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To the Graduate Council:

I am submitting herewith a thesis written by Carl A. Nelson entitled "Response of the Spinal Tract and Nucleus of the Trigeminal Nerve to Two Stimuli." I have examined the final electronic copy of this thesis for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Master of Science, with a major in Biochemistry and Cellular and Molecular Biology.

Frank Harrison, Major Professor

We have read this thesis and recommend its acceptance:

S. R. Brussels, J. Quigley

Accepted for the Council:
Carolyn R. Hodges

Vice Provost and Dean of the Graduate School

(Original signatures are on file with official student records.)

March 11, 1947

To the Committee on Graduate Study:

I submit herewith a thesis by Mr. Carl A. Nelson, Jr., "Response of the Spinal Tract and Nucleus of the Trigeminal Nerve to Two Stimuli", and recommend that it be accepted for eighteen quarter hours credit in fulfillment of the requirements for the degree of Master of Science, with a major in Anatomy.

Frank Harrison
Major Professor

At the request of the Committee on Graduate Study, I have read this thesis, and recommend its acceptance.

J. P. Dugley

Accepted by the Committee

E. A. Walters
Chairman

RESPONSE OF THE SPINAL TRACT AND NUCLEUS OF THE TRIGEMINAL NERVE TO TWO STIMULI

A THESIS

Submitted to the Graduate Committee

of

The University of Tennessee

in

Partial Fulfillment of the Requirements

for the degree of

Master of Science

by

CARL AUGUST NELSON, JR.

MEMPHIS, TENNESSEE

MARCH, 1947

ACKNOWLEDGEMENTS

The author wishes to express to Dr. Frank Harrison his sincere appreciation of the help and encouragement so generously given.

24 Oct 47 SLB 1.50

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INTRODUCTION AND REVIEW OF THE LITERATURE:

In a recent publication of results of oscillographic studies on the spinal tract and nucleus of the trigeminal nerve the problem of differentiating first from second or higher order neurons presented itself. Following a single electrical stimulus to a branch of the trigeminal nerve, action potentials were recorded in the spinal tract and nucleus. The form of the potentials varied with the position of the recording electrode in relation to the spinal tract and nucleus and with the conduction distance in the brain stem, but in general the action potential recorded was made up of two waves each having one or more peaks. It is the cause of this second wave that aroused our interest - whether it be due to second order neurons or to a discrete group of primary fibers of different size and conduction velocity from those producing the first wave. The first wave began 0.6 to 1.2 msec. after the stimulus, depending upon the conduction distance, and was completed within 2 msec. The second wave of the potential began 1.8 to 2.2 msec. after the stimulus, but was rather variable in size and time course. Increased frequency of stimulation or oxygen deprivation were found to vary the second wave and sometimes even abolish it. From the beginning of the first wave to the beginning of the second, the range of the

delay was 0.8 to 1.1 msec., which is within the limits of a single synapse (26). The synaptic delay has been found to be a minimum of 0.5 msec. and if appreciably longer than one msec. implies more than one synapse (37, 5, 2, 38, 45, 43, 31). The location from which the second wave is best recorded also is consistent with the belief that the second wave is produced by second order neurons (26).

This investigation was stimulated by the work of Harrison and Corbin (26) and Harrison and Bruesch (25). In the formers' work on the fifth nerve, and the latters' on the tenth nerve, a number of action potentials were recorded with the cathode ray oscillograph which presented the problem of differentiating first order from second and higher order neurons. It was thought that these waves might be broken down into groups of pre- and post-synaptic origin by using the recovery cycle of the waves as a possible index of their grouping.

In using the term recovery cycle, I am referring to the recovery of the spike height of the action potential recorded by the cathode ray oscillograph when tested by two supramaximal stimuli. The amount of recovery at various time intervals after the initial stimulus is determined by a second stimulus of the same magnitude. The initial stimulus is generally referred

to as the conditioning stimulus and the second as the testing stimulus. A series of recoveries is determined by starting with the interval between the conditioning and testing stimuli large enough so that the conditioning stimulus has no apparent effect on the size of the testing response. The interval is gradually decreased until the response to the testing shock is finally abolished, i.e., the testing shock is brought into the relatively refractory period of the conditioning shock until the absolutely refractory period is reached, which is manifest by no response at all.

Nerve fibers have been divided by their diameters and activities into fairly discrete groups(9). Axon diameter and excitability are closely related, the larger fibers being the more irritable. Speed of conduction also depends on the fiber diameter, being fastest in the large fiber types. Electrical shunting in the central nervous system prevents recording of the small fiber potentials because of the great amplification necessary to pick up their response. Therefore, the discussion will be limited to only the fibers of the larger type which fall in the A classification (10). The spinal tract of the trigeminal nerve mediates pain, temperature, and touch sensations (26), but it is

probably only the touch fibers which we are recording.

The general form of the action potential produced by neuron activity is rather simple in most instances. There is a period between the stimulus and the beginning of the response which depends on the distance of conduction and on a fluctuating "shock-response" delay (40, 3). The first sign of activity is a sharp negative elevation referred to as the spike, which lasts about 0.4 msec. in mammalian A fibers. Overlapping and immediately following the spike is the extremely variable negative after-potential, which is followed then by a positive after-potential. After-potentials are generally longer than the spike, show great variation, and are usually quite independent of the spike(8, 16).

The excitability of a nerve is usually measured as the reciprocal of the shock strength which will excite a constant number of fibers (14). Although not measuring the excitability proper of the nerve fiber in these experiments, the recovery cycle does depend on the excitability of the individual axons. As is well known, a fiber after responding to a stimulus remains momentarily unexcitable to any stimulus. During this absolutely refractory period no activity can be brought out by a shock of any strength. This period is approximately the duration of the spike potential which is between 0.41 and 0.44 msec. in the best preparations

of mammalian A fibers (14, 1). In smaller, less irritable, and slower conducting fibers, the absolutely refractory period is longer, being 1.1 to 1.5 msec. in mammalian B fibers (40, 39, 24). At the first return of responsiveness the spike is small and conduction is slowed. As the interval between the shocks is increased, both the size of the response and the rate of conduction increase rapidly, and then level off to normal. The interval between the earliest response and full recovery of the nerve is known as the relatively refractory period. During this time the threshold of the fibers which are being tested falls from the high value obtaining at the end of the absolutely refractory period to normal, and at the same time the magnitude of the response increases from its initial small value to full size (8). Thus the general form of the excitability cycle of mammalian A fibers is a short absolutely refractory period followed by a rapid rise to maximum, a gradual decline, and a slow return to the base line. Depending on the condition of the nerve and the extent of the activity, the initial maximum may occur at normal, supernormal, or subnormal irritability, and the subsequent decline may be small or very marked (22). Determinations of the absolutely refractory periods have been fairly consistent, being 0.41 to 0.44 msec. in determinations on sensory fibers (14) and not over 0.6 msec. in motoneurons (36). The relatively refractory period

lasts from 2.0 to 8.0 msec. (4, 34, 12, 14, 8).

Following the refractory period there are periods of supernormality and subnormality in excitability. The former is associated with the negative after-potential and the latter with the positive after-potential (12, 18, 11). The negative after-potential lasts 10 to 15 or 20 msec., and the positive potential often 20 to 40 msec.; however, it must be remembered that these after-potentials with their excitability changes are very variable and may be very long, or absent in some cases (34, 14). During the supernormal period the nerve is supernormal in excitability and conducts at supernormal velocity. During the subnormal period irritability is subnormal, but to a supramaximal shock the response during this period is supernormal, i.e. the ability to respond is at least normal during this period (15, 18).

The recovery of response of the spike height is determined by using stimuli several times that nesessary to elicit a maximal response. No response is obtainable during the absolutely refractory period, but immediately following there is a sharp rise from a minimal response to roughly 80 to 90 per cent of normal, and then a gradual rise to normal. Though the strength of the stimulus be varied fairly widely no change occurs in the shape of the curve (46). There are no late changes in responsiveness corresponding to the supernormal and subnormal periods of excitability. Supernormality of spike height is un-

observed according to Graham (20), but Von Brucke et al (46) recorded some curves that seemed to show a recovery of spike height to more than 100 per cent. They postulated error in their methods. Recovery of responsiveness and excitability during the relatively refractory period occur at quite different rates, responsiveness being recovered more promptly than excitability (46, 19). It was formerly thought that recovery of height and recovery of irritability in nerve required the same interval (20, 12).

The electrical potential produced at the synapse must also be considered. Eccles (7), by stimulating the dorsal root and recording from the ventral root in the spinal cord of the cat, found that when the spike potentials have been blocked by heavy anesthesia the synaptic potential appears as a brief negative potential with a quick rise, and a slower, approximately exponential decay. There was an 0.8 msec. latent period, 3.0 msec. time to summit, and 7.0 msec. time of half-decay (32). A much slower time course and electrotonic transmission are two criteria which distinguish the synaptic potential from the spike potential (6). A prolonged positive potential occurs on the end of the synaptic potential. The anesthesia does not affect the time course of the synaptic potential, but uncovers it by preventing the discharge of the impulses. The synaptic potential shows

spacial decrement and has the same refractory period as the axon. Similar potentials have been recorded by Gasser and Graham (13) and by Hughes and Gasser (27).

Electrical potentials recorded from the cuneate nucleus of the cat by Therman (45) were of 5.0 msec. average duration, and commonly there was a second negative elevation on the falling slope of the first, about 3.0 msec. after the primary spike. In testing the recovery cycle of the action potentials from the cuneate nucleus, Therman used two supramaximal shocks, 6 to 7 times threshold. In several cases he found that the negative wave had regained its full size at shock intervals of not more than 15 or 20 msec., but there was considerable variation from preparation to preparation in the time required for full recovery. It was often necessary to increase the shock interval to 50 msec. or even more until the negative wave had recovered completely. When the intervals between the conditioning and testing stimuli are shorter than 2 msec. the properties of the primary axons become a determining factor in the recovery curve, but in all cases if any second primary spike is evoked there is some negative wave, although much reduced in size (13). The form of the action potential in the cuneate nucleus is of the same general contour as that recorded by Gasser and Graham (13)

from the cord by dorsal root stimulation, but all potentials in the cuneate nucleus are larger, expecially the positive potential, and the negative potential following the primary spike is shorter.

Grundfest and Gasser (23) on studies of mammalian C fibers found that beginning after an absolutely refractory period of 2.0 msec., the height of response of the spike rises rapidly, but after recovery to 80 per cent of normal is attained, the rate of restoration is retarded and full height is not reached until 20 msec. have elapsed. No further increase takes place. The spike heights do not become supernormal, as they do in frog C fibers (17).

Recovery cycles of spike height in recording from the sciatic nerve showed about 90 per cent recovery in 5 msec., with complete recovery in about 14 msec. (21).

Skoglund (44) in testing recovery across the artificial synapse formed by the cut end of the cat's sciatic nerve, found 8 out of 10 series to be identical for direct and transynaptic stimulation of post-fibers. Six experiments showed subnormality, and 4 had supernormal periods. In 2 experiments transynaptic recovery was delayed.

Hughes and Gasser (28) in experiments stimulating afferent fibers of cats found two types of recovery curve which they correlated with features of

the action potential recorded from the spinal cord. When the potential contained only negative components, as is the case in acute preparations, recovery was rapid enough to be limited solely by refractoriness; but when positive components appeared in the action potential, as occur well developed in the chronic animal, it was associated with prolonged reflex unresponsiveness. These findings were also recorded in spinal monkeys by Hughes et al (29). Recovery was complete in 20 msec. which agrees well with values obtained by Lorente de Nó and Graham (34) in occulomotor motoneurones in the cat.

Lorente de Nó has extensively studied synaptic activity of motoneurones, and we make reference to some of his work on the third cranial nerve (33, 35, 39). It was found that the recovery cycle of the ocular motoneurones after one response consists of a protracted period of depressed excitability lasting 30 to 40 msec. The motoneurons never develop supernormality for synaptic stimuli, even when their axons show a pronounced supernormal phase for electrical stimuli. The recovery of motoneuron axon excitability showed four phases - absolutely refractory period, relatively refractory period, supernormal period, and subnormal period. The recovery of the soma was one

long period of depressed excitablilty to synaptic excitation, but to direct electrical stimuli is like that of the axon, and may include a supernormal phase. The subnormality in the axons and the soma lasts about the same length of time; however, there is no equivalent in the synaptic excitability of the soma to compare with the supernormality that develops in the axon excitability. It is true that supernormality did not develop in all cases of blood perfused nerve, but even in these the axon is 95 per cent recovered in 4 to 5 msec., while the soma is just beginning to recover at this interval (19). It was found that the absolutely refractory period of the entire synaptic arch of the oculomotor nerve when tested by two strong stimuli was 0.56 msec., thus no elements in the arc have an absolutely refractory period longer than that of the pre-synaptic axons.

METHODS AND MATERIAL:

The recovery cycle is determined by preexisting activity. Activity is produced by a stimulus which shall be referred to as the conditioning stimulus, and the return of function is measured by a second identical stimulus sent in at various intervals after the first. Both stimuli were 2 or 3 times threshold.

Eighteen cats were anesthetized with nembutal to a depth just sufficient to prevent muscular movement. In five preparations a section of the sciatic nerve was dissected out and placed on stimulating and recording electrodes in a moist chamber. In the remaining preparations the frontal branch of the trigeminal nerve was dissected out in the orbit and placed on hook electrodes. These served as the stimulating electrodes. In the same experiments an area of the occipital bone was removed with rongeurs, exposing the dorsal surface of the brain stem, and the recording electrode was oriented in the spinal tract or nucleus of the trigeminal nerve by means of the Horsley-Clarke stereotaxic instrument. At the beginning of each experiment the stimuli were separated by an interval more than sufficient to remove all apparent effect of the conditioning stimulus on the testing response. This varied from around 50 msec. to over 150 msec. The separation interval was gradually decreased until the

response to the testing stimulus was abolished. At each separation interval three photographs were made: one of the testing response alone, one of the conditioning reponse alone, and one of the two reponses together. A time base was taken from an audio-oscillator for each setting of the sweep of the screen of the cathode-ray tube. The recording electrode was connected to the plates of the cathode-ray oscillograph through a two-stage amplifier. Photographs of the fluorescent screen of the tube were made with a 35 mm. camera with an f2 lens on moderately fast film. To facilitate analysis of the photographs, each was enlarged to 5x7 inches. The height of the spikes was measured, and in some cases the areas of the action potentials measured with a planimeter. Also, the separation of the two stimuli was measured in each case.

To satisfy the need for two identical stimuli capable of being fired at very short intervals, a two channel stimulator was designed and constructed. The stimulator was built with two channels identical in construction in order to be certain that the stimuli were identical when used at the shortest intervals. See figures 1 and 2 for photographs and a circuit diagram. The basic plan of the circuit is a thyratron tube serving as an electric switch which fires stimuli as condenser discharges through a transformer.

The Thyratron tube is a gas filled tube of three necessary elements, the cathode, grid, and anode; some have additional elements depending on the characteristics desired (42). Electrons flow from the cathode to the anode. Depending on the function desired of the tube, the grid potential may be strongly negative preventing conduction through the tube, or it may be made positive permitting the tube to conduct continuously, or the grid charge may be at any gradation between. For our use, this charge is negative. When the grid loses its charge or becomes positive, conduction takes place through the tube. The condenser in the circuit becomes charged, then discharges through the thyratron tube, which causes a momentary pulse of current to flow through the tube, i.e. condenser voltage rises until it becomes equal to the breakdown voltage of the tube, and then it discharges through the tube. In this circuit the condenser may be one of ten different sizes, the size determining the duration of the discharge. Placed between the tube and the output transformer are potentiometers placed in series and in parallel to govern the size of the stimulus. The 175 ohm potentiometer in parallel serves as a coarse adjustment and the 400 ohm potentiometer in series serves as a fine adjustment. A voltage regulator tube (OC3/VR105) keeps the potential of the circuit constant at 105

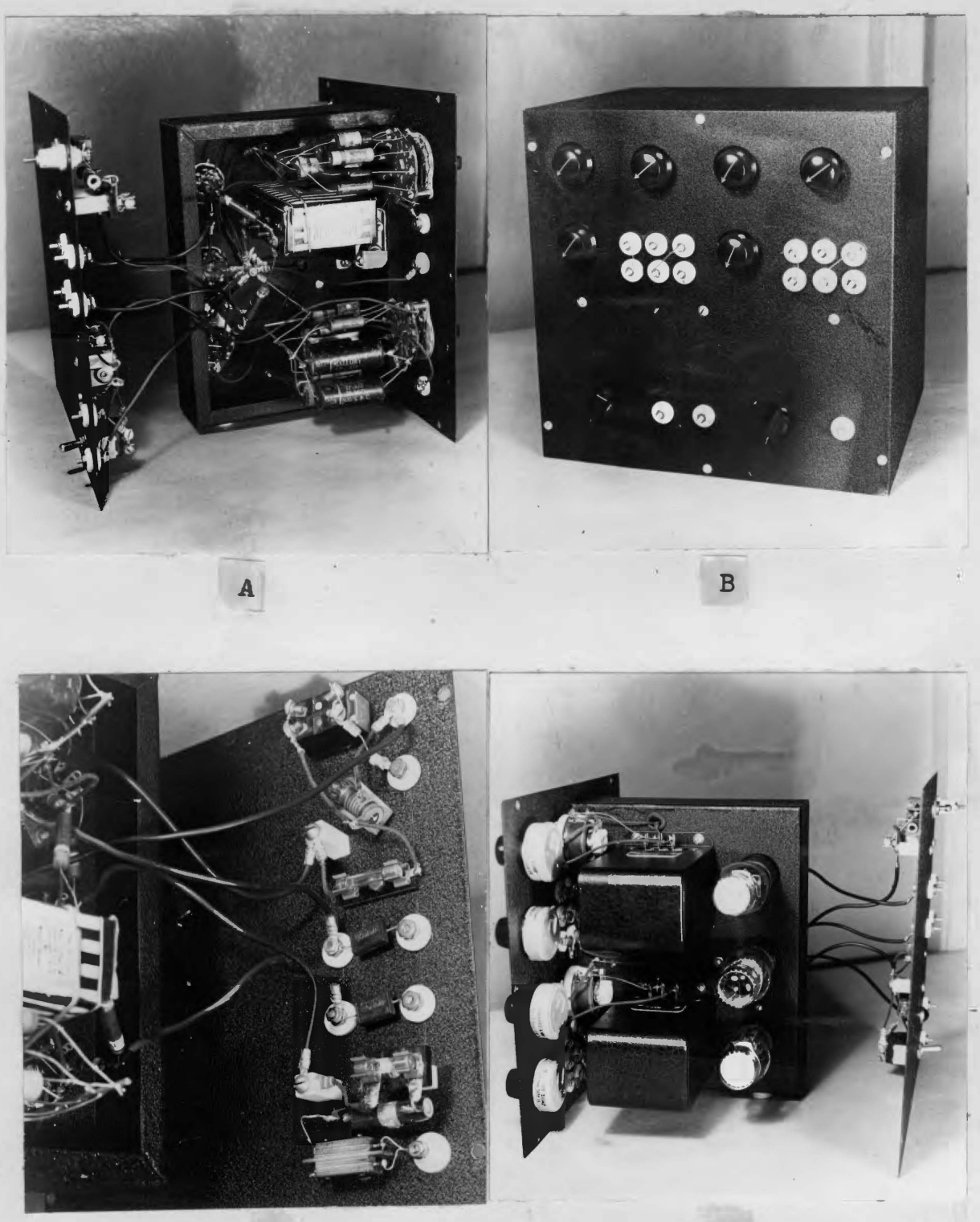
CAPTIONS FOR FIGURE 1

A. Interior view of front panel as seen from below.

B. Front view.

C. Interior view of back panel.

D. Interior view as seen from above.



A B

Figure 1. Stimulator

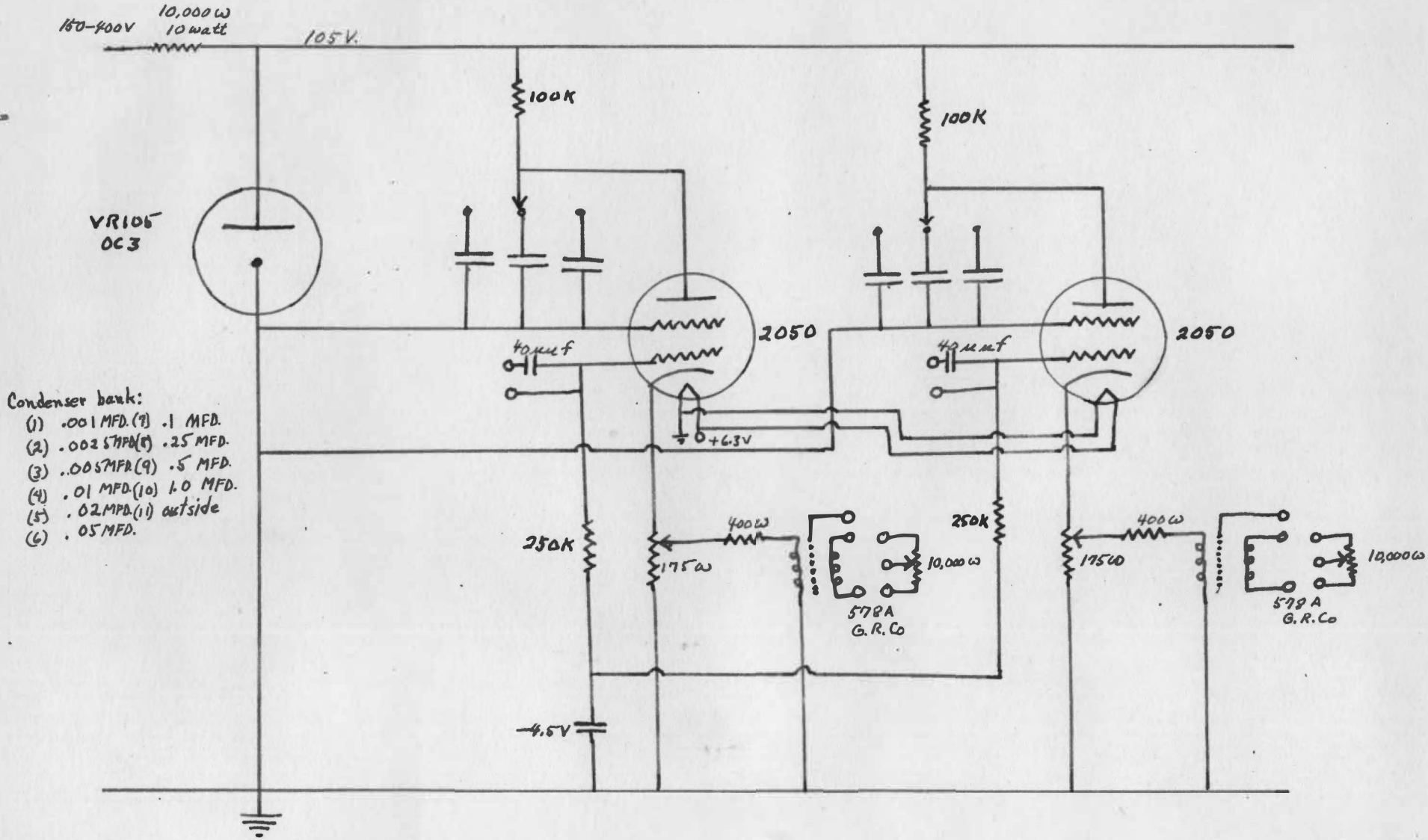


FIGURE 2 STIMULATOR CIRCUIT

volts D.C.

In order to be able to control the time interval between the two stimuli and to synchronize them with the sweep of the cathode-ray tube a circuit was designed and constructed which will be referred to as the synchronizer (see figure 4). The synchronizer consists of a master oscillator (see figure 3) and four subsidiary units. The master oscillator consists of a bank of condensers connected to the cathode of a thyratron tube, a 1 megohm potentiometer between cathode and ground, and a circuit breaking switch. The bank of condensers furnishes a coarse adjustment of the frequency of the firing of

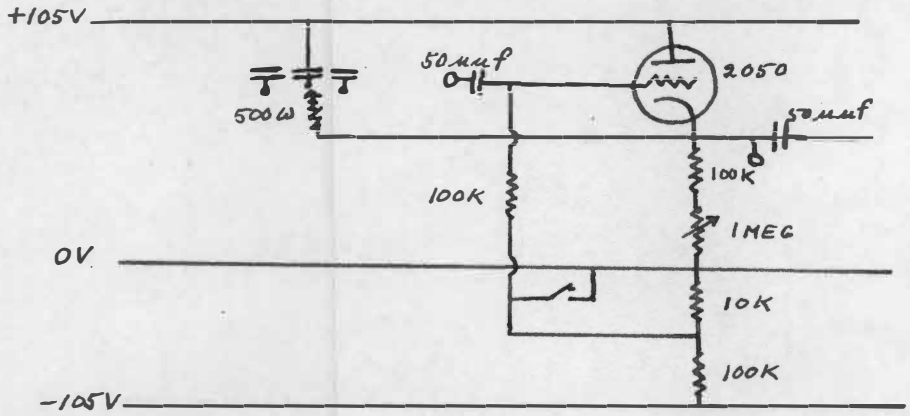


Figure 3. Master Oscillator Circuit

the thyratron tube, and the 1 megohm potentiometer a fine adjustment. The master oscillator operates on the same principle as the stimulator, but the grid voltage is adjusted so that the tube fires when the condenser

gets charged to a predetermined voltage. Each of the four subsidiary units (see figure 5) of the synchronizer consists of a thyratron tube which controls a Schmitt circuit (41). The Schmitt circuit is composed of two amplifier pentode tubes (6SJ7, 6AC7). These are coupled by two essential direct couplings: one a resistance coupling between the anode of the first and the grid of the second, and the other a common cathode coupling. In the resting condition the first tube does not conduct, but the grid voltage of the second is adjusted so that current flows continuously. Thus when the input potential to the grid of the first tube is zero, maximum current flows in the second tube, and the anode current of the first tube is cut off. If the potential of the grid of the first tube is increased so that current flows through the tube, the grid potential of the second tube will become negative enough to reduce the anode current, cutting it off momentarily. Output can be taken from either anode, giving a positive or a negative pulse.

The master oscillator sends a positive pulse onto the grid of the thyratron tube of the subsidiary unit which fires as a condenser discharge through the tube. The delay from the firing of the master oscillator to the firing of the Schmitt circuit is governed

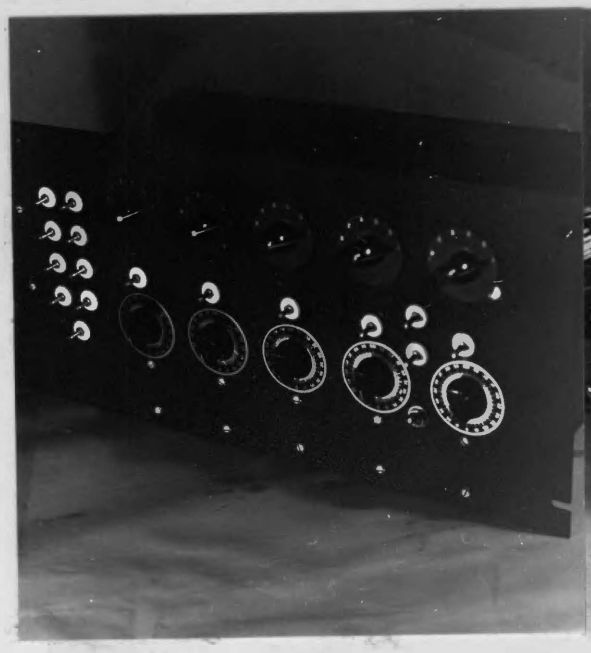
CAPTIONS FOR FIGURE 4

A. Anterior view.

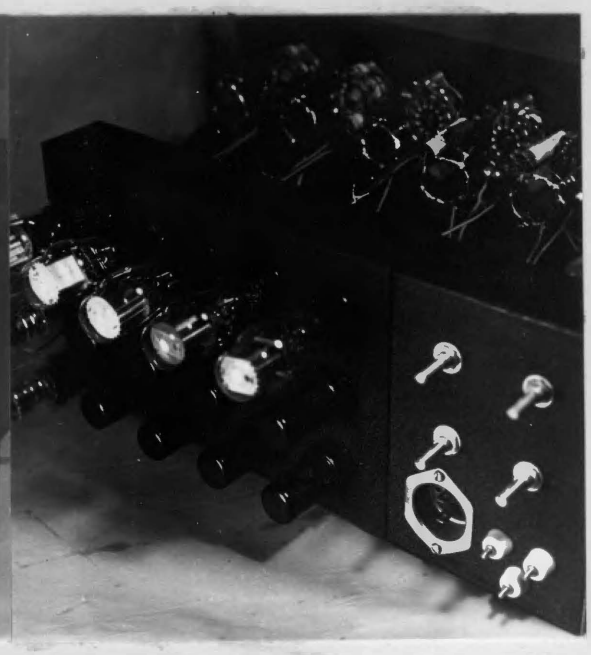
B. Interior view as seen from behind.

C. Interior view as seen from above.

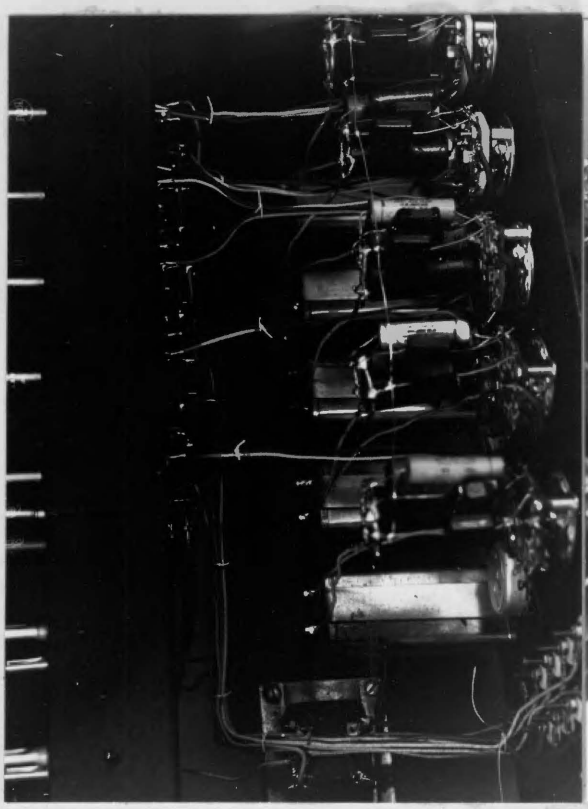
D. Interior view of front panel.

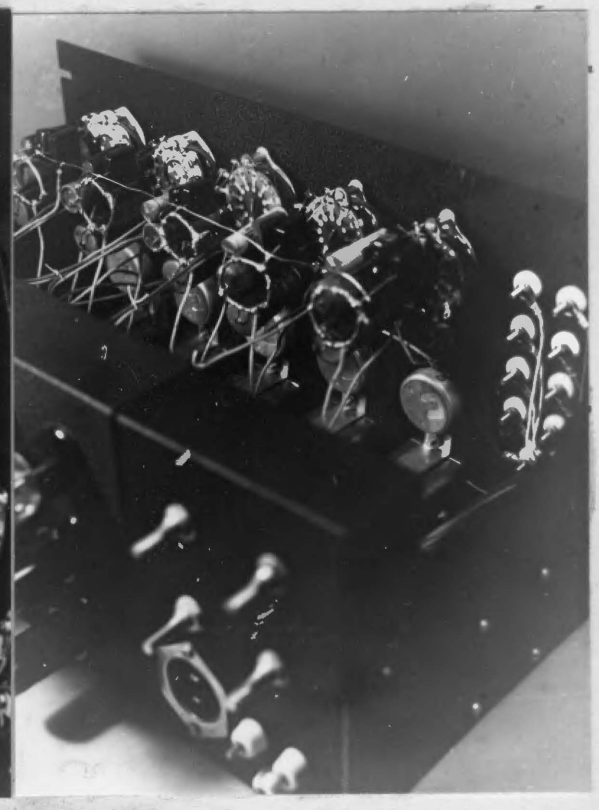


A



B





D

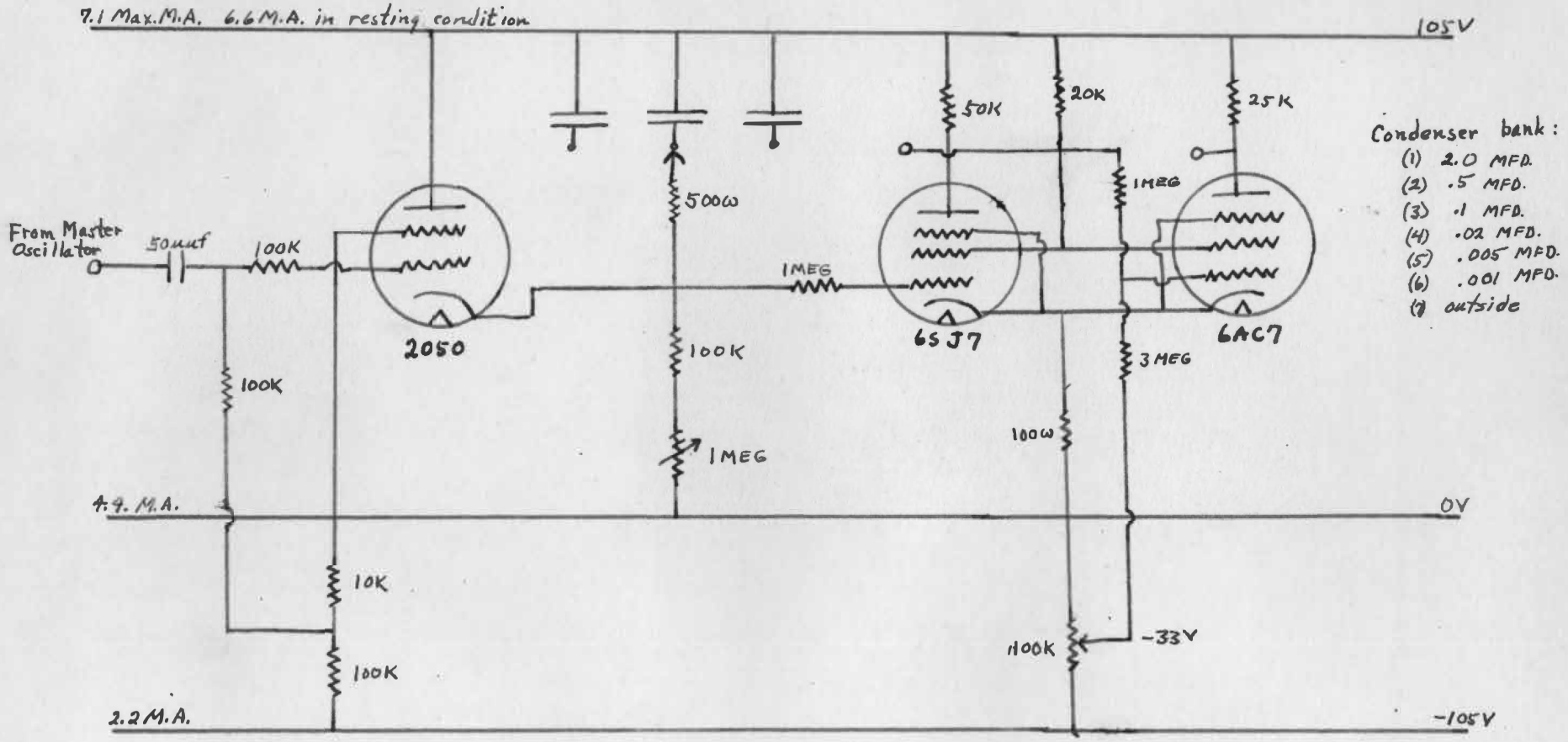


FIGURE 5 SYNCHRONIZER CIRCUIT — ONE CHANNEL

by a bank of condensers and a 1 megohm potentiometer. A negative pulse to the thyratron grid has no effect, but the positive pulse causes it to conduct. All the subsidiary units are discharged at the same time by the master oscillator, and each unit is adjusted so as to give the desired delay.

Two of the subsidiary units of the synchronizer were used to control the testing stimuli from the stimulator circuit, one unit released the sweep of the cathode-ray tube, and one was used to adjust the beam intensity of the screen of the tube.

The Horsley-Clarke stereotaxic instrument was designed for orientation of a needle electrode within the brain of an experimental animal (30). From the recording electrode in the stereotaxic instrument, impulses are lead through a two-stage amplifier to horizontal plates of the cathode-ray tube.

All electrodes were 22 gauge nichrome wire, the one used for recording in the brain being insulated except at its tip.

For a diagram of the entire experimental unit, see figure 6.

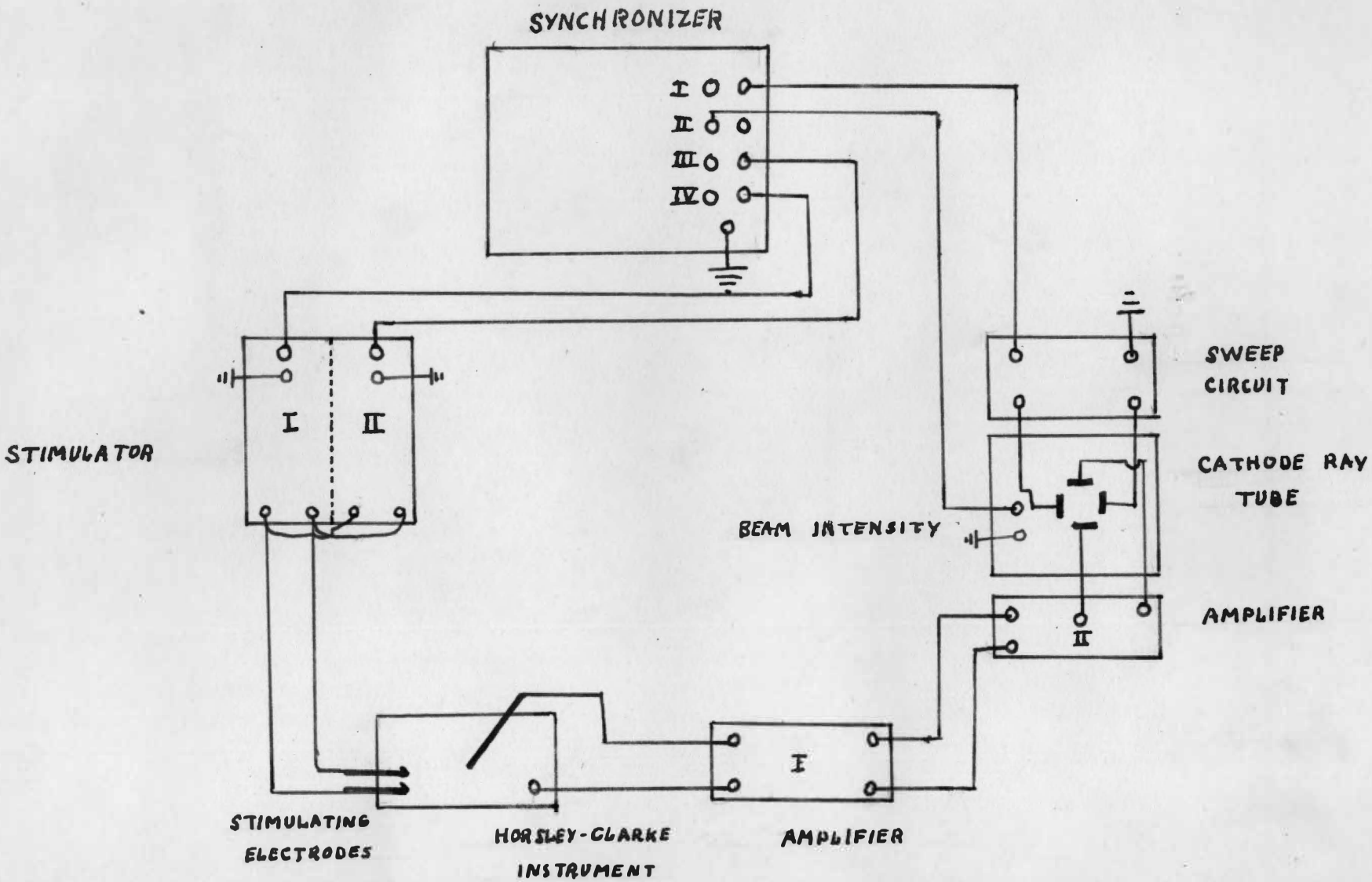


FIGURE 6 BLOCK DIAGRAM OF ELECTRICAL CONNECTIONS

OBSERVATIONS:

A. Peripheral nerve:

Oscillographic tracings from the five preparations of sciatic nerve appeared as a smooth line, since with isolated nerve there is no background activity to interfere with the studies. The recovery cycles of four of the five experiments were in reasonably close agreement, and these will be described together. Immediately following an absolutely refractory period of 1.5 msec., recovery rose rapidly to about 90 per cent of the unconditioned response, and from this point steadily rose to normal in approximately 13 msec. In one of these four, return to normal was followed by a supernormality of about 5.0 msec. duration. In the fifth experiment recovery was markedly different from the four described above. The absolutely refractory period was 1.47 msec., and, following it, recovery rose to 100 per cent in 6.3 msec., and continued to rise to 126 per cent of the unconditioned response. This peak was followed by a slow depression to 118 per cent by 22 msec., and remained at this level for 43.3 msec. which was the longest interval between stimuli used in the experiment.

Figure 7 is made up of samples from a typical experiment. All photographs are of the testing and

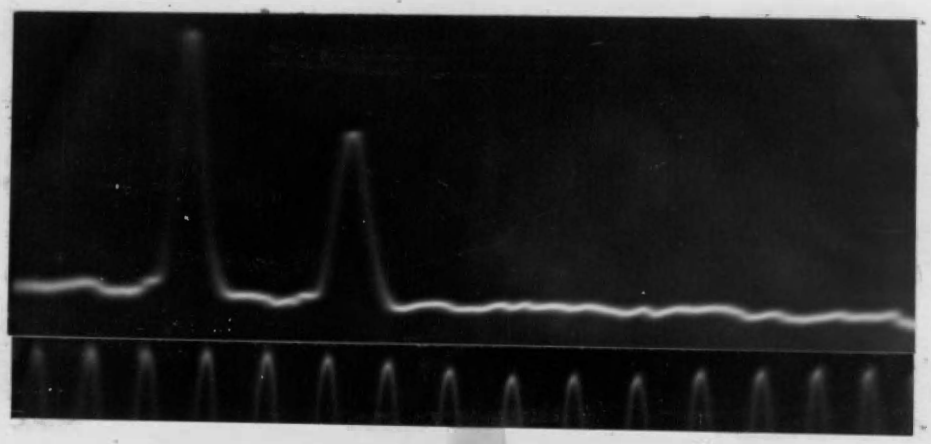
conditioning responses together. In photograph A the stimuli are separated by 8.9 msec., and the response to the testing stimulus is 97 per cent of the unconditioned response. Stimuli separation in photograph B is 2.54 msec., and the testing response is 66.5 per cent of the unconditioned response. Photographs A and B are from the same sweep circuit setting, as well as the time base of 1,000 cycles per second under photograph B. In photographs C and D the stimuli separations are 2.02 msec. and 1.51 msec., and the testing response is 37.5 per cent and 12.2 per cent of the unconditioned response respectively. Photographs C and D are from a faster sweep. The time base is 1,000 cycles per second.

Figure 8 is a graph showing the recovery curve produced in these experiments. The ordinates, as the per cent of the testing response of the unconditioned response, are plotted against the abscissa in milliseconds.

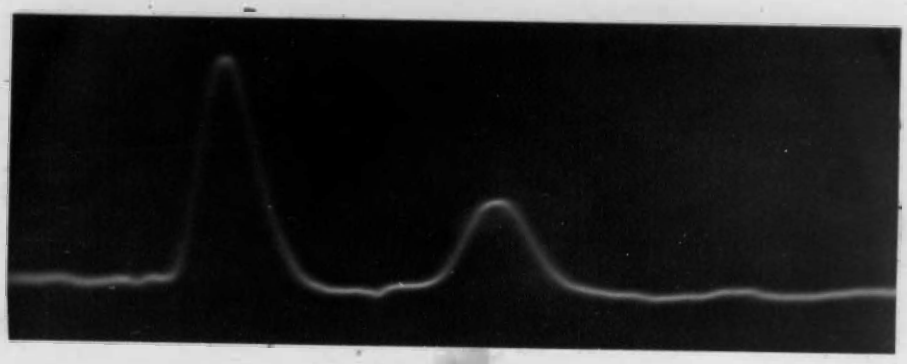
B. Central Nervous System:

The recovery cycles recorded in the spinal tract and nucleus of the trigeminal nerve may be divided into two fairly distinct groups. They have been separated on the basis of the form of the action potential and the speed of recovery. These groups will be referred to as primary and secondary potentials, there

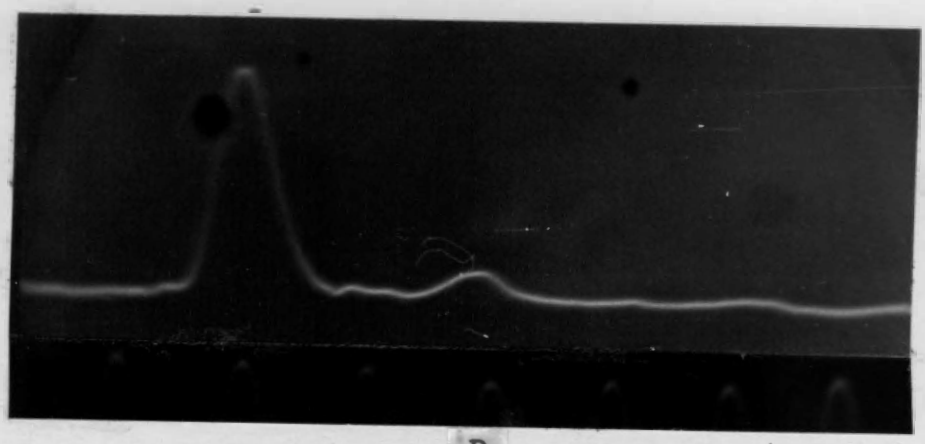
A



B



C



D

Figure 7.

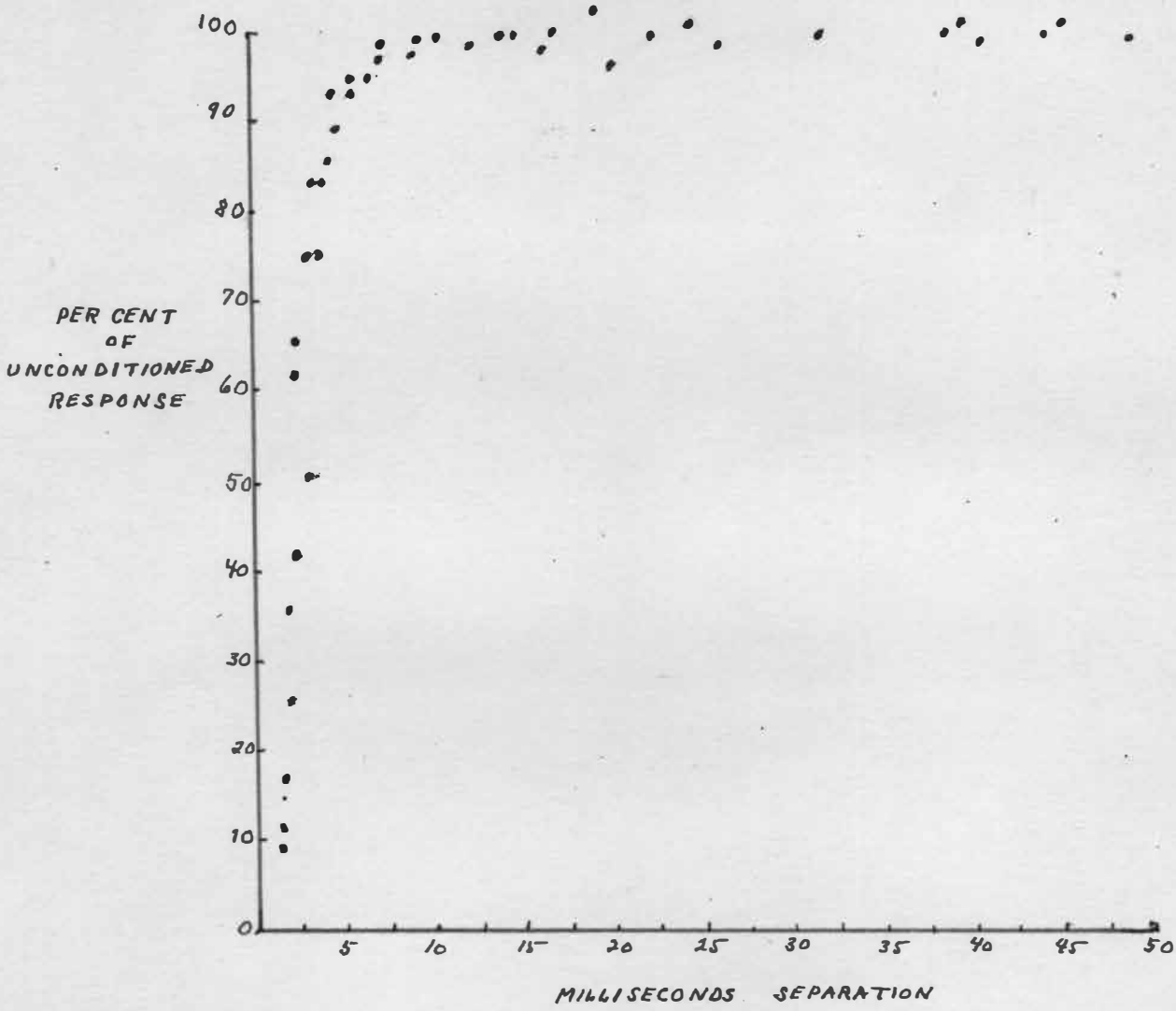

100
90
80
70
60
50
40
30
20
10
0
PER CENT
OF
UNCONDITIONED
RESPONSE
5
10
15
20
25
30
35
40
45
50
MILLISECONDS SEPARATION

FIGURE 8

being seven recovery cycles in the former and four in the latter group.

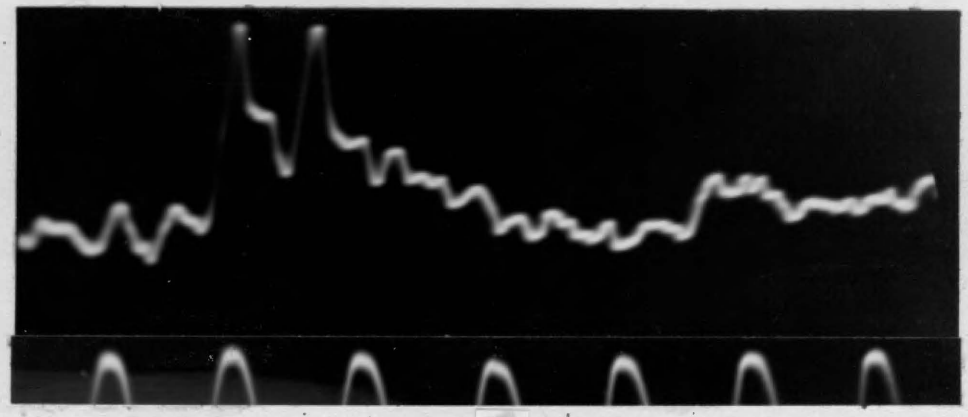
1. Potentials thought to be primary:

In this group the absolutely refractory period was 0.8 msec., and the relatively refractory period varied from 5 to 10 msec., with an average duration of 7.0 msec. Two of the seven series showed a slight supernormal period, one lasting 5 msec., and the other 20 msec. Supernormality never reached over 105 per cent of the unconditioned response. Five of the seven showed a slight subnormality which lasted from 8 to 46 msec. This depression varied only from 3 to 5 per cent below the unconditioned level.

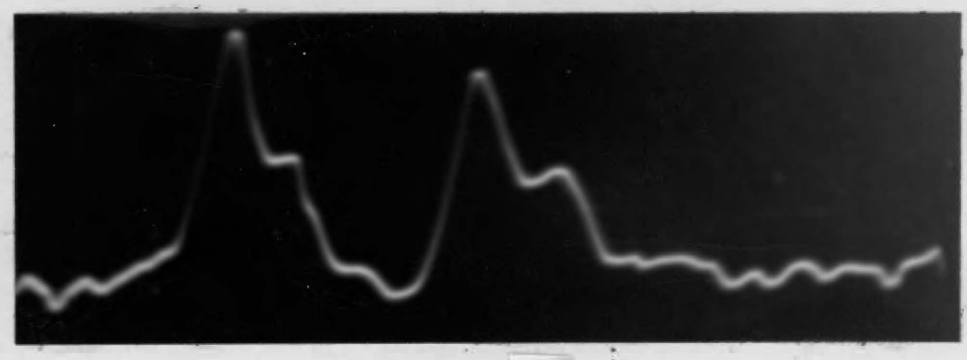
Figure 9 is composed of oscillographic tracings from a typical series of this group. Separation in photographs A and B are 5.55 and 1.26 msec., and the testing responses are 95.5 and 74.5 per cent, respectively, of the unconditioned response. The time line under B is 500 cycles per second. In C and D separations are 1.74 and 0.87 msec. with spike heights 83.5 and 30.3 per cent of the response when unconditioned by a previous stimulus. The time line for C and D is 1,000 cycles per second.

Figure 10 shows the typical type of recovery curve recorded in this group. Milliseconds separations are plotted against the height of the testing response in per cent of the unconditioned response. The solid

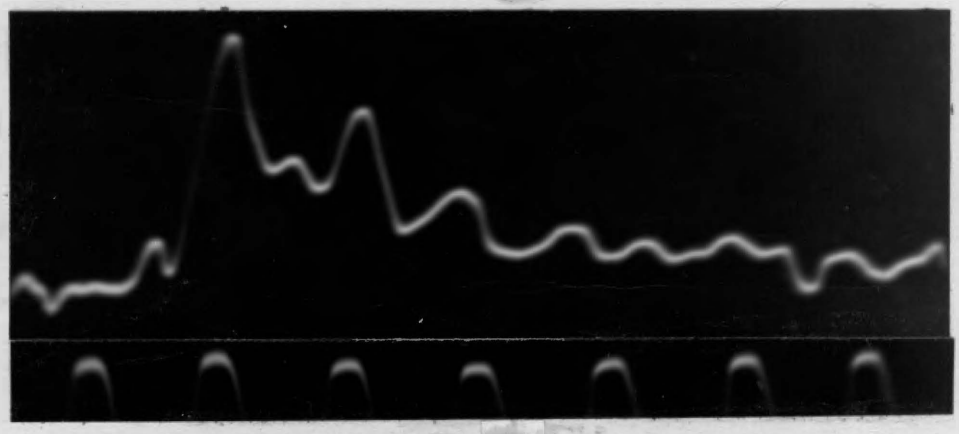
A



B



C



D

Figure 9.

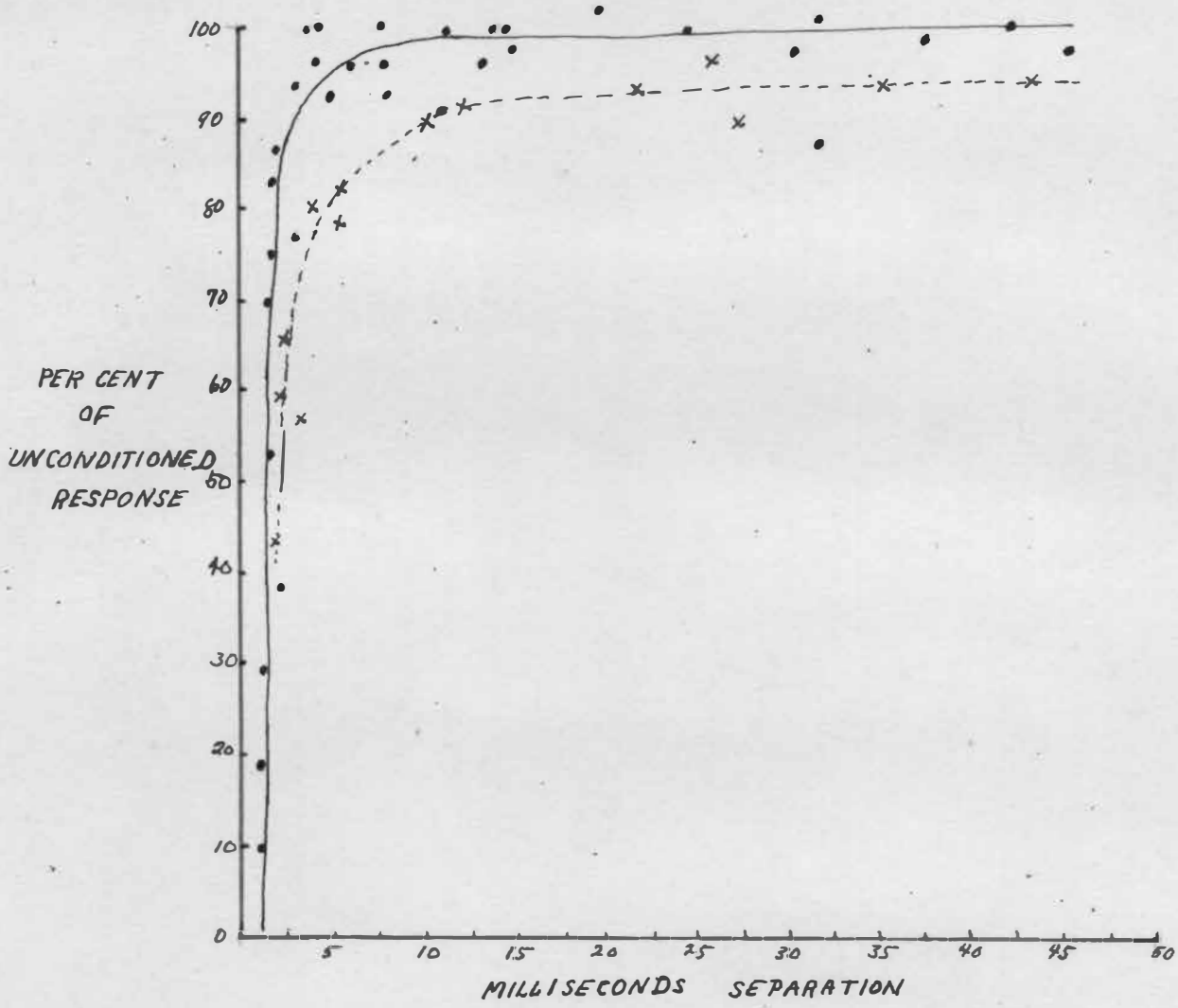

PER CENT
OF
UNCONDITIONED
RESPONSE
100
90
80
70
60
50
40
30
20
10
0
5
10
15
20
25
30
35
40
45
50
MILLISECONDS SEPARATION

FIGURE 10

line represents measurements on the first peak, and the dotted line is from the secondary elevation. This second elevation is considered to be a group of slower conducting fibers.

2. Potentials thought to be secondary:

In this series, the absolutely refractory periods were somewhat longer than those is the preceding group, varying from 1 to almost 2 msec., with the average being 1.4 msec. Spike height never recovered to the 100 per cent value in these 4 series, but rose to from 66 to 70 per cent in from 8 to 18 msec. (average 13.5) and either remained at that level throughout the remainder of the sweep or decreased slightly (not over 5 per cent) and remained at this lower level for even the widest separation (up to 150 msec.). In none of these four experiments did the recovery curve rise above 70 per cent.

Figure 11 is made up of photographs from a typical series of the group of potentials thought to be secondary. As can readily be seen, recovery is very much slowed, being only 59 per cent of the unconditioned height with a separation of 67.7 msec. in photograph A. The duration of the action potentials was quite long, positivity lasting ten to fifteen msec. followed by a prolonged negativity in most instances.

The time line for A is 100 cycles per second. In photograph B the stimuli are separated by 4.9 msec. and the response to the testing stimulus is 67.4 per cent of the unconditioned response. The point of this response when plotted on the curve in figure 10 is quite divergent, but the form of the potentials serves well for illustrative purposes. The time line is 1,000 cycles per second. C and D are separated by 4.1 and 2.24 msec., and recovery is 57 and 23 per cent of the unconditioned response respectively. The time line is 1,000 cycles per second. Sequence of events are: small spike due to primary neurons followed by the large potential due to secondary neurons. The primary spike is not so apparent in record A, and in none is a shock artifact evident.

Figure 12 shows milliseconds separation plotted against the height of the testing response in per cent of the unconditioned response, all curves in this group appearing very similar.

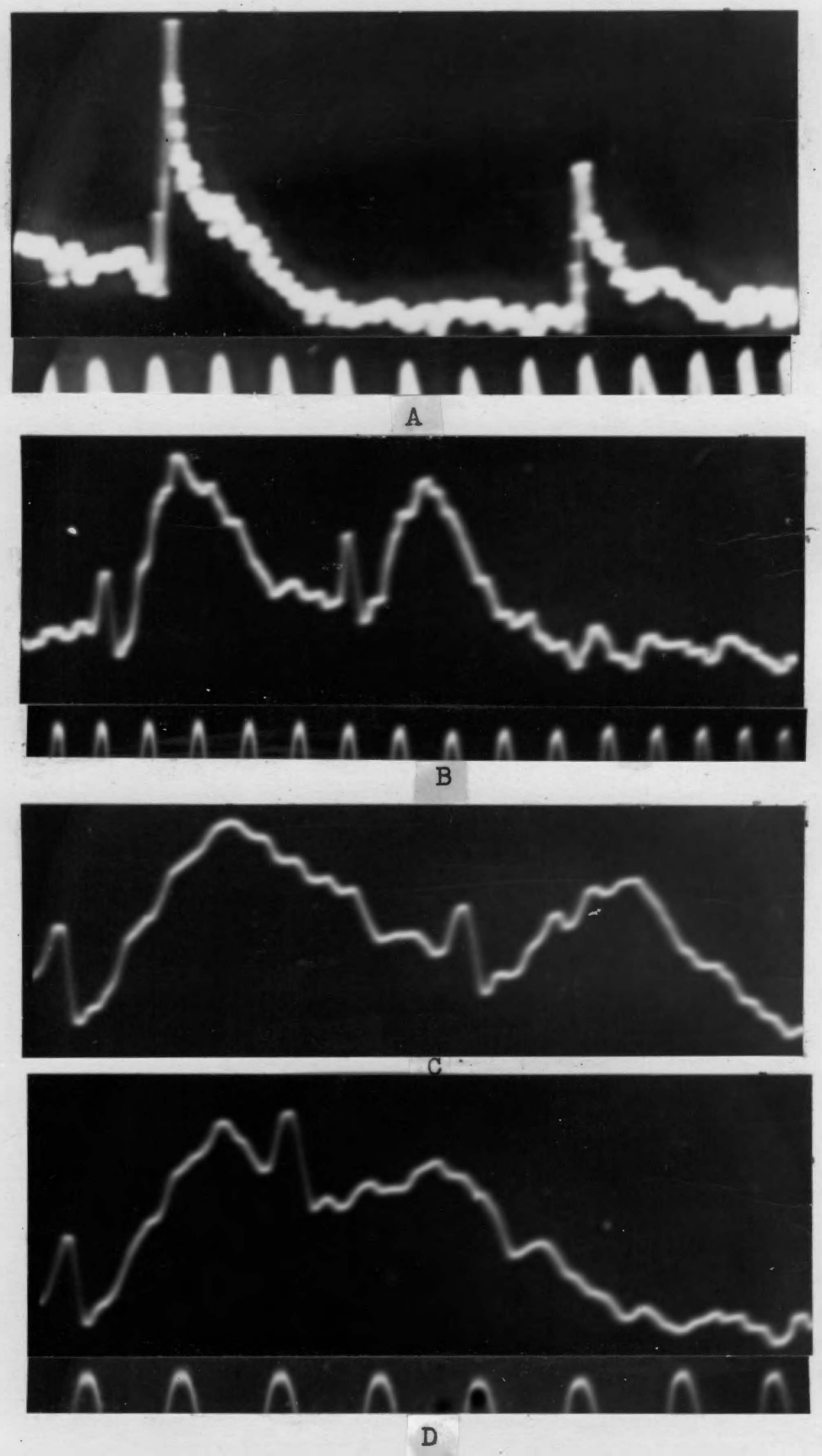


Figure 11.

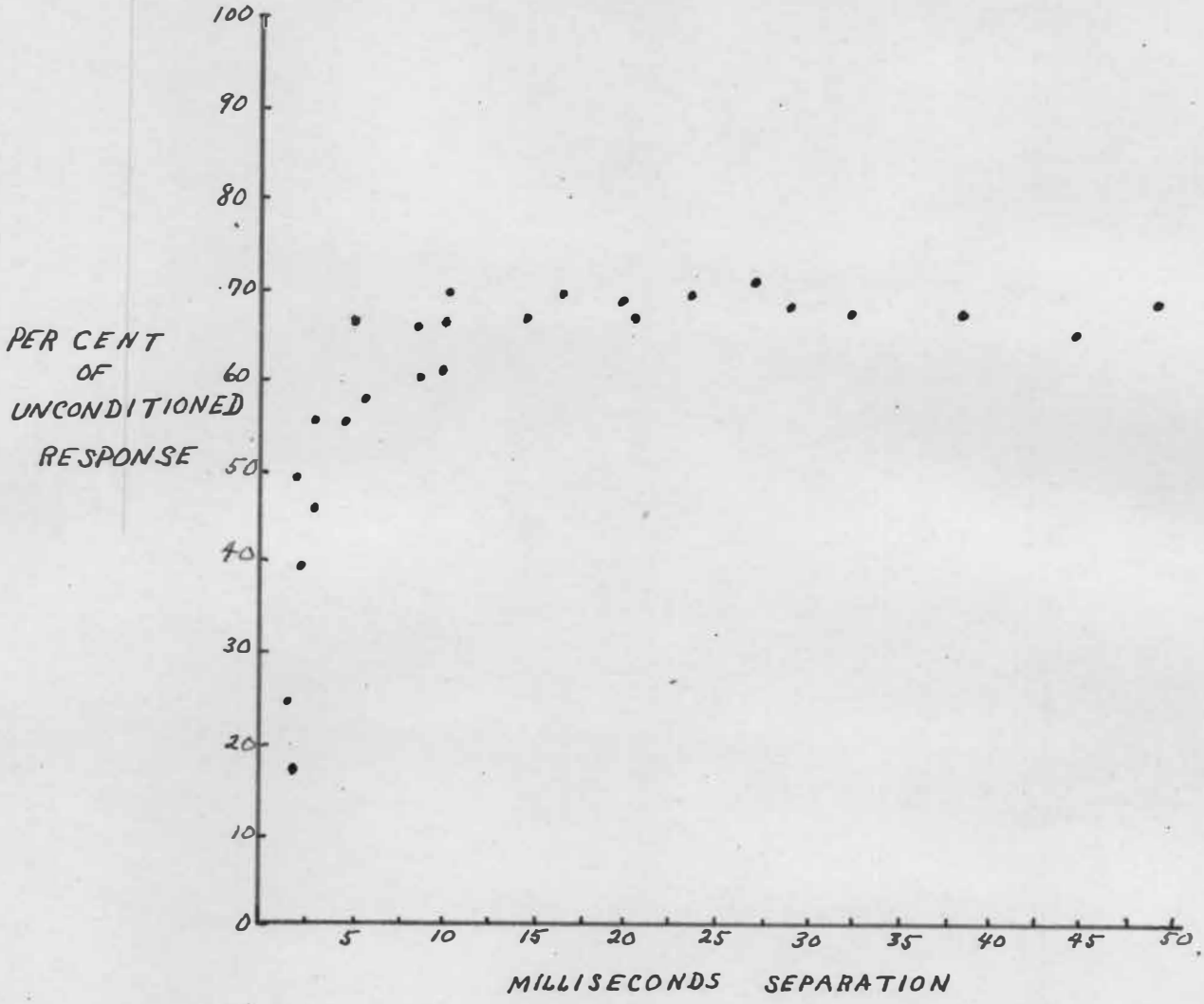

100
90
80
70
60
50
40
30
20
10
0
PER CENT
OF
UNCONDITIONED
RESPONSE
5
10
15
20
25
30
35
40
45
50
MILLISECONDS SEPARATION

FIGURE 12

DISCUSSION:

Since interest was centered primarily on the trigeminal nerve, the experiments on the sciatic nerve were more or less preliminary, and experimental conditions could have been greatly improved by making them more nearly physiological. The isolated piece of nerve was placed in a moist chamber lying on the stimulating and recording electrodes. No effort was made to control the temperature, and often a nerve was used for over an hour.

Measurements were made on an entire nerve, and this is admittedly not satisfactory in studying the finer points of neuron conduction; however, the properties of individual axons of all types have been thoroughly studied and are well known. The method of testing we have chosen to use limits our interest to the more irritable mammalian fibers which fall into the A group. Stimuli which were used were 2 to 3 times that necessary to elicit a maximal A spike. This is far below the threshold of the much less irritable B fibers.

After a maximal stimulus and response, no response is obtainable until the end of the absolutely refractory period of the most irritable fibers. Over a short time interval all the fibers of the A group will add their submaximal response to the recorded

response which causes its rapid increase following the measured absolutely refractory period of the nerve. Recovery then returns to normal during the relatively refractory period. Since stimuli used were supramaximal, the complete recovery of spike height occurs somewhat before the actual end of the relatively refractory period. The largest fibers tested recovered long before some of the smaller ones.

The recovery cycles recorded from the sciatic nerve compare well with those measured by Grundfest (21). It may be assumed that all elements of the recovery cycle were prolonged somewhat, because the nerve in the moist chamber was not kept at body temperature.

The spinal tract and nucleus of the trigeminal nerve contain fibers that mediate touch, pain, and temperature. In the sciatic nerve, there are all fiber types, and because of the somatic motor and large proprioception fibers the first part of recovery is comewhat faster, but other smaller components add to the total height so that the time to complete recovery is the same. Because of the differences in the conditions in which the recordings were made of the central and the peripheral series, the results can not be compared directly. The central

recordings were made in the living animal in an unexposed region, and thus simulated physiological conditions as nearly as possible. Minimal distortion from the recording electrode was obtainable by making it very sharp, and slowly lowering it into position.

The group of recordings from the spinal tract and nucleus that were thought to be secondary indicated an absolutely refractory period that appeared longer than that of the group thought to be primary. Lorente de No (39) found that the oculomotor nucleus and nerve have no elements in the entire arc with an absolutely refractory period longer than that of the presynaptic axons. This apparent discrepancy is probably due to the fact that both stimuli reached the spinal nucleus, in our experiments, by way of fibers in the spinal tract; the second stimulus, for the duration of the relatively refractory period of the primary fibers, was therefore less intense than the first, as far as the second order neurons were concerned. In Lorente de No's experiments the testing stimulus was applied directly to the motoneurones, or at least through fibers not previously stimulated.

Recovery of spike height of the series classed as presynaptic potentials was in good agreement with those recorded by other investigators (19, 46, 28)

with the exception of the supernormality which was observed. Supernormality was marked in one series on the sciatic nerve and showed up slightly in two of the central series. Graham (20) stated that supernormality does not occur. When supernormality was recorded by Von Brucke et al (46) it was attributed to error in their methods. In our experiments, the supernormality that is described is real, but is not necessarily contradictory to the statements of Graham and of Von Brucke. Although the conditioning stimulus was supramaximal at the beginning of the experiment, the threshold of some fibers may have increased during the experiment to where the stimulus was not adequate to fire them. They may then have responded to a second stimulus which fell in the supernormal period of a previous subthreshold conditioning stimulus. This, of course, does not occur when the conditioning stimulus is maintained supramaximal throughout the experiment.

The amplitude of the waves varied rather widely, but this is attributable to variation in the amount of shunting tissue, the number of active nerve fibers, and the distance of the recording electrode from the active tissue.

The form of the action potentials recorded

varied as to the location in the brain stem. The samples we have selected to represent the primary and secondary groups of figures 7 and 9 are fairly typical of the two general groups; however, these varied somewhat, as action potentials so notoriously do under slightly changing conditions. Their general characteristics compare rather well with those recorded in other brain stem nuclei (45) (39).

Recovery curves plotted from measurements of potentials which we have classed in the secondary or post-synaptic group have not been presented by previous workers, to our knowledge. It would be expected that the recovery of post-synaptic fibers would be slowed in comparison to the rate of recovery of the primary fibers, because of the slow recovery to synaptic stimuli of the soma of the neurons, (19). We would expect, however, a gradual increase to the normal level, and not the leveling-off at about 70 per cent recovery which we recorded. This level was maintained for the duration of the slowest sweep that was available, approximately 150 msec. The actual drawing of the curves was difficult in some cases, but the agreement of the group as a whole tends to eliminate this difficulty. As to the cause of this depressed recovery, we are not able to offer any suggestions, and we have found no adequate explanation in the literature. We did not determine just how long

it lasted since it was still present with the longest intervals which we were able to measure with our equipment.

It is an interesting point that the soma of the neuron recovers its exitability to direct electrical stimulation, or to a second stimulus sent in over different fibers, as rapidly as the axon itself, but recovers more slowly to a second stimulus sent in over the same presynaptic fibers. Several workers have found that the refractory period of the soma itself is no greater than that of axons (39) (28) under certain conditions, but there is almost universal agreement that synaptic recovery is slow where both stimuli are applied through the same fibers.

From the results presented here, it appears that the second peak of the potential wave recorded in the spinal tract and nucleus of the fifth nerve, upon stimulation of afferent fifth nerve fibers, is a post-synaptic potential. This is the wave that appears no earlier than 1.0 msec. and may last 10 to 15 msec. From the long duration of this post-synaptic potential in some experiments it very likely included neurons of higher order than the second, but these experiments do not give the data necessary to distinguish between second and higher order neurons. Since the synaptic delay is 0.5 to 1 msec.

(37, 5, 2, 38, 45, 43) and since the duration of the spike potential of any one neuron is not over 1 msec., it is unlikely that a wave due to second order neurons alone would have a duration greater than a few msec., even after allowing for different conduction times in the presynaptic fibers. Additional work would have to be done, however, to prove such a point.

SUMMARY & CONCLUSIONS:

1. An attempt was made to separate pre- and post-synaptic action potentials on the basis of recovery of spike height to the second of two supramaximal stimuli.

2. Two distinct groups of action potentials were recorded from the spinal tract of the trigeminal nerve.

3. A series of recovery-cycles of the spike potentials of the sciatic nerve was plotted for comparison with the spike potential of the spinal tract of the fifth nerve.

4. A 2 channel stimulator and a 5 unit synchronizer circuit were designed and constructed for use in these experiments. The utilization of a Schmitt circuit to achieve time delay is believed to be a new application of that circuit.

5. From the date presented here, it may not be certain that the second peak of the potential wave recorded from the spinal tract and nucleus of the fifth nerve is from second or higher order fibers, but it gives strong support to the belief that it is actually post-synaptic.

6. The methods used in these experiments are not necessarily restricted to use in trigeminal pathways but should be applicable to any synaptic region.

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