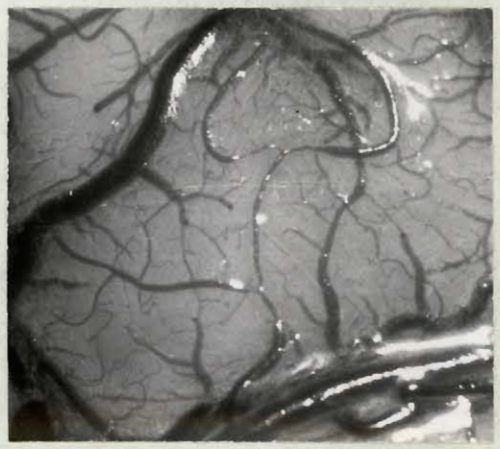

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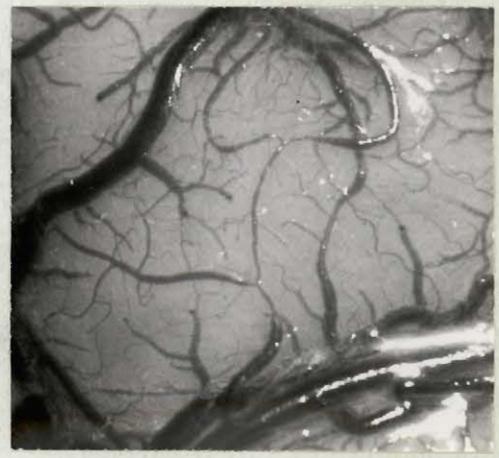

Fig. 13.

Fig. 14. Lateral Striate Arteries

The temporal lobe is strongly retracted with the tip of the retractor on the uncus. The middle cerebral artery is branching over the surface of the insula. The lateral striate branches of the middle cerebral artery are seen arising proximally and entering the anterior perforated space. They are just inferior to the limen insulae and between the uncus and the medial inferior frontal lobe. Running toward the uncus along the optic tract is the anterior choroidal artery and just proximal to its origin is the posterior communicating artery. Two branches from the posterior cerebral artery are seen entering the posterior perforated space just behind the mammillary bodies. The medial striate branches from the anterior cerebral artery are not seen.

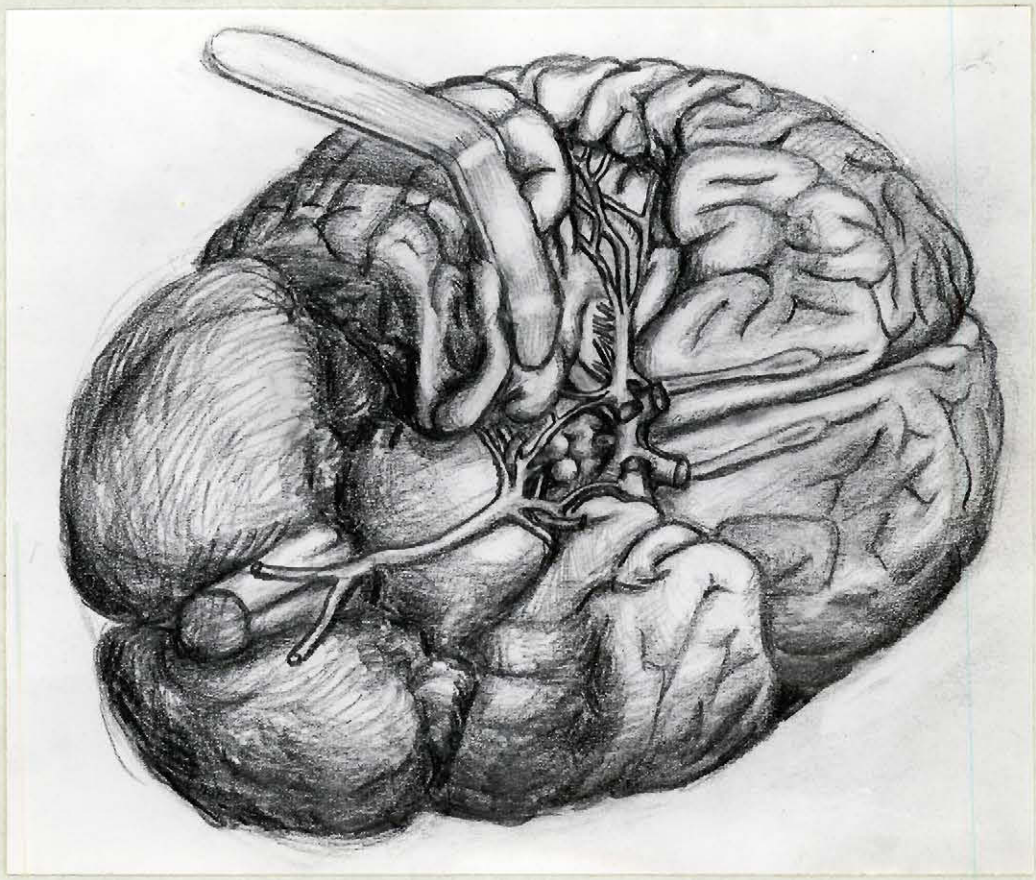

Fig. 14.

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