ACTION POTENTIALS FROM INDIVIDUAL ELEMENTS IN CAT GENICULATE AND STRIATE CORTEX[1]

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IN RECENT YEARS, application of hyperfine glass microelectrodes (15, 19) to electrophysiological studies of the central nervous system has started to yield some promising results (in the cat spinal cord, 6, 24; in the frog spinal cord, 23; in the mammalian cerebral cortex, 7, 14). In the present investigation attempts have been made to record, to analyze and to classify unitary responses observed with these submicroscopic electrodes introduced into the cat brain. We are concerned in this paper mainly with the responses recorded from the visual system, namely, from the lateral geniculate body and the striate cortex, following electric stimuli to optic nerve or radiation.

Introduction of a glass capillary of approximately 0.3 μ into a neurone soma injures the cell seriously. Although the records obtained under certain circumstances with these internal electrodes are of great physiological significance, it was sometimes difficult to analyze the functions of the neurones from them. Extracellular recording of action potentials with these electrodes, on the contrary, gave us satisfactory, undistorted pictures of the function of the nerve fibers, cell bodies and dendrites in the central nervous system.

With the extracellular electrodes, we obtained four different types of electric response from the lateral geniculate body, namely, responses of the pre- and postsynaptic axons, responses from the cell bodies and those from the dendrites.[5] In agreement with what has been postulated by Lloyd (16), Chang (8, 9), and Bishop and Clare (4), the dendritic responses were found to show a much longer and slower configuration than the cell body responses. The potential field produced by a neurone in the cerebral cortex will be discussed in this connection.

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[5] According to Lloyd (16), the words "neurone soma" are used in this paper to include both the dendrites and the cell body of a neurone. The term "responses of a soma" is therefore used to indicate that not only the cell body but also the dendrites could make contribution to those responses.

METHOD

Material and preparation. Cats were anesthetized, as described by Bishop and Clare (2), with a mixture of half doses of nembutal (0.2 cc./kg. body weight) and of magnesium sulphate solution (0.13 gr. of $MgSO_4$/kg. body weight). By removing a part of the bony wall of the orbital cavity, the optic nerve was exposed for electric stimulation. In so doing, the hydrostatic pressure of the eyeball was first released by making a large incision through the cornea and by subsequent removal of the lens. A small curved strip of silver, insulated with "lucite" except on the inner surface, was placed around the optic nerve and was used as the stimulating cathode. The anode was a silver hook, inserted into the sclera. Square voltage pulses or induction shocks from a transformer were used as stimuli.

The skull was opened, generally on both sides, to expose the lateral, suprasylvian and ectosylvian gyri. The geniculate body usually was not exposed. The microelectrode was pushed toward the geniculate body through a small hole made through the pia on the surface of suprasylvian gyrus. Both electrophysiological and anatomical controls indicated that the lateral geniculate body is reached at the depth of 12–15 mm. from the surface of the cortex. For direct stimulation of the radiation fibers, a pair of steel wire electrodes, fixed at about 2 mm. apart, was inserted into the substance of the cortex and directed towards the geniculate body. The size and latency of the response recorded from the surface of the visual cortex with gross electrodes served as a criterion for successful placement of the stimulating electrode. For recording unitary responses from the striate cortex, a small hole was made on the surface of the lateral gyrus, and through this hole in the pia a microelectrode was inserted into the cortex, either tangentially or vertically to the surface.

Microelectrode. Glass microelectrodes were drawn from either soft or pyrex glass tubing of about 1 mm. diameter. The electron microscope showed that most of the capillaries, selected under an ordinary microscope with high dry objective, had orifices of between 0.2 and 0.3μ, the diameter increasing at the rate of approximately one-tenth with distance from the tip. A 3 molar KCl solution was drawn into the capillary by the following procedure: Capillaries were fixed with rubber bands to a glass plate with their tips directed downward and were gently boiled for about 10 minutes in absolute alcohol under reduced pressure (temperature 25–40°C.). The capillaries were then kept in alcohol under atmospheric pressure until the air bubbles within them disappeared completely (5–20 minutes). Then they were placed in a beaker of distilled water for 2–2.5 minutes.[6] Usually they were then dipped in a 3 molar KCl solution (below 45°C.) for 5–7 minutes under atmospheric pressure, followed by about 30 minutes under reduced pressure; but this step of evacuation in KCl solution was sometimes omitted. The capillaries were kept in the KCl solution at room temperature overnight, and those with D.C. resistances (measured in Ringer) of between 8 and 30 megohms were selected for experiments. This alcohol method of introducing KCl solution was devised by Mrs. I. Tasaki, when she found that, with many kinds of glass tubing, boiling the capillaries in 3 molar KCl solution under atmospheric pressure caused very extensive destruction of their sharp tips. The alcohol method always gave satisfactory results, provided the alcohol and the KCl solution were clean. Another advantage of this alcohol method is that absorption of air bubbles is much faster in alcohol than in water.

Electrical equipment. Equipment used for recording action potentials from the geniculate body with microelectrodes was similar to that used by one of us previously (23). A piece of fine silver wire (about 100μ diameter) of 10–15 cm. length was used to connect the fluid in the capillary with the input of a cathode-follower preamplifier (RCA 1620 in triode connection). The indifferent electrode was a silver plate, imbedded in a large mass of cotton and placed in most cases on the surface of the contralateral cerebral cortex. The potential differences between the micro- and the indifferent electrodes were amplified with a low-gain D.C. amplifier and simultaneously with a high-gain condenser-coupled amplifier, and the outputs were recorded with three beams of two double-beam cathode-ray oscillographs. One of the oscillograph beams was used for continuous recording of the resting potential, the second for continuous recording of the action potentials and a third for recording at high transit speed responses to stimulation of the optic nerve. A Grass camera was used.

For recording unitary responses from the striate cortex, a double-beam oscillograph was employed. Since a direct-coupled amplifier was not available in this series of experiments, a mechanical chopper was inserted between the two output terminals of the push-

[6] If methyl alcohol is used, this step is not absolutely necessary.

pull cathode-follower stage. By brief closure of this contact, the D.C. voltage was recorded as a rectangular pulse in each sweep of the oscillograph beam.

In the records presented in this paper, an *upward* deflection represents a *positive* potential at the tip of the recording microelectrode.

RESULTS

PART I. LATERAL GENICULATE BODY

A. *Four different kinds of extracellularly recorded responses*

When a hyperfine microelectrode was pushed slowly into the lateral geniculate body with a micro-manipulator, sizable D.C. potentials (generally 10–50 mV.) were found to appear from time to time as the electrode penetrated one element after another. Since the start and the end of these resting potentials were, in most cases, fairly abrupt, it was generally easy to decide whether or not the tip of the electrode was inside a cell. By the term "extracellularly recorded" responses, we mean the responses taken when there was practically no resting potential at the tip of the microelectrode. These responses, unlike those associated with a resting potential, did not show any progressive deterioration during the course of observation. They disappeared when the position of the electrode changed either gradually or suddenly by circulatory or respiratory movements of the animal. The extracellularly recorded action potentials, induced in all-or-none manner by electric stimulation of the optic nerve, were of four different kinds, namely, responses from (i) presynaptic medullated axons, (ii) from postsynaptic medullated axons, (iii) from cell bodies and (iv) from dendrites. The criteria for this classification and the physiological properties of these responses are as follows.

(i) *Presynaptic axons.* The latencies of the unitary responses recorded from the region of the geniculate body were either longer or shorter than 1 msec.; this 1 msec. has therefore served for distinguishing presynaptic from postsynaptic responses. The latency for the presynaptic responses was between 0.4 and 0.8 msec. These responses showed a sharp rising phase, a sharp positive peak and a gradual falling phase, followed frequently by a slight negativity which we ascribe to the capacitative effect of a thin film of myelin covering the tip of the microelectrode. The duration of these responses was 1 msec. or less; but it was difficult to determine its value accurately because of distortion by the capacity of the myelin layer and of the recording microelectrode. The spike height was in many cases only a few millivolts and never exceeded 20 mV.

In an isolated frog nerve fiber (23), such monophasic responses without a resting potential appeared when the microelectrode pushed into the fiber reached the interface between the myelin layer and the axis cylinder or when the tip of the electrode caused a dimpling of a layer of myelin into the axis cylinder. A resting potential appeared only when the tip of the microelectrode reached the axis cylinder. Since all the responses recorded here with latencies shorter than 1 msec. showed this simple monophasic configuration, there seemed no doubt that these responses derived from individual medullated axons in the optic tract, namely, from presynaptic axons. The length of the optic tract between the site of stimulation and the geniculate body is approximately 30 mm. The latency of our presynaptic axons coincides approximately with the value of 0.6 msec. obtained by Bishop and O'Leary (5) under similar experimental conditions but with larger recording electrodes (see also 18).

Column A in Fig. 1 gives an example of the responses from individual presynaptic axons. Each shock gave rise to one spike in all-or-none manner.

When the frequency of stimulation was increased to about 100 shocks per sec., it was found that the latency, the size and the threshold strength for these responses remained constant. In many cases such extracellular recording changed, because of some accidental movement of the microelectrode relative to the brain, into intracellular recording. The spike height became suddenly larger simultaneously with the appearance of a resting potential and then showed a progressive deterioration.

(ii) *Postsynaptic axons.* The extracellularly recorded responses of the postsynaptic axons appear after a latency of 1.2–2.2 msec. The size and the

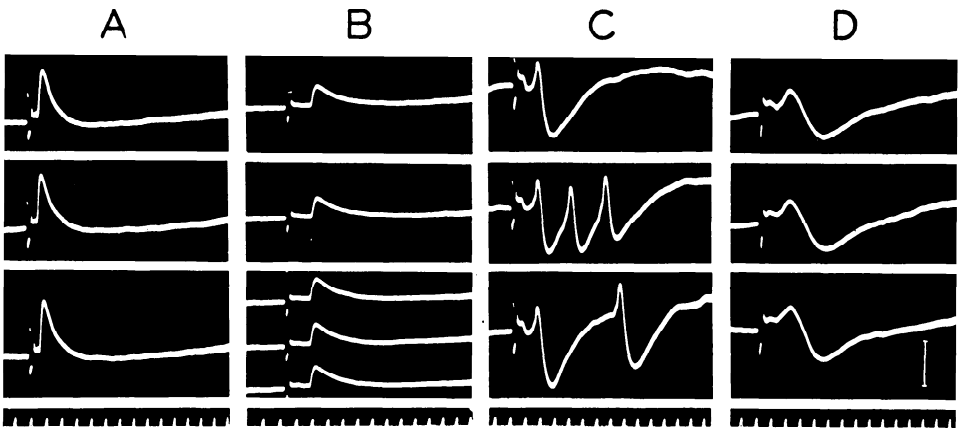

FIG. 1. Four different types of unitary responses taken with extracellular microelectrodes from lateral geniculate body of cat. Stimuli were electric shocks applied to contralateral optic nerve. No resting potential was observed when these records were taken. Voltage calibration, 2 mV., applies to all four columns. Time markers, 1 msec. apart. A: Responses of a presynaptic axon taken at intervals of 0.2 sec. B: Responses of a postsynaptic axon; stimulus frequency approximately 50 (bottom) and 5 (middle and top) per sec. C: Responses of soma of neurone. D: Responses of dendrite. Further detail in text.

shape of these responses resembled those from the presynaptic axons. Their configuration was "triangular," sometimes with slight diphasicity. These responses appeared either with or without an associated resting potential (see Fig. 2), indicating that they were from medullated axons. Our interpretation that these axons were from the postsynaptic fibers, *i.e.*, from the radiation fibers, was supported directly by the fact that similar responses could be obtained from the white matter above the geniculate body.

In addition to their longer latency, postsynaptic responses differed from presynaptic ones in the tendency to respond with multiple spikes to single shocks. In our experiments, double or triple responses appeared very often, even when there was no resting potential at the tip of the microelectrode (Fig. 2). This fact excludes the possibility that these multiple spikes were caused by some effect of the injury inflicted upon the axon by the microelec-

trode. The time intervals between these multiple spikes were in general 3–7 msec.

Another feature of the postsynaptic responses was their behavior to high-frequency stimulation. In many cases it was observed that, at high frequencies (30 100 shocks per sec.), every shock produced one spike at the usual long latency, while at low frequencies (1–5 shocks per sec.) each shock often induced more than one response. In some preparations, constant high-frequency stimulation caused rhythmical failure of synaptic transmission.

It is interesting to note that these responses from the postsynaptic axons sometimes exhibited "notch s" on or near their positive peaks (Fig. 3B).

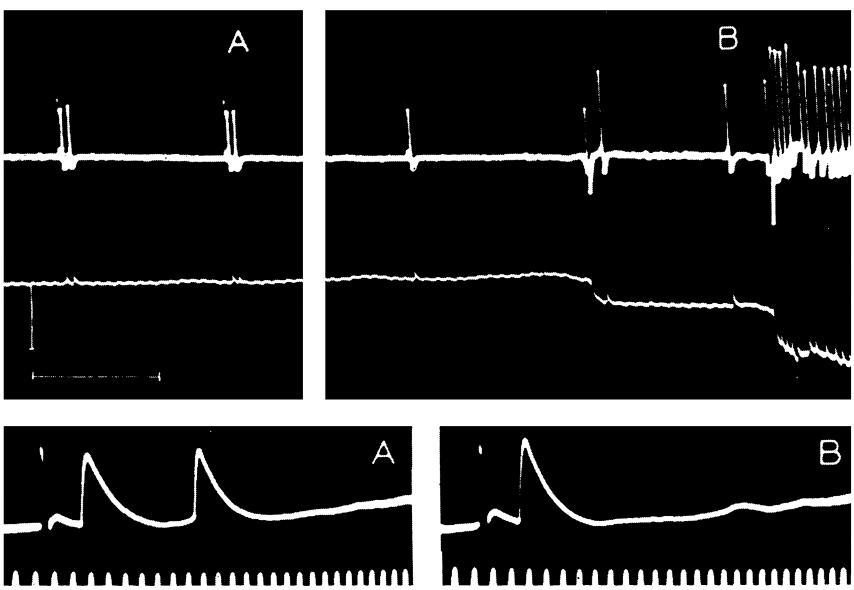

FIG. 2. Responses of postsynaptic axon. Top, continuous recording with condenser-coupled amplifier. Middle, continuous recording with direct-coupled (D.C.) amplifier. Bottom, high speed recording of responses A and B at top with a long time constant RC amplifier. Voltage calibration, 20 mV. for D.C. (middle) channel, and approximately 2 mV. for other two channels. Time markers, 100 msec. for continuous recording and 1 msec. apart for high speed recording.

These notches, the "nodal signs" of the injured axons (23), appeared only when the responses were associated with a resting potential at the tip of the microelectrode. They were undoubtedly the sign of delayed or weakened propagation of an impulse between two portions of a neurone which are each capable of developing electric responses of about the same size. Such notching has not been demonstrated in the responses from cell bodies or from dendrites. In the peripheral nerve fiber these notches appear only when propagation of an impulse across the internodal segment punctured by the microelectrode, from the proximal node to the distal one, is delayed by the injury. In the light of similar findings on the myelinated fibers in the frog dorsal

funiculus (23), we believe that the double peaks demonstrated in the radiation fibers are caused by the same mechanism.

(iii) *Cell body.* The responses of this category are characterized by their complicated configuration with a relatively long, negative spike potential. Their latency was practically the same as that of the postsynaptic axons (Figs. 1C, 3A). As in the case of postsynaptic axons, single shocks induced often double, sometimes triple, responses in these elements. The size of the negative spikes of these cell body responses was smaller than 3 mV.

The reason for attributing these negative spikes to the activity of the neurone soma is that they can be readily explained as being due to activity of

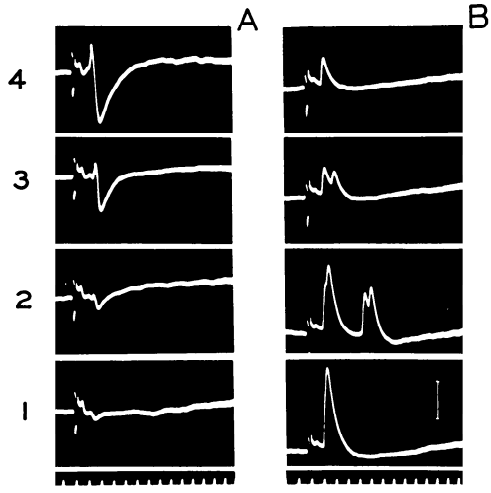

FIG. 3. A: Progressive increase in size of somatic responses caused by a gradual approach of recording microelectrode toward cell body of a neurone. Microelectrode was pushed gradually into geniculate body while induction shocks were being given repetitively to optic nerve. Note change in shape of response; absence of initial positive phase at a great distance indicates that potential field at this moment is localized in vicinity of cell body. No resting potential was observed at time of recording. Absolute distance of electrode movement was not clear. B: Development of notches near peak of spike potentials, or "nodal signs," during progressive deterioration of responses of postsynaptic axon. These four records were taken within 2 sec. after start of resting potential at tip of recording microelectrode. Voltage calibration, 2 mV.; time markers, 1 msec. apart.

a cell body with a number of dendrites extending from the cell body in all directions. We assume that the surface of an active cell body behaves, in a continuous conducting medium, as a sink of electric current and all the inactive dendrites behave as sources. The potential in the fluid medium around the soma should then be purely negative relative to remote points (see Fig. 13). The initial positivity in these responses of neurone soma we attribute to an outward-directed current through the surface of the soma caused by synaptic activity. A more detailed argument on these points will be presented in the Discussion.

(iv) *Dendrites.* During the course of our experiments we have encountered one more type of externally recorded response. Figure 1D shows a series of slow, diphasic, all-or-none responses. The latency for their positive initial phase is practically the same as that for other postsynaptic responses. Their slow initial positive phase and their gradual transition into the negative phase indicate that they derive from the slow propagation of an impulse along a single large strand of protoplasm. Since the possibility of their being

from axons has been excluded, we conclude that they are from the dendrite.[7] The conclusion that dendrites carry nerve impulses at a slow speed agrees with the conclusion drawn by Lloyd (16), Chang (8, 9), and Bishop and Clare (4) from their experiments with gross electrodes.

According to our interpretation, the first (positive) phase of these dendritic responses corresponds to the period in which the active-inactive boundary on the dendritic surface is approaching the site of the recording microelectrode. The second (negative) phase represents arrival of activity locus

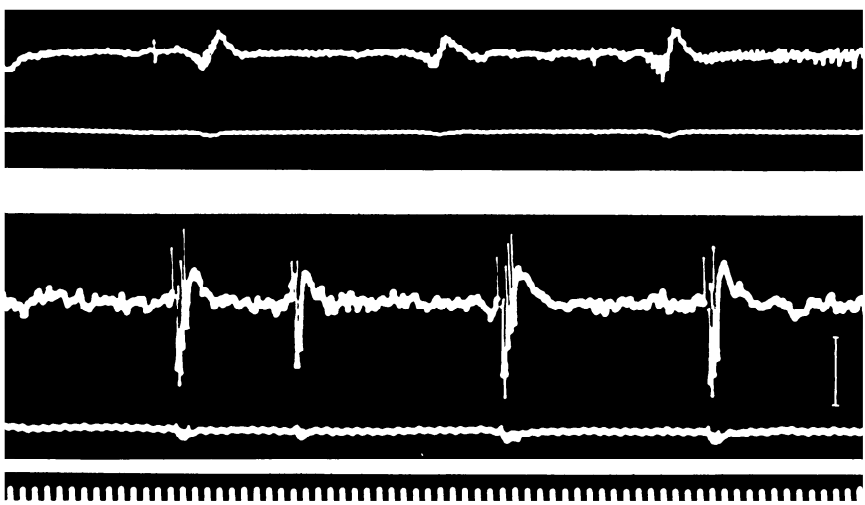

FIG. 4. Top: Extracellular recording of spontaneous repetitive impulse discharges in a "dendrite." Bottom: Spontaneous (1st, 3rd and 4th) and induced (2nd) responses of a "neurone soma." This induced response was photographed simultaneously at a high transit speed and record was presented in Figure 1C, bottom. Voltage calibration, 20 mV. for D.C. channel (lower beams) and 2 mV. for short time constant RC (upper) channel. Time markers, 10 msec. apart.

at the region under the recording electrode. The time course of these diphasic responses will be considered further in the Discussion.

B. *Spontaneous discharges recorded from individual elements in geniculate body*

By the term "spontaneous discharge" we mean a train of impulses which have no direct time relation to the electric shocks applied to the optic nerve. Under the conditions of our experiments, such spontaneous discharges were limited chiefly, if not exclusively, to the postsynaptic elements. Although the eyeball of our preparation was not deprived of its blood supply, it was

[7] Better evidence for the presence of extremely slow responses in dendrites was secured by intracellular recording of the responses of Mauthner cells of the catfish to antidromic stimulation. The lateral dendrite of this giant nerve cell is exceptionally thick and long. From inside this cell very prolonged action potentials were recorded (Tasaki *et al.*, *Jap. J. Physiol.*, 1954, *4*: 79–90).

unlikely that the retina preserved its normal function. This situation probably accounts for our failure to record spontaneous discharges in the presynaptic axons.

Many of the postsynaptic elements, from which action potentials were recorded without association of resting potentials, showed spontaneous discharges of impulses. Since the microelectrodes without doubt remained outside the cell membrane in these cases, they were not the discharges caused by injury. In some elements, the discharge was fairly regular (see Fig. 9, top) and in others it appeared to be completely irregular (Fig. 9, bottom). There were also elements which showed occasional bursts of impulses which were unrelated to the applied shocks. Other elements showed periodic bursts of

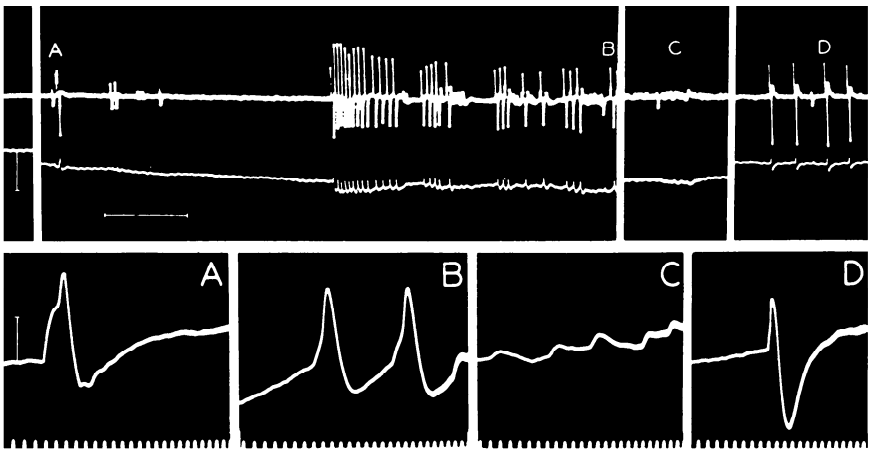

FIG. 5. Changes in shape of "neurone soma" responses associated with appearance and disappearance of the resting potential. Top: Continuous recording with short time constant RC amplifier. Middle: Continuous recording with D.C. amplifier. Bottom: Samples of high speed recording with long time constant RC amplifier. Voltage calibration, 20 mV. for D.C. channel and 2 mV. for condenser-coupled channels. Time markers, 100 msec. for continuous recording, and 1 msec. for high speed recording.

impulses, each burst consisting of 2–5 impulses following closely one after another and the bursts recurring at an interval of 0.1–0.2 sec. (Fig. 4, bottom). We did not make a serious attempt to investigate the frequency of these spontaneous discharges statistically.

The time courses of the spontaneously discharged impulses indicated that these responses recorded extracellularly from single elements in the geniculate body could be classified into the three different kinds described above, namely, responses of axon, cell bodies, and dendrite. The upper record in Fig. 4 shows typical dendritic responses. Those at the bottom of this figure and those in Fig. 5 and in the right column of Fig. 6 are the action potentials from neurone somata. Some of the elements from which spontaneous discharges were recorded did not show any response to the applied shocks. This does not necessarily mean that the lateral geniculate body con-

tains non-afferent neurones; our microelectrode could have been in the hippocampus instead of the geniculate body in such cases.

It was not possible for us to trace the origin of these "spontaneous" responses, whether they were induced by arrival of impulses from some other neurones or were derived from the periodic activity of the same neurone. There is good reason, however, to believe that most of these responses were not induced at the tip of the microelectrode. The large positive initial deflection in the record of Fig. 6, right, for instance, indicates the existence of a strong sink of electric current (hence the arrival of a full-sized impulse) in the

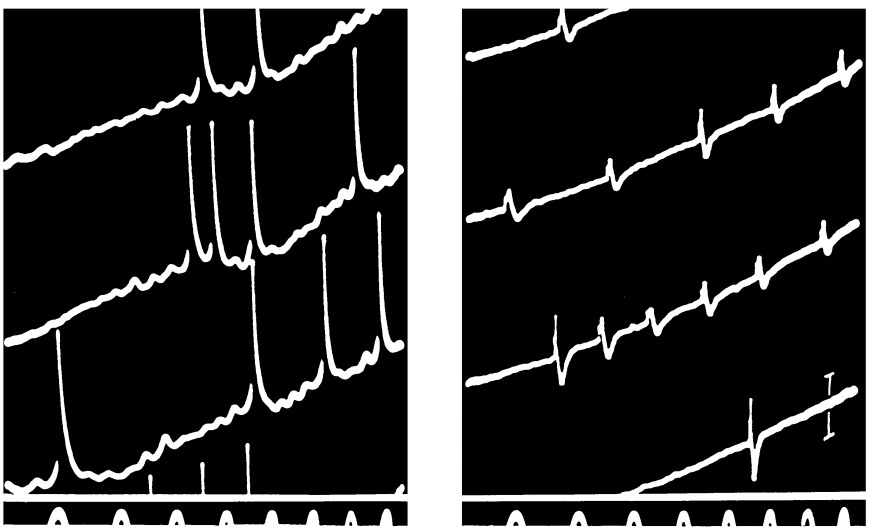

FIG. 6. Left: Intracellular recording of "cell body" responses (spontaneous) preceded by variable small responses. Right: Extracellular recording of spontaneous "neurone soma" responses. Voltage calibration, 2 mV.; time markers, 10 msec. apart.

neighborhood of, but not underneath, the tip of the recording microelectrode.

It is interesting to note that small and irregular responses of variable sizes were recorded from the vicinity of and also from inside the neurone soma (see Fig. 4, bottom). Probably they are of electric origin, similar to the subthreshold endplate potentials described by Fatt and Katz (12). The upper record in Fig. 4 shows that these subthreshold responses increase their size periodically, indicating a definite relationship between these responses and the repeating dendritic action potentials.

With an intracellular microelectrode, namely, when there was a large resting potential at the tip of the microelectrode, records were obtained which suggest release of full-sized action potentials by the variable subthreshold responses (Fig. 6, left). These small responses are seen to increase their amplitude gradually, and, from the tops of these large (a fraction of mV.) subthreshold responses, all-or-none neurone cell body action poten-

tials are seen to start. Similar records have been obtained by Brock *et al.* (6).

It is generally easy to distinguish these spontaneous discharges of impulses from discharges induced directly by injury of the neurone with the recording microelectrode. Injury discharges are initiated by the start of a D.C. potential at the tip of the recording electrode. At the beginning their rhythm is regular and their frequency is high (300–100 impulses per sec.), and, as time elapses, both the regularity and the frequency of the discharge (as well as the size of the responses) d cline fairly rapidly. It was our impression that injury discharges could be induced more readily with blunt than with sharp microelectrodes.

In Fig. 7 is given an example of a repetitive discharge, induced probably by injury in a slow element of which the action potential lasted almost 20 msec. Since, according to our interpretation of the previous records, dendrites are capable of developing such long action potentials, we conclude that they are intracellularly recorded dendritic responses. We shall discuss later the relationship between the shapes of the intra- and extracellularly recorded responses.

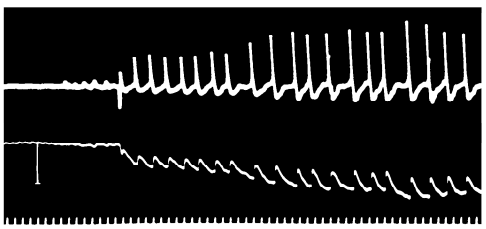

FIG. 7. Intracellular recording of "dendritic" responses with short time constant RC amplifier (top) and with D.C. amplifier (bottom). Voltage calibration, 20 mV. for D.C. channel and 2 mV. for other channel. Time markers, 10 msec. apart.

C. *Compound character of cell body responses*

In many of the records of the cell-body action potentials presented above, the complex nature of their temporal configuration is obvious. In Fig. 6, right, for example, a clear-cut notch is seen on the ascending limb of the action potential curve. The records in Fig. 5 show further that this notch becomes more prominent when the microelectrode penetrates the surface membrane of the neurone, suggesting that this notch is due to a jump of impulse in the vicinity of the recording electrode from one region of the neurone to another. At present it is difficult to decide experimentally what parts of the neurone are responsible for these notches. But, owing to the fact that synapses are found on both cell body and dendrites, a sudden spread of activity from the region of initial activation to adjacent regions would not be surprising.

Following the start of a resting potential recorded at the tip of the microelectrode, a simple spike potential sometimes starts to separate into two distinct components. Figure 8 is an example of such records. Immediately after the start of the resting potential, the spikes were large and were preceded, as in the records of Fig. 6, left, by small subthreshold responses. As time elapsed, these simple spikes began to segregate into two components, short and long. It is seen in this figure that the duration of the short component

coincides with that of the axon spikes (about 1 msec.) and that of the longer one to that of the cell body. This element showed no response to the shock applied to the optic nerve; we are not sure, therefore, whether reactions came from the geniculate body or from some neighboring region in the brain.

The point of interest in this type of record is that there is no definite time relation between these two different components of responses; in other words, these components appear independently of each other. Our interpretation of these records is as follows: in this experiment the microelectrode happened to be inserted into the spot at which both the axon and cell body responses could be picked up. Since the activity spreads, in the normal and lightly damaged neurone, readily and quickly from the axon to the cell body and

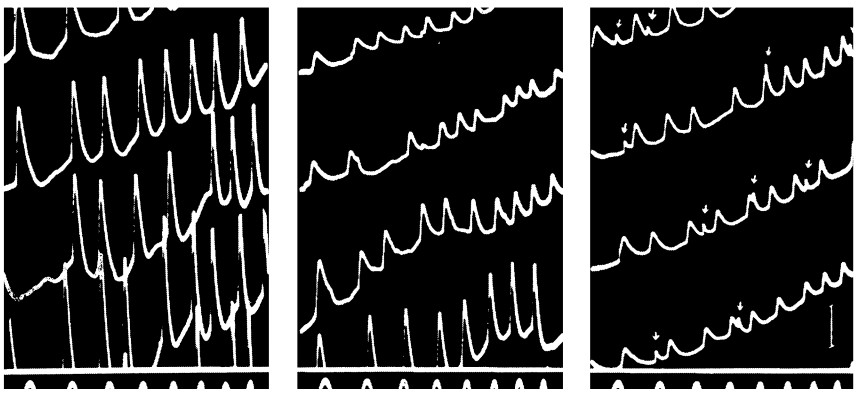

FIG. 8. Separation of "cell body" responses into "axonal" responses (indicated by arrows) and "pure cell body" responses during progressive deterioration of potentials following start of injury potential. Spontaneous discharge recorded with an intracellular microelectrode from region of lateral geniculate body. Voltage calibration, 2 mV. Time markers, 10 msec. apart.

also in the reverse direction, the short axon responses are always masked by the long cell body responses. Later on, when the local injury of the neurone by the recording electrode becomes severe enough to block spread of activity from the axon to the cell body and from the cell body to the axon, the two components recur independently of each other. On one occasion, we encountered an element which, at the beginning, produced a train of long, relatively simple, monophasic spikes and later a mixture of very long (15–20 msec. duration) and medium long (2–3 msec.) spikes. Although these chance observations could not be reproduced at will, these progressive changes are still strong evidence that the spike durations of the responses are considerably different in different parts of one and the same neurone. Our records taken from the lateral geniculate body tell us that the axon responses are approximately 1 (probably less than 1) msec. in duration, the cell body responses 1.5–3 msec., and the dendritic responses 15–20 msec.

D. *Cessation of spontaneous discharge following stimulation*

When a postsynaptic element in the lateral geniculate body was discharging impulses spontaneously, electric stimuli applied to the optic nerve often caused a temporary cessation of the discharge following each stimulus. In Fig. 9 are presented two examples of such an inhibitory effect of stimulus. In the upper record (A) of this figure, responses were taken from a postsynaptic axon. There was no resting potential at the tip of the microelectrode in

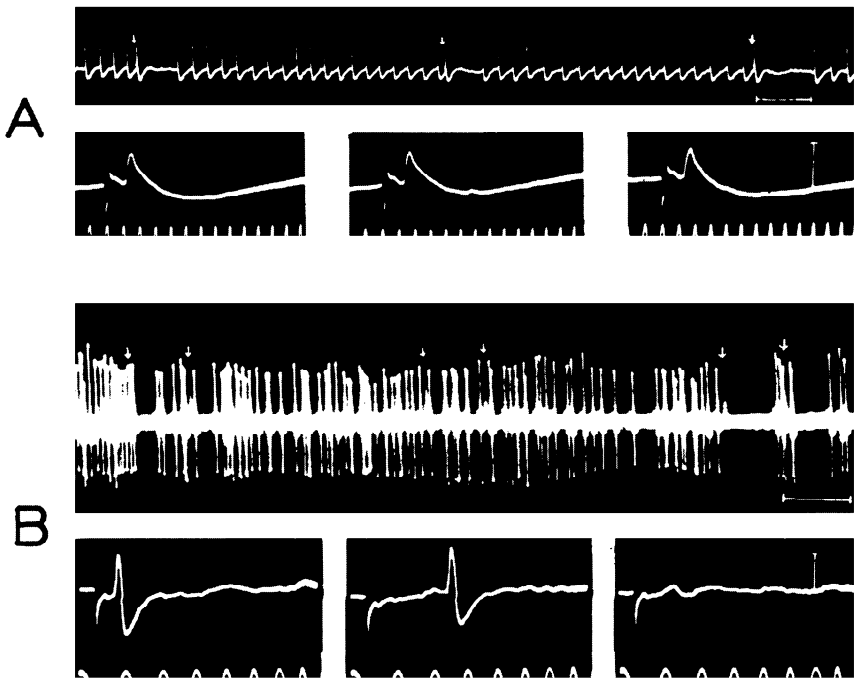

FIG. 9. Cessation of spontaneous impulse discharges in postsynaptic axon (A) and in "neurone soma" (B) caused by shocks applied to contralateral optic nerve. Recording microelectrodes were pushed into lateral geniculate body. Voltage calibration, 2 mV. Time markers, 100 msec. for continuous recording, and 1 msec. (A) and 10 msec. (B) for high speed recording.

this case, and the sharp rise and the gradual fall of the recorded action potential was characteristic of the responses of a medullated axon. To each shock applied to the optic nerve the axon responded with a spike which appeared at a constant latency of approximately 1.2 msec. Following this response to the shock, there was cessation of spontaneous discharge for a period of approximately 0.1 sec.

The lower record (B) in Fig. 9 shows a case in which stimulation of the optic nerve caused cessation of spontaneous discharge without inducing any direct response to the stimulus. Although the inhibitory effect of the shock was somewhat erratic in this unit, cessation of the discharge following each

shock did not seem to be accidental. In this and other cases, an impression was received that the inhibitory effect appears only after a certain latency and, as the consequence, the first impulse after the shock is liable to escape inhibition. This delayed start of the inhibitory effect was quite common in the discharge recorded from the cell body in the striate cortex.

PART II. STRIATE CORTEX

On a number of occasions, unsuccessful attempts were made to record unitary responses from the lateral gyrus of the cortex to stimulation of the optic nerve. The reason for our failure is not altogether clear. We may well attribute this to the fact that, with increasing distance from the site of stimulation, the effectiveness of the stimulus and the latency of the responses become more and more labile and the density of the responding cells is certainly

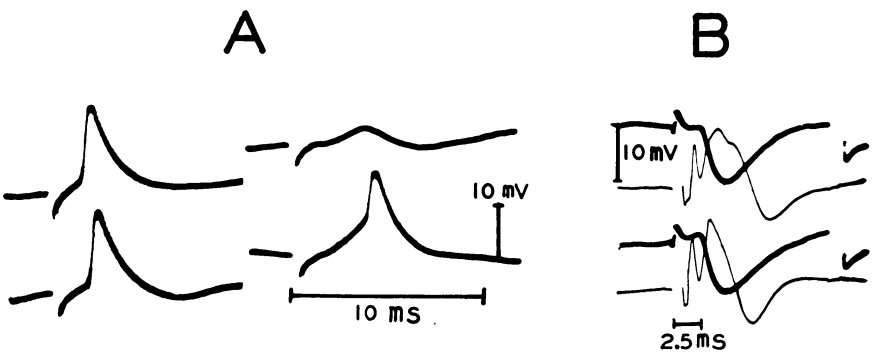

FIG. 10. A: Intracellular recording of responses of a "cell body" in striate cortex to electric shocks applied to radiation fibers. The two records on left were taken immediately after start of resting potential at tip of microelectrode; those on right, approximately 2 sec. later. B: "Negative swings" recorded with intracellular microelectrode from "cell body" in striate cortex. Stimuli were applied to radiation fibers. Thin line shows time course of whole cortex response.

lower in the cortex than in the lateral geniculate body. In repetitive stimulation of the optic nerve, the response of the whole cortex is known to vary from time to time and to be subnormal unless an interval as long as 5 sec. separates individual shocks (2, 18).

When shocks were applied directly to the radiation fibers, instead of to the optic nerve, through a pair of steel wire electrodes inserted towards the geniculate body (6–10 mm. from the surface of the cortex), it was found possible to record responses to the stimuli from several different elements in the cortex. These responses were found to come, as in the case of the responses from the geniculate body, under one of the four different categories, namely, into presynaptic and postsynaptic axon responses, cell body responses and dendritic responses.

Presynaptic or radiation-axon responses were characterized by their short latency (less than 0.5 msec.). They often appeared without being associated

with a resting potential. These responses were, like those in Fig. 1A, triangular in shape, with a duration of approximately 1 msec.

From the striate cortex, cell body responses were recorded both extra- and intracellularly. The latency of these cell body responses was longer than 1 msec. The shape and the size of the extracellularly recorded cell body responses did not seem to differ appreciably from those recorded from the lateral geniculate body.

The record in Fig. 10A, left, is an example of intracellular recording of the cell body responses. The long latency and the relatively long duration

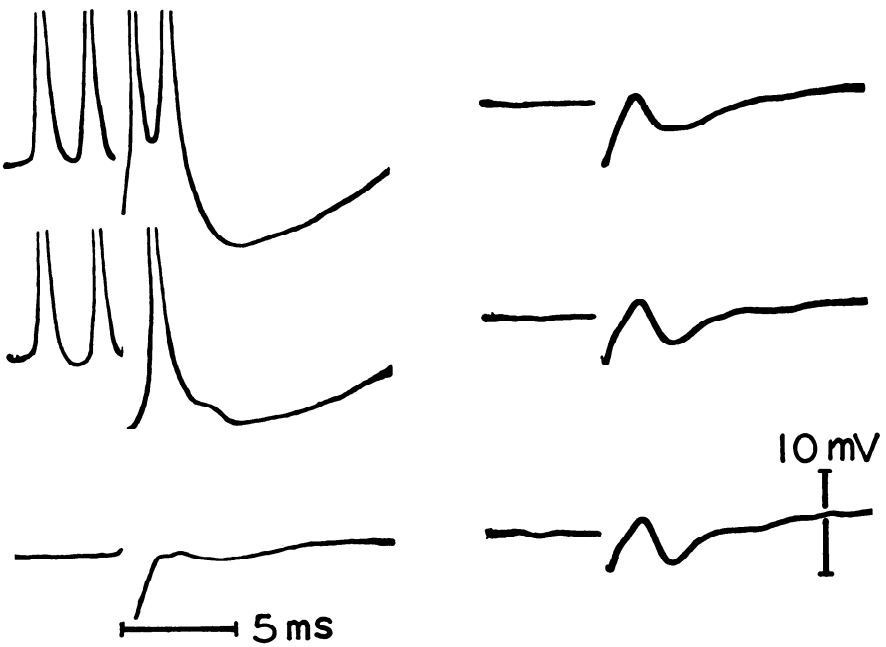

FIG. 11. Cessation of "injury discharges" by electric shocks applied to radiation fibers. Microelectrode was pushed into striate cortex. Left bottom: immediately before start of resting potential at tip of microelectrode. Left, middle and top: injury discharges stopped by shocks which initiated "negative swings." Right: records taken approximately 30 sec. later.

of the responses in this figure indicate that they are from a postsynaptic cell body. On several occasions extracellular recording from a cell body was followed by intracellular recording from the same element; such records indicate that the records of the type of Fig. 10A are actually taken from the body of a neurone. The two records on the right side of this figure show how such responses deteriorate following the puncture of the cell body with the microelectrode. At this critical stage, the latency of the large response varied considerably from one sweep to the next, and the full-sized responses seemed to start from the top of the small (but probably all-or-none) responses which is shown in the upper right-hand corner of Fig. 10A. We interpret this small

response as being the activity of the soma membrane near the synapses, which failed to activate the whole body of this neurone. The observed size of the cell body action potential was in general less than 30 mV.

The point of interest in the intracellular recording of cell body responses is that purely negative swings of potential of the neurone interior have often been elicited by the stimulus applied to the radiation fibers. Although the condition of the neurone in which a microelectrode has been inserted is certainly abnormal, this negative swing of the intracellular potential is indicative of the existence of some process other than the one known as depolarization (cf. Eccles, 11). The size of such negative swings amounted to 10–20 mV., and the resting potential at the time of recording varied from 20 to 60 mV. The negative swings were often preceded by positive spikes which were in some cases very large and in others quite small.

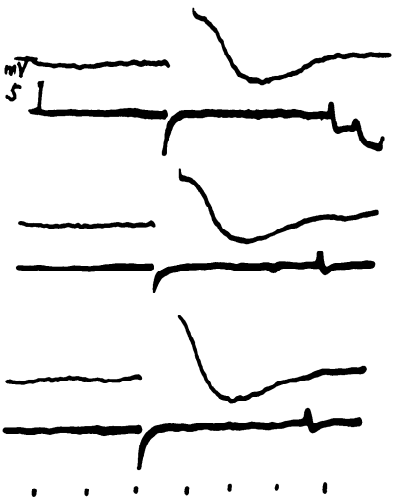

FIG. 12. Responses of axon in lateral gyrus to electric shocks applied to radiation. Time markers, 10 msec. apart; voltage calibration, 5 mV. No resting potential was observed at time of recording. This long latency response persisted for more than 1 min.

There is some evidence that this negative swing is connected in some way with the process of inhibition, as in the case of the similar phenomenon in the spinal cord (6, 11). It was frequently observed that a spontaneous discharge of impulses (recorded from inside a neurone) was completely suppressed by the start of a negative swing (Fig. 11, left). Since the latency of the negative swing was 2–2.5 msec., it sometimes happened that the first impulse after the shock remained unsuppressed (Fig. 11, left). In many cases, the first one or two spikes after the period of suppression showed a height greater than that of the spikes before the suppression. This fact suggests strongly that this negative swing is actually associated with an increase or restoration of the resting membrane potential.

We have examined the relationship between the latencies of the spikes of the whole cortex response (2, 10) and those of the unitary responses. It was our impression that the unitary responses tend to start at the peaks of the whole cortex responses. But we encountered many unitary responses which appeared near the valleys of the whole cortex responses.

In Fig. 12 are shown the responses with the longest latency we encountered. The absence of a resting potential and the shape of the responses indicated that they were derived from a medullated axon. At present we cannot account for this extremely long, but surprisingly constant, latency in terms of propagation of impulses in the central nervous system.

Discussion

Let us now consider the field of potential produced by the activity in a single neurone in the cortex. In Fig. 13 the circles represent the body of a neurone, and the spaces between the thin straight lines, the dendrites. The axon which, as we shall see later, makes practically no contribution to the electric field about an active neurone is omitted in the diagram. The shaded areas of the neurone are supposed to be the active, or the depolarized, regions (*i.e.*, the regions with low membrane resistance and low membrane voltage) and the unshaded parts are the resting region of the neurone. Due to this difference in the membrane voltages in different parts of the neurone, the active

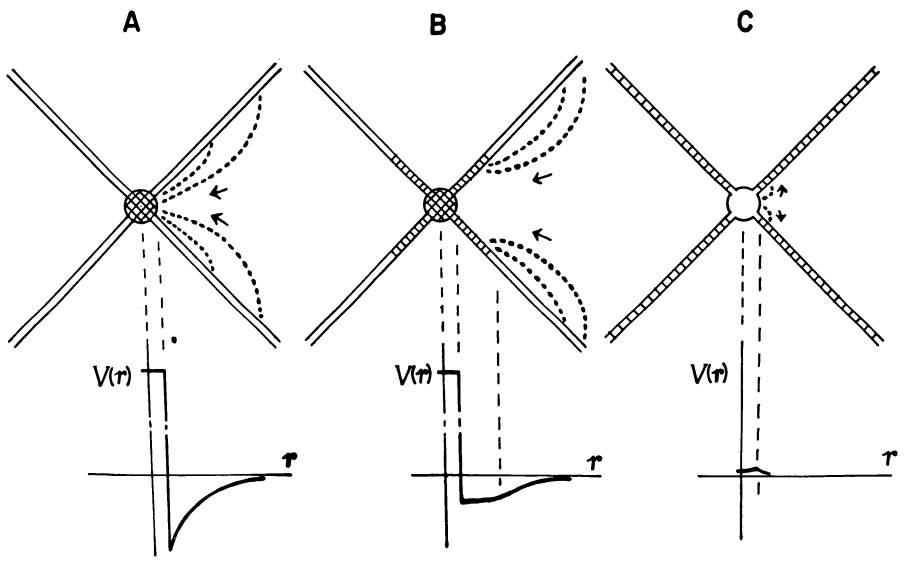

Fig. 13. Top: Diagrams showing lines of current flow around cell body (circles) with a number of dendrites (straight lines) extending from cell body in all directions. Shaded areas are assumed to be active. Bottom: Field of potential obtainable from assumption of spherical symmetry; $V(r)$ represents the magnitude of action potential recorded with a condenser-coupled amplifier at the position r. Further detail in text.

regions are traversed by inward-directed currents and the resting regions by outward-directed currents. In other words, the active regions behave as the sinks and the resting regions as the sources of electric currents in the volume conductor.

Diagram A in Fig. 13 represents the state in which the cell body of a neurone is active and its dendrites, which are radiating from the body in all directions, are still inactive. This is the case which Lorente de Nó (17) has already considered in his analysis of the antidromically induced responses of the hypoglossus nucleus and arrived at a correct qualitative result. Here we are interested in a semi-quantitative treatment of the problem. In this case, the currents flowing longitudinally through the dendrites are considered

to decay approximately exponentially as the distance from the cell body. Thus, the sources of currents are distributed continuously along the surface of the dendrites, while the sink is localized on the surface of the cell body. The potential of the fluid around the neurone soma is given by the IR drop caused by passage of the currents through the conducting fluid medium between the dendrites.

Let $V(r)$ be the potential at the distance r from (the center of) the cell body, subjected to the condition $V(\infty)=0$. We are now taking the approximation that the potential field about the cell body is spherically symmetrical. Then,

$$V(r) = \int_{\infty}^{r} \frac{ISe^{-r/l}}{4\pi r^2} dr,$$

where S: the average specific resistance of the mass of brain,
I: the total current flowing through the surface of the cell body,
l: the characteristic length (space constant) of the dendrite.
(Note that $Ie^{-r/l}(Sdr/4\pi r^2)$ is the IR drop across the two concentric spherical surfaces at the distance r and at $r+dr$). In the large medullated axons, l is of the order of 2 mm.; in the dendrite, along which a nerve impulse travels more slowly than in the axon, this value would be smaller than 2 mm. At present we are interested in the potentials in the vicinity of the cell body; in other words, we are dealing with the region where $r \ll l$, or $e^{-r/l} \doteqdot 1$. Then the above equation becomes

$$V(r) = \frac{-IS}{4\pi r}.$$

Our experimental results show that, near the surface of the cell body, namely, when $r \doteqdot 10^{-3}$ cm., $V(r)$ is of the order of -2×10^{-3} volt. Introducing these figures into the last expression, we have $IS \doteqdot 2\times10^{-5}$ volt-cm. Assuming S to be 2×10^{2} ohm-cm., we finally have $I \doteqdot 10^{-7}$ ampere. This current is about 50 times as strong as the action current from a large medullated axon.[8]

Diagram B in Fig. 13 represents the state in which the wave of activity is propagating along all the dendrites of the neurone. The lines of current flow are now distributed near the active-resting boundaries of the dendrites. In the resting region, the current should decay in accordance with the exponential law. In the active region, the current should decay very abruptly towards the cell body, because the characteristic length of the active dendrites should be far smaller than that of the resting ones. Under these circumstances, the radial component of the current in the medium is still directed toward the cell body. The potential of the fluid near the cell body, therefore, should still be negative to the potential at a distance. This potential distribution is shown in diagram B (bottom) of Fig. 13, together with the level of action potential inside the cell body which is still strongly positive to the potential outside.

[8] During his recent trip to Japan, one of us (I.T.) carried out, in collaboration with Mr. H. Uchiyama at Tokyo Medical and Dental University, a simple measurement of the average specific resistance of the grey matter of the cat's cortex. For frequencies between 2.5 and 6 kc. per sec., the impedance of the grey matter, measured with a silver plate electrode of 2–4 mm. diameter, was approximately 5 times as high as that of the mammalian ringer. Since this high impedance is due to the presence of many neurones in the cortex, the average specific resistance S of the medium about a soma should be smaller than this. In our argument here we have assumed S to be about 3 times as large as the resistance of mammalian ringer.

In a still later stage (Fig. 13C), the activity reaches the peripheral end of the dendrites and the cell body recovers from the previous activity. The distribution of currents along the dendrites is now determined simply by the difference in the rate of recovery in different parts of the neurone. If we assume the conduction rate along the dendrite to be about 1 m./sec. (8, 9), then the time required for an impulse to travel all along these relatively short dendrites of the neurones in the geniculate body (20) is negligible in view of the long duration of a dendritic action potential. The currents flowing along the dendrites at this moment would therefore be very small. Through the surface of the cell body, however, there should be a strong outward-directed current which would make the potential of the fluid in the immediate vicinity of the cell body slightly positive to the potential at a distance.

Thus, we have arrived at a satisfactory interpretation of the cell body action potentials presented Fig. 3A. The initial positive phase of these responses can be interpreted as being due to the local current flowing between the synaptic region and the still inactive soma surface. Next, spread of activity over the whole surface of the cell body and subsequent propagation of the impulse along the dendrites cause the large negative potential in the vicinity of the cell body. From this statement it is clear that our externally recorded "cell-body responses" derive from activity of the whole neurone soma, namely, both the cell body and the dendrites. In a neurone without any dendrite (*e.g.*, neurones in the spinal ganglia, 22), the cell-body response should be very different from those presented in Results.

When the tip of the microelectrode is lying directly on, or very close to, the surface of a dendrite, the observed potential should be quite different from what is shown by the curve in Fig. 13, which is derived from the consideration of symmetry. We now have to consider the strong potential field near the source or the sink of current, instead of the average field about the soma. Thus, the outward flow of current ahead of the active region of the dendrite should make the microelectrode positive to the remote indifferent electrode. As the impulse travels at a slow speed across the site of recording, the potential should reverse because of the reversal of the membrane current. This situation seems to account for the time course of the dendritic potential presented in Fig. 1D.

It seems to us that there have been some controversial arguments concerning the potential field produced by a neurone in the central nervous system (see 1, 13, 17, 21, etc.). We believe that some of the arguments arise from the confusion of the following three different quantities, namely, (i) the electric charge across the Bernstein membrane which is supposed to determine the membrane voltage, (ii) the sources and sinks of electric current in the volume conductor distributed on the surface of the neurone, and (iii) the potential at the point in question relative to a certain indifferent point. The frequent use of the same symbols "+" and "−" to express the signs of these three different quantities is certainly misleading.

We shall now discuss some of the implications of our experimental findings. In the first place, the fact that the extracellularly recorded action potentials of individual neurones are smaller than about 2 mV. tells us that the direct electric interaction between two neighboring neurones should be physiologically insignificant. It is most unlikely that a voltage pulse of less than 2 mV. applied from outside could bring about an appreciable stimulating or electrotonic effect upon a neurone.

The response of the whole cortex recorded with a gross electrode is far smaller than the action potential of a single neurone recorded extracellularly with a microelectrode. The external somatic or dendritic potentials amount to a few millivolts, while the whole cortex responses taken from the surface

of the brain are generally a few tenths of a millivolt. This fact indicates that the relatively strong field of potential, recordable only with a microelectrode, is limited to the immediate vicinity of the cell body of each neurone and that it has an approximately spherical symmetry. The potential recordable with a gross electrode is the sum of small potentials produced by slight asymmetry in the potential fields about individual neurones.

Next, the finding that the action potentials produced by dendrites (extracellular recording) are slow in time course and long in duration has an important bearing on the problem of production of slow potential waves, spontaneous or induced, which are recordable from the whole cortex. When small potentials produced by individual elements in the cortex are superposed to form the whole cortex response, it is unlikely that the contribution from the sharp spike potentials of axons and cell body to the summated potential wave is greater than that from the slow, monophasic dendritic potentials. Synaptic potentials are also short in duration and small in size even when they are recorded from inside the cell body. We therefore do not believe that they can make a large contribution to the production of slow brain waves. *We propose, therefore, a hypothesis that brain waves, such as Berger rhythms, are the summation of rhythmical dendritic potentials,* of which two examples are shown in Fig. 4 (see the D.C. channels). This statement is consistent with the conclusion reached by Bishop and Clare (3) that the units of response in spontaneous activity are waves of the order of 15 msec. duration, which seem to us to be dendritic potentials. The slow potentials recorded by Renshaw *et al.* (21) from the hippocampus seem to consist also of more or less synchronized volleys of impulses in the dendrites.

The finding that there are, within one and the same neurone, elements with short and with long spike durations suggests to us a simple explanation of the mechanism of multiple responses in postsynaptic elements, such as those shown in Figs. 1C and 4 (bottom). We noticed that the duration of such individual bursts of impulses does not exceed the duration of the internally recorded dendritic potential, namely, about 20 msec. It seems to us very probable that these individual bursts are caused by the stimulating effect of the local current flowing between the dendrites and the cell body. In the case of a neurone shown in Fig. 13C there should be a strong outward-directed current through the surface membrane of the cell body. And, if the process of accommodation in this membrane is slow enough, the cell body should respond to this strong stimulating current with multiple responses.

Summary

1. With intra- and extracellular micropipette electrodes, responses of single units in the lateral geniculate body and the striate cortex were recorded. The recorded responses were classified, according to their latencies and their shapes, into (i) presynaptic axonal responses, (ii) postsynaptic axonal responses, (iii) cell body responses and (iv) dendritic responses.

2. It was concluded that the duration of the axonal response was ap-

proximately 1 msec. or slightly less, that of the cell body response 1.5–3 msec. and that of the dendritic potential 15–20 msec. The intracellularly recorded responses were generally less than about 50 mV. Extracellularly recorded cell body and dendritic responses were less than 3 mV.

3. Monophasic axonal spikes were recorded with the tip of a microelectrode apparently in the axis cylinder or in the innermost layer of the myelin sheath. Notches near the peak of an axonal response, or "nodal signs," were observed in the action potential records taken from the radiation fibers.

4. Spontaneous discharge of impulses in some element in the lateral geniculate body was depressed by stimulation of the optic nerve. Spontaneous and injury discharges in the soma of a neurone in the striate cortex were often depressed by stimulation of the radiation fibers. This process of depression was associated with "negative swings" of the inside potential, or a temporal increase in the resting membrane potential.

5. Insertion of a glass pipette electrode of about 0.3 μ diameter into a nerve cell was found to bring about a strong injurious effect upon the cell.

6. The field of potential around the soma of a neurone, the process of repetitive discharge of impulses, and the possible origin of brain wave are discussed.

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