EFFECT OF VASOMOTOR NERVE SECTION ON EXPERIMENTAL EPILEPSY

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by

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Table of Contents

INTRODUCTION

Epilepsy (from the Greek ἐπιλεψία meaning "I seize" or "seizure") is defined by Lennox and Cobb (1928) as a "syndrome characterized by the sudden appearance of paroxysms, of which convulsive movements or loss of consciousness or both, are a principal element". This definition, although not including the purely sensory paroxysms which Hughlings Jackson emphasized as epilepsy, is accepted in this research, and a study is made of the epileptic syndrome as it occurs clinically in man and as it is produced experimentally in animals.

The work herein reported represents part of an experimental study of epilepsy which is being carried on in the Department of Neurosurgery. It is in part a continuation of the work of Evans (1930) on post-traumatic epilepsy and is in addition a study of the effect of resection of the cervical sympathetic ganglia and nerves and of section of the greater superficial petrosal nerve on epilepsy produced in monkeys and cats. The thesis underlying the work was briefly as follows:

1. Nervous control of the vascular supply to the brain must be regarded as an experimentally proven fact. (Lennox and Cobb (1928); Penfield (1931).)

2. The vasomotor mechanism of the epileptic convulsion as suggested by Brown-Sequard (1858), discussed by Hughlings Jackson (1863), and later elaborated by A. E. Russel (1909) and others becomes a definite possibility.

3. Influences which would produce unnatural stimulation

of the vasomotor nerves to the brain (contracting cerebral cicatrix pulling on vessels or nerves in the scar, lesions of the cervical sympathetics, endotoxins, exotoxins, etc.) could, theoretically, cause a vasomotor change which would in turn cause or enhance an epileptic seizure.

Following this reasoning the experimental approach readily suggested itself, for, if the source of the vasomotor nerve supply to the cerebral blood vessels were found and removed, improvement or cure of an existing epilepsy might be expected.

Forbes and Wolff (1928) showed definitely that stimulation of the cervical sympathetic nerve caused constriction of the pial arteries and that stimulation of the vagus in the neck caused dilatation of these vessels to a measurable degree. The cervical sympathetics are, therefore, one of the sources of vaso-constrictor fibers to the cerebral arteries, and on the basis of this information the following plan of experimental study was outlined.

Using cats (felès domesticus) and monkeys (macacus rhesus) for the experimental animals:

1. Determine the minimal dose of a convulsant drug (10% oil of wormwood in gum acacia emulsion by stomach tube for the cats, and 20% camphor ($C_{10}H_{16}O$) in olive oil intramuscularly for the monkeys) which will produce convulsions in each normal animal.

2. Operate upon the animal aseptically doing a craniotomy.

Then (a) determine the amount of electrical stimulation (galvanic and faradic) necessary to produce Jacksonian seizures, and (b) produce a brain wound in the fore-paw and face area of the motor cortex.

3. Allowing the animal a minimum recovery time of 5 weeks again establish the minimal convulsant dose of the drug, this to be called the first post-operative dose.

4. Again operate upon the animal, this time doing a complete cervical sympathectomy, taking out the superior cervical, the middle cervical (when present), and stellate ganglia, the chains, the vertebral branches, the branches to the carotids with any attached accessory ganglia, and the adventitial fibers of the carotid and vertebral arteries.

5. Allowing 10 days as a minimum recovery time establish the minimal convulsant dose of the drug, this to be called the second post-operative dose.

It was believed that this procedure should give physiological evidence of the effect, or lack of effect, which removal of sympathetic impulses to the cerebral arteries has on experimental epilepsy.

6. Using the surviving animals it was planned to cut such of the cranial nerves as the anatomical and histological studies being carried out in the Department of Neurosurgery by other workers might suggest as possible sources of origin for the cerebro-vascular nerve fibers.

7. Allowing a minimum recovery time of 10 days, again

establish the minimal convulsant dose of the drug, this to be known as the third post-operative dose.

8. Finally it was hoped to repeat the craniotomy in the animals of the brain wound series and again determine the amount of electrical stimulation necessary to produce a Jacksonian seizure, and thus use the electrical dosage as a check on the drug dosage.

In a second group of animals it was planned to omit the stage of craniotomy and to carry out procedures 1, 4, 5, 6 and 7 as outlined for group one.

It was hoped that this attack upon the problem of epilepsy would accomplish the following ends:

1. Supply experimental evidence concerning the value of sympathectomy in the treatment of epilepsy.
2. Furnish physiological evidence concerning the effect upon experimental epilepsy of cerebrovascular fibers coming from the cranial nerves.
3. Add information concerning electrical stimulation of the cortex and its use in the study of epilepsy.
4. Furnish additional data concerning the effect of brain wounds upon experimental epilepsy.

The experimentation as planned has been carried out in several animals and the procedures, results, conclusions, and protocols of the experiments are recorded in the chapters which follow. Observations on a number of additional animals are not complete as planned, and several animals have died

before complete observation could be made on them; but where conclusions are possible from the observations already made regarding either drug dosage, brain wound or sympathectomy, the protocols of these animals are included.

Chorobski (1931), in the Department of Neurosurgery, has found gross and histological evidence of nerve fibers from the greater superficial petrosal nerve to the internal carotid artery. On the basis of these findings we have cut this nerve in one of our animals and the results are included in the protocol.

The anatomical and histological studies concerning the sources of nerve fibers to the cerebral vessels will be recorded in another report from the Department of Neurosurgery.

CLINICAL EPILEPSY AND VASOMOTOR PHENOMENA

The relationship between epilepsy and vasomotor phenomena has long been recognized. In the first volume of the Journal de la Physiologie published in 1858, there is a résumé of Claude Bernard's original work on the sympathetic nervous system published that year (Comptes rendues des séances et memoires de la société de biologie, Paris, 1858, vol.iv, de la 2e serie) and in the same Journal Brown-Séquard (1858),p.203, states his belief that the exciting cause of the epileptic seizure may be an anaemia of the cerebral hemispheres due to vaso-constriction. He wrote as follows expressing his views:

"J'ai essayé d'établir avant Kussmaul et Tenner ces deux propositions fondamentales:

1) que dans la vertige epileptique avec ou sans convulsions les vaisseaux des lobes cérébraux se contractent et chassent le sang de cet organe, et y determinent en consequence l'état ou il se trouve dans une syncope.

2) que le crane ne permettant pas à la pression atmosphérique d'agir sensiblement sur l'encéphale, il suffisait que les lobes cérébraux reçussent moins de sang pour que la base de l'encéphale en reçût davantage ce qui, par suite de plusieurs raisons que j'ai mentionnées dans mon livre sur l'epilépsie, contribué à la production des convulsions."

Hughlings Jackson (1863) said the fundus oculi was pale before a fit but during the seizure the veins became large and dark. However, he introduced his remarks by the statement: "I have never had the opportunity of examining the retina during a fit of epilepsy under favourable conditions." He suggested that the sympathetic supply to the retinal artery and the cerebral vessels might be different from that to the meningeal vessels, the face, and the iris.

Echeverria in 1870, quoted by Levy and Patrick (1928), writing of epilepsy said: "Paroxysm may occur without muscular spasm; it does not, however, without a disturbance of the vasomotor elements in its inception; and hence paleness of the face or loss of consciousness or vertigo not infrequently are the whole symptoms of the epileptic attack in the early stage of the disease."

Echeverria (1870) quoted by Lennox and Cobb, described the optic disc just before a convulsion as pale with indistinct arteries.

Gowers (1881) discussed the theory of vasomotor spasm as a cause of convulsions bud did not lend his support in favour of the idea.

Horsley (1882) in vigorous fashion discredited the theory of cerebral anaemia as a cause of convulsions because, as he says, in his observations of the vascular supply of the nerve centres during fits started with absinthe, these nerve centres "so far from being anaemic, they are actually hyperaemic".

This description is typical of the cortex seen at the operating table in the middle of a convulsion, but this stage of hyperaemia as well as the immediate onset of the fit is usually preceded by a brief wave of cortical pallor while the pulsation of the cortical arteries has greatly diminished or ceased.

Pollock and Treadway (1913) indicated circulatory and respiratory changes which may occur in relation to epileptic convulsion. They reported the case of a patient with petit mal on whom they took blood pressure tracings and showed a rise in blood pressure from 26 to 60 seconds before convulsion, then preceding the convulsion by 9 to 12 seconds a fall in blood pressure which remained relatively low during the attack. The aura followed the blood pressure change and a period of apnoea in inspiration preceded the attack by 4 to 9 seconds.

Guillaume (1922) reported two cases of epilepsy, one following war injury and one with cerebral abscess, both of whom showed a marked rise in blood pressure, and pallor of the skin during the attack, followed by flushing and sweating after the attack. The cortex exposed at operation in each case during an attack showed a diminution in the calibre of the arterioles. During the tonic phase there was cyanosis and great engorgement of the veins, and then when the attack had ceased, one observed vaso-dilation of the arterioles and capillaries characterized by very noticeable augmentation of the calibre of the arteries and the rosy colour of the tissues which had replaced the cyanosis. Guillaume concluded that these observations seemed to indicate that the vasomotor phenomena in epilepsy are generalized (and not entirely limited to the brain) and that the vasomotor phenomena coincide with or precede the motor phenomena of the underlying muscles.

Kennedy (1923) described the pallor of the brain before a convulsion and suggested a vascular basis for the "spread" of a focal attack. He said: "such spread is too slow to be explicable by the passage of a nerve impulse and might well be dependent upon a quickly widening area of cerebral anaemia."

Riesman and Fitzhugh (1927) after presenting 12 cases of late epilepsy and suggesting a classification, state that they believe that moments of deranged cerebral circulation are responsible in part at least for the convulsions of epilepsia tardia.

Lennox and Cobb (1928) quote Horrax as telling of pallor of the brain followed by congestion and bulging, and Forster (1926) described a sequence of events repeatedly seen by him at the operating table: first the brain becomes pale and sinks away from the skull, then it is suffused with blood and bulges greatly as the convulsion starts.

Olkon (1927) reported the case of a boy of 13 who developed throbbing of the head and generalized convulsions. Polygraphic tracings with a manometric oscillometer gave unique tracings showing vascular intermittent tetanic spasms. Atropin gr.1/300 given twice daily made the patient attack-free. Olkon (1931) also reported the most interesting occurrence of epilepsy of angiospastic variety in monozygotic twins. The two boys developed true epilepsy with attacks which appeared simultaneously or within twenty-four hours of each other. Laboratory studies were negative but examination of the capillaries of the nail beds showed striking similarity of pathology and the capillaries became spastic during an attack and some ruptured. Under antispasmodic treatment of 5 minims of tincture of Belladonna 4 times daily and 10 grains calcium lactate daily, the twins became attack-free and have continued so for three years.

These clinical observations furnish confirmation that one factor associated with the initiation of convulsions is cerebral vasomotor change. Further consideration of the literature reveals additional evidence concerning the subject.

Physiological Evidence

In 1830 Bracket, after cutting the cervical sympathetic chain and extirpation of the superior cervical sympathetic ganglion, noted a dilatation of the pial vessels on the same side (in a dog). Callenfels (1855) found in 2 of 12 rabbits that stimulation of the cervical sympathetic caused homolateral constriction of the pial arteries followed by dilatation; and Ackerman (1858), using a skull window, found that section of the cervical sympathetic nerve caused dilatation of the vessels on the same side and that stimulation caused constriction. Donders (1859) through a closed window in the skull observed on stimulation of the cervical sympathetic nerve in the neck a constriction of the pial arteries followed by dilatation. Nothnagel (1867) noted dilatation of the pial arteries on the side of the transected sympathetic nerve of the neck. Faradic stimulation of the cut nerves caused constriction of the pial arteries, as did stimulation of sensory nerves as well. The findings of these workers and the views of Brown-Sequard favouring arterial spasm as the initiating factor in convulsions furnished an important basis for the early section and avulsion of the cervical sympathetics in the treatment of epilepsy.

Alexander in 1883 performed the first cervical sympathectomy for this purpose. Winters (1902) and, as I shall show later, many other operators, followed his example by performing this operation in the last three decades of the 19th century.

There was, however, another side to the question of vasomotor control of cerebral vessels and many outstanding workers believed no such control existed. Schültz (1866) in experiments on rabbits observed neither contraction nor dilatation of the pial vessels following cutting and stimulation of the cervical sympathetic and the effect on the vessels of the ear was only barely demonstrable. From these observations Schültz concluded that the motor nerves to the pial vessels of the rabbit only pass through the cervical sympathetics in an abnormal manner. Riegal and Joly (1871) in a large series of animals could note only the slightest change in the degree of filling of the cerebral vessels after cutting the cerebral sympathetic chain. Hürthle (1889) confirming the result of Riegal and Joly, found no marked change in the vessels of the ear or in the pupil on stimulation of the central end of the cut cervical sympathetic, and agreed with the conclusion of Schültz. However, in his research with measuring the pressure in the central and peripheral ends of the carotid, Hürthle stated that the "results speak unequivocably that the cervical sympathetics carry vasomotor fibers for the cerebral vessels of the same side, this being true for the rabbit, cat and dog."

Roy and Sherrington (1890) after a series of experiments on dogs concluded that the changes in cerebral blood pressure and blood flow followed and were dependent upon changes in systemic blood pressure. Secondly, they concluded that there

was no evidence that vasomotor nerves to the brain were to be found outside the cerebro-spinal cavity and that there was no reason to believe that vasomotor nerves were to be found in the nerves to the neck.

Leonard Hill (1896) in his monograph on the cerebral circulation reviewed the Munroe-Kellie doctrine of invariability of the intracranial blood quantity and agreed with it. He sketched the work which had been done on cerebral circulation and quoted experiments which he and Bayliss had carried out. He them summarized his conclusions on the cerebral circulation as follows:

"1. No evidence has been found of the existence of cerebral vasomotor nerves, either by means of stimulation of the vasomotor centre, or central end of the spinal cord after division of the cord in the upper dorsal region, or by stimulation of the stellate ganglia, and, that is to say, the whole sympathetic supply to the carotid and vertebral arteries.

2. Evidence is not forthcoming of the existence of any local vasomotor mechanism.

3. In every experimental condition the cerebral circulation passively follows the changes in the general arterial and venous pressures. The intracranial or cerebral venous pressure varies directly and absolutely with general venous pressure, but only proportionately with general arterial pressure.

4. The intracranial pressure is in all physiological conditions the same as the cerebral venous pressure.

5. The volume of the blood in the brain is in all physiological conditions but slightly variable.

6. There is no compensatory mechanism by which the intracranial pressure is kept constant. The intracranial pressure or cerebral tension, which in all physiological conditions is circulatory in origin, may vary with the circulatory pressure from zero to 50 millimetres mercury. The functions of the brain matter continue in this varying condition of pressure.

7. In all physiological conditions a rise of arterial pressure accelerates the flow of blood through the brain and a fall slackens it. The cerebral circulation is controlled by the vasomotor centre acting on the splanchnic area.

8. There is no evidence of the causation of cerebral anaemia by spasm of the cerebral arterioles.

9. Arterial hyperaemia of the brain produces no experimental results of importance. Cerebral venous congestion, on the other hand, is of great pathological significance."

Hill's conclusions, although some of them have since been proven incorrect, had a definitely unfavourable influence upon the use of cervical sympathectomy in the treatment of epilepsy, and certainly, if the conclusions were true, cervical sympathectomy had no physiological basis. The total

extent to which Hill's monograph effected the use of sympathectomy we can only conjecture, but as Mosser (1926) points out, there was a distinct decline of interest in sympathectomy from 1905 to 1915.

Now the pendulum of cerebrovascular physiology has again swung to the side favouring sympathetic control of cerebral vessels and interesting new work has recently been reported on the subject. Muller and Siebeck (1907) carried out experiments which indicated that there was a distinct and fairly rapid increase in the volume of the brain after section of the cervical sympathetic, the systemic blood pressure remaining at a constant level. In 1908 Webber experimenting with cats found a decrease in brain volume in 75% of his animals following stimulation of the cervical sympathetic. He criticized Hill's method because it did not take into account changes in pressure due to increase in the amount of cerebrospinal fluid, a factor which might well mask the effects of vascular change as determined by Hill. This work of Webber seems to have had little consideration until its merits were emphasized by Lennox and Cobb (1928).

The conflict of opinion concerning the presence or absence of nervous control of cerebral vessels existed up to the time of the publication of a series of papers from the Neuropathological Laboratory of Harvard University. (Forbes (1928); Forbes and Wolff (1928); Talbott, Wolff and Cobb (1929); and Cobb (1929)).

Forbes (1928) by means of an ingenious apparatus which

he devised was able to study, measure, and photograph the vessels of the pia in cats. Spinal fluid pressure and systemic blood pressure were recorded at the same time as vessel measurements were taken. By means of Forbes' apparatus, he and Wolff (1928) made an extensive study of the effect of stimulation of the cervical sympathetics and the vagus, and the effect of adrenalin locally and in the blood stream. The results of their experiments are most striking:

1. "Sympathetic stimulation was followed by constriction of arteries in the pia in each of the 23 animals examined. In 75 trials in which there was no fall in blood pressure, constriction of at least sufficient extent to be accurately measured (9 microns or more) was noted in 87%, and constriction of 13.5 microns or more in 60%".

2. "Vagus stimulation was followed by dilatation of pial arteries, of the same size as those just mentioned in 12 of the 13 animals examined. A sudden and often striking fall in general systemic arterial pressure occurred in almost every case. Of the 35 trials 97% showed dilatation of 9 microns or slightly more, and 87% showed dilatation of much more than that amount."

3. "Change in diameter of the pial arteries was not noted after stimulation of the vagus or the cervical sympathetic nerve on the opposite side of the head from that of the observed vessel. It was interesting, however, that stimulation of the nerve either on the right or on the left

was followed by an equal fall in intracranial pressure."

4. "Local irrigation with epinephrine (1:10,000 in 7 cases; 1:250,000 in 2 cases; and 1:500,000 in 3 cases) beneath the cranial window - i.e., directly over the surface of the pia, was not attended by an appreciable change in systemic blood pressure but was followed by constriction of the pial artery (bathed by the epinephrine solution) in each of the 11 trials. Once at least constriction of a pial vein also resulted. Intravenous injection of epinephrine, on the other hand, often caused a great rise in systemic arterial pressure, and, coincidently, a dilatation of the pial arteries. When the blood pressure began to fall, though it was still far above the initial level, a true constriction of the pial artery (the diameter now being less than the initial) was noted in 5 of 5 trials. Injections of epinephrine into the carotid artery always caused a constriction of the pial artery, in spite of the coincident rise in the blood pressure."

(Note: Forbes' and Wolff's paper appends a complete resume and bibliography of the literature on cerebral vasomotor phenomena.)

Talbott, Wolff and Cobb (1929) found that cutting the cervical sympathetic nerve causes an increase in the capillary bed of the homolateral cerebral hemosphere as measured by microscopic counting of the capillaries in sections of the brain tissue following injection of the vessels of the head with 2% aqueous solution of Berlin blue.

These workers in Cobb's laboratory have furnished conclusive evidence of the relationship between the cervical sympathetics and the intracranial vessels.

Anatomical Evidence

Turning again to Hill's (1896) monograph we find (page 45) the following statement: "In a recent and exhaustive research, Gulland has failed to demonstrate by every known histological means the existence of any vasomotor nerves in the pial vessels."

Lennox and Cobb (1928, page 53) write concerning this quotation: "The last statement quoted from Hill, to the effect that no nerve fibers have been found going to cerebral vessels has been proved erroneous. In fact, Gulland, who did the histological studies for Hill in 1895 and found no nerves, published a paper in 1897 retracting his statement and showing that nerves are present. In a letter to Dr. J. W. Courtney in 1899, Gulland says: "I am afraid there is no doubt about the nerves on the intracranial blood vessels. Their actual distribution and arrangement are very much the same as those on other vessels, except that they are perhaps a little more scanty. I'm rather sorry I've found them, for the discovery rather takes the legs from Hill's and Bayliss' work, but you may take it from me that they are there"." However, as Lennox and Cobb point out, histological methods do not differentiate between motor and sensory nerve fibers.

Huber (1899) described nerves of two kinds on pial blood vessels: a) medullated fibers which terminated in non-medullated branches and which he considered sensory and b) non-medullated nerves which he considered vasomotor. Stöhr (1922) published illustrations of nerves and nerve endings on the fine pial vessels. In 1928 he published beautiful illustrations of rich plexuses of nerves on arteries, veins and capillaries in the pia and in the chorioid plexuses of the ventricles, and he also described nerve endings. In 1931 he called attention to the fact that many of these nerve endings on the chorioid plexus are sensory and he suggested that they may serve as the afferent portion of a circulation regulatory mechanism.

Kolliker (1893) mentioned nerve fibers entering the brain upon blood vessels of a diameter of 90 micra and less and Hunter (1900) stained a delicate plexus which seemed to be nervous in nature upon vessels of the cerebellum and brain stem of young rabbits, but he could not follow such a plexus into the white matter of the cerebrum. Clarke (1928) demonstrated perivascular nerves in the medulla and spinal cord of cats and dogs but failed to stain them elsewhere in the central nervous system.

Penfield (1931), with a modified silver impregnation method worked out in his laboratory, demonstrated that nerve fibers can be found and appear essentially the same in the vessels of the various areas of the cerebrum, cerebellum, medulla oblongata, and spinal cord. He showed that the

"nerve fibers are continuous with those of the pial vessels and they often pass irregularly around an artery or arteriole, giving off numerous collaterals and forming a loose net. They may course like a long thread upon the artery, gradually passing about it but without branching. These fibers may lie upon or in the adventitia, but on the smaller arteries they run between the adventitia and media."

Penfield stated: "Study of the intracerebral vascular nerves following sympathectomy in a number of animals indicates that their parentage is not altogether in the sympathetic ganglia. The same conclusion was reached tentatively in regard to the pial vascular nerves by Huber (1899) after extended experimental work." He then concluded: "The intracerebral and intramedullary arteries (and to some extent the veins) are innervated in a manner similar to that of the blood vessels of the pia mater, and the two nerve plexuses are continuous. From a purely morphological point of view, intracerebral vasomotor reflexes are possible."

This review of clinical, physiological and anatomical evidence indicates clearly that an epileptic seizure resulting from cerebral vasomotor change is a reasonable possibility. It also is reasonable to believe that the removal of sympathetic constrictor influence from the cerebral vessels should prevent their constriction and thereby avoid convulsions due to this cause. The following review of the literature of cervical sympathectomy in the treatment of epilepsy illustrates the application of this reasoning.

William Alexander in 1883 performed the first cervical sympathectomy for the treatment of epilepsy. Having reached the conclusion that an important factor in initiating an epileptic seizure is abnormality of the blood supply to the brain he had (1881) tried ligation of the vertebral artery on one side in three cases of epilepsy. The success which attended ligation of this vessel in the early cases encouraged further use of the procedure, and in 1882 he enthusiastically reported the cure of a number of patients with epilepsy by ligation of one or both vertebral arteries. In the last paragraph of his report (1882) Alexander calls attention to the fact that in his patients whenever he ligated the vertebral artery there was contraction of the pupil on the side of ligation. He wrote concerning this observation:

"The inferior cervical ganglion rests upon the carotid and sends branches along these vessels. These branches are included in the ligature and somehow affect the pupil. Or is the pupil affected by a change in the circulation at the base of the brain? "

Alexander exchanged vertebral ligation for sympathectomy after concluding that his beneficial results were due to the sympathetic paralysis following ligation. It was not until 1889 that he published his book, "The Treatment of Epilepsy", concerning the results which he had obtained by sympathectomy.

Following Alexander's leadership, operations of various kinds were performed upon the sympathetics of the neck. In

1889 Baracz reported one case in which following the ligature of the vertebral arteries he had resected the superior and inferior vertebral ganglia. In 1892 Jaksch reported two cases in which in addition to ligation of the vertebral arteries the inferior cervical ganglion was removed. Kümmel (1892) reported a unilateral resection of the superior ganglion and Bogdanik (1893) reported a case in which bilateral resection of the middle cervical ganglion had been carried out. Péan (1897) and Jaboulay (1893) each reported a case in which the cervical sympathetic nerve had been merely sectioned.

These occasional cases had very little influence on the general treatment of epilepsy by the medical profession, but at the meeting of the Surgical Congress in Paris in December of 1896, Thomas Jonnesco reported the results he had obtained by use of his methods of sympathectomy. Jonnesco (1897) favoured bilateral removal of all three cervical sympathetic ganglia and the complete chains. He (Jonnesco - 1899) expressed the theoretical basis for his operation in the following manner.

"Bei der Epilepsie wollen wir eine tiefgehende Anderung der Hirncirkulation herbeiführen, indem wir die cerebrale Anämie in eine permanente Kongestion umwandeln,- eine Kongestion, die die schlechte Ernährung der Nervenzellen verändert oder dieselben von den toxischen Produkten befreit. In anderen Fällen, bei der Visceren zum Hirn laufenden

Reizungen ändern."

He then further explained his operation for the removal of all three ganglia as follows:

"Denn die Resection des oberen Ganglion hebt die Vasomotoren des Carotis-Gebiets auf, die des unteren Ganglion dieselben Nerven des vertebralen Gebiets, man muss also beide entfernen, um eine möglichst vollkommeme Zerstörung der Vasomotoren beider vasculären Gebiete zu Stande zubringen. Auch muss man, um die Unterdrückung der Leitungswege der visceralen Reizungen zum Hirn zu erhalten, sowohl die praevertebralen wie auch die intervertebralen Nerven den ganzen Halsympathicus, entfernen."

This very reasonable presentation may well be called the first step in the understanding of sympathectomy as a treatment for epilepsy.

In 1902 Winter collected the cases of sympathectomy which had appeared in the literature up to that time. He found 213 cases of sympathectomy from which he eliminated 91 cases because post-operative observation was too short or too incomplete. The remaining 122 cases (reported by 22 operators) are included in his summary. I have included Winter's collected cases (reading the original case reports where possible) and have reviewed the additional cases of sympathectomy which I have found in the literature.*

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* The following references have not been available up to the time of this thesis and are therefore not included.

Winter's Table

OPERATOR	Number of Operations	Cured	Preliminarily Helped	Improved	Without Change	Died	Sum of Cases Completely Followed	Without Further Observation
Baracz	1				1		1	
Alexander	24	4	2	3	13	1	23	1
Jaksch	2		2				2	
Kümmel	1			1			1	
Bogdanik	1			1			1	
Péan	1				1		1	
Jaboulay	16		1	4	10	1	16	
Jonnesco	96	4	8	7	11	3	33	63
Minin	1				1		1	
Bayer	1				1		1	
Chipault	26		3				3	23
Donath	3				3		3	
Schapiro	1				1		1	
Ricard	1				1		1	
Patemsky-Sciamanra	7			1	6		7	
Bourneville	1				1		1	
Deschamps	2						2	2
Souques	1				1		1	
Dejerine	1				1		1	
Braun	9			3	4	2	9	
Marian	8			2	6		8	
Winter	9		1	1	5		7	2
TOTAL	213	8	17	23	67	7	122	91
PERCENTAGE		6.6	13.9	18.9	54.9	5.7		

Winter states that he has placed in the "Cured" column only those cases which have remained attack-free for three years or more. Of these Alexander had 4 and Jonnesco 4, making a total of 8, or 6%. Alexander and Jonnesco each had one case attack-free for four years. In the column "Preliminarily Cured" are the cases that had remained attack-free up to the time of the publication of the report and had been observed for a period of eight months to two years. Of these Alexander had 2 (observed one and two years respectively); Jaksch, 2 (observed eight months and one year); Jaboulay, 1 (observed eight months); Jonnesco, 8 (observed one to two years); Chipault, 3 (the observation time not specified); and Winter, 1 case (observed one year). This makes a total of 17 cases, 13.9%, some of which might have a remission but others, no doubt, which would remain attack-free and be included in the "Cured" column of later reports.

In the column "Improved" are included the cases in which the attacks, although still present, are much less frequent and less severe. Of these cases Alexander had 3 (one of these attack-free for two years); Kümmel, 1 (attack-free for one year); Bogdanik, 1; Braun, 3; and Winter, 1. In several of these cases, as in those of Bogdanik and in one of Braun's, the mental condition had been improved. The total number of cases improved is 23, or 18%.

The deaths which were recorded in the literature at the time of Winter's report were as follows: Alexander and Braun

each reported 1 case of respiratory death following broncho-pneumonia four and two days after operation. One of Jaboulay's patients died the following day in status epilepticus. One case of Donath's died eleven days after operation, and 3 cases of Jonnesco's and 1 case of Braun's died several days after operation. One of Winter's own cases died at home four months after operation. These were not all included as operative deaths in Winter's report.

Summarizing the types of operation which had been used up to the time of this report (1902) we find the following:

Resection of the superior cervical ganglia:

Alexander, Kümmel, Donath, Chipault.

Resection of the middle cervical ganglion:

Bogdanik, Shapiro.

Resection of the inferior ganglion:

Jaksch.

Resection of the superior and middle cervical ganglia:

Braun.

Resection of the middle and inferior cervical ganglia:

Baracz. (Later used complete bilateral resection).

Transection of the cervical chains only:

Jaboulay and Pean.

Bilateral resection of all 3 cervical sympathetic ganglia and chains:

Jonnesco and Winter.

It is evident from this range of surgical procedures that statistics from the general heading of sympathectomy are of

little value, but comparison of results obtained in each procedure may furnish useful information.

Spratling and Park (1905) record 5 cases of bilateral cervical sympathectomy reported by Hopkins (1904) and then report three of their own cases with records of the histological studies made on the chains and ganglia. The findings of note were:

1. Pigmentation of a greater or less number of nerve cells of the cervical ganglia in all three cases.

2. Presence in every one of the three cases of at least one nerve cell with double nucleus in some one of the extirpated ganglia. In one case about half a dozen such cells were found.

(Brueckner (1898) pointed out the fact that cells with double nucleus are rather rare in the sympathetic nervous system normally.)

3. Degenerative changes in the medullated nerve fibers in the sympathetic cord and ganglia of the excised portion.

4. In one case a focus of inflammation - i.e., of perivascular round cell infiltration.

These authors made a commendable attempt at analysis of vasomotor epilepsy from the standpoint of abnormality in the sympathetic system.

In 1906 Jonnesco reported 12 of 117 cases of idiopathic epilepsy absolutely cured (Mosser 1926). (This shows an addition of 19 cases to those of Jonnesco's in Winter's series.)

Jaboulay (1906) reported a case of combined epilepsy and trigeminal neuralgia. The patient, a woman of 54 who had been having epileptic attacks two or three times a week, was subjected to a unilateral cervical sympathectomy. She had only one fit during the two months after operation and from the day of operation the pain was absent from her face. (The observation time is too short for conclusions).

Witzel (1924) reported a case of migraine and epilepsy greatly improved by resection of one carotid body and the homolateral superior cervical ganglion. As migraine and epilepsy are seldom associated in the same person or family, and as the epilepsy was of Jacksonian nature, the probability of a brain tumour being present seems likely.

Tinel (1925) reported the case of a patient who had epileptic attacks from the age of 20 to 38 with gradually increasing severity. Bilateral carotid peri-arterial sympathectomy (the right side 21 days after the left side) was performed and six months later the patient was distinctly improved although not attack-free. Babitsky (1925) recommended the use of sympathectomy (he used superior and middle cervical ganglionectomy) plus subtemporal decompression. He reported several cases thus operated upon, but all of such short duration that conclusions were not justified.

Sicard, Hagnenar and Lichtwitz (1925) report a case of bilateral carotid and vertebral peri-arterial sympathectomy with no improvement in the epilepsy. Tinel (1925) presented

7 cases of carotid peri-arterial sympathectomy with one death, one case definitely improved and the others seemingly improved. He notes that the pericarotid sympathectomy, if it does not cure the attacks, at least abates them.

Mosser (1926) writes as follows in his review of sympathectomy:

"In theory Jonnesco and Jaboulay agree that interruption of the continuity of the sympathetic system in the cervical region paralyzes vasoconstrictor influence, thus leading to a congestion of the motor cortex of the brain through passive dilatation of the cerebral vessels. This deduction was due, no doubt, to the very evident connection found between the sympathetic ganglia and internal carotid artery. They seem to disregard, however, that all investigations, anatomic and physiologic, tend to prove that the cerebral vessels, whether the brain is normal or abnormal, are entirely free of vasomotor influences. Their results, therefore, would seem to be unsound in principle, unsubstantiated by experimentation and dubious in actuality. Jonnesco himself appears to have recognized the fallacy of his theory as he discarded the procedure soon after his report to the German Surgical Congress." He further states that "from 1905 to 1915 there was a distinct decline of interest in sympathectomy, but in 1916 interest was again revived when Jonnesco first tried the operation as a treatment for angina pectoris."

Mosser's survey clearly indicates that the writings of Hill (1896) and others played a definite part in overthrowing

cervical sympathectomy as a treatment for epilepsy early in the 20th century.

In the light of the recent work proving the relationship between the cervical sympathetics and vasomotor control of cerebral vessels (Forbes and Wolff (1928); Penfield (1931)), I want here to consider the writings of E. Vidal which seem to have been largely overlooked or disregarded. Vidal (1899b) after discussing the theories of cause and treatment of epilepsy and reporting some original work (to be considered later) wrote as follows: (Translation)

"Regardless how far flown the theories, we have acquired two points:

1. Sympathectomy is in general inefficient in purely reflex epilepsy.

2. It produces in cases of toxic epilepsy where the intoxication is not too profound a favourable action, if one of the two following conditions is present:

a) Mechanical irritation of the sympathetic by a tumour of the nerve trunk or vicinity.

b) The ability of the poison to cause vasoconstriction."

He then emphasized the necessity of careful diagnosis and choice of patients suitable for sympathectomy and said: (translation)

"Clinically, epileptics are capable of being classed in three groups:

1. Cases in which amyl nitrite administered in the

period premonitory to the crisis does not exert the least effect on the attack.

2. Cases in which under the same conditions the attack is arrested.

3. Cases in which the inhalation of amyl nitrite is capable of producing outwardly all the premonitory signs of an attack.

In the first group it is probable that the circulatory phenomena do not play any part. One would not know what result would follow resection of the sympathetic if one were to practice it. The second group in which the attack is happily influenced by vasodilation we have theoretically judged favourable for sympathectomy. The results of the last group constitute a definite contraindication to sympathectomy."

The author of these constructive suggestions put them into practice and in 1903 published this report of 14 cases which he had chosen and operated using Jonnesco's bilateral complete sympathectomy.

Mortality.....	0	
Absolute cure after 2 years or more..	5	(35%)
Considerable improvement.....	4	
Slight improvement.....	2	
Entirely unsuccessful.....	1	
Patients lost sight of.....	2	

The results of these selected cases is remarkable when compared with a series of unselected cases published by

Jaboulay (1902) using the same operative procedure, whose results were as follows:

Dead	0	
Made worse	2	
Unchanged	15	
Improved	3	
Cured	2	(9%)

Vidal's suggestion of selection of cases may be considered the second advance in the understanding of cervical sympathectomy in the treatment of epilepsy.

Wagner (1925) reported two cases in which superior cervical sympathectomy was performed without much improvement. He reports the study of the ganglion microscopically as revealing abnormal pigmentation of the ganglion cells.

Hirsch, Weiss, Izgur and Lauerman (1927) obtained improvement in four of nine patients by carotid peri-arterial sympathectomy, but their observation period was not long enough to allow conclusions. Dogs which they operated upon showed no dilatation of the homolateral cerebral vessels. Lennox and Cobb (1928) report ultimate improvement following sympathectomy in one of their cases which showed a Horner's syndrome before operation.

Brünning, quoted by Forster (1923), suggested the combined operation of cervical sympathectomy and carotid peri-arterial sympathectomy for epilepsy. Laignel, Lavawtine, Girode and R. Largeau (1929) reported 3 cases of epilepsy

treated by carotid peri-arterial sympathectomy. These cases were improved at first but at the end of six months were in the same condition as before operation. Geyelin and Penfield (1929) report a case in which the right superior cervical ganglion was dissected free from the carotid and surrounding structures but was left intact, the right stellate was freed from its fibers to carotid and vertebral arteries but was left intact. The accessory sympathetic ganglion, which was reported "in our experience, has always been found fastened like a saddle about the vertebral artery", was removed together with the vertebral nerve. A right peri-arterial sympathectomy was performed and in addition a right vertebral peri-arterial sympathectomy was carried out. The patient was definitely improved by the operation. The attacks became left-sided. He had previously had an amputation of the right occipital lobe. A second patient operated upon in a similar manner on the left side showed but little change. Both patients had cerebral calcification epilepsy.

In this report we have another important addition to the list of sympathectomy operations, namely vertebral peri-arterial sympathectomy with avulsion of the vertebral nerve and accessory sympathetic ganglion.

McClintic (1930) reported 18 cases of epilepsy which he had treated by bilateral superior cervical ganglionectomy and bilateral injection of 95% alcohol beneath the peri-arterial nerve-bearing sheath of the common, internal and

external carotid arteries and into the carotid bodies. Many of these were recently operated cases and were not reported in detail, but 4 cases, one of convulsions following birth injury, were reported as greatly improved or cured. He stated: "To date we have no case of epilepsy from whom we have heard who has been operated upon as long as two months ago who had any seizures to this date."

The author recommended that any case which might not respond to this treatment should be subjected to the additional operation of alcoholic injection under the peri-arterial nerve-bearing sheath of the vertebral arteries and section of the vertebral nerve. He further stated: "We have been very careful in selecting our cases of epilepsy in order to avoid hysterical cases and those with a psychosis."

McClintic's report did not include all of the details concerning the cases, but his suggestion of peri-arterial alcohol is interesting and constructive.

Several writers have called attention to untoward extraneous effects which have occurred following cervical sympathectomy. Kümmel (1892) noted a constriction of the pupil and nasal hypersecretion on the side corresponding to the avulsed ganglion. Winter (1922) observed the following changes after operation:

1. A strong flush of the operated side of the neck and face.

2. A rise in temperature of the operated side of

the face and head.

3. A congestion of the conjunctiva on the operated side.

4. Decrease in the side of the pupil on the operated side and a ptosis on the operated side.

Laignel, Lavastine, Girode, and R. Largeau (1929) in 3 cases found a rise in temperature of the neck and head, and flushing of the face following carotid peri-arterial sympathectomy. There was, however, a gradual subsidence of these signs and complete return of the convulsions at the end of six months.

Vidal (1903) noted a marked change in the heart beat, cardiac irregularity and depression of respiration in two cases when the superior cervical ganglion was forcibly resected. By injection of a drop of 1% solution of cocaine into the ganglion before the resection was carried out he no longer had the cardiac and respiratory changes following the resection.

Analysis of the foregoing clinical material permits the following deduction:

The percentage of epileptic patients cured by sympathectomy is directly proportional to the completeness of operation plus the care used in selection of suitable cases. Thus, in Winter's (1902) series of mixed cases there were 8 of 122 patients, or 6.6% cured. In Jaboulay's (1902) series, using complete bilateral cervical sympathectomy, there were 2 of 22 patients, or 9%, cured; and in Jonnesco's (1906) series there were 12 of

117 patients, or 10%, cured. In Vidal's (1903) series, he having used the action of amyl nitrite as a criterion for selection of cases and bilateral complete cervical sympathectomy, there were 5 of 14 patients, or 35%, cured.

By way of criticism it might be said that in Vidal's results a minimum of two years was considered a cure, whereas Winter required a minimum of three years for cure. On the other hand, analysis of Winter's figures shows that adding the cases "Preliminarily Cured" (observation eight months to two years, which included 8 of Jonnesco's) would then bring the cures to but 20.5%, and if Jonnesco's 8 cases of complete sympathectomy were subtracted from those preliminarily cured and only the cases of incomplete sympathectomy included, the total percentage of "Cured" and "Preliminarily Cured" patients would be but 13.8.

It is difficult to reach conclusions concerning the cases which have been reported more recently because of various types of incomplete sympathectomies and short periods of observation. McClintic's peri-arterial alcoholic injection combined with superior cervical sympathectomy has shown good results for a short period of observation. It would seem then, that epileptic patients carefully selected and subjected to complete cervical sympathectomy (bilateral removal of cervical sympathetic ganglia and chains, the vertebral nerves and the adventitia of the carotid and vertebral arteries) should be improved or cured.

Experimental Sympathectomy

Jonnesco's report at the Congress of Surgery in Paris, 1896, aroused not only the interest of clinicians but also of research workers.

Guinea pigs having "Brown-Séquard epilepsy" were subjected to sympathectomy to test experimentally the therapeutic effect of the procedure. Laborde (1889), quoted by Jaboulay and Lannois, found that in the guinea-pig rendered experimentally epileptic by hemisection of the medulla, producing an epileptogenic zone in the cervical region, section of the sympathetics did not remove the epileptogenic zone but attenuated it considerably. If the resection of the two cervical sympathetics were made in a preventative manner before the production of epilepsy, it did not exert the least influence. Dejerine (1889), quoted by Rodolfo, using experimental epilepsy, concluded that operative procedures only aggravated the condition. In the light of the work of Brown (1909-1910) and Alford (1911) who showed that Brown-Séquard epilepsy is but an exaggerated scratch reflex and not a true epilepsy, one can readily understand the failure of sympathectomy to effect a cure.

Vidal (1899a and b) carried out experiments which were unique and ingenious. He, also, using guinea pigs, produced convulsions by giving them: 1) a decoction of tobacco, and 2) potassium chloride. He then experimented with the animals and reported the following findings: (Translation)

1. "An intoxication insufficient to produce an attack, with the aid of electrical stimulation of the cervical sympathetic, results in a convulsion (in a guinea-pig)."

2. "An intoxication insufficient to produce an attack in the normal guinea-pig becomes sufficient after the ligation of one of the nutrient arteries of the brain."

3. "A guinea-pig was subjected to whirling in a horizontal plane, the head being fixed at the axis of the circle, thus producing a cerebral anaemia by centrifugal force. An epileptogenic drug formerly insufficient to produce an attack now results in a convulsion."

He continued:

"The conclusion to be drawn from these experiments is that the toxin used in these experiments (decoction of tobacco and potassium chloride) require the help of a decrease in the cerebral circulation to produce the attack. It seems that this theory is applicable to clinical use in man. There are cases in which there exist the conditions which have been used in the experiments, namely tumours, etc., causing permanent mechanical irritation of the cervical sympathetics and at the same time there being an autogenous toxin in the body. There are, then, two convulsant actions of the cortex: 1) Direct, specific stimulation to the cells of the cortex by the poison; and 2) Indirect stimulation of the motor cells by vaso-constriction."

"If the toxin is light and the primary factor is the vaso-constriction, one should be able to remove one of

the causes and thus cause a disappearance of the attacks. The following experiments were carried out:

1. In the guinea-pig whose cerebral circulation had been diminished by partial ligation of the arteries supplying the brain, total resection of the cervical sympathetic caused the dose of a convulsant drug which had been markedly diminished to return to normal.

2. In a guinea-pig with moderate cerebral congestion produced by centrifuging the animal with the head at the periphery of the centrifuge, a dose of convulsant drug much larger than normal is required to produce a convulsion.

If certain convulsant poisons are combined with a vaso-dilating drug not having convulsant properties (amyl nitrite) a larger dose than normal of the convulsant drug is required to provoke an epileptic seizure.

Complete cervical sympathectomy increases the resistance of normal healthy guinea-pigs to certain convulsant poisons."

The report of Vidal's work was not found until this present research was well under way, but the agreement in results from sympathectomy is worthy of note.

Ravdin (1931) in a personal communication stated that in experimenting with dogs he had produced convulsions with hypodermic injections of insulin after first producing hydration with 500 cubic centimetres of water by stomach tube. After removal of the stellate ganglia he was unable to produce

the convulsions in the same manner. He could offer no explanation of the phenomenon.

It seems evident that further application of experimental methods in determining the relationship of the vasomotor system to epilepsy is warranted.

EXPERIMENTAL METHODS

This research was undertaken to determine what effect the removal of vasomotor influences from the cerebral vessels of epileptic animals would have on the convulsions. The first need, therefore, was a number of animals which were spontaneously or artificially epileptic.

Sauerbruch (1913), quoted by Evans (1930), found that spontaneous convulsions followed some time post-operatively in a few of his monkeys; Pavlov (1927) reported a number of spontaneous convulsions in dogs after cerebral operations, and Bagley (1928) reported severe convulsions in several puppies after injection of blood into the cisterna magna and lateral ventricles. On the other hand, Dandy and Elman (1925), Muncie and Schneidie (1928), Evans (1930) and others had not obtained spontaneous convulsions in any of their animals. It was, therefore, deemed advisable to use a convulsant drug in all the animals and base conclusions upon changes in the minimal convulsant dose, but in addition to perform the operation of craniotomy on a number of the animals, stimulate the cortex (to localize motor areas and to measure the minimal electrical

stimulus which would produce convulsions) and then produce a brain wound in the hand and face areas, in the hope of producing spontaneous convulsions.

Cats and monkeys were selected as experimental animals because of their availability, their place well up in the phylogenetic scale, and the satisfactory anatomical situation of their cervical sympathetics.

A large list of pharmacologic convulsants was available from which to choose a drug:

Absinthe (Marce, 1864; Magnan, 1876; Horsley, 1892; Pike and Elsberg, 1925).

Acid Fuchsin (Syz, 1927).

Amyl Nitrite.

Camphor (Evans, 1930).

Cocaine (Sauerbruch, 1913).

Homocamfin (Lennox, Nelson and Beetham, 1929).

Insulin (Abel, 1929; Ravdin, 1931).

Oil of Wormwood (Florey, 1925; Dandy and Elman, 1925; Muncie and Schneidie, 1928).

Picrotoxin. (Grünwald)

Thujone (Cobb, 1929; Uyematsu and Cobb, 1922; Florey, 1925).

Evans (1930) in his experimental work had found camphor ($C_{10}H_{16}O$) to be the drug which gave the most uniform results in monkeys, and thujone in the form of oil of wormwood (10% emulsion in gum acacia, by stomach tube) to be the most satisfactory in cats. As camphor and oil of wormwood act on the nerve cells, and the effect of the former in particular is

chiefly cortical (Florey, 1925, and Cushney, 1924) these drugs were chosen for this research.

The Care of the Animals

The cats were kept in large, airy, individual cages in a room where there was good ventilation and morning sunlight; and in the autumn and winter sufficient steam heat was supplied to keep the room comfortable. On one or two very cold days only was the room too cool for comfort. During the summer months the windows and door, being screened, were opened wide and on two of the hot days an electric fan was supplied to give the animals as much comfort as possible. Each day the cages were cleaned, and the cats fed on a good grade of raw beef and milk. A few of the cats had slight colds during the spring months but were, on the whole, healthy and maintained or gained weight.

The monkeys were all kept in one large cage in the animal house, but had continuous access to the wire sun-cage on the roof. On cold days in the winter they stayed in the steam-heated cage below, but when the weather was less severe they chose to sit in the sun on the roof even with snow all about them. In the summer they spent the entire day on the roof.

The monkeys' food consisted of fruits in season (apples, bananas, peaches), vegetables and greens (carrots, lettuce, cabbage), bread, a mash of corn meal, eggs, milk, and ground lean meat (recipe of Dr. Herbert Fox). In the latter part

of the summer of 1931 during an epidemic of enteritis, a mash of milk and wheat germ was added to the diet in an effort to correct possible vitamin deficiency.

Tuberculosis and enteritis constantly threatened the monkeys and despite early isolation of sick and suspected animals, there were numerous deaths which meant the loss of both the animals and the incompleted experiments.

Method of Dosing

The cats were not fed for 24 hours before each dosing. Each cat was carefully weighed and the dose of oil of wormwood (10% in gum acacia emulsion) calculated on the basis of the weight in kilograms, after which a #14 French soft rubber catheter lubricated with olive oil was passed into the cat's stomach and the drug, measured in a graduated syringe, was given by gavage. The animal was returned to its individual cage and carefully watched for four hours. When the cat convulsed it was removed from the cage and placed on the floor so that all its actions could be more easily noted.

The monkeys were fed the day before the dosing and no precaution was taken against their eating the residual food on the morning of dosing as the drug was given intramuscularly. The animals were caught, placed in individual bags and weighed. The dose of camphor (20% in olive oil, sterilized and kept in air-tight bottles) was calculated on the basis of the weight in kilograms. Each monkey was taken from the bag, his thigh shaved, and the skin prepared with

tincture of iodine and alcohol. The dose of camphor in oil, measured in a sterile syringe, was then injected intramuscularly and the animal transferred to a wire cubicle where he was watched for four hours.

Operative Procedures

The technique in the animal operating rooms was essentially the same as that used in the Neurosurgical Clinic. The sterile supplies were in charge of a graduate nurse who also assisted at the operations. Great care was taken in preparation of the field of operation and constant vigil helped prevent slips in technique. This care was rewarded, for only two serious wound infections occurred, one in cat No.4305, undoubtedly the result of intentional opening of the frontal sinus at operation, and the other in monkey No.124, who died five days after craniotomy and showed moderate wound infection plus tuberculosis. This monkey's wound infection must be considered as due to a slip in technique.

Anaesthesia

A few of the first operations were performed under amytal anaesthesia, a dose of 0.5 cubic centimetre per kilogram for the monkeys and 0.6 cubic centimetre per kilogram for the cats, given intraperitoneally. Later, on the recommendation of Fulton et al. (1930) "Dial" Ciba (diallylbarbitaric acid) was tried and used in the majority of the operations in the dose of 0.5 cubic centimetres per kilogram for the cats

and 0.4 cubic centimetre per kilogram for the monkeys given intraperitoneally. The drug and dosage proved very satisfactory for the craniotomies, where cortical stimulation was successfully carried out, and for sympathectomies. In a few animals a slight addition to the dose of Dial or a supplementary whiff of ether was used, but these instances were few.

The administration of the anaesthetic was aseptically carried out, the animal's abdomen being shaved and the skin prepared with tincture of iodine and alcohol. The needle was inserted just below the umbilicus and directed laterally, thus avoiding the liver, stomach and bladder.

One animal (monkey No.132) had a partial intestinal obstruction from omental bands five days after operation which may have been due to the injection. No other untoward effects were noted.

The monkeys recovered from the anaesthetic in 18 to 28 hours, but the cats required 36 hours or more. The animals were kept warm with hot water bottles and electric heater during this period, and the cats were fed milk by stomach tube the day after operation.

Surgical Care

In preparation for each operation (after the animal was asleep) the skin of the operative site was shaved and the animal placed in the necessary position. It was then covered

with a blanket and a warm sand bag placed at either flank. When stimulation of the cortex was to be carried out the limbs of the contralateral side either were not restrained or were held with rubber bands to allow free movement. The operator having scrubbed and donned sterile gloves, the skin of the operative field was prepared by washing with tincture of green soap, 95% alcohol, ether, and mercurochrome-acetone solution. Sterile towels were then sutured in place, leaving only the site of the incision uncovered. The entire operating table was draped with sterile sheets.

In the monkeys' operations the additional preparation of placing the needles of a hypodermoclysis unit under the skin of the monkeys' thighs, after proper sterilization, was carried out. This enabled the operator to give normal saline at once if undue bleeding was encountered and undoubtedly saved the lives of some animals. Caffein-sodium-benzoate, grains 2, was kept in readiness and given to both cats and monkeys hypodermically if the pulse or respiration lagged.

Sterile gauze dressings were kept in place on the cats with liquid adhesive (Johnson and Johnson) and on the monkeys with collodion.

Craniotomy

In both monkeys and cats the skin incision was made from a point just above the lateral angle of the supra-orbital ridge arching up to the midline of the head and thence back to a point just behind the ear. The incision was made clear

to the bone and the skin and subcutaneous tissue laid back exposing the skull and fan-shaped temporal muscle.

In the cats an incision was made in the temporal muscle one-quarter centimetre from the attachment to the skull, thus leaving an edge of fascia for suturing. The temporal muscle was separated from the bone by a periosteal elevator and was then held away from the skull by a suture and rubber band attached to the sterile drapes of the table. A small trephine opening was made in the skull and enlarged with rongeurs. When the exposure was sufficient for stimulation, the dura, which is extremely delicate in the cats, was opened with a dural hook and small scissors.

In the monkeys a rectangular bone flap to which was attached the temporal muscle was outlined, five small trephine holes were made and three sides of the flap cut with a Gigli saw. The flap was then broken on the temporal muscle and the dura opened with dural hook and scissors.

As soon as the cortex was exposed the operator sketched with sterile pencil and paper the outline of the operative field, showing the cortical landmarks and vessels as well as possible. The cortex was then stimulated with gradually increasing amounts of both galvanic and faradic currents. The charts showing the point of stimulation and the result for each animal are included in the chapter of Experimental Results.

In the early experiments unipolar stimulation was used, the indifferent electrode being bandaged to a shaved area on

the animal's leg. In the majority of the operations a bi-polar electrode was used.

After stimulation of the cortex a small but deep brain wound was made in the cortical area most nearly representing the forepaw and face. In the early operations the wound was made by cutting the cortex to bits with small scissors. This frequently produced tremendous bleeding and after finding cerebral softening in the frontal and parietal lobes of a monkey (118) following this procedure, it was decided that it caused too much vessel destruction. Thereafter cortical wounds were made by thrusting a small hemostat deep into the cortex and opening it, repeating the procedure several times.

In all cases after the wound was made a piece of temporal muscle was cut free and thrust deep into the cerebral tissue. This muscle aided hemostasis and, it was hoped, would encourage scar formation.

No attempt was made to close the cat's dura. The temporal muscle was sutured in place, being in contact with the cortex, and the fascia and skin closed in layers with interrupted silk sutures.

The monkey's dura was sutured in place with the exception of a portion over the cortical wound which was left exposed. The bone flap was held in place by two double silk sutures through small drill holes in the bone. The incisions in the temporal muscle, the fascia and subcutaneous tissue were closed in layers with interrupted silk sutures, and the skin

was closed with a continuous subcuticular suture of split silk.

Sympathectomy

The incision for this operation in both cats and monkeys extended from the angle of the jaw along the anterior border of the sterno-cleido-mastoid muscle to a point just lateral to the midline at the sternum. After going through the skin, the fascial plane to the nerves and vessels was located by blunt dissection with Mayo scissors, and the sterno-cleido-mastoid muscle was retracted laterally. The great vessels of the neck and the vagus and sympathetic nerves in their sheath were easily exposed and the sheath of the nerves was carefully picked up and opened with small scissors. A mosquito hemostat was then slipped into the sheath to hold it open and the sympathetic chain was grasped with forceps, care being taken not to pinch the vagus. The sympathetic chain was then carefully dissected free from the vagus and followed cephalad until the superior cervical ganglion was located. This was usually about the level of the bifurcation of the common carotid artery in cats and somewhat nearer the skull in monkeys. The ganglion was freed from surrounding fascial attachments by blunt dissection with a mosquito hemostat, and the nerve fibers from the ganglion to the vagus nerve and carotid artery were cut. The ganglion was then grasped by a hemostat and removed by avulsion, taking as much of the post-ganglionic chain as would come away with it.

Working caudad, the sympathetic chain was then dissected free from the vagus, great care being taken that the vagus was never grasped in an instrument or pulled upon severely. In some of the animals it was necessary at this stage to divide the sterno-cleido-mastoid muscle in order to obtain sufficient exposure. In other animals this procedure was unnecessary. The tubercle of Chasseignac was then palpated, and in the earlier operations the region dorso-medial and caudad to the tubercle was explored in search of the vertebral artery and nerve. In the later operations, however, the sympathetic chain was followed down to the stellate ganglion (which is extremely low down in the cat) and then after freeing the ganglion and cutting the branches to the carotid and the thoracic chain, the vertebral nerve was followed to the foramen and removed by avulsion. In none of the animals was an accessory ganglion seen on the vertebral nerve.

Following the removal of the nerves and ganglia, the fine adventitial network was stripped from the carotid and vertebral arteries with forceps and scissors. In the last two operations a more extensive deep decortication of these arteries was carried out to make sure of removing all vasomotor fibers. In two monkeys (No.163, No.127) it was necessary to ligate one vertebral artery. The muscles and superficial parts of the wound were closed in layers with interrupted silk sutures.

The posterior approach to the stellate ganglion by removal of the head of the first rib was tried on one cat

(No.4207), but the difficulty of exposure of the ganglion and the inaccessibility of the vertebral artery and nerve by this approach made the anterior approach the necessary one.

Bilateral superior cervical ganglionectomy was tried in one operation (cat No.4339) but the cat died.

Because of the possible trauma to the vagus in removing the sympathetic chain it seemed advisable to operate on only one side at a time with an interval of at least 10 days between operations. This plan was therefore carried out in all of the monkeys.

Before this research, all the monkeys which had been subjected to complete cervical sympathectomy by members of the Department of Neurosurgery had died in 1 to 5 days after operation with signs of either pulmonary oedema, pneumonia or circulatory instability. Following the removal of the cervical sympathetics from the right side of monkey No.110, the left side having been previously operated upon, he began to drool saliva from his mouth, breathe with difficulty and act much as some of the other monkeys had done. Because of the noticeable irrespiratory retractions of the intercostal spaces on the right side, an X-ray was made of the chest and it showed a collapse of the upper lobe of the right lung. Reasoning that in the operation the vagus might well have been traumatized just enough to cause excessive peripheral stimulation, I gave the monkey what I judged was about 1/150 grains of atropin. (The atropin at the animal house was in bulk). The monkey lived (the first complete cervical sympathectomy)

and a second X-ray taken three days after the first shows the chest clear.

Following this experience all the monkeys were given atropin, grains 1/150, after the final stage of sympathectomy. Four have survived and one (No.132) died, but autopsy showed that he had pulmonary tuberculosis and partial intestinal obstruction.

Section of Greater Superficial Petrosal Nerve

This operation was performed on only one monkey (No.110). Incision was made as for a craniotomy, the scar of the former craniotomy being reopened and the bone flap turned down. The skin was separated from the outer surface of the temporal muscle and from the zygoma. The periosteum of the zygoma was incised and intraperiosteal removal of that bone was carried out, but care was taken that the spongy portion close to the ear was not entered. With the zygomatic arch out of the way, the temporal muscle to which was attached the bone flap was stripped from the skull well down toward the base, and the subtemporal decompression remaining from the former craniotomy was enlarged to expose the base of the skull. The dura was not opened and was seen to be entirely intact despite the defect which had been left at the former operation.

When sufficient opening had been made in the skull the dura was slowly and carefully elevated from the petrous portion of the temporal bone and the temporal lobe elevated to expose the base of the skull. About a centimetre medial

from the lateral edge of the skull was a small elevation of bone which caused a little difficulty in the freeing of the dura. Directly dorso-medial to this bony prominence was the sulcus of the greater superficial petrosal nerve extending from the hiatus of the facial canal to the foramen lacerum. This nerve was freed from its fascial attachment to the bone and was cut close to the facial canal. The slight bleeding from a small vessel accompanying the nerve was easily controlled by irrigations with warm saline, the temporal lobe and dura settled back to the base of the skull, the bone flap was replaced and the wound closed as in the craniotomies.

EXPERIMENTAL RESULTS

As a help in their analysis the dosings of the animals have been divided into five groups - group 1 being the pre-operative doses of normal animals, both cats and monkeys; group 2 the first post-operative doses or the doses following craniotomy and brain wound; group 3 the doses after complete cervical sympathectomy; and group 4 the doses after section of the greater superficial petrosal nerve; in group 5 are placed those animals whose doses have not been completely established, or have been so irregular that they could not be placed in the other groups. These animals are included because each illustrates some particular problem that has arisen during the research. The animals in each group are recorded by their numbers which refer to the protocols.

Minimal Pre-operative Convulsant Dose

Group 1.

Cat No.	Dose Wormwood per kilogram	Monkey No.	Dose Camphor per kilogram
4207	0.9 c.c.	110	0.7 c.c.
4300	1.1 c.c.	118	0.75 c.c.
4301	1.2 c.c.	121	1.15 c.c.
4302	1.0 c.c.	122	0.7 c.c.
4304	1.0 c.c.	123	0.7 c.c.
4305	1.15 c.c.	124	0.65 c.c.
4332	1.75 c.c.	127	0.8 c.c.
4333	0.8 c.c.	128	0.7 c.c.
4346	1.0 c.c.	132	0.8 c.c.
4355	1.75 c.c.		
4365	1.6 c.c.		
4371	2.0 c.c.		
4378	1.2 c.c.		

The average minimal pre-operative convulsant dose of oil of wormwood in 13 cats was 1.18 cubic centimetres per kilogram, the largest dose being 2.0 cubic centimetres and the smallest 0.8 cubic centimetre per kilogram.

The average minimal pre-operative convulsant dose of camphor in oil in 9 monkeys was 0.77 cubic centimetre per kilogram, the largest dose being 1.15 cubic centimetres and the smallest 0.65 cubic centimetre per kilogram.

First Post-operative Minimal Convulsant Dose

(After Brain Wound)

Group 2.

Dose Wormwood per kilogram

Cat. No.	After Brain Wound	Before Brain Wound
4207	0.6 c.c.	0.9 c.c.
4302	1.1 c.c.	1.0 c.c.
4304	1.0 c.c.	1.0 c.c.
4333	0.6 c.c.	0.8 c.c.
4346	1.15 c.c.	1.0 c.c.
4301	Not established definitely but well above 1.2c.c.	1.2 c.c.

Dose Camphor per kilogram

Monkey No.	After Brain Wound	Before Brain Wound
110	0.6 c.c.	0.7 c.c.
122	0.55 c.c.	0.7 c.c.
128	0.65 c.c.	0.7 c.c.

Analysis of these doses shows the following results:

Two cats and all the monkeys had their minimal convulsant dose of the drugs lowered by the production of a brain wound.

Three cats showed an elevation of minimal convulsant dose after brain wound.

One cat remained exactly the same as before operation.

The average minimal post-operative convulsant dose of wormwood in 5 cats was 0.89 cubic centimetre per kilogram.

The pre-operative dose in these same cats was 0.898 cubic centimetre per kilogram, a negligible elevation of 0.008 cubic centimetre per kilogram.

The average minimal post-operative convulsant dose of camphor in 3 monkeys was 0.6 cubic centimetre per kilogram, and the average minimal pre-operative dose in these same monkeys was 0.7 cubic centimetre per kilogram, a reduction of 0.1 cubic centimetre by brain wound.

Second Post-operative Minimal Convulsant Dose
(After Complete Sympathectomy)

Group 3.

Cat No.	Dose Wormwood per kilogram After Complete Sympathectomy	After Unilateral Sympathectomy	After Brain Wound	Original Dose
4207	-	0.9 c.c. (sup. cervical only)	0.6 c.c.	0.9 c.c.
4304	-	more than 1.0 c.c.	1.0 c.c.	1.0 c.c.

Monkey No.	Dose Camphor per kilogram After Complete Sympathectomy	After Unilateral Sympathectomy	After Brain Wound	Original Dose
110	0.7 c.c.	0.7 c.c.	0.6 c.c.	0.7 c.c.
121	1.25 c.c.	1.25 c.c.	-	1.15 c.c.
123	0.75 c.c.	0.7 c.c.	-	0.65 c.c.
127	-	0.75 c.c. (Had one fit at this dose but dose not yet established)	-	0.8 c.c.
128	more than 0.7 c.c.	more than 0.7 c.c.	0.65 c.c.	0.7 c.c.
132	-	0.8 c.c.	-	0.8 c.c.

Analysis of these tables of Group 3 shows the following facts:

All the animals which were subjected to a complete cervical sympathectomy required a larger dose of convulsant drug to produce a fit after the sympathectomy than before it.

Of the animals subjected to only unilateral cervical sympathectomy, two cats showed an elevation of the minimal convulsant dose of the drug after the operation, one monkey's dose was unchanged and one monkey had one convulsion on a slightly smaller dose,but his minimal convulsant dose is not yet established.

A striking coincidence which may be significant occurred in the cases of cat No.4207 and monkey No.110. These animals, following a brain wound, had a definite reduction in the minimal convulsant dose of the respective drugs. Following left superior cervical ganglionectomy in the cat and complete cervical sympathectomy in the monkey the convulsant dose of the drug returned to <u>exactly</u> the original pre-operative dose (group 1). The sympathectomies were on the same side as the brain wounds. Sympathectomy of the right side of monkey No.110 did not further elevate his dose.

Following complete cervical sympathectomy the minimal convulsant dose of camphor in monkey No.128 has been elevated even above the original pre-operative dose.

These results plus the result of McClintic's (1930) "prize case" - a little girl whose epilepsy was cured and post-

traumatic quadraplegia greatly improved by cervical sympathectomy and carotid peri-arterial alcoholic injection, should encourage further study of cervical sympathectomy in clinical and experimental post-traumatic epilepsy.

The average minimal convulsant dose of the completely sympathectomized animals of Group 3 before sympathectomy (not including monkey No.128 whose post-operative dose is not yet definite), was 0.83 cubic centimetre per kilogram. The average minimal convulsant dose of the same animals after complete cervical sympathectomy was 0.9 cubic centimetre per kilogram, an increase of 0.06 cubic centimetre per kilogram.

The average minimal convulsant dose of the two monkeys with brain wounds was 0.625 cubic centimetre per kilogram before sympathectomy and after complete cervical sympathectomy monkey No.110 required 0.7 cubic centimetre per kilogram and monkey No.128 required more than 0.7 cubic centimetre per kilogram to produce a convulsion.

The average minimal pre-operative convulsant dose of the animals without brain wounds was 0.9 cubic centimetre per kilogram, and after complete cervical sympathectomy the average minimal convulsant dose of the same animals was 1.0 cubic centimetre per kilogram, an increase of 0.1 cubic centimetre per kilogram.

Third Post-operative Minimal Convulsant Dose

Group 4.

Only one monkey can be included in this group at this time, for thus far section of the greater superficial petrosal nerve has been performed on only the one animal of the series.

Monkey No.110 had a minimal pre-operative convulsant dose of camphor of 0.7 cubic centimetre per kilogram. Following brain wound this dose was reduced to 0.6 cubic centimetre per kilogram and after sympathectomy it returned to 0.7 cubic centimetre per kilogram. Following section of the greater superficial petrosal nerve the monkey, in the four dosings since this operation, first failed to convulse on a dose of 0.65 cubic centimetre per kilogram; then he had a seizure on 0.7 cubic centimetre per kilogram, had no seizure on 0.65 cubic centimetre per kilogram, and then also failed to convulse on 0.7 cubic centimetre per kilogram but had a fit on 0.75 cubic centimetre per kilogram. The dosing has not progressed beyond that point. It would seem that this operation had little or no effect on the dose in this one monkey but more complete observation in a larger number of animals is necessary before conclusions can be drawn.

Miscellaneous

Group 5.

In this group are included four monkeys and three cats. These are monkeys Nos. 110, 115, 116 and 120; and cats Nos. 4303, 4345, and 4356. Each of the animals will be comsidered

individually because of the problem which it illustrates.

Monkey No.109 was one of the hardiest animals. His dosing was commenced on January 7th, 1931, but a survey of his protocol will show that it was impossible to establish definitely his pre-operative dose of camphor. He was finally operated upon and a brain wound produced in the hope of stabilizing the convulsant dose, but up to the time of this thesis he has had no fits since operation although the dose of the drug has been considerably increased. The chart of the cortical stimulation at operation of this animal shows one of the most satisfactory results of the series.

Monkey No.115 was given the initial dose of 0.7 cubic centimetre of camphor per kilogram body weight. This was the dose at which all the monkeys, previously dosed, had been started. The protocol shows his severe reaction to the convulsant and despite special care he died following status epilepticus. At autopsy the lungs and spleen were found to be masses of caseous tuberculosis and there were tubercles in the other organs. As Evans (1930) noted in one of his monkeys, the severe tuberculosis infection proved an accessory convulsant.

Monkey No.120, with an initial dose of 0.65 cubic centimetre, less than that of No.115, had several severe convulsions and later became ill and died in three weeks. The autopsy showed a few tuberculous nodules in the left lung and an extensive enteritis. It seems likely that the dose of camphor or the resulting convulsions enhanced the illness. Animals

with any recognized illness were not dosed.

Monkey No.116 merely illustrates the loss of time devoted to experimentation through death of the animal. This loss was even greater when the experiment was nearly completed before death, as in some of the operated animals.

Cat No.4394 has failed to convulse in spite of rather large doses of drugs and a brain wound (the operation was performed for demonstration purposes). This is the only completely resistant animal encountered in the series.

Cats No. 4345 and No.4356 illustrate an unexplained development of resistance to the convulsant. As one or two of the other cats simultaneously failed to convulse on a dose which had previously caused a convulsion, a new mixture of wormwood was obtained. However, the resistance of these two animals continued despite the freshly prepared drug. No change in feedings or surroundings could be found coincident with the development of resistance.

The protocol of cat No.4345 illustrates a problem which arose in dosing the cats, and which at first proved most disturbing. This cat and a few of the others, following return to the cage after dosing, began suddenly to retch and regurgitate most of the dose of wormwood. This of course destroyed the results of the day's dosing as one could not be sure how much drug was retained. It was finally decided that the cats had learned to regurgitate voluntarily. They were then closely watched and the moment vomiting was

suggested a firm hand was closed upon the trachea and oesophagus for a few seconds. The epidemic of voluntary vomiting ceased following this somewhat barbaric but effective procedure.

Cortical Stimulation

As mentioned in the Operative Procedures the cerebral cortex, when exposed during each craniotomy, was sketched on a sterile sheet of paper, the point of electrical stimulation noted and the result recorded. Following the operation the sketch was carefully transposed to more permanent paper and the results of stimulation typed on the new record. In the protocols are photostatic reproductions of these records which not only illustrate the effect of stimulation at the various points on the individual cortex, but also serve as permanent records of the amount of current used (as near as it could be measured), so that comparison may later be made with the results of a second stimulation.

A unipolar electrode, as previously described, was used in the cases of cats Nos. 4207, 4301, 4302 and 4304. Both unipolar and bipolar electrodes were used at the operation of cat No.4305, and all other cortical stimulations were carried out with a bipolar electrode. A post-stimulation convulsion of Jacksonian nature was obtained in the cases of Cats Nos. 4301 and 4333 and monkey No.110. These convulsions were consistently of clonic type and involved chiefly the muscles

controlled by the cortical area which had been stimulated.

In cat No.4346, on stimulation of area (1) (with faradic current) there was a definite retraction of the nictitating membranes of both eyes. This phenomenon had not been observed in the previous cat operations and could not be duplicated in the one cat operated on later.

Review of the cortical stimulation of monkey No.109 shows definite localization of the area in his case for turning of head and eyes to the contra-lateral side. As noted on the record of stimulation, the result in this one case suggests that the centre for head and eye turning in the monkey may be further forward than that for head turning alone.

From the results of stimulation in these experiments it would seem that before accurate conclusions can be drawn concerning animal stimulation, it will be necessary to develop a procedure using local anaesthesia as is done in the Neurosurgical Clinic when cortical stimulation is carried out.

Deaths in Animals

Monkeys:

No. 115: Died in afternoon following dosing and status epilepticus. Generalized tuberculosis - lungs, spleen and mesenteric lymph nodes.

No. 116: Died of entercolitis.

No. 118: Died after craniotomy brain wound. Extensive parietal and frontal softening, probably due to ischemia.

Monkeys: (Continued)

No. 120: Died of entercolitis and slight tuberculous infection of left lung.

No. 124: Died 5 days after craniotomy. Had superficial infection of wound. Bilateral pulmonary tuberculosis. Fatty degeneration of liver and pinworm infestation of colon.

No. 132: Died 3 days after second stage of cervical sympathectomy. The monkey was in poor condition before this operation but was making no progress and the risk was taken. Autopsy showed bilateral pulmonary tuberculosis and partial intestinal obstruction.

No. 122: Died three months after brain wound of entercolitis.

No. 133: Died 4 days after unilateral cervical sympathectomy of fulmonating entercolitis and hepatitis.

No. 163: This animal died immediately after operation from haemorrhage into the mediastinum which occurred when the vertebral artery was torn in removing the stellate ganglion.

Cats:

No.4300: Died of ruptured stomach and enormous hair-ball containing ascaris lumbracoides.

No.4305: Was killed because of extensive infection which developed secondary to the intentional opening of the frontal sinus at operation.

No.4332: Died 3 days after unilateral cervical sympathectomy and no cause could be found for her death. Autopsy

Cats:

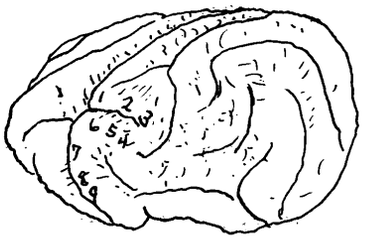
No.4332: (Continued)

revealed a clean wound and no other abnormalities.

No.4207: Died 4 days after bilateral stellate ganglionectomy by posterior approach, of mediastinal haemorrhage.

OUTLINE OF CAT'S BRAIN (From Muncie and Schneider).

Frontal pole -----



-----Occipital pole.

Areas 1 to 9 constitute principal motor area.

Cat No. 4207.

Group 1. Pre-operative dosing with wormwood (10% emulsion); stomach tube.

Date.	Weight.	Dose per kg.	Total.	Result.
1/12/31.	5.5 kg.	1.1 cc.	6.00 cc.	Seizure (2); seizure(2)
1/17/31.	5.5 kg.	1.0 cc.	5.5 cc.	Seizure (3).
1/17/31.	5.50 kg.	1.0 cc.	5.5 cc.	Seizure (2).
1/28/31.	5. 45 kg.	.9 cc.	4.9 cc.	Seizure (3).
2/7/31.	5. 35 kg.	.8 cc.	4.3 cc.	Quiet.

Minimal pre-operative convulsant dose 0.9 cc. per kilogram body weight.

Operation, February 12th 1931. Left fronto-parietal craniotomy; stimulation of motor cortex; production of cortical wound of the motor area. (See chart for stimulation).

Group 2. Post-operative dosing with wormwood after brain wound.

4/7/31.	4.6 kg.	.7 cc.	3.2 cc.	Seizure (2); turning counter-clockwise.
4/22/31.	4.67 kg.	.65 cc.	3.0 cc.	Seizure (2); rolling counter-clockwise; (looking at head).
4/25/31.	4.67 kg.	.60 cc.	2.8 cc.	Quiet.
4/27/31.	4.55 kg.	.60 cc.	2.7 cc.	Quiet.

1st minimal post-operative convulsant dose wormwood (after left brain wound)0.6 cc. per kilogram body weight.

Operation, May 3rd 1931. Left superior cervical sympathetic ganglionectomy.

5/19/31.	4.35 kg.	.6 cc.	2.6 cc.	Quiet.
6/6/31.	4.2 kg.	.65 cc.	2.7 cc.	Quiet.
6/13/31.	4.3 kg.	.7 cc.	3.0 cc.	Quiet.
6/17/31.	4.2 kg.	.75 cc.	3.15 cc.	Quiet.
6/20/31.	4.2 kg.	.8 cc.	3.36 cc.	Quiet.
6/24/31.	4.3 kg.	.85 cc.	3.6 cc.	Seizure (3).
7/11/31.	4.55 kg.	.8 cc.	3.6 cc.	Quiet.
7/23/31.	4.47 kg.	.85 cc.	3.8 cc.	Quiet.
7/25/31.	4.45 kg.	.9 cc.	4.0 cc.	Seizure (2).
7/29/31.	4. 35 kg.	.85 cc.	3.7 cc.	Quiet.
8/1/31.	4.25 kg.	.9 cc.	3.8 cc.	Very angry and excited.

Post-operative dose 0.9 cc per kilogram.

8/7/31. Bilateral stellate ganglionectomy.
8/11/31. Died. Hemorrhage into mediastinum; extrapleural hemorrhage.

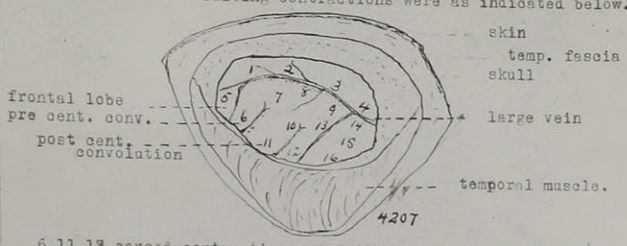
Cat No. 4207 continued.

Summary Minimal pre-operative convulsant dose wormwood 0.9 cc. per kilogram.
Minimal post-operative convulsant dose wormwood (after brain wound, left) 0.6 cc. per kilogram.
Dose lowered 0.3 cc. per kilogram.
Minimal post-operative convulsant dose wormwood (after left superior cervical sympathectomy 0.9 cc. per kilogram
Dose raised 0.3 cc. per kilogram.

Autopsy Notes: Examination of the abdomen revealed no pathological findings.
Thorax: There was moderate bloody fluid in each pleural cavity suggesting slight post-operative effusion rather than perforation of the pleura. The mediastinum was infiltrated with blood and this, we believe, was the cause of the animal's death.
Central Nervous System: At the site of the brain wound a new dura had formed over the cortex under the temporal muscle. This dura was thicker than that over the right cortex. There was a crater-like pocket in the brain which was densely adherent to the new-formed dura, which was in turn adherent to the temporal muscle. The traction of the scar was sufficient to pull the temporal muscle well within the edges of the bone defect. The adhesions between the cortex, pia-arachnoid and the temporal muscle were quite firm and there were in addition smaller adhesions between the arachnoid and dura well under the bone edge and away from the temporal muscle. This seems to suggest that there was some bleeding about the wound after the closure for these adhesions are of the type described by Bagley in his puppies, with blood injected into the cisterna magna.
The spinal cord was normal.
(Photographs of the brain and adherent dura and muscle are included)

Drawing of the left cortex Cat No. 4207 made at operation.
Stimulation with galvanic and then Faradic current. Unipolar.

1.5 to 2 milliamperes of galvanic current were used in the stimulation and the resulting contractions were as indicated below.



6,11,12 caused contraction and twitching of the muscles of the right face with twitching of the right eyelid. There was also very slight twitching of the right hind leg.

7,8,19 more pronounced contraction of the right fore and hind paws in flexion. Remainder of the field produced no contraction with this strength of current.

Using 2.5 milliamperes of galvanic current a generalized extension of the muscles of the neck and back as well as the fore and hind legs on both sides resulted from stimulation of any area on the cortex. there was however in addition to the above a twitching of the muscles of both sides of the face when areas 5 & 6 were stimulated.

Using Faradic current of the lowest amount obtainable on the machine in the laboratory gave the following contractions on the of the areas indicated;

Stimulation Cat No.4207 (continued)

6,11 contraction of the face and eyelids more marked on the right than on the left.

5 clonic contractions of the muscles of the neck, back and fore and hind legs the fore legs more marked than the hind legs.

the remainder of the cortex when stimulated with Faradism produced a generalized clonic convulsion of the entire set of trunk muscles and the four limbs . These rapid clonic twitchings in the parts mentioned continued as long as the contact was maintained between the electrode and the cortex.

There was in no case a continuation of the convulsive movement after the electrode had been removed from contact with the cortex.

CAT NO. 4207.

Lateral view of brain showing crater of brain wound with adherent temporal muscle.

CAT NO. 4207.

Lateral view of brain showing crater of brain wound with adherent temporal muscle.

CAT NO. 4207.

Dorsal view of brain showing adherent meninges and temporal muscle.

Cat No. 4300.

Group 1. Pre-operative dosing with wormwood (10% emulsion).

Date.	Weight.	Dose per kg.	Total.	Result.
1/6/31.	2.5 kg.	1.1 cc.	2.8 cc.	Hypersalivation.
1/12/31.	2.4 kg.	1.2 cc.	2.9 cc.	Seizure (2) tonic.
1/17/31.	2.45 kg.	1.1 cc.	2.7 cc.	Series of jerks. Seizure (2).
1/28/31.	2.95 kg.	1.0 cc.	2.95 cc.	Quiet.

Minimal pre-operative convulsant dose 1.1 cc. per kilogram body weight

Operation No. 1. February 3rd 1931. Right fronto-parietal craniotomy; stimulation of the motor cortex; production of cortical wound of the motor area. (See chart for stimulation).

February 4th 1931. The cat was found dead in the cage the morning after operation. Late on the night of operation the animal's condition was good, and we look to the autopsy for explanation of cause of death

Autopsy Findings: At the site of the brain wound there a small blood clot which was insufficient to cause death. No other pathology was found in the central nervous system.

Heart and lungs were normal. The abdomen was swollen, and on opening it a small amount of fluid and considerable gas was found. There was a rupture of the greater curvature of the stomach from which protruded a portion of an enormous hair ball. In the hair ball and in the peritoneal cavity about the hole in the stomach, were numerous small round worms of the type of ascaris lumbracoides.

Death due to ruptured stomach and peritonitis.

Summary: Minimal pre-operative convulsant dose, wormwood, 1.1cc. per kilogram.

Operative death - indirectly.

Cat No. 4301.

Group 1. Pre-operative dosing with wormwood (10% emulsion); stomach tube.

Date.	Weight.	Dose per kg.	Total.	Result.
1/6/31.	3.3 kg.	1.1 cc.	3.6 cc.	Hypersalivation.
1/13/31.	3.35 kg.	1.2 cc.	3.9 cc.	Seizure (2), vomited.
1/17/31.	3.45 kg.	1.1 cc.	3.8 cc.	Slightly excited.
1/28/31.	4.00 kg.	1.15 cc.	4.6 cc.	Quiet.

Minimal ore-operative convulsant dose 1.2 cc. per kilogram body weight.

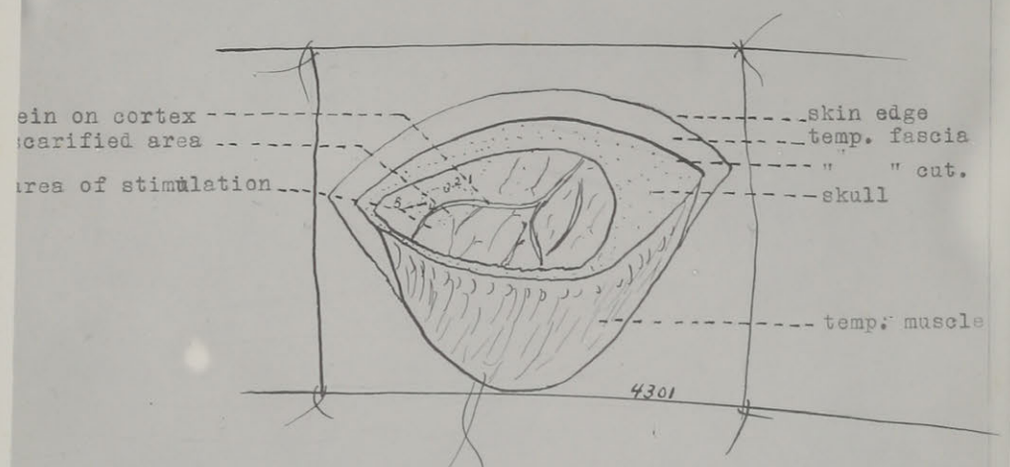
Operation, January 29th 1931. Left tempero-parietal craniotomy; stimulation of motor cortex; production of cortical wound of the motor area. (See chart for stimulation).

Group 2. Post-operative dose wormwood after brain wound.

4/7/31.	4.25 kg.	.9 cc.	3.8 cc.	Vomited.
4/22/31.	4.25 kg.	.9 cc.	3.8 cc.	Quiet.
4/25/31.	4.10 kg.	.95 cc.	3.9 cc.	Quiet.
4/27/31.	4.05 kg.	1.00 cc.	4.05 cc.	Vomited.
5/7/31.	3.85 kg.	1.0 cc.	3.85 cc.	Vomited.
5/9/31.	3.87 kg.	1.0 cc.	3.9 cc.	Quiet.
5/15/31.	3.85 kg.	1.1 cc.	4.2 cc.	Vomited.
5/19/31.	3.83 kg.	1.1 cc.	4.2 cc.	Vomited; given 1 cc. in addition.
6/6/31.	3.55 kg.	1.2 cc.	4.4 cc.	Quiet.
6/8/31.	3.58 kg.	1.2 cc.	4.29 cc.	Vomited.
6/13/31.	3.45 kg.	1.2 cc.	4.1 cc.	Vomited; given 2.5 cc
6/17/31.	3.47 kg.	1.25 cc.	4.3 cc.	Vomited.
6/20/31.	3.45 kg.	1.3 cc.	4.5 cc.	Vomited; given 2 cc.
6/24/31.	3.42 kg.	1.4 cc.	4.8 cc.	Quiet.
7/11/31.	3.6 kg.	1.45 cc.	5.2 cc.	Quiet.
7/23/31.	3.57 kg.	1.5 cc.	5.3 cc.	Quiet.
7/25/31.	3.47 kg.	1.65 cc.	5.7 cc.	Quiet.
7/29/31.	3.47 kg.	1.8 cc.	6.2 cc.	Quiet.
8/1/31.	3.45 kg.	2.0 cc.	6.9 cc.	Vomited; given 2.5 cc
8/8/31.	3.47 kg.	2.1 cc.	7.3 cc.	Seizure (2).

Summary: Minimal pre-operative convulsant dose wormwood 1.2 cc. per kilogram.
Minimal post-operative convulsant dose not determined but is well above the pre-operative dose.

Cat No. 4301
Drawing at operation. Area on left cortex. Stimulation.
Production of brain scar.



1. 0.6 milliamp. galv nic. - generalized jerk.
2. 0.4 " " " - backward jerk of head.
3. 0.4 " " " - extension jerk of neck and trunk.
4. 0.4 " " " - jerking of neck and trunk.
5. 0.8 " " " - marked jerking of the muscles of the neck and trunk. By prolongation of the stimulus there developped a clonic jerking of these muscles but not of the extremities. Following the prolonged stimulation in area 5 there continued to be spontaneous jerks of the trunk muscles especially those of the neck. These jerks continued from time to time until the c closure of the incision was nearly complete.

CAT NO. 4301.

Cat No. 4302.

Group 1. Pre-operative dosing with wormwood (10% emulsion); stomach tube.

Date.	Weight.	Dose per kg.	Total.	Result.
1/6/31.	2.65 kg.	1.1 cc.	2.9 cc.	Several jerks;seizure(2).
1/12/31.	2.7 kg.	1.05cc.	2.8 cc.	Seizure (2).
1/17/31.	2.7 kg.	1.00 cc.	2.7 cc.	Seizure (2).
1/28/31.	2.75 kg.	.9 cc.	2.5 cc.	Quiet.

Minimal pre-operative convulsant dose wormwood 1.0 cc. per kilogram body weight.

Operation, February 6th 1931. Right fronto-parietal craniotomy; stimulation of the motor cortex; production of cortical wound of the motor area. (See chart for stimulation).

Group 2. Post-operative dose wormwood after brain wound.

4/7/31.	2.55 kg.	.8 cc.	2.0 cc.	Several jerks;seizure (3) generalized; no focal signs.
4/22/31.	2.65 kg.	.75 cc.	2.0 cc.	Seizure (2); not localized.
4/25/31.	2.57 kg.	.70 cc.	1.8 cc.	Quiet.
4/27/31.	2.55 kg.	.70 cc.	1.8 cc.	Quiet.
5/19/31.	2.47 kg.	.75 cc.	1.85 cc.	Quiet.
6/6/31.	2.57 kg.	.75 cc.	1.9 cc.	Quiet.
6/8/31.	2.52 kg.	.8 cc.	2.0 cc.	Quiet.
6/13/31.	2.57 kg.	.85 cc.	2.2 cc.	Quiet.
6/17/31.	2.84 kg.	.9 cc.	2.55 cc.	Quiet.
6/20/31.	2.72 kg.	1.0 cc.	2.7 cc.	Quiet.
6/24/31.	2.62 kg.	1.1 cc.	2.9 cc.	Seizure (2).
7/11/31.	2.77 kg.	1.0 cc.	2.8 cc.	Quiet.
7/23/31.	2.72 kg.	1.1 cc.	3.0 cc.	Seizure (2).

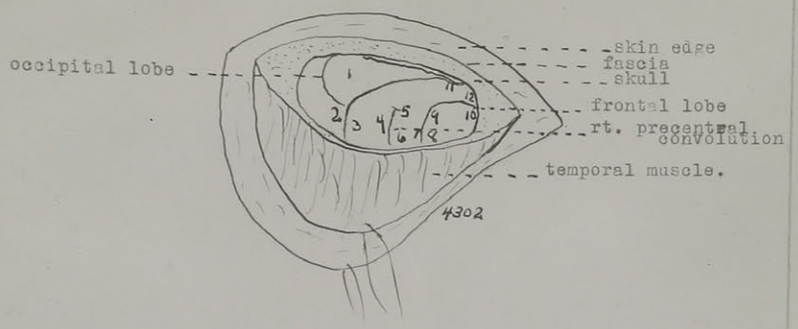
Minimal post-operative convulsant dose wormwood (after brain wound) 1.1 cc. per kilogram.

7/24/31.	Exposure of vagus and sympathetics; no removal.			
8/30/31.	2.8 kg.	1.1 cc.	3.08 cc.	Several jerks; no seizure

Summary: Minimal pre-operative convulsant dose wormwood 1.0 cc. per kilogram.
Minimal post-operative convulsant dose wormwood (after brain wound) 1.1 cc per kilogram.
Dose raised 0.1 cc. per kilogram.
Dosing after exposure of vagus and sympathetic not complete.

Diagram of stimulation drawn at the time of operation.

Right tempero-parietal cortex. Cat No. 4302.



The motor cortex of the right side was first stimulated with galvanic current of 1 milliampere strength in all areas. No muscular movement resulted. The current was then raised to 3 milliamperes when contractions of the muscles were produced as follows:

1. general stiffening and extension of all of the muscles of the back.
2. slight jerking backward of the head and contraction of the temporal muscles.
3,4,5,6, combined extension of the back and jerking of the head dorsally.
7,8,9, extension and abduction of the right leg . With current increased to 4 milliamperes the left leg extended with the right.
10,11,12, with 3 milliamperes current the left leg extended and abducted while the right leg remained quiet. Increase of the current to 4 milliamperes caused slight extension of the right leg as well.

Faradism

Using the smallest possible amount of current obtainable on the machine used (about 3/4 on the scale) the following results were obtained in the designated areas.

1,2. stiffening and extension of the muscles all along the back. The stiffening was clonic in nature thus making it comparable to a tremor of the muscles in the stimulated area.
3,4,5,6, Clonic twitching of the muscles of the back and the right leg. Areas 7,&8 produced approximately the same type of movement in the same areas but an occasional twitch was noted in the left rear leg as well.
9,10,11,12 clonic movement of the left rear leg, chiefly extension, and slight clonic or twitching movement of the muscles along the left side of the body. head, face and fore paw not noticed to move.

With the addition of more current by moving the Faradic indicator up to 1.5 the reactions above were all increased in magnitude. In areas 1 to 5 inclusive both legs were noted to be in clonic extension and abduction.

In the areas 6 to 12 the use of this stimulus produced a clonic generalized extension of the body with extension of the rear legs and extension of the head on the body.

Although practically a generalized convulsion could be produced as long as the contact of the electrode was maintained with the cortex in the area (6 to 12) there was only a momentary continuation of the movement after the electrode was removed from contact with the cortex.

CAT NO. 4302.

Cat No. 4303.

Group 1. Pre-operative dosing with wormwood (10% emulsion).

Date.	Weight.	Dose per kg.	Total.	Result.
1/6/31.	4.00 kg.	1.1 cc.	4.4 cc.	Quiet.
1/12/31.	3.95 kg.	1.15 cc.	4.5 cc.	Vomited.
1/17/31.	4.05 kg.	1.15 cc.	4.7 cc.	Vomited.
1/28/31.	4.45 kg.	.90 cc.(error)	4.0 cc.	Quiet.
2/7/31.	4.62 kg.	1.15 cc.	5.3 cc.	Quiet.
2/16/31.	4.5 kg.	1.2 cc.	5.4 cc.	Excited.
2/28/31.	4.35 kg.	1.25 cc.	5.4 cc.	Excited slightly.
3/5/31.	4.45 kg.	1.3 cc.	5.8 cc.	Quiet.
3/12/31.	4.47 kg.	1.4 cc.	6.3 cc.	Vomited.
3/16/31.	4.47 kg.	1.45 cc.	6.5 cc.	Vomited.
3/19/31.	4.45 kg.	1.45 cc.	6.4 cc.	Quiet.
4/4/31.	5.00 kg.	1.5 cc.	7.5 cc.	Quiet.
4/7/31.	4.92 kg.	1.6 cc.	7.9 cc.	Quiet.
4/16/31.	4.95 kg.	1.7 cc.	8.4 cc.	Quiet.
4/22/31.	5.1 kg.			Changed to camphor (20%) in oil, intramuscularly.
4/22/31.	5.1 kg.	.7 cc.	3.57 cc.	Quiet.
4/25/31.	5.15 kg.	.8 cc.	4.1 cc.	Quiet.
4/27/31.	4.95 kg.	.9 cc.	4.25 cc.	Quiet.
5/7/31.				Wormwood because of sore legs.
5/7/31.	5.1 kg.	2.00 cc.	10.2 cc.	Vomited.
5/9/31.				Camphor again used(intra-
5/9/31.	5.05 kg.	1.1 cc.	5.6 cc.	muscularly). Over-reacts to sound.

5/22/31. Right fronto-parietal craniotomy.

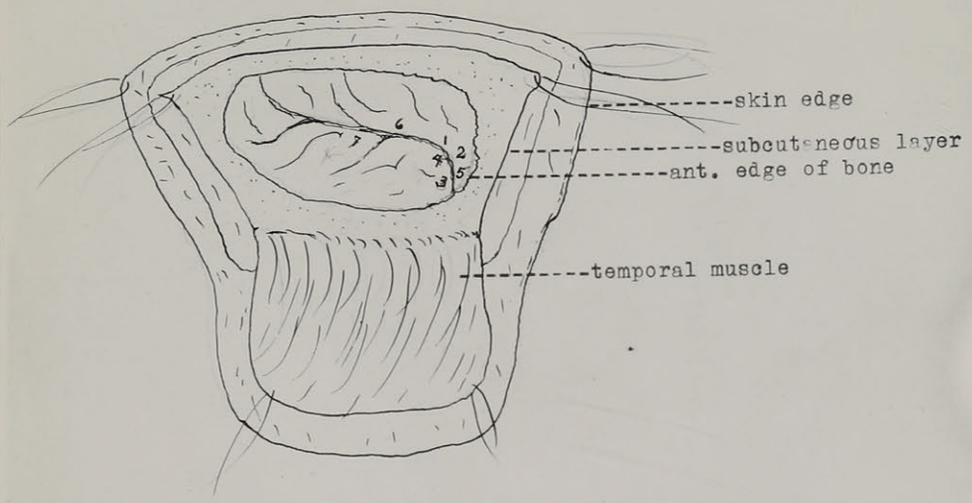
Group 2. Post-operative dose wormwood after brain wound.

7/23/31.	5.05 kg.	1.2 cc.	6.0 cc.	Quiet.
7/25/31.	4.95 kg.	1.4 cc.	6.9 cc.	Quiet.
7/29/31.	4.7 kg.	1.8 cc.	8.4 cc.	Quiet.
8/1/31.	4.58 kg.	2.0 cc.	9.1 cc.	Quiet.
8/8/31.	4.54 kg.	2.2 cc.	10.0 cc.	Quiet, vomited small amount.

Summary: This animal was resistant to both wormwood and camphor. It was operated upon in the hope of causing a lower threshold but it has failed to convulse on large doses of wormwood.

Stimulation of the cortex of CatNo. 4303 at operation.

Galvanic current was not used in this case because the operation was for demonstration purposes and the faradic current has given more uniform and satisfactory results.
Faradism was begun at the set No. 4 as that has given most of the minimum results of active contraction.
Resulta of Stimulation



Faradic at 4. Area 1. Flexion of the left fore paw, & hind leg.
Faradic at 3. Area 1. No contraction after prolonged contact.
Faradic at 4. Area 2. Flexion of the front paw.(left)
" at.4. Area 5. Flexion of the front paw and contraction of the muscles of the neck with pulling of the ear over to left.
Faradic at 4 Area 4. Flexion of the front paw, left.
Faradic at 4 Area 3. Flick of left front paw.
Faradic at 8 Areas2,3,4,5, convulsive jerking of the left fore and hind leg with slight contraction of the neck muscles and flick of the left ear. No true convulsion was obtained which would persist more than 5 seconds after breaking of the contact.

CAT NO. 4303.

Cat No. 4304.

Group 1. Pre-operative dosing with wormwood (10% emulsion); stomach tube.

Date.	Weight.	Dose per kg.	Total.	Result.
1/6/31.	2.5 kg.	1.1 cc.	2.8 cc.	Seizure (2).
1/12/31.	2.6 kg.	1.05 cc.	2.7 cc.	Seizure (3);incontinenc
1/17/31.	2.65 kg.	1.0 cc.	2.65 cc.	Seizure (2).
1/28/31.	2.15 kg.	.9 cc.	2.8 cc.	Quiet.
2/7/31.	3.2 kg.	.95 cc.	3.0 cc.	Quiet.

Minimal pre-operative convulsant dose wormwood 1.0 cc. per kilogram body weight.

Operation, February 10th 1931. Left fronto-parietal craniotomy; stimulation of the motor cortex; production of cortical wound of the motor area. (See chart for stimulation).

Group 2. Post-operative dose wormwood after brain wound.

4/7/31.	3.75 kg.	.8 cc.	3.0 cc.	Quiet.
4/22/31.				Pregnant; not dosed.
5/14/31.				Gave birth to 4 kittens
7/11/31.	2.9 kg.	.8 cc.	2.3 cc.	Quiet.
7/23/31.	3.22 kg.	.9 cc.	2.9 cc.	Quiet.
7/29/31.	2.95 kg.	1.1 cc.	3.2 cc.	Seizure (2).
8/1/31.	2.8 kg.	1.2 cc.	3.3 cc.	Seizure (3);seizure(2)
8/8/31.	2.82 kg.	1.0 cc.	2.8 cc.	Seizure (3) left sided

Minimal 1st post-operative convulsant dose wormwood 1.00 cc. per kilogram.

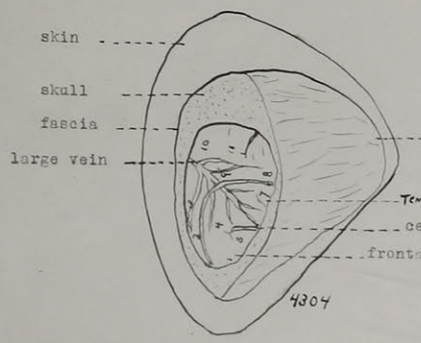
8/21/31. Right sympathectomy, superior and stellate ganglia.

Summary: Minimal pre-operative convulsant dose wormwood 1.0 cc. per kilogram.
Minimal 1st post-operative dose wormwood (after brain wound) 1.0 cc. per kilogram.
Dose unchanged by brain wound.

Minimal post-operative dose wormwood after complete right cervical sympathectomy not determined, but the animal failed to convulse on the previous dose.

Left motor cortex Cat No.4304 drawn at operation.
Stimulation with galvanic and then Faradic current.

When the cortex was exposed galvanic stimulation with a needle point electrode was carried out at the various points indicated on the drawing by numbers.
Using 0.06 milliamperes of galvanic current the following results were obtained in the areas indicated:



Stimulation of the cortex with 0.6 to 0.8 milliamperes of galvanic current. The resulting contractions in the various areas were as indicated below.
1,3, marked twitching of the right side of the face, slight jerking of the right fore and hind paws.
2,4,5,6, twitching of the fore and hind legs and slight jerking of the extensor muscles of the back.
7,8,9,10, 11, & 12 generalized jerk of the entire back with jerk of the four legs, the jerks on the right side being somewhat more pronounced than those on the left.
Using the smallest current of faradic type obtainable on the machine in the laboratory(Monopol made by Nye-Sherring Corperation of New York) stimulation in any area on the cortical surface caused marked contractiona of clonic type in all four legs and slight twitching of the face and eyelids on both sides but most marked on the right.

Despite this marked demonstration of the excitability of the exposed cortex to galvanic and Faradic current I was unable to produce a convulsion of epileptic nature which would persist after the contact between the cortex and the electrode was broken.

CAT NO. 4304.

Cat No.4305.

Group No. 1. Pre-operative dosing with wormwood (10% emulsion); stomach tube.

Date.	Weight.	Dose per kg.	Total.	Result.
1/6/31.	2.5 kg.	1.1 cc.	2.8 cc.	Quiet.
1/12/31.	2.3 kg.	1.2 cc.	2.8 cc.	Seizure (3), seizure (2) Seizure (2), seizure (2)
1/28/31.	2.43 kg.	1.1 cc.	2.7 cc.	Excited; no seizure.
2/7/31. c	2.67 kg.	1.15 cc.	3.0 cc.	Seizure (2), bilateral,

Minimal pre-operative convulsant dose wormwood 1.15 cc. per kilogram body weight.

Operation, February 19th 1931. Left fronto-parietal craniotomy; stimulation of the motor cortex; production of cortical wound in the motor area. (See chart for stimulation).

February 24th 1931. A moderate pus collection in the anterior end of the operative wound was drained. Mercurochrome irrigation showed communication between wound and the nose through the frontal sinus which had purposely been opened at operation in order to expose more of the frontal lobe for stimulation.

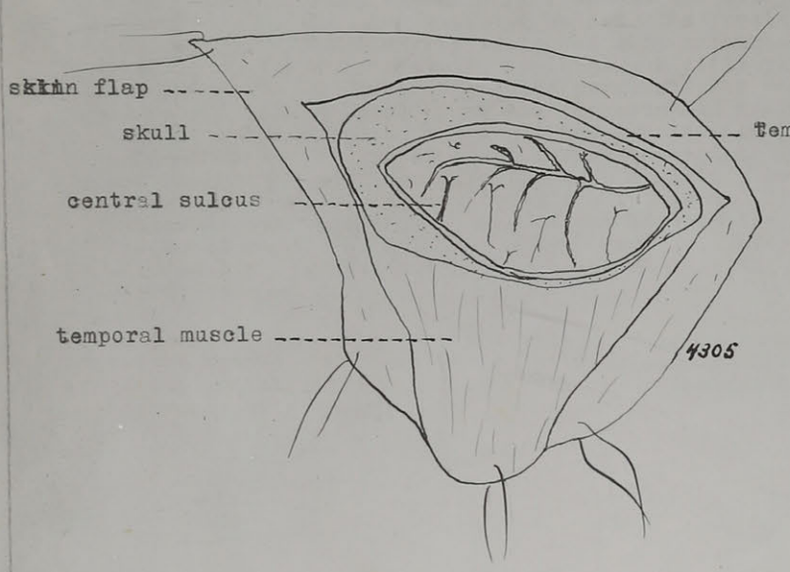
March 2nd 1931. Despite free drainage, careful irrigation and frequent dressings, the infection spread widely. The animal was chloroformed and the brain and cord used for routine histological studies in the laboratory.

Autopsy Findings: Extensive infection of the brain at the site of the cortical wound, with spread of the infection throughout the subarachnoid space. Necrosis of bone in region of frontal sinus. (Gross findings).

Summary: Minimal pre-operative convulsant dose wormwood 1.15 cc. per kilogram.

Operative death.

Drawing of the motor cortex of the left side made at operation Stimulation of the cortex with bipolar electrode with the maximum strength of both galvanic and faradic currents produced no contraction of any muscle.



Stimulation of the cortex with unipolar current both Galvanic and Faradic produced either no contraction at any point or when the current was increased slightly there resulted a generalized jerk of all of the trunk muscles from all points on the cortex when stimulated.

CAT NO. 4305.

Cat No. 4332.

Group 1. Pre-operative dosing with wormwood (10% emulsion); stomach tube.

Date.	Weight.	Dose per kg.	Total.	Result.
2/7/31.	3.55 kg.	1.0 cc.	3.55 cc.	Quiet.
2/16/31.	3.0 kg.	1.1 cc.	3.3 cc.	Excited; salivating.
2/28/31.	3.05 kg.	1.2 cc.	3.7 cc.	Excited; increased respiration.
3/5/31.	3.0 kg.	1.3 cc.	3.7 cc.	Seizure (2); weakness of left hind leg after seizure.
3/12/31.	2.87 kg.	1.25 cc.	3.6 cc.	Excited.
3/16/31.	2.75 kg.	1.3 cc.	3.6 cc.	Quiet.
4/7/31.	3.15 kg.	1.3 cc.	4.0 cc.	Quiet.
4/16/31.	3.10 kg.	1.3 cc.	4.0 cc.	Seizure (2).
4/22/31.	3.07 kg.	1.25 cc.	3.8 cc.	Vomited.
4/25/31.	3.0 kg.	1.25 cc.	3.75 cc.	Quiet.
4/27/31.	3.0 kg.	1.3 cc.	3.9 cc.	Hypersalivating.
5/7/31.	3.15 kg.	1.3 cc.	4.1 cc.	Vomited.
5/9/31.	3.12 kg.	1.3 cc.	4.0 cc.	Quiet.
5/15/31.	3.0 kg.	1.35 cc.	4.0 cc.	Quiet.
5/19/31.	3.0 kg.	1.4 cc.	4.2 cc.	Quiet.
6/6/31.	3.1 kg.	1.45 cc.	4.5 cc.	Quiet.
6/8/31.	3.0 kg.	1.5 cc.	4.5 cc.	Quiet.
6/13/31.	3.02 kg.	1.6 cc.	4.8 cc.	Vomited; given 2.5 cc.
6/17/31.	3.04 kg.	1.65 cc.	4.0 cc.	Quiet.
6/20/31.	3.0 kg.	1.7 cc.	5.1 cc.	Excited.
6/24/31.	3.0 kg.	1.75 cc.	5.25 cc.	Seizure (2).
7/11/31.	3.05 kg.	1.75 cc.	5.3 cc.	Quiet.
7/23/31.	2.95 kg.	1.75 cc.	5.1 cc.	Seizure.
7/25/31.	2.8 kg.	1.7 cc.	4.76 cc.	Quiet.

Minimal pre-operative convulsant dose wormwood 1.75 cc. per kilogram.

7/31/31. Bilateral superior cervical sympathetic ganglionectomy.
8/2/31. Died. Autopsy revealed no cause for death. Operative site in excellent condition.

Summary: Minimal pre-operative convulsant dose wormwood 1.75 cc. per kilogram.

Operative death.

Cat No. 4333.

Group 1. Pre-operative dosing with wormwood (10% emulsion); stomach tube.

Date.	Weight.	Dose per kg.	Total.	Result.
2/7/31.	3.47 kg.	.9 cc.	3.1 cc.	Seizure (2),generalized.
2/16/31.	3.35 kg.	.75 cc.	2.5 cc.	Seizure (2),spastic gait
2/28/31.	3.42 kg.	.65 cc.	2.2 cc.	Quiet.
3/3/31.	3.45 kg.	.7 cc.	2.4 cc.	Quiet.
3/12/31.	3.55 kg.	.75 cc.	2.7 cc.	Quiet.
3/16/31.	3.4 kg.	.8 cc.	2.7 cc.	Seizure (2), rolling clockwise, seizure (2).
3/19/31.	3.4 kg.	.75 cc.	2.5 cc.	Quiet.

Minimal pre-operative convulsant dose wormwood 0.8 cc. per kilogram body weight.

Operation, March 21st 1931. Left fronto-parietal craniotomy; stimulation of motor cortex; production of cortical wound of themotor area.

Group 2. Post-operative dose wormwood after brain wound.

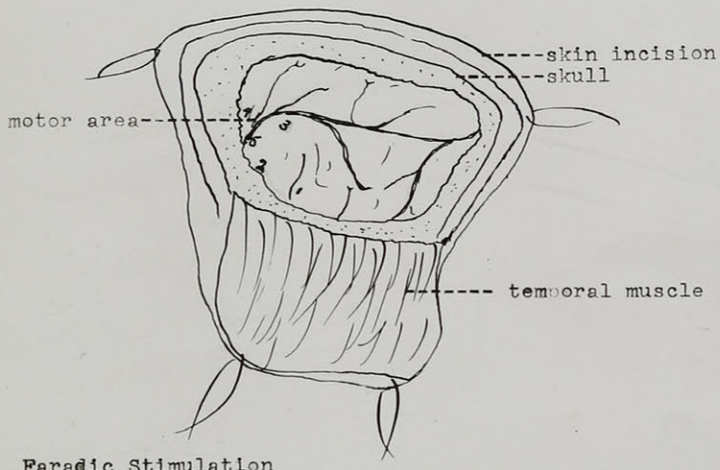
5/9/31.	3.95 kg.	.5 cc.	2.0 cc.	Quiet.
5/15/31.	3.8 kg.	.55 cc.	2.1 cc.	Quiet.
5/19/31.	3.7 kg.	.6 cc.	2.2 cc.	Seizure (2).
6/6/31.	3.15 kg.	.6 cc.	1.9 cc.	Quiet.
6/8/31.	3.1 kg.	.6 cc.	1.86 cc.	Quiet.
6/13/31.	2.95 kg.	.65 cc.	1.9 cc.	Seizure (2).
6/17/31.	2.82 kg.	.6 cc.	1.7 cc.	Quiet.
6/20/31.	2.7 kg.	.65 cc.	1.75 cc.	Quiet.
6/24/31.	2.6 kg.	.65 cc.	1.7 cc.	Quiet.
7/11/31.	2.65 kg.	.7 cc.	1.8 cc.	Seizure (2).
7/23/31.	2.42 kg.	.65 cc.	1.6 cc.	Seizure (2).
7/25/31.	2.37 kg.	.6 cc.	1.4 cc.	Quiet.
7/29/31.	2.35 kg.	.65 cc.	1.5 cc.	Seizure (2).

Minimal post-operative convulsant dose wormwood 0.6 cc. per kilogram.

Summary: Minimal pre-operative convulsant dose wormwood 0.5 cc. per kilogram.
Minimal post-operative convulsant dose wormwood (after brain wound) 0.6 cc. per kilogram.
Dose lowered 0.2 cc. per kilogram.

Stimulation of left motor cortex of cat No.4333 at operation.

Galvanic Stimulation: Region 1. pull down rt, ear. 2 milliamp.
Region 2 - 2 milliamp. adduction of right fore leg and pulling down of right ear. Following the stimulation there was slight twitching of right ear and eye as well as right fore and hind legs.
Region 3. Slight twitch of rt, hind leg.
Region 2. 3milliamp. contraction of rt, side of the body with adduction of both legs and flick of right ear.
Region 2. 5 milliamp. More marked adduction and flexion of righ. legs. Flick of rt, ear.



Faradic Stimulation
Faradic 2. area 2. Slight convulsion of rt. side including both legs ear , and dorsiflexion of head in clonic convulsion
After the attack the stimulation failed to produce another convulsion and only after raising the current to 5 Faradic did the ear begin to flick on stimulation.
This failure of response after the convulsion may have been due to fatigue of the given centers.

CAT NO. 4333.

Cat No. 4345.

Group 1. Pre-operative dosing with wormwood (10% emulsion); stomach tube.

Date.	Weight.	Dose per kg.	Total.	Result.
2/28/31.	3.52 kg.	1.0 cc.	3.5 cc.	Seizure (2),generalized
3/5/31.	3.25 kg.	.9 cc.	2.9 cc.	Vomited.
3/12/31.	3.5 kg.	.95 cc.	3.3 cc.	Vomited 1 cc.Seizure(2)
3/16/31.	3.2 kg.	.9 cc.	2.9 cc.	Seizure (2),seizure (2)
3/19/31.	3.25 kg.	.85 cc.	2.8 cc.	Seizure (3). Stood rigidly on four legs for fifteen minutes.
4/4/31.	3.8 kg.	.80 cc.	3.04 cc.	Quiet.
4/7/31.	3.6 kg.	.86 cc.	3.0 cc.	Quiet.
4/16/31.	3.8 kg.	.85 cc.	3.3 cc.	Quiet.
4/22/31.	4.05 kg.	.9 cc.	3.6 cc.	Quiet.
4/25/31.	3.95 kg.	.9 cc.	3.5 cc.	Quiet.
4/27/31.	3.95 kg.	.95 cc.	3.75 cc.	Quiet.
5/7/31.	4.00 kg.	.95 cc.	3.8 cc.	Vomited.
5/9/31.	4.02 kg.	1.0cc.	4.0 cc.	Vomited.
5/15/31.	3.95 kg.	1.0 cc.	3.95 cc.	Vomited.
5/19/31.	3.85 kg.	1.0 cc.	3.85 cc.	Quiet.
6/6/31.	4.12 kg.	1.1 cc.	4.5 cc.	Quiet.
6/8/31.	4.13 kg.	1.2 cc.	4.95 cc.	Vomited; given 1 cc.
6/13/31.	4.05 kg.	1.3 cc.	5.26 cc.	Quiet.
6/17/31.	4.02 kg.	1.35 cc.	5.4 cc.	Quiet.
6/20/31.	4.05 kg.	1.4 cc.	5.7 cc.	Quiet.
6/24/31.	4.0 kg.	1.5 cc.	6.0 cc.	Quiet.
7/11/31.	4.25 kg.	1.6 cc.	6.8 cc.	Quiet.
7/23/31.	3.87 kg.	1.7 cc.	6.6 cc.	Quiet; vomited small amount.
7/25/31.	3.75 kg.	1.8 cc.	6.75 cc.	Jerks.
7/29/31.	3.67 kg.	1.85 cc.	6.8 cc.	Quiet.
8/1/31.	3.7 kg.	1.95 cc.	7.2 cc.	Quiet.
8/8/31.	3.6 kg.	2.05 cc.	7.4 cc.	Seizure (2).

Cat No. 4346.

Group 1. Pre-operative dosing with wormwood (10% emulsion); stomach tube.

Date.	Weight.	Dose per kg.	Total.	Result.
2/28/31.	3.45 kg.	1.0 cc.	3.45 cc.	Quiet.
3/5/31.	3.65 kg.	1.1 cc.	4.00 cc.	Seizure (2), seizure (2).
3/12/31.	3.7 kg.	1.0 cc.	3.7 cc.	Seizure (2), jerks and sham rage, seizure (2).
3/16/31.	3.65 kg.	.9 cc.	3.3 cc.	Vomited 1cc. Quiet.
3/19/31.	3.75 kg.	.95 cc.	3.6 cc.	Quiet.

Minimal pre-operative convulsant dose wormwood 1.0 cc. per kilogram body weight.

Operation April 7th 1931. Right fronto-parietal craniotomy; stimulation of the motor cortex; production of cortical wound of motor area. (See chart for stimulation.)

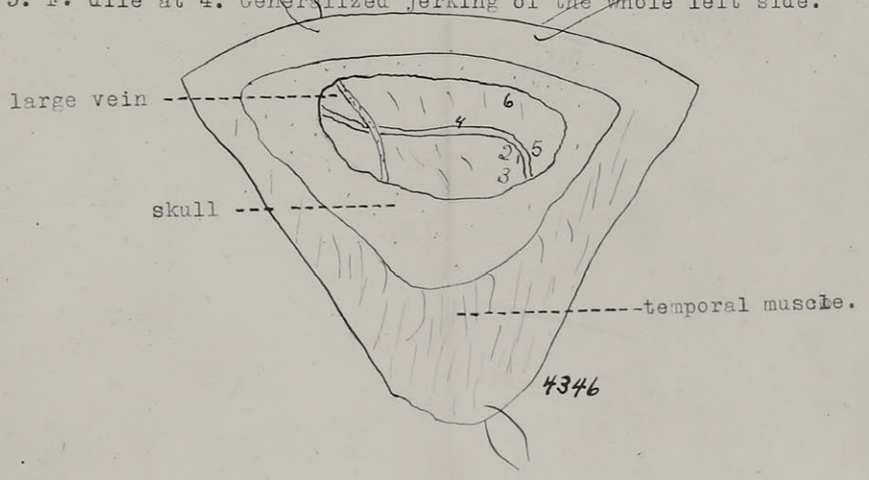
Group 2. Post-operative dose wormwood after brain wound.

5/19/31.	4.1 kg.	.8 cc.	3.3 cc.	Quiet.
6/6/31.	3.95 kg.	.85 cc.	3.3 cc.	Quiet.
6/8/31.	3.95 kg.	.9 cc.	3.55 cc.	Quiet.
6/13/31.	3.98 kg.	.95 cc.	3.8 cc.	Quiet.
6/17/31.	3.96 kg.	1.0 cc.	4.0 cc.	Quiet.
6/20/31.	3.95 kg.	1.1 cc.	4.77 cc.	Quiet.
7/11/31.	4.0 kg.	1.3 cc.	5.2 cc.	Quiet.
7/23/31.	3.85 kg.	1.4 cc.	5.4 cc.	Quiet.
7/25/31.	3.76 kg.	1.5 cc.	5.6 cc.	Seizure (2).
7/29/31.	3.72 kg.	1.45 cc.	5.4 cc.	Quiet.
8/1/31.	3.62 kg.	1.5 cc.	5.4 cc.	Quiet.
8/8/31.	3.65 kg.	1.5 cc.	5.5 cc.	Seizure (2), head to right

Minimal post-operative convulsant dose wormwood 1.5 cc. per kilogram.

Summary: Minimal pre-operative convulsant dose wormwood 1.0 cc per kilogram.
Minimal post-operative convulsant dose wormwood (after brain wound) 1.5 cc. per kilogram.
Dose raised 0.5 cc. per kilogram.

Record of Stimulation of the motor cortex Cat No.4346
Bipolar electrode. Stimulation first with galvanic and then faradic.
Galvanic. Area numbers below.
1. 2 milliamp. Flick of the left ear.
2. 4 " " . Elevation of the left eyebrow.
3. 4 " " . Wink of both eyes.
Faradic Current Numbers below.
1. F. dile at 3. Retraction of the nictitating membranes of both eyes . Same result with repeated stimulation.
5. F. dile at 4. Generalized jerking of the whole left side.



6. F.dile at4. Bilateral generalized convulsing as long as the contact was maintained with the electrode.
1. F. dile at 8. Bilateral jerking of the muscles of the torso and the four extremities . The left side showed more jerking than the right.

Following the stimulation of the cortex a rather extensive wound was made in the cortex in the area including the area marked 1,2,3,5. . A large piece of muscle was placed in the brain wound and thus the bleeding was checked and the means for producing a retracting scar was left in place.

CAT NO. 4346.

Cat No. 4355.

Group 1. Pre-operative dosing with wormwood (10% emulsion); stomach tube.

Date.	Weight.	Dose per kg.	Total.	Result.
4/4/31.	3.78 kg.	1.0 cc.	3.8 cc.	Seizure (2).
4/16/31.	3.62 kg.	.95 cc.	3.4 cc.	Quiet.
4/22/31.	3;67 kg.	1.0 cc.(error)	3.4 cc.	Quiet.
4/25/31.	3.6 kg.	1.0 cc.	3.6 cc.	Retching, but no vomiting
4/27/31.	3.57 kg.	1.1 cc.	3.9 cc.	A series of jerks.
5/7/31.	3.65 kg.	1.15 cc.	4.2 cc.	Vomited.
5/9/31.	3.62 kg.	1.15 cc.	4.2 cc.	Quiet.
5/15/31.	3.56 kg.	1.2 cc.	4.3 cc.	Quiet.
5/19/31.	3.55 kg.	1.25 cc.	4.4 cc.	Quiet.
6/6/31.	3.8 kg.	1.3 cc.	4.9 cc.	Quiet.
6/8/31.	3.67 kg.	1.4 cc.	5.1 cc.	A series of jerks.
6/13/31.	3.45 kg.	1.45 cc.	5.0 cc.	Vomited.
6/17/31.	3.25 kg.	1.45 cc.	4.7 cc.	Quiet.
6/20/31.	3.1 kg.	1.5 cc.	4.65 cc.	Several single jerks.
6/24/31.	3.02 kg.	1.55 cc.	4.7 cc.	Vomited.
7/11/31.	3.4 kg.	1.55 cc.	5.3 cc.	Quiet.
7/23/31.	3.2 kg.	1.6 cc.	5.1 cc.	Quiet; vomited small amount.
7/25/31.	3.05 kg.	1.7 cc.	5.2 cc.	Violent jerks,
7/29/31.	2.92 kg.	1.75 cc.	5.1 cc.	Seizure (2), jerks continuing.
8/1/31.	2.79 kg.	1.7 cc.	4.7 cc.	Quiet.
8/8/31.	2.82 kg.	1.75 cc.	4.9 cc.	Seizure (2), bilateral,

Minimal pre-operative convulsant dose wormwood 1.75 cc. per kilogram.

Summary: Minimal pre-operative convulsant dose wormwood 1.75 cc. per kilogram.

Cat No. 4356.

Group 1. Pre-operative dosing with wormwood (10% emulsion); stomach tube.

Date.	Weight.	Dose per kg.	Total.	Result.
4/4/31.	4.35 kg.	1.0 cc.	4.35 cc.	A few jerks.
4/16/31.	4.1 kg.	1.05 cc.	4.3 cc.	Seizure (2).
4/22/31.	4.1 kg.	1.0 cc.	4.1 cc.	Seizure (2).
4/25/31.	4.05 kg.	.95 cc.	3.8 cc.	Quiet.
4/27/31.	3.97 kg.	1.0 cc.	4.0 cc.	Quiet.
5/7/31.	4.2 kg.	1.05 cc.	4.4 cc.	Quiet.
5/9/31.	4.1 kg.	1.1 cc.	4.5 cc.	Vomited.
5/15/31.	4.0 kg.	1.1 cc.	4.4 cc.	Quiet.
5/19/31.	3.87 kg.	1.2 cc.	4.65 cc.	Quiet.
6/6/31.	3.6 kg.	1.2 cc.	4.3 cc.	Quiet.
6/8/31.	3.57 kg.	1.3 cc.	4.25 cc.	Quiet.
6/13/31.	3.67 kg.	1.4 cc.	5.1 cc.	Quiet.
6/17/31.	3.67 kg.	1.6 cc.	5.9 cc.	Quiet.
6/20/31.	3.67 kg.	1.7 cc.	6.2 cc.	Quiet.
6/24/31.	3.75 kg.	1.8 cc.	6.75 cc.	Quiet.
7/11/31.	4.0 kg.	1.8 cc.	7.2 cc.	Quiet.
7/23/31.	3.9 kg.	1.85 cc.	7.2 cc.	Seizure (2).
7/25/31.	3.77 kg.	1.8 cc.	6.8 cc.	Vomited.
7/29/31.	3.77 kg.	1.85 cc.	7.0 cc.	Quiet.
8/1/31.	3.65 kg.	1.85 cc.	6.75 cc.	Quiet.
8/8/31.	3.85 kg.	1.9 cc.	7.3 cc.	Quiet.

Cat No. 4365.

Group 1. Pre-operative dosing with wormwood (10% emulsion); stomach tube.

Date.	Weight.	Dose per kg.	Total.	Result.
4/22/31.	1.9 kg.	1.0 cc.	1.9 cc.	Excited.
4/25/31.	1.87 kg.	1.05 cc.	1.96 cc.	Quiet.
4/27/31.	1.85 kg.	1.1 cc.	2.0 cc.	Quiet.
5/7/31.	1.9 kg.	1.2 cc.	2.3 cc.	Quiet.
5/9/31.	1.9 kg.	1.25 cc.	2.4 cc.	Quiet.
5/15/31.	1.85 kg.	1.3 cc.	2.4 cc.	Quiet.
5/19/31.	1.92 kg.	1.35 cc.	2.6 cc.	Quiet.
6/6//31.	1.9 kg.	1.45 cc.	2.7 cc.	Excited.
6/8/31.	1.82 kg.	1.5 cc.	2.7 cc.	Over-reacts.
6/13/31.	1.87 kg.	1.55 cc.	2.9 cc.	Quiet.
6/24/31.	1.72 kg.	1.6 cc.	2.76cc.	Quiet.
7/11/31.	1.87 kg.	1.6 cc.	3.0 cc.	Seizure (2).
7/23/31.	1.87 kg.	1.55 cc.	2.9 cc.	Seizure (2).
7/25/31.	1.84 kg.	1.5 cc.	2.76 cc.	Quiet.
7/29/31.	1.9 kg.	1.55 cc.	2.9 cc.	Quiet.
8/1/31.	1.87 kg.	1.6 cc.	3.0 cc.	Seizure (2).
8/8/31.	2.02 kg.	1.55 cc.	3.14 cc.	Quiet.

Minimal pre-operative convulsant dose of wormwood 1.6 cc. per kilogram.

Summary: Minimal pre-operative convulsant dose wormwood 1.6 cc. per kilogram.

Cat No. 4371.

Group 1. Pre-operative dosing with wormwood (10% emulsion); stomach tube.

Date.	Weight.	Dose per kg.	Total.	Result.
5/7/31.	3.62 kg.	1.0 cc.	3.6 cc.	Quiet.
5/9/31.	3.5 kg.	1.1 cc.	3.85 cc.	Quiet.
5/15/31.	3.4 kg.	1.1 cc.	3.7 cc.	Quiet.
6/6/31.	3.42 kg.	1.15 cc.	3.9 cc.	Quiet.
6/8/31.	3.3 kg.	1.2 cc.	3.96 cc.	Quiet.
6/13/31.	3.25 kg.	1.3 cc.	4.2 cc.	Quiet.
6/17/31.	3.18 kg.	1.4 cc.	4.45 cc.	Quiet.
6/24/31.	3.15 kg.	1.5 cc.	4.7 cc.	Quiet.
7/11/31.	3.37 kg.	1.6 cc.	5.4 cc.	Quiet.
7/23/31.	3.22 kg.	1.7 cc.	5.5 cc.	Quiet.
7/25/31.	3.15 kg.	1.8 cc.	5.7 cc.	Quiet.
7/29/31.	3.05 kg.	1.9 cc.	5.8 cc.	Quiet.
8/1/31.	2.96 kg.	2.0 cc.	5.9 cc.	Seizure (2), bilateral
8/8/31.	3.05 kg.	1.9 cc.	5.8 cc.	Quiet; vomited small amount.

Minimal pre-operative convulsant dose wormwood 2.0 cc. per kilogram.

Summary: Minimal pre-operative convulsant dose wormwood 2.0 cc. per kilogram.

Cat No. 4378.

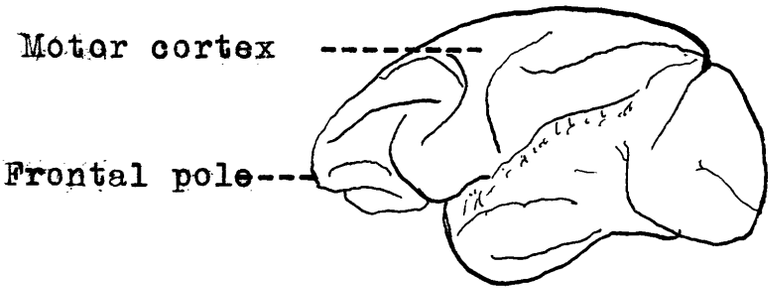
Group 1. Pre-operative dosing with wormwood (10% emulsion) stomach tube.

Date.	Weight.	Dose per kg.	Total.	Result.
6/4/31.	2.27 kg.	1.0 cc.	2.27 cc.	Quiet.
6/17/31.	2.39 kg.	1.05 cc.	2.5 cc.	Vomited.
6/20/31.	2.27 kg.	1.1 cc.	2.5 cc.	Quiet.
6/24/31.	2.27 kg.	1.2 cc.	2.7 cc.	Quiet.
7/11/31.	2.4 kg.	1.2 cc.	2.9 cc.	Seizure (2)
7/23/31.	2.4 kg.	1.15 cc.	2.76 cc.	Quiet.
7/25/31.	2.45 kg.	1.2 cc.	2.9 cc.	Quiet.
7/29/31.	2.55 kg.	1.2 cc.	3.0 cc.	Seizure (3)plus.
8/1/31.	2.32 kg.	1.15 cc.	2.8 cc.	Quiet.
8/8/31.	1.2 kg.	1.2 cc.	2.8 cc.	Seizure (2).

Minimal pre-operativ3 convulsant dose - wormwood - 1.2 cc. per kg.

Summary. Minimal pre-operative convulsant dose wormwood 1.2cc per kilo.

OUTLINE OF MONKEY'S BRAIN (SCHÄFER).



Monkey No. 109. Male.

Group 1. Pre-operative dosing with camphor (20% in olive oil) intramuscularly.

Date.	Weight.	Dose per kg.	Total.	Result and Remarks.
1/7/31.	1.84 kg.	.7 cc.	1.3 cc.	Seizure (2), bilateral. Seizure (2) bilateral.
1/14/31.	1.7 kg.	.6 cc.	1.00 cc.	Quiet.
1/21/31.	2.2 kg.	.65 cc.	1.4 cc.	Quiet.
2/4/31.	1.8 kg.	.70 cc.	1.26 cc.	Quiet.
2/26/31.	1.74 kg.	.70 cc.	1.20 cc.	Quiet.
3/3/31.	1.7 kg.	.75 cc.	1.3 cc.	Quiet.
3/13/31.	1.6 kg.	.8 cc.	1.2 cc.	Seizure (2),bilateral. A series of short seizures followed by longer convulsions; given ether.
3/17/31.	1.7 kg.	.75 cc.	1.3 cc.	Seizure (2); head, and later body turned left.
3/31/31.	1.73 kg.	.7 cc.	1.2 cc.	Seizure (2), bilateral. Seizure (2), bilateral.
4/10/31.	1.76 kg.	.65 cc.	1.1 cc.	Quiet.
4/14/31.	1.89 kg.	.7 cc.	1.3 cc.	Quiet.
4/17/31.	1.78 kg.	.75 cc.	1.3 cc.	Quiet,
4/21/31.	1.79 kg.	.8 cc.	1.4 cc.	Quiet.
4/24/31.	1.9 kg.	.8 cc.	1.5 cc.	Quiet.
4/29/31.	1.86 kg.	.85 cc.	1.6 cc.	Seizure (2),seizure (2), seizure (2), seizure (3); given ether.
5/6/31.	1.8 kg.	.8 cc.	1.4 cc.	Quiet.
5/12/31.	1.9 kg.	.85 cc.	1.6 cc.	Seizure (2), bilateral.
5/19/31.	1.85 kg.	.8 cc.	1.5 cc.	Seizure (2),bilateral; head slightly to left.
5/21/31.	1.9 kg.	.75 cc.	1.4 cc.	Seizure (2), bilateral.
6/2/31.	1.8 kh.	.7 cc.	1.26 cc.	Quiet.
6/5/31.	2.9 kg.	.75 cc.	1.4 cc.	Quiet.
6/11/31.	1.58 kg.	.8 cc.	1.58 cc.	Seizure (2), bilateral. Head to left.
6/16/31.	1.99 kg.	.75 cc.	1.5 cc.	Quiet.

Minimal pre-operative dose indefinite; ranges between .7 cc. and .85cc per kilogram.

6/23/31. Left brain wound.

Group 2. First post-operative dosing with camphor, after brain wound.

7/22/31.	1.8 kg.	.65 cc.	1.2 cc.	Quiet.
7/24/31.	1.85 kg.	.7 cc.	1.3 cc.	Quiet.
7/29/31.	1.76 kg.	.75 cc.	1.3 cc.	Quiet.
7/31/31.	1.84 kg.	.8 cc.	1.47 cc.	Quiet.

Monkey No. 109 continued.

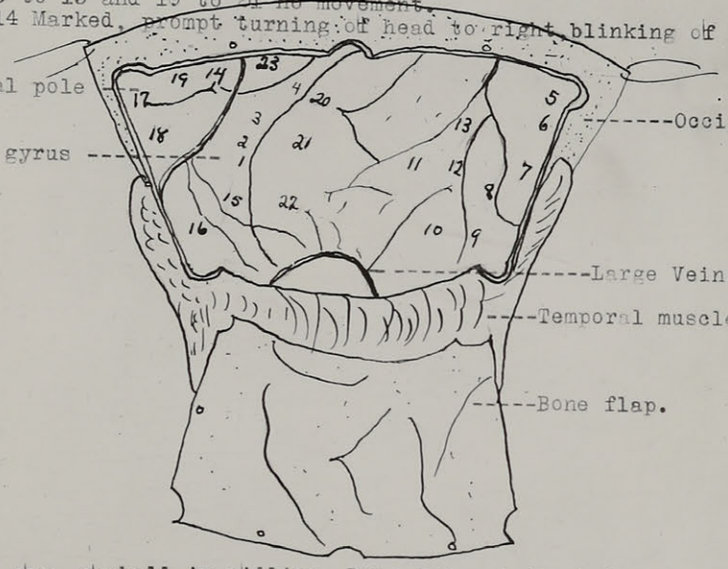
8/4/31.	1.87 kg.	.85 cc.	1.6 cc.	Quiet.	
8/7/31.	1.89 kg.	.9 cc.	1.6 cc.	Quiet; jerks.	several short
8/10/31.	1.89 kg.	.95 cc.	1.8 cc.	Quiet.	
8/14/31.	1.86 kg.	1.0 cc.	1.86 cc.	Quiet.	
8/18/31.	1.89 kg.	1.1 cc.	2.07 cc.	Quiet.	
8/21/31.	2.14 kg.	1.2 cc.	2.57 cc.	Quiet.	
8/25/31.	1.9 kg.	1.3 cc.	2.47 cc.	Quiet.	

Summary: Minimal pre-operative convulsant dose camphor indefinite; ranges between .7 cc. and .85 cc. per kilogram.

This animal is entirely inconsistent in his reaction to the convulsant drug. He was operated upon in hopes of a more constant first post-operative dose.

Chart of the Stimulation of the Cortex of Monkey No. 109 at Operation

Galvanic - Minimum contraction current - 3 milliamperes.
Area 1. Upper lip drawn upward and to the right. Repeated.
" 2. Movement of right eye lid.
" 3. No movement with 3 milliamperes.
Increase of galvanic current produced accentuation of the above and nothing additional. Change to Faradic.
Faradic. Set at 4.
Area 1. Twitching of the right upper lip.
" 2,3. Slight movements of the right upper lip.
" 4. Very slow turning of the head to the right and slight twitch of the right hind foot. Repeated and checked.
" 5 to 13 and 19 to 21 no movement.
" 14 Marked, prompt turning of head to right, blinking of right



eye, eyeball in midline. Repeated and checked.
Faradic Current - Full.
Area 14 Prompt turning of the head to right, blink of right eye, eyeballs in midline.
" 15 Marked twitching of the mouth on the right side. Mouth pulled to right. Persisted 5 to 8 seconds after stimulation.
" 16 Marked twitching of right upper lip.
" 17 Head turned far over to the right. Repeated.
" 18 Less marked turning of the head to the right.
" 19 Most pronounced turning of the head to the right with turning of the eyes far over to the right . On release of the contact the eyes tended to drift back and forth from left to right as the animal was very light. They would then finally come to rest in the midline. The stimulation was then repeated twice with the same result. In the third repetition the eyes failed to move but the head turned as before. This suggests that the center for the head and eyes is forward of the center for the head alone.
Area 23 No turning.

MONKEY NO. 109.

Monkey No. 110.

Group 1. Pre-operative dosing of camphor (20% in olive oil) intramuscularly.

Date.	Weight.	Dose per kg.	Total.	Result and Remarks.
1/7/31.	2.66 kg.	.7 cc.	1.9 cc.	Seizure (2), head left, then right; jerks bilateral; sham rage.
1/14/31.	2.46 kg.	.6 cc.	1.4 cc.	Quiet.
1/21/31.	2.55 kg.	.7 cc.	1.8 cc.	Series of single jerks.

Minimal pre-operative dose camphor 0.7 cc. per kilogram body weight.

Operation February 21st 1931. Left fronto-parietal craniotomy; stimulation of the motor cortex; production of cortical wound in the motor area. (See chart for stimulation).

Group 2. Post-operative dosing camphor after brain wound.

Date.	Weight.	Dose per kg.	Total.	Result and remarks.
4/10/31.	2.41 kg.	.55 cc.	1.3 cc.	Quiet.
4/14/31.	2.39 kg.	.6 cc.	1.4 cc.	Quiet.
4/17/31.	2.54 kg.	.65 cc.	1.65 cc.	Seizure (2) head right, then left. Right arm tonic before rest of body. Seizure (2) eyes to right. Jerks of right arm - Jacksonian.
4/21/31.	2.5 kg.	.6 cc.	1.5 cc.	Seizure (2) right sided jerk fell on right side, then bilateral. Head to right, then to left.
4/24/31.	2.45 kg.	.55 cc.	1.3 cc.	Quiet.
4/29/31.	2.49 kg.	.6 cc.	1.5 cc.	Quiet.
5/6/31.	2.6 kg.	.6 cc.	1.56 cc.	Seizure (2) bilateral; eyes right. Jacksonian attacks of right arm and neck.

Minimal 1st post-operative dose camphor 0.6 cc. per kilogram body weight.

Operation May 7th 1931. Left superior and stellate ganglionectomy and vertebral sympathectomy.

Group 3. Post-operative dosing of camphor after sympathectomy.

Monkey No. 110 continued.

Date.	Weight.	Dose per kg.	Total.	Result and remarks.
6/2/31.	2.48 kg.	.6 cc.	1.5 cc.	Quiet.
6/5/31.	2.58 kg.	.7 cc.	1.8 cc.	Seizure (2),seizure (2).
6/11/31.	2.49 kg.	.65 cc.	1.6 cc.	Quiet.
6/16/31.	2.6 kg.	.7 cc.	1.8 cc.	Seizure (2),seizure (2).

Post-operative dose 0.7cc per kilogram.

6/25/31. Right superior cervical and stellate ganglionectomy.

Group 3. Dosing after bilateral sympathectomy.

7/14/31.	2.5 kg.	.65 cc.	1.6 cc.	Quiet.
7/22/31.	2.4 kg.	.7 cc.	1.7 cc.	Some of dose lost. 1.8cc given in addition.
7/24/31.	2.49 kg.	.7 cc.	1.7 cc.	Seizure, not general. Face head and left arm. Seizure (2).
7/29/31.	2.49 kg.	.65 cc.	1.6 cc.	Quiet.
7/31/31.	2.6 kg.	.7 cc.	1.8 cc.	Seizure (2), right sided.

2nd post-operative minimal convulsant dose camphor 0.7 cc.

8/5/31. Section of greater superficial petrosal nerve.

Group 4. Dosing after section of superficial petrosal nerve.

8/14/31. 2.36 kg. .7 cc. 1.65 cc. Seizure (2) bilateral.
Note: Following operation cutting greater superficial nerve, the monkey could not close his eye on the side of the operatio The upper lid not only refused to close but had the appearance of being retracted into the orbit. There was also a moderate amount of left sided facial weakness.
Early in the first dosing after this operation the monkey had athetoid movements of both hind legs. These were similar to the movements seen when the monkeys recover from an attack. There were then a few very small jerks on the left side, whereas before operation the preliminary jerks were right sided. At 2.40 p.m. the monkey was having numerous jerks of the neck and torso; he was chattering wildly..

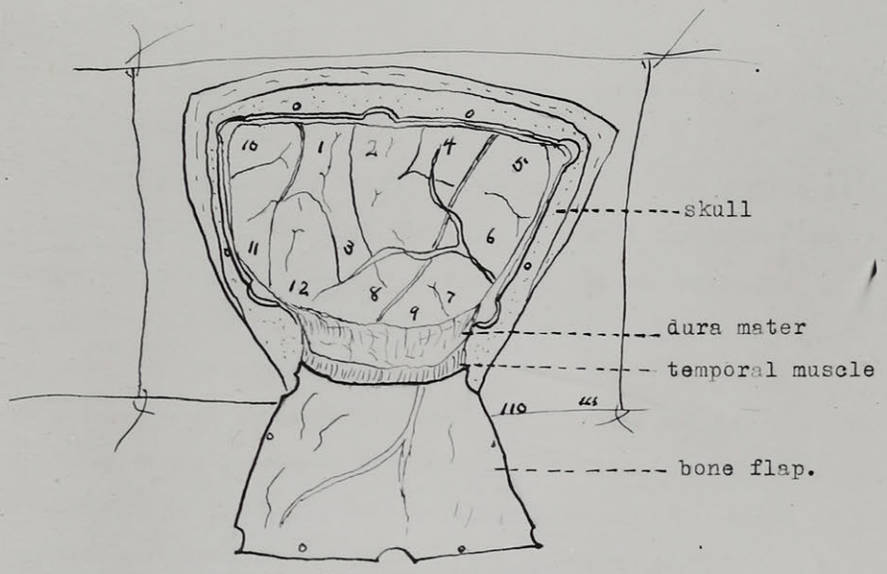
8/18/31.	2.4 kg.	.65 cc.	1.56 cc.	Quiet.
8/21/31.	2.6 kg.	.7 cc.	1.8 cc.	Quiet.
8/25/31.	2.49kg.	.75 cc.	1.86 cc.	Seizure (2), bilateral.

Monkey No. 110 continued.

Summary.

Minimal pre-operative dose camphor 0.7 cc. per kilogram.
1st minimal post-operative dose camphor (after left brain wound) 0.6 cc.per kilo
Dose lowered 0.1 cc per kilo.
Minimal post-operative dose camphor (after left complete cervical sympathectomy)0.7 cc. per kilo.
2nd minimal post-operative dose camphor (after complete cervical sympathectomy) 0.7 cc. per kilo.
3rd minimal post-operative dose camphor (after section of left greater superficial petrosal nerve).
Had one fit on 0.7 cc. per kilo but later failed to fit on same dose, but had convulsion on 0.75 cc per kilo.

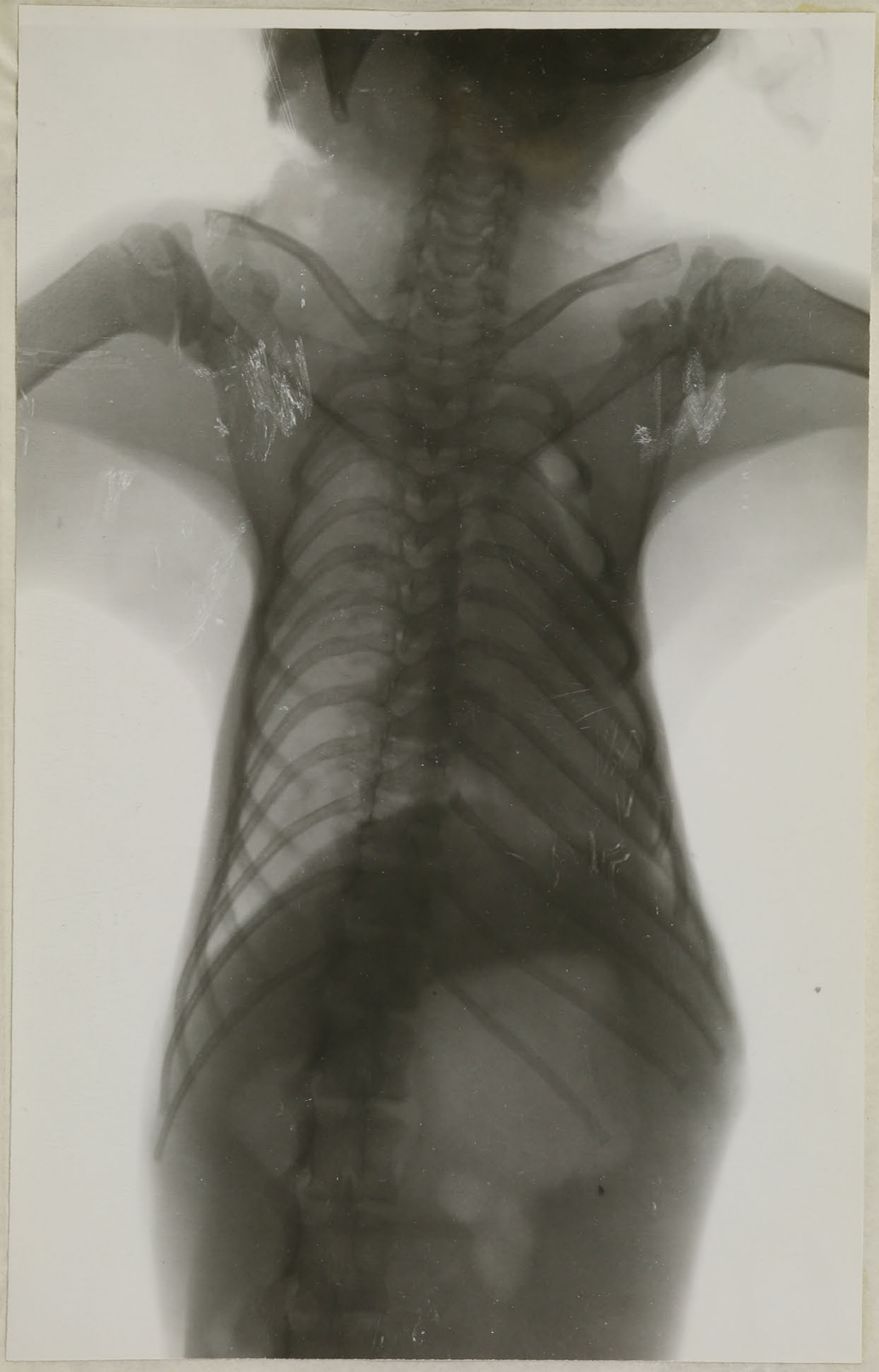
Drawing of motor cortex in monkey No.110. Operation Feb.21,1931
Left fronto-parietal osteoplastic craniotomy. Stimulation of
the motor cortex.



Stimulation with the Galvanic current.
1 movement of the right hand . 2 milliamperes motor full
1 radial deviation of rt. wrist and partial closure of fingers and thumb. 1 and 1.5 milliamperes (add.2 milliamp correction) motor full.
2 closure of hand and supination. 2 milliamperes. motor full.
2 began with supination and closure of rt. hand clonic in character and with clonic movements. 2.4 milliamperes motor full.
3 slight movement of muscles below jaw with movement of tongue and pharynx. 3 milliamperes . motor full.
4 flick of the fingeres. 5 milliamperes. motor full. (probably a spread of the current to this area)
1 movement of the entire right side. 4 milliamperes. motor full.
2 supination of fore arm. 3 milliamperes. motor full.
All other areas of the cortex were negative and produced no motor responce with galvanic current.

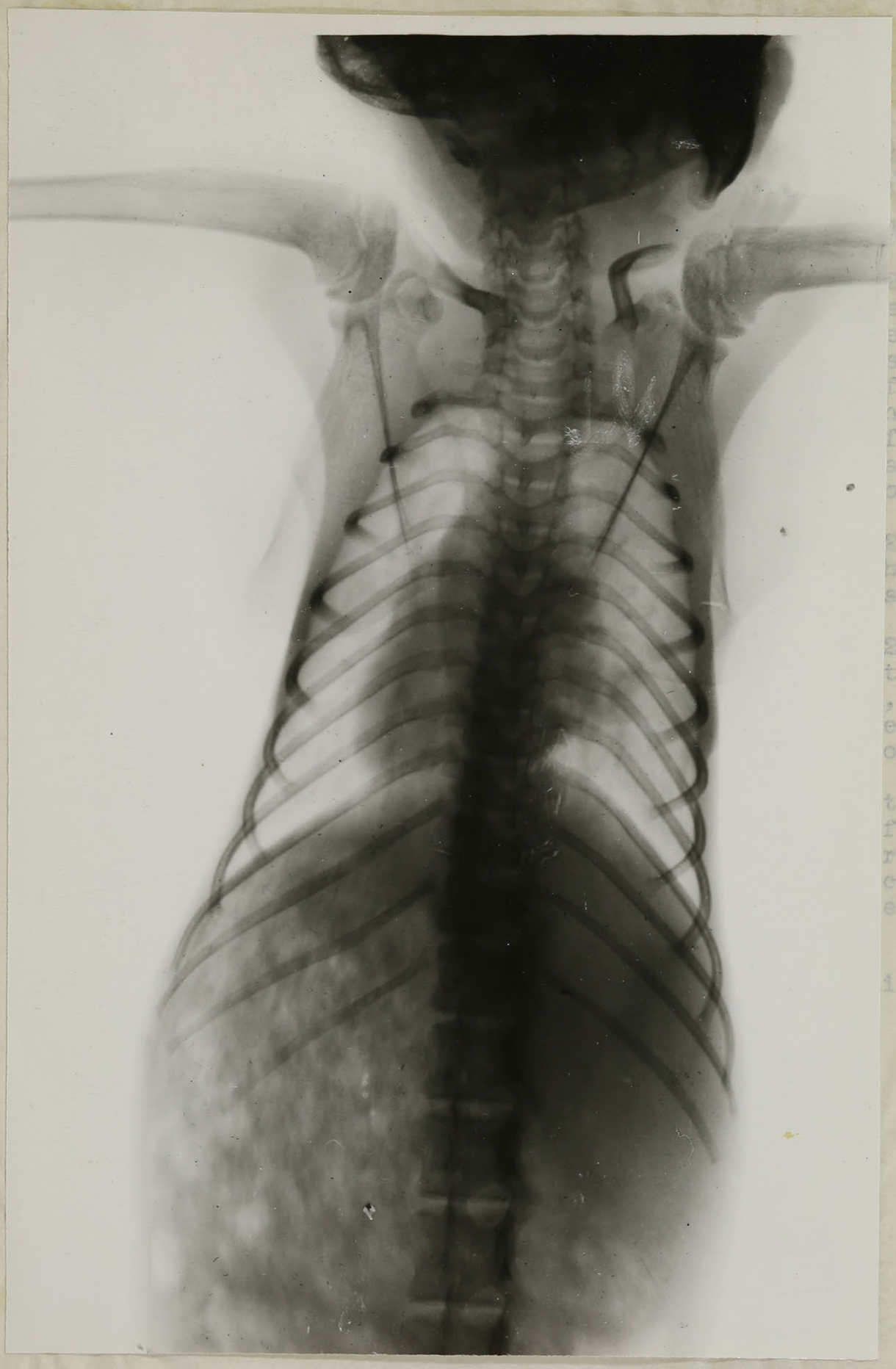
Faradic stimulation of the following areas.
1 supination and closure of the right hand. 1.5 indicator
1 Jacksonian seizure of right hand lasting 15 sec. 3 indicator.
8 twitch of muscles under the mouth. 3 indicator.
2 clonic seizure 33 seconds in duration involving thr rt. hand and arm and spreading to the right leg. 5 indicator.
This last attack was a typical Jacksonian convulsion. It began in the right hand and spread with quite typical epileptic march.

MONKEY NO. 110.



MONKEY NO. 110.

X-ray taken 3 hours after operation.



MONKEY NO. 110.

X-ray taken 3 days after operation.

Monkey No. 115.

Group 1. Pre-operative dosing camphor (20% in olive oil) intramuscularly.

Date.	Weight.	Dose per kg.	Total.	Result and remarks.
2/26/31.	2.6 kg.	.7 cc.	1.8 cc.	Seizure (2) bilateral; jerks general, then eyes to left. Respirations ceased; started with artificial respiration, then tonic stat seizure of clonic jerks of hands and feet. Slight frothing at the mouth. Seizure (2) bilateral. Eyes, right face jerking Body jerks more right-sided. Seizure (2) bilateral, eyes front, twitching both arms, legs, both sides face, jerking backward of head. Dial, one half cc. given intraperitoneally. Jerking of hands continued for some minutes Quieter, cold; respirations regular. Died late in afternoon.

2/26/31. Died - generalized tuberculosis, caseous and miliary.

Monkey No. 116.

Group 1. Pre-operative dosing camphor (20% in olive oil) intramuscularly.

Date.	Weight.	Dose per kg.	Total.	Result and remarks.
3/3/31.	3 kg.	.65 cc.	2 cc.	Quiet.
3/13/31.	3 kg.	.7 cc.	2.1 cc.	Quiet.
3/17/31.	2.96 kg.	.75 cc.	2.22 cc.	Quiet.
3/31/31.	3.01 kg.	.8 cc.	2.4 cc.	Quiet.
4/10/31.	3.1 kg.	.8 cc.	2.5 cc.	Quiet.
4/14/31.	3.06 kg.	.85 cc.	2 cc.	Quiet.
4/17/31.	3.19 kg.	.9 cc.	2.87 cc.	Seizure (2) bilateral. Vomited.
4/21/31.	2.79 kg.	.85 cc.	2.37 cc.	Quiet.
4/24/31.	2.54 kg.	.9 cc.	2.3 cc.	Quiet.
4/25/31.	Died - entercolitis.			

Monkey No. 118.

Group 1. Pre-operative dosing camphor (20% in olive oil) intramuscularly.

Date.	Weight.	Dose per kg.	Total.	Result and remarks.
1/7/31.	4.1 kg.	0.7 cc.	2.9 cc.	Seizure (2) bilateral.
1/14/31.	3.85 kg.	0.6 cc.	2.3 cc.	Quiet.
1/21/31.	3.9 kg.	0.7 cc.	2.7 cc.	Quiet.
2/4/31.	3.9 kg.	0.75 cc.	2.9 cc.	Quiet.
2/26/31.	3.4 kg.	0.80 cc.	2.7 cc.	Quiet.
3/3/31.	3.51 kg.	0.8 cc.	2.8 cc.	Seizure (2)
3/13/31.	3.48 kg.	0.75 cc.	2.6 cc.	Seizure (2), seizure (2 Downward nystagmus and cyanosis at end of seizure. Seizure (2), seizure (2). Given a few whiffs of ether.
3/17/31.	3.5 kg.	0.70 cc.	2.45 cc.	Quiet.
3/31/31.	3.61 kg.	0.75 cc.	2.7 cc.	Seizure (3) staggering to right.

Minimal pre-operative convulsive dose camphor 0.75 cc. per kilogram body weight.

Operation May 13th 1931. Left fronto-parietal craniotomy; stimulation of the motor cortex; production of cortical wound in the motor area. (See chart for stimulation).

Died - 6/21/31. Enterocolitis. No other pathological lesion found at autopsy.

Brain Wound: Slight softening of cerebral tissue about the muscle core. No infection.

Monkey No. 120.

Group 1. Pre-operative dose camphor (20% in olive oil) intramuscularly.

Date.	Weight.	Dose per kg.	Total.	Result and remarks.
3/31/31.	2.49 kg.	.65 cc.	1.6 cc.	Seizure (2) weakness of right hand. Seizure (2) bilateral. Seizure (2) bilateral. Downward nystagmus after. Seizure (2) bilateral.
4/20/31.	Animal ill; not dosed.			
4/20/31.	Died. Showed entercolitis and a few small tuberculous nodules in left lung.			

Monkey No. 12.

Group 1. Pre-operative dosing camphor (20% in olive oil); intramuscularly.

Date.	Weight.	Dose per kg.	Total.	Result.
4/2/31.	3.02 kg.	.65 cc.	1.96 cc.	Quiet.
4/10/31.	2.86 kg.	.7 cc.	2.00 cc.	Quiet.
4/14/31.	2.7 kg.	.75 cc.	2.2 cc.	Quiet.
4/17/31.	2.89 kg.	.8 cc.	2.3 cc.	Quiet.
4/21/31.	2.86 kg.	.85 cc.	2.4 cc.	Quiet.
4/24/31.	2.9 kg.	.9 cc.	2.4(error)	Quiet.
4/29/31.	3.0 kg.	.95 cc.	2.85 cc.	Quiet.
5/6/31.	2.9 kg.	1.00 cc.	2.9 cc.	Quiet.
5/12/31.	2.94 kg.	1.1 cc.	3.2 cc.	Quiet.
5/19/31.	2.9 kg.	1.2 cc.	3.5 cc.	Seizure (2), bilateral.
5/21/31.	2.86 kg.	1.1 cc.	3.1 cc.	Quiet.
6/2/31.	2.86 kg.	1.15 cc.	3.3 cc.	Quiet.
6/5/31.	2.75 kg.	1.2 cc.	3.3 cc.	Seizure (2), bilateral.
6/11/31.	2.97 kg.	1.15 cc.	3.4 cc.	Seizure (2), seizure (3)
6/16/31.	2.78 kg.	1.1 cc.	3.0 cc.	Quiet.
6/18/31.	2.84 kg.	1.15 cc.	3.2 cc.	Quiet.
6/26/31.	2.89 kg.	1.15 cc.	3.3 cc.	Seizure (2), seizure (2) seizure (2).
7/1/31.	2.9 kg.	1.1 cc.	3.2 cc.	Excited.

Minimal pre-operative dose 1.15 cc. per kilogram.

7/2/31. Right cervical and stellate ganglionectomy.

Group 3. Dosing after sympathectony.

7/22/31.	2.5 kg.	1.15 cc.	2.9 cc.	Quiet.
7/24/31.	2.56 kg.	1.2 cc.	3.0 cc.	Seizure (2).
7/29/31.	2.62 kg.	1.15 cc.	3.0 cc.	Quiet.
7/31/31.	2.54 kg.	1.2 cc.	3.0 cc.	Quiet.
8/4/31.	2.44 kg.	1.2 cc.	2.9 cc.	Slightly excited.
8/7/31.	2.6 kg.	1.25 cc.	3.25 cc.	Seizure (3),seizure (2).
8/10/31.	2.54 kg.	1.22 cc.	3.0 cc.	Quiet.

Post-operative dose 1.25 cc. per kilogram.

8/12/31. Left cervical and stellate ganglionectomy.

Group 3. Dosing after complete sympathectomy.

8/21/31.	2.89 kg.	1.25 cc.	3.6 cc.	Seizure (2), seizure (2) light ether.
8/25/31.	2.56 kg.	1.2 cc.	3.0 cc.	Quiet.

8/25/31. Post-operative minimal convulsant dose of camphor 1.25 cc. per kilogram.

Monkey No. 121 continued.

Summary: Minimal pre-operative dose camphor 1.15 cc. per kilogram.

Minimal post-operative convulsant dose (after right complete cervical sympathectomy) 1.25 cc. per kilogram.

2nd minimal post-operative dose camphor (after complete cervical sympathectomy) 1.25 cc. per kilogram.

Dose raised after sympathectomy 0.1cc.per kilogram.

Monkey No. 122.

Group 1. Pre-operative dosing camphor (20% in olive oil) intramuscularly.

Date.	Weight.	Dose per kg.	Total.	Result and Remarks.
4/2/31.	3.03 kg.	.65 cc.	1.96 cc.	Quiet.
4/10/31.	3.2 kg.	.70 cc.	2.24 cc.	Seizure (2), bilateral. Seizure (2), bilateral, one started suddenly when dog ran into room; seizure (2) began when frightened.
4/14/31.	2.99 kg.	.65 cc.	1.99 cc.	Quiet.
4/17/31.	3.16 kg.	.7 cc.	2.2 cc.	Seizure (2),bilateral. Seizure (2), bilateral. Seizure (2), bilateral.

Minimal pre-operative convulsant dose camphor 0.7 cc. per kilogram body weight.

Operation, May 1st 1931. Left fronto-parietal craniotomy; stimulation of the motor cortex; production of cortical wound in the motor area. (See chart for stimulation).

Group 2. Dosing after brain wound.

6/18/31.	3.06 kg.	.5 cc.	1.53 cc.	Quiet.
6/26/31.	2.95 kg.	.6 cc.	1.8 cc.	Quiet.
7/1/31.	2.94 kg.	.65 cc.	1.9 cc.	Seizure (2).
7/14/31.	2.9 kg.	.6 cc.	1.7 cc.	Seizure (2).
7/22/31.	2.9 kg.	.6 cc.	1.7 cc.	Seizure (2) jerks.
7/24/31.	2.85 kg.	.55 cc.	1.6 cc.	Seizure (2),seizure(2)

Minimal post-operative convulsant dose camphor 0.55.

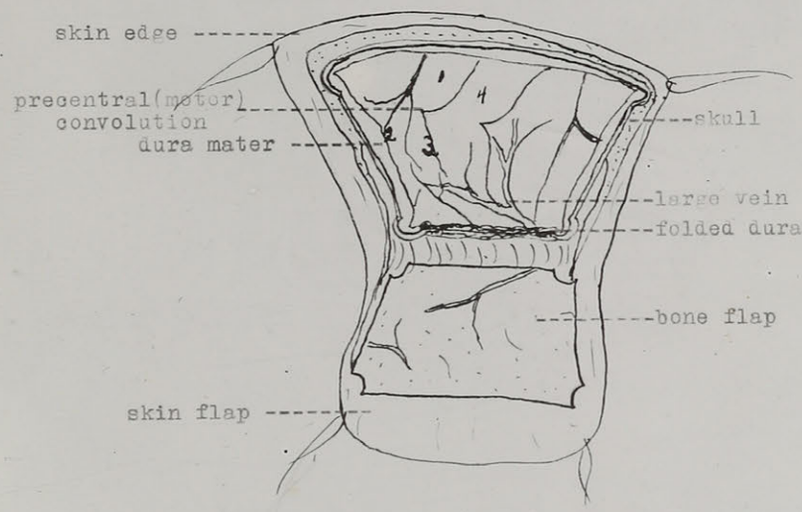
7/28/31. Dead - enterocolitis.

Summary: Minimal pre-operative convulsant dose camphor 0.7 cc. per kilogram.
Minimal post-operative convulsant dose camphor (after left brain wound) 0.55 cc. per kilogram.
Dose lowered - 0.15 cc. per kilogram.

Stimulation of the motor cortex Monkey No. 122 at Operation.

Area No. 1 Galvanic 2 milliamp. Twitch of rt. small finger.
Area 1 " 6 " movement of tips of rt. fingers
Area 2 Faradic 2 Twitch of rt. upper lip.
Area 1 " 4 Violent twitch of rt hand and clonic closure. Pronation of rt. hand.

At area 2 with the electrode extended well under the edge of the bone with the dial set at full for Faradic current there was marked jerking of the head into the extended position and movement of the two arms.



MONKEY NO. 122.

Monkey No; 123.

Group 1. Pre-operative dosing camphor (10% in olive oil); intramuscularly.

Date.	Weight.	Dose per kg.	Total.	Result.
4/2/31.	2.18 kg.	.65 cc.	1.4 cc.	Seizure (2).
4/10/31.	2.54 kg.	.60 cc.	1.5 cc.	Quiet.
4/14/31.	2.44 kg.	.65 cc.	1.6 cc.	Quiet.
4/17/31.	2.54 kg.	.65 cc.	1.65 cc.	Seizure (2); sham rage.
4/21/31.	2.61 kg.	.6 cc.	1.5 cc.	Quiet.
4/24/31.	2.67 kg.	.65 cc.	1.7 cc.	Quiet.
4/27/31.	2.22 kg.	.65 cc.	1.4 cc.	Quiet.
5/6/31.	2.26 kg.	.7 cc.	1.58 cc.	Seizure (2); head to right
5/12/31.	2.34 kg.	.65 cc.	1.5 cc.	Seizure (2); head right and then left.
5/19/31.	2.5 kg.	.6 cc.	1.5 cc.	Quiet.
5/21/31.	2.37 kg.	.65 cc.	1.5 cc.	Quiet.
6/2/31.	2.46 kg.	.65 cc.	1.6 cc.	Quiet.
6/5/31.	2.38 kg.	.7 cc.	1.66 cc.	Quiet.
6/11/31.	2.51 kg.	.7 cc.	1.76 cc.	Seizure (2),seizure (2).
6/16/31.	2.56 kg.	.65 cc.	1.66 cc.	Quiet.
6/18/31.	2.59 kg.	.7 cc.	1.8 cc.	Quiet.
6/26/31.	2.56 kg.	.7 cc.	1.8 cc.	Seizure (2).
7/1/31.	2.66 kg.	.65 cc.	1.7 cc.	Seizure (2).

Minimal pre-operative convulsant dose 0.65 cc. per kilogram.

7/2/31. Operation; Right cervical sympathectomy.

Group 3.. Dosing after sympathectomy.

7/14/31.	2.67 kg.	.65 cc.	1.7 cc.	Quiet.
7/29/31.	2.5 kg.	.65 cc.	1.6 cc.	Quiet.
7/31/31.	2.5 kg.	.7 cc.	1.75 cc.	Seizure (2).
8/4/31.	2.46 kg.	.65 cc.	1.6 cc.	Quiet.

Minimal post-operative dose, convulsant, 0.7 cc. per kilogram.

8/6/31. Left cervical sympathectomy.

Group 31. Dosing after sympathectomy.

8/14/31.	2.44 kg.	.7 cc.	1.7 cc.	Quiet.
8/18/31.	2.33 kg.	.75 cc.	1.7 cc.	Seizure (2).
8/21/31.	2.47 kg.	.7 cc.	1.7 cc.	Quiet.
8/25/31.	2.3 kg.	.75 cc.	1.7 cc.	Quiet.

Summary: Minimal pre-operative convulsant dose camphor 0.65 cc. per kilogram.

Minimal post-operative convulsant dose camphor (after complete right cervical sympathectomy) 0.7 cc. per kilogram.

Minimal post-operative convulsant dose camphor (after complete bilateral cervical sympathectomy) 0.75 cc. per kilogram

Dose raised o.1cc per kilogram by sympathectomy.

Monkey No. 124.

Group 1. Pre-operative dosing camphor (20% in olive oil) intramuscularly.

Date.	Weight.	Dose per kg.	Total.	Result and remarks.
4/2/31.	2.96 kg.	.65 cc.	1.92 cc.	Seizure (2), bilateral.
				Seizure (2), bilateral.
4/10/31.	2.95 kg.	.6 cc.	1.77 cc.	Vomited, quiet.
4/14/31.	2.86 kg.	.65 cc.	1.85 cc.	Seizure (2), bilateral.
4/17/31.	2.86 kg.	.6 cc.	1.7 cc.	Vomited.

Minimal pre-operative convulsant dose 0.65 cc. per kilogram body weight.

Operation, April 30th 1931. Left fronto-parietal craniotomy; stimulation of the motor cortex; production of cortical wound in the motor area. (See chart for stimulation).

5/5/31. Died. Autopsy showed pulmonary tuberculosis, bilateral. Fatty degeneration of liver, pin-worm infestation of colon, and infection of wound. There was a slight peritonitis about the site of the intraperitoneal injection of Dial.

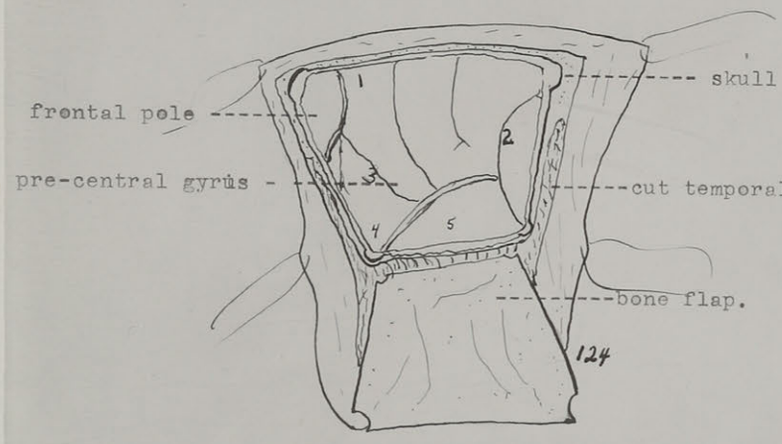
Summary: Minimal pre-operative convulsant camphor 0.65 cc. per kilogram.

Stimulation of the cortex of monkey No. 124 at operation.

Left motor cortex. Stimulation with Galvanic and then far dic currents.

Galvanic - 2 milliamperes.Point no. 1. Flexion of the index finger of the right hand.

8 milliamperes.Point No.1Flexion of the right leg with flexion and closure of the right hand and pronation.



Faradic set at No.2. Cortical location No.1. Fibrillary movement of right flexor carpi radialis longus and brevis.

Faradic set at 4. Cortical location No.1. Flexion of the fingers of the right hand.

Far dic set at full strength. Cortical location No. 2 Large vein stimulated with resulting tremor of the right thumb and little finger

MONKEY NO. 124.

Monkey No. 127.

Group 1. Pre-operative dosing camphor (20% in olive oil); intramuscularly.

Date.	Weight.	Dose per kg.	Total.	Result.
4/24/31.	2.4 kg.	.65 cc.	1.5 cc.	Quiet.
4/29/31.	2.53 kg.	.7 cc.	1.8 cc.	Seizure (2); head first turned right, then left eyes ditto. Rt. arm flexed, left extended. Seizure (2); head first left and then right. Weakness left hand.
5/6/31.	2.5 kg.	.65 cc.	1.6 cc.	Quiet.
5/12/31.	2.34 kg.	.7 cc.	1.6 cc.	Quiet.
5/19/31.	2.4 kg.	.7 cc.	1.7 cc.	Quiet.
5/21/31.	2.33 kg.	.75 cc.	1.7 cc.	Quiet.
6/2/31.	2.45 kg.	.8 cc.	1.96 cc.	Seizure (2),seizure (2)
6/5/31.	2.41 kg.	.75 cc.	1.8 cc.	Quiet.
6/11/31.	2.39 kg.	.8 cc.	1.9 cc.	Quiet.
6/16/31.	2.43 kg.	.8 cc.	1.95 cc.	Seizure (2).
6/18/31.	2.44 kg.	.75 cc.	1.8 cc.	Quiet.
6/26/31.	2.51 kg.	.8 cc.	2.0 cc.	Seizure (2), seizure (2
7/1/31.	2.39 kg.	.8 cc.	1.9 cc.	Seizure (2).
7/22/31.	2.34 kg.	.75 cc.	1.75 cc.	Seizure (2).
7/24/31.	2.37 kg.	.75 cc.	1.8 cc.	Seizure (2), seizure(2)
7/29/31.	2.46 kg.	.7 cc.	1.7 cc.	Quiet.
7/31/31.	2.37 kg.	.75 cc.	1.8 cc.	Quiet.
8/4/31.	2.26 kg.	.75 cc.	1.7 cc.	Quiet.
8/7/31.	2.16 kg.	.8 cc.	1.72 cc.	Seizure (2),seizure (2) seizure (2).
8/10/31.	2.34 kg.	.75 cc.	1.75 cc.	Quiet.

Minimal pre-operative convulsant dose 0.8 cc. per kilogram.

8/13/31. Left cervical and stellate ganglionectomy.

Group 3. Dosing after sympathectomy.

8/21/31.	2.19 kg.	.75 cc.	1.64 cc.	Seizure (2).
8/25/31.	2.14 kg.	.7 cc.	1.5 cc.	Quiet.

Summary: Minimal pre-operative convulsant dose camphor 0.8 cc. per kilogram.

Monkey No. 128.

Group 1. Pre-operative dose of camphor (20% in olive oil); intramuscularly.

Date.	Weight.	Dose per kg.	Total.	Result and remarks.
4/24/31.	2.66 kg.	.65 cc.	1.7 cc.	Quiet.
4/29/31.	3.00 kg.	.7 cc.	2.1 cc.	Seizure (3), sympathetic signs with sham rage following.
5/6/31.	2.9 kg.	.65 cc.	1.9 cc.	Quiet.
5/12/31.	2.7 kg.	.7 cc.	1.9 cc.	Seizure (3); head right and then left; salivating, sham rage Seizure (3), fell to left; head turning to left. Seizure so severe that ether was given.

Minimal pre-operative convulsant dose camphor 0.7 cc. per kilogram body weight.

Operation, May 14th 1931. Left fronto-parietal craniotomy; stimulation of the motor cortex; production of cortical wound in the motor area. (See chart for stimulation).

Group 2. Dosing after brain wound.

6/18/31.	3.0 kg.	.5 cc.	1.5 cc.	Quiet.
6/26/31.	3.11 kg.	.6 cc.	1.86 cc.	Seizure (2); sham rage
7/1/31.	3.05 kg.	.55 cc.	1.67 cc.	Seizure (2).
7/14/31.	3.2 kg.	.5 cc.	1.6 cc.	Quiet.
7/22/31.	2.9 kg.	.55 cc.	1.6 cc.	Jerks.
7/24/31.	3.09 kg.	.55 cc.	1.7 cc.	Quiet.
7/29/31.	3.18 kg.	.6 cc.	1.9 cc.	Quiet.
7/31/31.	3.3 kg.	.6 cc.	2.0 cc.	Some of dose lost.
8/4/31.	3.02 kg.	.6 cc.	1.8 cc.	Quiet.
8/7/31.	3.38 kg.	.65 cc.	2.63 cc.	Seizure (3).
8/10/31.	3.16 kg.	.6 cc.	1.9 cc.	Excited.

1st post-operative convulsant dose camphor 0.65 cc. per kilogram.

8/11/31. Left sympathectomy, superior and stellate ganglia.

Group 3. Dosing after sympathectomy.

8/21/31.	2.94 kg.	.65 cc.	1.9 cc.	Quiet.
8/25/31.	2.8 kg.	.7 cc.	1.96 cc.	Quiet.

Dose after left sympathectomy - did not fit on .7 cc. per kilogram.

8/27/31. Right sympathectomy, superior and stellate ganglia.

8/30/31.	2.8 kg.	.7 cc.	1.9 cc.	Quiet.

Monkey No. 128 continued.

Summary: Minimal pre-operative dose camphor 0.7 cc. per kilogram.
Minimal 1st post-operative dose camphor (after brain wound) 0.65 cc. per kilogram.
Minimal 2nd post-operative dose camphor (after complete cervical sympathectomy) not yet established, but the anima failed to convulse on either of the former doses.

Monkey No. 132.

Group 1. Pre-operative dosing with camphor (20% in olive oil); intramuscularly.

Date.	Weight.	Dose per kg.	Total.	Result.
6/5/31.	4.2 kg.	.7 cc.	2.94 cc.	Quiet.
6/11/31.	3.84 kg.	.75 cc.	2.9 cc.	Quiet.
6/16/31.	3.69 kg.	.8 cc.	2.95 cc.	Seizure (2),bilateral.
6/18/31.	3.6 kg.	.75 cc.	2.7 cc.	Quiet.
6/26/31.	3.59 kg.	.8 cc.	2.9 cc.	Quiet; some of dose lost
7/1/31.	3.59 kg.	.8 cc.	2.9 cc.	Seizure (2); seizure (2) head to right; seizure (2) head to left; seizure (2); ether given. Seizure (2) head to right; seizure (2) head to left.

Minimal pre-operative convulsant dose camphor 0.8 cc. per kilogram.

7/7/31. Operation - complete right cervical sympathectomy.

Group 3. Post-operative dose camphor (after sympathectomy).

7/22/31.	2.93 kg.	.8 cc.	2.34 cc.	Seizure (3); eyes and head to left; pivoted to right;
8/4/31.	2.79 kg.	.75 cc.	2.1 cc.	Seizure (3).
8/7/31.	2.74 kg.	.7 cc.	1.9 cc.	Many severe jerks.
8/10/31.	2.8 kg.	.75 cc.	2.1 cc.	Jerks.

1st Minimal post-operative convulsant dose camphor 0.8 cc. per kilogram

8/19/31. Operation - complete left cervical sympathectomy.
8/21/31. Died, two days after left cervical sympathectomy.

Summary: Minimal pre-operative convulsant dose camphor 0.8 cc. per kilogram.
Minimal first post-operative convulsant dose (after right sympathectomy) 0.8 cc. per kilogram.
Dose remained the same.

Autopsy Note: Operative site healing well, sympathectomy complete.
Partial intestinal obstruction.
Pulmonary tuberculosis.
Very few adhesions in cisterna magna and at base of skull

DISCUSSION

As stated in the introduction, Lennox and Cobb's definition of epilepsy emphasizing convulsive movements and loss of consciousness was accepted in this research, and throughout the work generalized convulsions have been the standard by which doses were judged. Camphor and its isomer thujone in the form of oil of wormwood were chosen as the convulsant drugs for the monkeys and cats respectively, because the convulsant action of these drugs is predominantly cortical.

The convulsions obtained have been of the clonic type, and although some of the monkeys showed phenomena of sham rage and athetosis it has been impossible from the limited observations after operation to come to any conclusion as to the effect of complete sympathectomy on these phenomena, which may be from a lower level. At the outset it was hoped that a second craniotomy and second stimulation of the cortex could be done, but further observations are desirable on the animals before the risk of such procedure is justified.

Brain Wounds

The brain wounds used in the animals of group 2, both monkeys and cats, were all produced in the motor cortical area controlling the forepaw and face (as nearly as could be determined by stimulation), yet only two of the cats had a lowering of the convulsant dose (one of these, No.4333, had

spontaneous convulsions as a kitten), whereas all the monkeys of group 2 had a lowering of the minimal convulsant dose after the brain wound. Analysis of the operative procedures shows the following difference between the operations on the cats and on the monkeys: The cranial opening in the cats was in the form of a skull window which was left unclosed because of the technical difficulties in doing an osteoplastic operation and furnished a decompression over a large proportion of the cerebrum of the operated side. The cranial opening in the monkeys, on the other hand, was in the form of a bone flap which was sutured back in place at the close of the operation. The decompression in the monkeys was therefore only the small window where the bone flap had been broken, and it covered only a small proportion of the cerebrum of the operated side. It is realized that this difference may be of significance and that the size of the decompression may influence the experimental results in post-traumatic epilepsy. This factor has no bearing on the conclusions concerning complete sympathectomy in this research, as they have been drawn only from monkeys in which an osteoplastic flap was used. It is pointed out only because extensive decompression operations have been carried out in the treatment of epilepsy.

Cervical Sympathectomy

Survey of the literature of sympathectomy in its relation to epilepsy reveals several interesting facts: First, that by

combining some of the various operations that have been carried out on the sympathetics of the cervical region one can, in all probability, remove the vaso-constrictor influences from the intracranial vessels.

Since Kuntz and Morehouse (1930) have shown that a certain percentage of the fibers to the cardiac accelerator apparatus come from below the second thoracic sympathetic ganglion, it seems theoretically necessary to remove not only the two complete cervical sympathetic chains with their three ganglia, but also the vertebral nerves (and accessory ganglia if present) and the nerve-bearing peri-arterial sheaths of the carotid and vertebral arteries. This procedure has, in this research, been considered a complete cervical sympathectomy, and its effect on the doses of the animals suggests that it lessens the tendency to the convulsions of experimental epilepsy.

McClintic (1930) has suggested the peri-arterial injection of alcohol beneath the adventitia as a substitute for decortication of carotid and vertebral arteries. The method may have advantages and it merits investigation.

The degree of regeneration of the sympathetics after various types of removal is still an unsettled question. Lee (1930) and others have done constructive work on the subject, but much remains undetermined. The theory that regeneration may occur even after ganglionectomy as suggested by changes in the peripheral vasomotor signs awaits

confirmation or contradiction. Prognosis concerning the permanence of sympathectomy depends upon this knowledge.

As noted before, the careful choice of cases of clinical epilepsy which are suitable for sympathectomy greatly increases the probability that the operation will effect a cure. Vidal suggested the use of amyl nitrite as a means of determining how vasodilatation will effect the individual case before undertaking the operation, while others have used flushing, sweating, etc. as a criterion for diagnosis. Winter (1902), Forster (1923), McClintic (1930) and others have emphasized the value of discrimination in selecting cases for sympathectomy. It may be said, then, that in the literature the percentage of reported cures of epilepsy by sympathectomy seems to be proportional to the completeness of operation plus the care in the selection of cases.

Vasodilator Nerves

Throughout this research consideration has been given to the vaso-constrictor nerves of the cerebral vessels, and it has been shown that the removal of their influence from the cerebral vessels raises the convulsant threshold. Recently it has been demonstrated that there are also vasodilator fibers to the cerebral blood vessels. Forbes and Wolff (1928) showed that stimulation of the vagus nerve causes dilatation of the pial vessels. Penfield and Cobb in unpublished researches have shown that stimulation of the seventh nerve at its point of origin causes dilatation of the pial vessels, and Chorobski

(1931) has demonstrated nerve fibers running from the greater superficial petrosal nerve to the internal carotid artery. The greater superficial petrosal nerve was cut unilaterally in one monkey who had previously had a complete sympathectomy and he had a fit on the same convulsant dose as before the section. More work must be done to determine the effect of the vasodilator fibers on epilepsy.

CONCLUSIONS

A. From the Literature

1. The percentage of cases of epilepsy cured by sympathectomy is proportional to the completeness of the operation plus the care used in selection of cases.

2. There has been a tendency in the last two decades toward the use of numerous procedures in cervical sympathectomy, very few of which result in complete removal of sympathetic influence to the intracranial vessels. If sympathectomy is to be done it should be complete.

3. More complete data is needed concerning untoward symptoms following complete cervical sympathectomy.

B. From This Research

1. Complete cervical sympathectomy increases the convulsant threshold in monkeys rendered epileptic by doses of camphor.

2. In two animals removal of the cervical sympathetics from the side of the brain wound raised the convulsant threshold which had been lowered by the brain wound.

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