

SPREAD OF DIRECTLY EVOKED RESPONSES IN THE CAT'S CEREBRAL CORTEX

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ABSTRACT

A study has been made of the electrical responses to direct stimulation of the exposed cerebral cortex of cats that had been immobilized with neuromuscular blocking drugs, and whose muscle and skin wounds had been locally anesthetized. The characteristics and spread of the first and second surface-negative responses are described. It was found that the first surface-negative response to weak stimuli decays linearly to zero at 3 to 6 mm. from the point of stimulation. Intermediate stimuli cause farther and non-linear spread: responses are re-initiated, or reinforced, at 6 to 10 mm.; and supramaximal stimulation produces reinforcement both at 5 and at 10 mm. The conduction velocity of these responses is uniform for linear spread (0.7 to 2.0 m./sec.), but reinforced responses occur 1 to 3 msec. earlier than would be expected for simple conduction. The phenomenon of re-initiation, or reinforcement, depends upon the excitatory state of the brain; circulation and previous stimulation are important factors. Connections outside the gyrus matter only in so far as they provide other sources of general excitation. It is concluded that two types of transmission: slow and fast, can lead to generation of similar surface-negative responses. The suggestion is made that the slowly conducted surface-negative potentials are due to direct or to synaptic excitation of pyramidal cells; while the responses with shortened latency are initiated synaptically on other pyramidal cells after fast conduction at about 10 m./sec. in tangential fibres.

INTRODUCTION

Electrical stimulation of the surface of the cat's cerebral cortex elicits responses that can be detected electrically with recording electrodes placed upon the cortical surface. Weak shocks cause the surface briefly to become negative with respect to ground potential (the surface-negative response), while stronger stimuli produce a later surface-positive response as well. Adrian (1936) showed that the former is generated by elements near the surface, and the latter by deep-lying units. Burns and Grafstein (1952), using isolated slabs of suprasylvian gyrus, demonstrated the two responses to originate from different cells, which they named A and B respectively. Their type A cells (Fig. 9 A) resemble pyramidal cells with long axons leaving the grey matter while type B cells possess only short intragriseal axons.

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Burns and Grafstein (1952) suggested that the surface-negative potential reflects a conducted response that spreads up to 10 mm. along superficial tangential processes of type A cells (see Fig. 9 A). Chang (1951 *a*) adopted a similar view by proposing that the surface-negative potential is propagated up to 6 mm. along apical dendrites of pyramidal cells, with possible involvement of interneurons. However, it is difficult to reconcile these views with measurements by Sholl (1955) that limit the extent of arborization of apical dendrites to about 200 μ . Spread of the surface-negative response could occur in recurrent collaterals that are known to extend for about 2 mm. (Lorente de N6, 1922); or in cortico-cortical axons as has been suggested for the rabbit by Ochs (1956). Eccles (1951) first suggested, and Purpura and Grundfest (1956) have elaborated, the view that the surface-negative response does not represent action potentials of tangential conductors but that instead it reflects synaptic potentials generated probably on apical dendrites of successive pyramidal cells. All authors describe constant conduction velocities of 1 to 2 m./sec. and stress linear decreases of amplitude from the site of stimulation to zero in 5 to 10 mm.

The spread of the surface-negative response is re-examined in the present work, and an attempt is made to define the simplest arrangement of cells and their relevant activities that could produce the observed electrical potentials.

Methods

Cats were anesthetized with ether, and tracheal and venous cannulae fitted. In later experiments initial induction was by means of ethyl-chloride. The scalp was divided in the middle, the temporal muscles were removed, and all injured or exposed skin and muscles were infiltrated with a long lasting local anesthetic: a 1 per cent solution of procaine in propylene glycol (efocaine, E. Fougere & Co., New York). The ether was discontinued after about 30 minutes, and the animal was immobilized by gradual intravenous injection of succinylcholine (anectine, Burroughs-Wellcome & Co., Tuckahoe, New York) or of gallamine triethiodide (flaxedil, American Cyanamid Co., Danbury, Connecticut), after artificial respiration had been started. The left cerebral cortex was then exposed by removal of overlying bone and of dura. The head was held in a modified Palmer holder in a frame that has already been described (Brooks, Winsbury, and Jernberg, 1959). The edges of the scalp were sutured to a metal ring to form a pool for mineral oil with which to cover the brain. Before the pool is filled, sponges should be packed temporarily against the skin injected with local anesthetic to absorb anesthetic leakage that might otherwise reach the exposed brain. Anal temperatures were kept between 36° and 38°C. and oil temperatures between 36° and 37°C. All experiments were carried out upon the suprasylvian gyrus. In some experiments a channel into the ventricle was made by suction at the posterior end of the suprasylvian gyrus, or in the ectosylvian gyrus. The channel served as a drain to let out excess cerebrospinal fluid and prevented swelling of the brain. Bleeding was controlled by electrocautery. Radial cuts and isolated slabs were made by the method described by Burns and Grafstein (1952). Records were never taken until at least 2 hours, and usually 3, had elapsed after discontinuation of the ether anesthesia.

The electrodes were made of thin platinum wires (0.004 inch diameter) with ends that were fused into smooth balls (about 0.01 inch diameter). The stimulating leads were 0.5 to 1.0 mm. apart. Conditions of stimulating and recording are indicated in the text and figures. Stimuli were usually of 0.15 msec. duration and were given at rates of 0.3 to 1.0 per sec. Records were taken relative to ground with a capacity-coupled amplifying system (time constant 1 sec.), whose frequency response was flat from 10 to 2000 c.p.s., with a 5 per cent loss up to 10,000 c.p.s. Amplified potentials were displayed on an oscilloscope (tektronix 532) and photographed. All pictures of electrical potentials show negativity to ground as upward deflections. The space constant of the recording system was 1.5 mm. It was determined by recording the

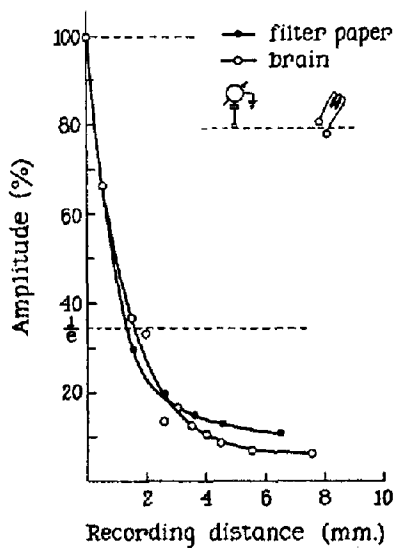


FIG. 1. Graphs of amplitude of stimulus artefact (ordinate) against recording distance from stimulating leads (abscissa). Space constant marked by broken line.

amplitude of the stimulus artefact at various distances from the stimulating leads both on brain and on wet filter paper. The relations between amplitude and distance as tested on moist filter paper and on the brain are shown in Fig. 1. The usual procedure during the experiments was to keep one recording electrode at 2 mm. from the point of stimulation, and to move another as required. Points of stimulation and recording were marked on drawings of the surface of the brain. Experimental arrangements are shown diagrammatically in the illustrations, as are the measured parameters.

RESULTS

Appearance of Potentials

When a weak electrical shock is applied to the surface of the suprasylvian gyrus a surface-negative response is produced, the amplitude of which attains

maximum at 3 to 8 \times threshold stimulating voltage (mean of 37 trials in 11 experiments = 6 \times threshold). Large surface-negative responses are usually preceded by small positive "pre"-potentials. Shocks of about 2 \times threshold strength for the surface-negative response elicit also a later surface-positive response; *i.e.*, the threshold of the surface-positive response occurs when the surface-negative response is about 20 per cent maximal. At about 50 per cent maximal amplitude of the first surface-negative response a second surface-negative response appears superimposed on the falling edge of the first response and on the trough of the surface-positive one. Thirty-seven trials in 11 experiments gave thresholds of the second response, expressed as above, from 20 to

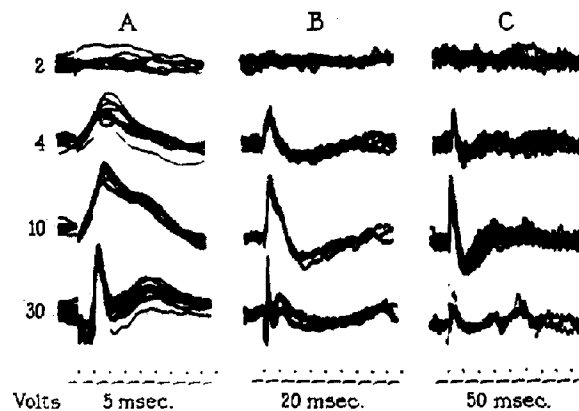


FIG. 2. Responses recorded 2 mm. from point of stimulation. Each record contains 10 superimposed traces. Stimulus strengths given at left margin apply to all records in that row. The three columns (A to C) show equivalent responses at progressively slower sweep speeds, as indicated by time markers. For details see text.

100 per cent with a mean of 60 per cent. In addition, sometimes a third surface-negative response was seen. Stimuli yielding more than 10 to 20 per cent maximal first surface-negative responses initiate a wave, or series of waves, occurring with a delay of about 100 msec., that resemble those previously identified as originating from the thalamus by Dempsey and Morison (1942). These waves are better synchronized with stronger shocks and are most easily visible with slow sweep speeds.

The traces in Fig. 2 were recorded 2 mm. from the point of stimulation. They are reproduced at 3 sweep speeds to display the two surface-negative, the surface-positive, and the thalamic responses to best advantage. The growth of the surface-negative responses with increasing stimulus strength is best examined in column A. At 30 volts the positive "pre"-potential preceding the negative response can also be seen. The surface-positive response first appears at

4 volts, (column B), with the second surface-negative response superimposed upon it plainly at 10 volts. The "thalamic" waves are best seen in column C.

The amplitudes of the first surface-negative responses of Fig. 2 are plotted as a "stimulus-response" curve in Fig. 3 A. The inset diagram indicates the relevant parameter of measurement: height from base line to peak potential. Thresholds of the second surface-negative responses (T_2) and of the "thalamic" waves (T_1) are marked upon the graphs. Responses to supramaximal shocks were found to be depressed within about 2 mm. of the stimulated point, but

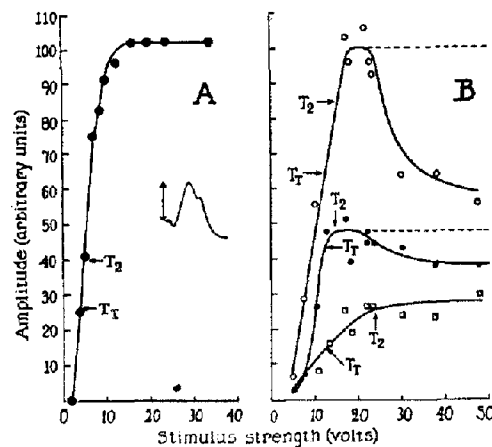


FIG. 3. A: Stimulus-response curves from the same experiment as for Fig. 2. Ordinates: amplitudes of first surface-negative responses in arbitrary units recorded at 2 mm. Abscissae: stimulus strength in volts. T_2 : threshold of second surface-negative response. T_1 : threshold of thalamic waves.

B: Stimulus-response curves from another experiment. Recording distances: 1.4 mm., (\circ); 2.5 mm. (\bullet); 4.1 mm. (\square). For detail see text.

sometimes this depression extended further. An example is provided in Fig. 3 B, in which are shown 3 stimulus response curves from one experiment, constructed from simultaneous records taken at 1.4 (\circ), 2.5 (\bullet), and 4.1 (\square) mm. respectively: the depression was noticeable at 2.5, but not at 4.1 mm. This depression does not depend on polarity of stimulating leads, and it is inconstant from one trial to another. It probably represents algebraic summation of superficial (surface-negative) activity and of deep activity that is surface-positive, but it is also possible that some local inhibitory process is engaged by strong shocks. At any rate, the excitable elements are not driven maximally by "maximal" single stimuli, because drugs such as strychnine greatly increase the amplitude of previously "maximal" surface-negative responses (Chang, 1951 *b*).

If the cerebral circulation was functioning well, and if there was no swelling

of the brain or other adverse condition, relatively low thresholds were obtained for the first and second surface-negative responses, and the stimulus-response curves had steep slopes. The threshold of the second response in relation to the maximum of the first was found to be most sensitive to these factors.

Spread of the First Surface-Negative Response

To make different experiments comparable, response amplitudes are reported in this paper by expressing them as per cent of the amplitudes at 2 mm. from the stimulated point. The distance of 2 mm. was chosen for reference because potentials may be measured there relatively free of the depression near the stimulating leads. Graphs depicting spread, called "distance-response" graphs, can only be compared when adjustments for effective stimulus strength have been made. Therefore stimulus strengths are not reported in units of current, but instead their effectiveness is measured by the surface-negative responses produced by them. The practise in these experiments has been to test the excitability of the brain at least every 30 minutes by recording responses to stimuli of different strengths at the reference distance of 2 mm. In the resultant stimulus-response curves maximal amplitudes are called 100 per cent, and stimulus strengths are then expressed as per cent of the maximal response that can be recorded at 2 mm. This method permits adjustment of stimulus strengths during prolonged experiments to obtain equivalent stimuli besides providing a basis for comparison of different experiments.

Stimulation with Weak Shocks.—In accordance with descriptions by previous authors, linear decreases of amplitude with distance were found when weak shocks were used. The distance-response graphs in Fig. 4 A represent the spread found with four different stimulus strengths in one experiment. The effect of weak shocks that produced only 10 per cent of maximal responses at 2 mm. (○) declined linearly to zero at 5 mm., while 20 per cent responses (●) reached zero at 7 mm., and reappeared at 9 mm. This pattern of re-initiation was still present with 50 per cent responses (□), but the initial decline ceased to be linear. Maximal responses (△) showed two points of reinforcement: at 5 and at 10 mm. The latencies of these responses are plotted with the same symbols in Fig. 4 B. It is apparent that weak shocks generated processes that travelled at velocities of 0.7 to 0.8 m./sec., but that the responses at the points of reinforcement occurred earlier than would be expected on the basis of constant conduction velocities. Although the dependence of peak latencies on rate of rise of the potentials is recognized, it was considered a better parameter than latency of onset, because the latter is often hard to distinguish owing to the presence of positive "pre"-potentials (see Fig. 2). Statements about extent of spread need to be qualified by reference to Fig. 1, which shows that a stationary (artefact) potential is still recorded at 2 mm. distance from its source as one-third of its amplitude at that source. Contribution to the surface-negative response from distant sources cannot be large, however, because latencies in-

crease regularly with distance. At any rate, reinforcement cannot be accounted for by any such artefact.

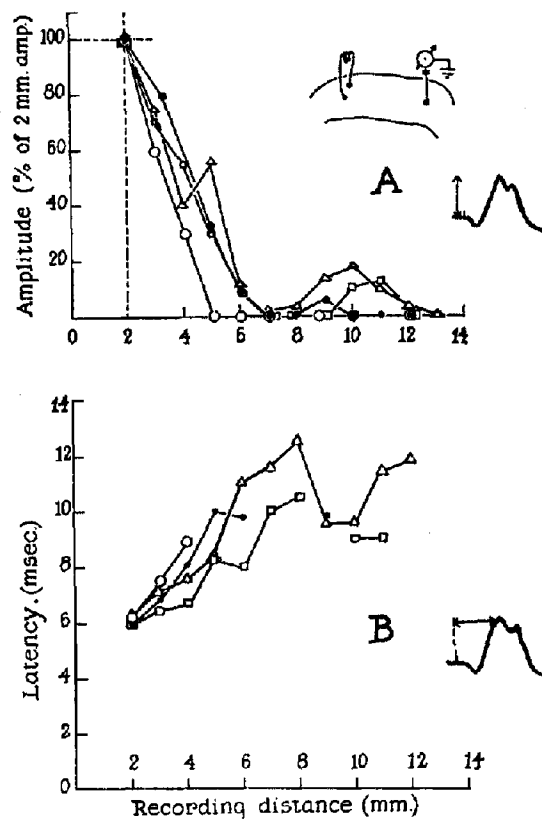


FIG. 4. A: Distance-response graphs. Ordinates: amplitudes of first surface-negative responses expressed as per cent of the amplitudes recorded at 2 mm. from the stimulated point. Abscissa: recording distances anterior to point of stimulation, in mm. 100 per cent amplitude and 2 mm. distance are marked by dotted lines. (○), 10 per cent response; (●), 20 per cent response; (□), 50 per cent response; (△), 100 per cent response; for detail see text.

B: Plots of peak-latencies (ordinates: msec.) of first surface-negative responses against recording distance (abscissa: mm.). Symbols as in A.

Stimulus strength is only one of many parameters that determine the pattern of spread of the first surface-negative response. Repeated stimuli before tests with weak shocks can transform a linear decline into a pattern with reinitiation or, if the original response did not decline to zero, with reinforcement. Thus it was noticed in one experiment when trials were carried out in 15 minutes, with a pause of 30 minutes between, that responses, which were about

30 per cent maximal and decayed linearly at first, were reinforced 5 mm. from the point of stimulation only after two trials. The effect persisted for about 30 minutes, thereafter linear decline of amplitude with distance was again observed.

Stimulation with Strong Shocks.—As has already been mentioned in the last section, strong stimulation of the cortical surface yields non-linear spatial decline of the first surface-negative response. The re-initiation, shown in Fig. 4 A (●) at 9 mm., sometimes occurs as close as 6 mm. to the site of stimulation. However, in all cases further increase of stimulus strength caused the single reinforcement to be displaced by two such elevations of amplitude: at 5 and 10 mm. indicated by (△) in Fig. 4 A. Usually the responses at both points of reinforcement occurred with shortened latencies (Fig. 4 B). The maximal pattern (△) shown in Fig. 4 was reached with shocks of just maximal strength. Yet, the presence of maximal first surface-negative responses does not guarantee their distribution with the maximal pattern: in several experiments shocks of 2 to 3 times maximal strength had to be employed to produce this pattern. Whatever the other factors are, they are highly sensitive to the state of the capillary circulation and also as to whether the brain tends to swell or not. Deterioration of the cerebral circulation can simplify distributions reinforced at 5 and at 10 mm. to the type usually found for intermediate strengths with brains in good condition: with only one reinforcement at an intermediate point.

Conversely, in a few cases, even submaximal stimulation produced spread with two reinforcements, of which an example is given in Fig. 5. Mean distributions of amplitudes were the same for maximal responses (Fig. 5 A) and for those ranging from 15 to 65 per cent of maximum (Figs. 5 B and 5 C), regardless of whether direction of spread was posterior (●) or anterior (○, □, △, ▽, ×) (see inset diagram of Fig. 5). In this experiment four recording stations were kept on the brain simultaneously; their positions were varied during the experiment as indicated by the six symbols, and curves were constructed by considering all trials together. Some stimulus-response curves measured between the distance-response runs marked (○) and (△) have already been presented in Fig. 3 B. The stimuli used for the trials of Fig. 5 A were 1 to 1.3 × maximal, except the run marked × when stimuli 2 × maximal were used. Amplitudes are expressed as per cent of the (calculated) maxima at 2 mm. The amplitudes shown in graphs 5 B and 5 C were elicited by submaximal stimuli of strengths near the threshold of the second surface-negative response, after previous strong stimulation had been applied. Responses were 15 to 30 per cent maximal, except those marked × and ○ that were 65 and 50 per cent maximal respectively. The tests were run continuously: the ones illustrated were obtained at intervals of about 1 hour. The amplitudes of the submaximal responses are displayed both as per cent of the maximal response obtained at 2 mm. with the supramaximal stimulus strengths used (graph 5 B), and as

per cent of the biggest responses to submaximal stimuli at 2 mm. (graph 5 C). It is apparent that the decline of amplitudes of the potentials is approximately linear for 3 to 4 mm., and that they are reinforced both at 5 and at 10 mm.

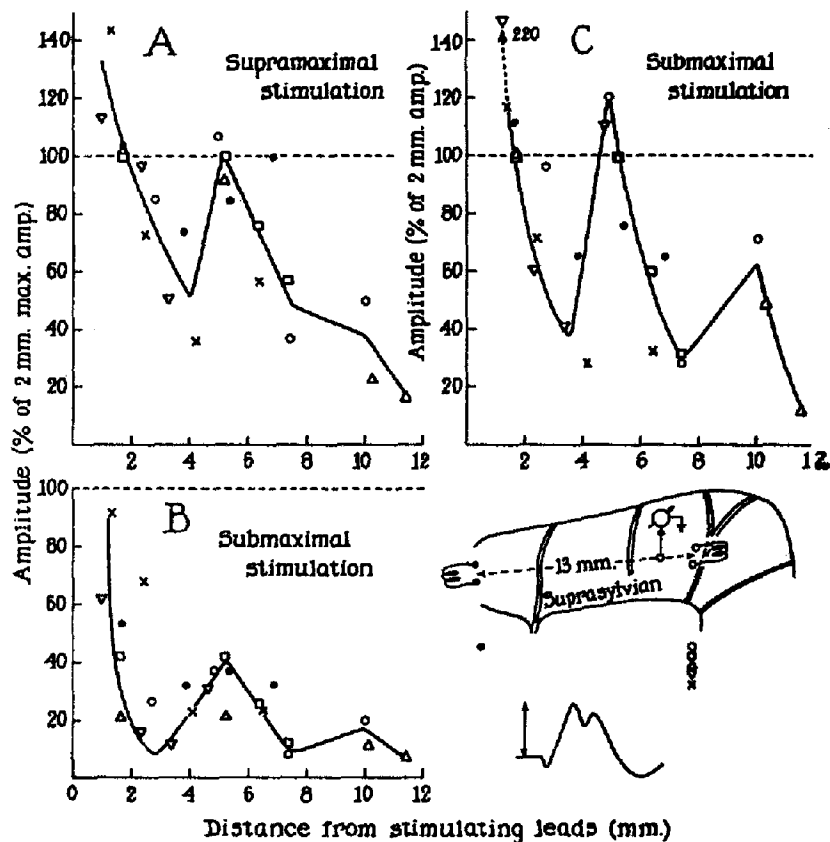


FIG. 5. Graphs of amplitude of first surface-negative response against recording distance (abscissae). Same trials and symbols as in Fig. 3 B, diagram shows arrangement. Ordinates: A and B: amplitude as per cent of maximum obtained at 2 mm. with *supramaximal* stimulus. C: amplitude as per cent of 2 mm. response with *submaximal* stimulus.

The positions of the points of reinforcement do not depend upon stimulus strength, although the extent of the two reinforcements is roughly related to the strength of the stimulus (Figs. 5 A and 5 B). Yet, the same *percentage* change occurred at both stimulus strengths (Figs. 5 A and 5 C) indicating that the effect of weak and of strong stimuli is mediated by similar systems. Both with maximal and submaximal stimuli, peak latencies of reinforced responses

occurred 1 msec. earlier than would be predicted on the basis of linear conduction velocities.

In all experiments with maximal (or near maximal) responses, increased amplitudes of the first surface-negative response occurred at 5 and at 10 mm. with decreased latencies. In Fig. 6 A the amplitudes of these maximal responses

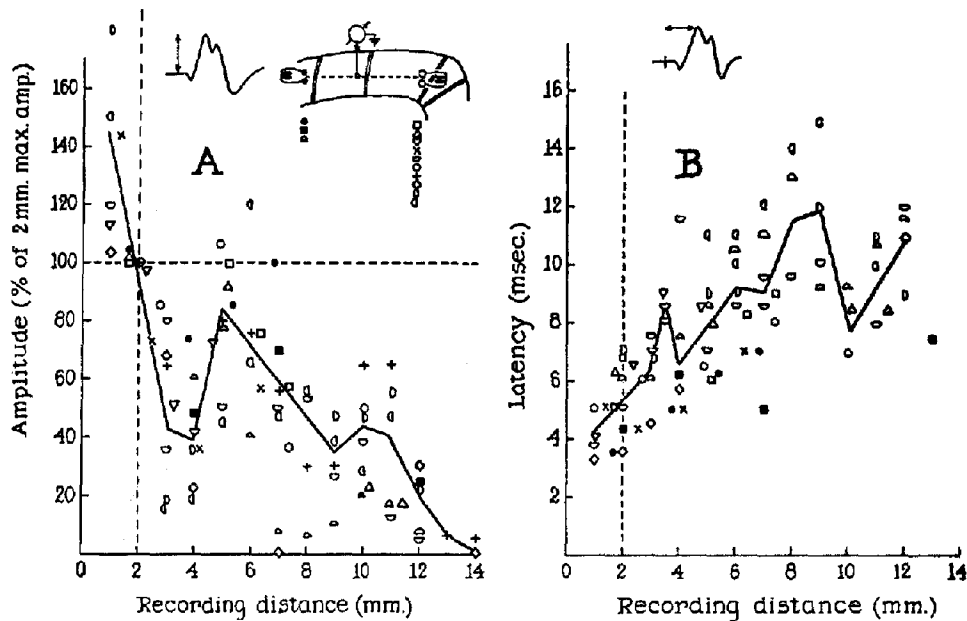


FIG. 6. A: Composite distance-response curve of maximal first surface-negative responses from six experiments. Abscissa: recording distance (mm.). Ordinate: amplitude of first surface-negative response as per cent of maximum response at 2 mm. from stimulating leads.

B: Composite graphs of latencies (ordinate) of first surface-negative response against recording distance (abscissa) from same 6 experiments as in A. Ordinate: latency in msec. Same symbols as in A. For details see text.

are plotted against distance, while the latencies are graphed in Fig. 6 B. The trials from the experiment illustrated in Fig. 5 (\circ , \bullet , \square , \triangle , ∇ , \times) should be regarded as one set because the points of recording overlapped in position from one test to another. The decreases of latency of the first surface-negative response at points of reinforcement imply the existence of slow and fast processes. It follows from the results with weak stimuli which do not produce reinforcement, that the slow process predominates near the point of stimulation, while more distal responses are produced in greater measure by the fast process. The interpretation of these components will be deferred until Discussion.

Spread of the Second Surface-Negative Response

Fig. 7 A shows strength-response curves of the second surface-negative response, taken from the same experiment as Figs. 3 B and 5. Comparison with Fig. 3 B shows that the slopes of the graphs for the second response are steeper than those of the first. The amplitude is a little difficult to assess because the potential usually is superimposed on the falling phase of the first surface-

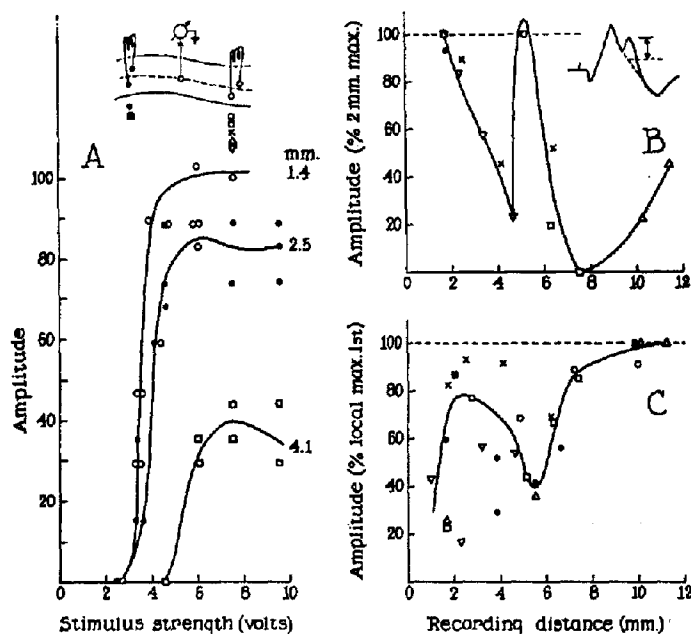


FIG. 7. A: Stimulus-response graphs for second surface-negative response, same experiment and symbols as in Figs. 3 B and 5. B: Distance-response graph of second surface-negative response for that experiment. C: Distance-threshold graph of second response for the same experiment. Abscissa: recording distance; ordinate: per cent of first maximum response at that distance.

negative potential and upon the trough of the surface-positive potential as shown in Fig. 2 and as indicated in the inset diagram of Fig. 7 B. There is a discontinuity in the distance-response graphs (Fig. 7 B) at 5 mm. as there is with the first surface-negative response. The amplitude of the first surface-negative response reached at threshold of the second response declines sharply at the 5 mm. region, which means that the second response is generated at nearly constant amplitudes of the first (see Fig. 7 C). The conduction velocity of the second response is approximately 1 to 2 m./sec., and in different trials it was always identical with that of the first surface-negative response. At no

time were potentials with properties of the second surface-negative response seen to spread beyond the measurable confines of the first response.

Anatomical Considerations

The distribution patterns of the first or of the second surface-negative responses appear to depend neither upon direction of travel along the suprasylvian gyrus, nor upon which part of the gyrus is being studied (see inset diagram of Fig. 6). The absence of specific areas or of unidirectional conduction

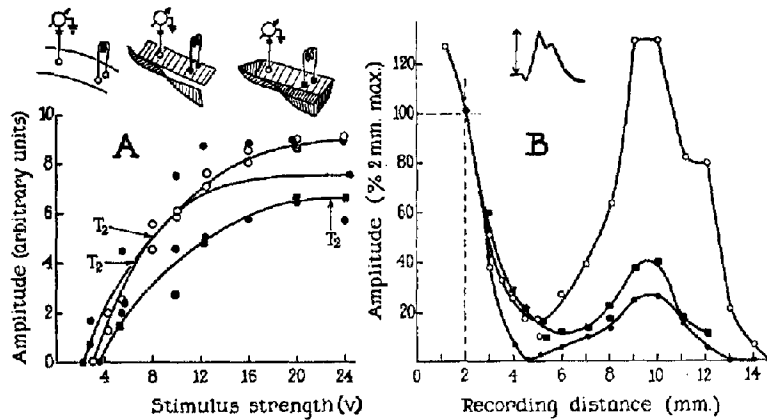


FIG. 8. A: Stimulus-response graphs of first surface-negative responses. Ordinates: peak amplitude (arbitrary units), abscissa: stimulus strength (volts). (○): intact brain. (●): radial cuts made. (■): isolated slab. T_2 denotes threshold of second surface-negative response.

B: Distance-response graphs of first surface-negative response of same experiment. Ordinate: amplitudes as per cent of 2 mm. maximal responses. Abscissa: recording distance (mm.). (○): intact brain. (●): radial cuts made. (■): isolated slab.

suggests the existence of a network of cells that has approximately equal excitability everywhere.

Connections with Other Parts of the Brain.—If the gyrus is isolated from its neighbors by radial cuts along its sides, sparing the pial vessels (see Methods), then the spread of the first surface-negative response is reduced. Reinforcements of amplitude occur at the same distances from the point of stimulation as before, but the amplitudes fall off to smaller values. Loss of excitability increases with distance from the point of stimulation. Four experiments have been carried out with such cuts. In only two cases controls were taken before the cuts were made, but in all four the patterns of spatial decay found after the cuts were non-linear. Stimulus strengths were $1.2 \times$ maximal both before and after the cuts. The persistence, after the cuts had been made, of the rein-

forcement at about 5 mm. makes it very unlikely that this distribution of the surface-negative response is due to invasion of neighboring gyri.

Alternately, afferent paths to the suprasylvian gyrus could be responsible for the discontinuities of the surface potentials. Two tests were made with undercut suprasylvian gyri that also had radial cuts along the sides. Two trials, made 1 hour apart, employing stimuli of $2 \times$ maximal strength, showed that the position of reinforcement did not shift significantly. After undercutting, there were no major changes in the appearance of the first surface-negative potentials, but the second surface-negative response disappeared.

A series from a more complete experiment is illustrated in Fig. 8. Stimulus-response graphs are shown in A, and distance-response graphs in B; the same symbols apply in both. The diagrams indicate the sequence from intact brain (○), through a stage with radial cuts (●), to complete isolation of a "slab" of cortex (■). The three trials were made with stimuli of $2 \times$ maximal strength at intervals of about 3 hours. The brain was tested almost continuously for excitability or for distribution of potentials. Reinforcement of the first surface-negative response became less powerful as isolation proceeded (Fig. 8 B), and as the threshold of the second surface-negative response rose to higher values (Fig. 8 A).

DISCUSSION

Reinforcement of the First Surface-Negative Response

The responses described in this study are similar to those seen by previous authors (Burns, 1958; Chang, 1951 *a*; Purpura and Grundfest, 1956). The main difference arises over the extent of spread: reinforcement, or re-initiation, of the surface-negative responses has not been reported before, although it was subsequently noted that some of the information is contained in Fig. 5 of Chang (1951 *a*), but was not recognized by that author.

The present evidence states that weak stimulation, evoking no more than 10 to 15 per cent of a maximal first surface-negative response, produces a process that travels outward from the stimulating electrodes to extinction at 5 mm. or less at 0.7 to 2 m./sec. Stronger stimulation, evoking up to 60 per cent maximal responses, causes re-initiation of the response at 6 to 10 mm., from where it also travels at 1 to 2 m./sec. Maximal surface-negative responses typically have two points of re-initiation or reinforcement: at 5 and 10 mm., both responses travelling from their respective points of origin at 1 to 2 m./sec. (Fig. 4). When neural connections to the suprasylvian gyrus are severed, excitability of the first surface-negative response decreases only slightly as measured by the strength-response curve, but excitability of the second surface-negative response does decrease, sometimes to the point of its abolition (T_2 : indicated in Figs. 3 and 8). This may account for its absence in the experiments of Burns (1958).

Since the site of stimulation on the suprasylvian gyrus is of no consequence to the initial pattern of distribution of the first surface-negative response (Fig. 6), it is unlikely that the points of re-establishment described above depend upon a special distribution of the responsible cells. Instead it may be more useful to consider the gyrus as containing a network of cells, all capable of producing directly evoked and re-initiated responses. In view of the similarity of the two processes both with regard to appearance and to conduction velocity *away* from the point of reinforcement (Fig. 6), it seems easiest to ascribe the origin of both slow and fast responses to type "A" cells of Burns and Grafstein (1952), that probably are pyramidal cells (see Fig. 9 A). Sholl (1955) in his classification of pyramidal cells includes cells of the general shape of type A cells in his groups "P-2" and "P-3," and type B cells in group "P-1," but as noted earlier he failed to find dendrites longer than 200 μ . It still appears undecided to the present authors whether the responses represent electrotonic or propagated spread in tangential fibres or in dendrites of various lengths (Burns, 1950; Chang, 1951 *a*; Clare and Bishop, 1955) or alternately whether they reflect their synaptic activation (Purpura and Grundfest, 1956), or if perhaps they are a mixture of all types of events.

The assumption that the surface-negative response is *entirely* accounted for by activity in tangential branches of type A cells (Fig. 9 A) is made untenable by the present observation of slow and fast components. The new evidence suggests that strong shocks discharge, in addition to the slowly travelling response, some structures with mean tangential lengths of 5 mm., which after fast conduction, synaptically excite other pyramidal cells. This latter event is observed as the fast response. Provided a sufficient number of cells are discharged, the sequence is then repeated at 10 mm. This property of summation is one commonly associated with synaptic transmission, as is the sensitivity of the reinforced response to the central excitatory state and to stimulus strength.

The structures that provide synaptic excitation for the fast response could be cortico-cortical axons, or recurrent collaterals of pyramidal cells, or axons of stellate cells, or a mixture of all. In Fig. 9 modified reproductions of Fig. 10 of Burns and Grafstein (1952) and of Fig. 3 from Sholl (1955) are reproduced, only irrelevant parts having been deleted. It is a point of interest that Burns and Grafstein (1952) and the present authors both obtained units of tangential conduction with average lengths of 5 mm. However, the absence of re-initiation with submaximal shocks (20 to 60 per cent maximal) in isolated slabs found by Burns (1951) is not surprising in view of the attenuation found for re-initiation of maximal responses after undercutting (Fig. 8 B). Since it has been shown by Lorente de N6 (1922) and by Sholl (1955) that neither apical dendrites nor recurrent collaterals of pyramidal cells extend for more than 2 mm., but that axons of stellate cells (type S3) do so close to the cortical surface (Sholl, 1955) it seems possible that surface-negative responses are reinforced or re-initiated

after conduction in axons of stellate cells. One further point of circumstantial evidence can be cited in favor of this surmise: Burns and Grafstein (1952) found lowered thresholds for initiation of the surface-negative response with a stimulating electrode at a depth of 1.2 mm., which they assumed to be due to

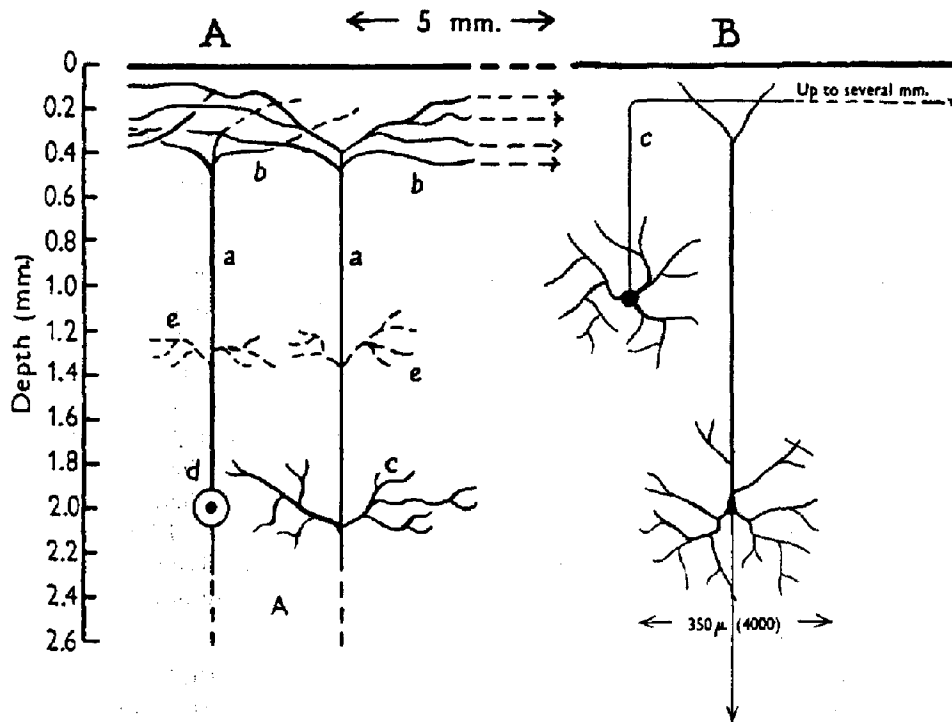


FIG. 9. A: Modified from Burns and Grafstein (1952). The drawing shows the most likely shape and location of type A cells in the suprasylvian gyrus, deduced from electrophysiological studies.

B: Modified from Sholl (1955). The drawing shows the most common shape and location of pyramidal and of stellate cells in the lateral gyrus based on histological studies.

dendrites, marked *e* in Fig. 9 A. The greatest concentration of stellate cells occurs near that depth (Fig. 9 B), both in the lateral gyrus (Sholl, 1955) and in the sigmoid gyri (Mitra, 1955).

The conduction velocities of the slow and fast components can be approximated by assuming that the responses at 1 and 2 mm. from the stimulated point are mostly due to the slow process; and that those at 5 and 10 mm. points of reinforcement are predominantly due to the fast process. Inspection of latencies

in Fig. 6 B, which is representative of the results of all experiments with maximal stimulation on "normal" brains, provides values of 1 m./sec. and 5 m./sec., respectively. However, if allowance is made for one synaptic delay of 0.5 msec. for the fast response, its velocity would be doubled, to be 10 m./sec. If the rule of Hursh (1939) applies in this case, the outside diameters of the responsible fibres would be about 1 to 2 μ .

The Second Surface-Negative Response

The origin of this response is still obscure. It may represent discharge of interneurons (Chang, 1951 *a*), but it might also be a second discharge of type A cells. Presumably the differences between its appearance in Chang's paper (Fig. 2) in contrast to that of Purpura and Grundfest (1956) and in ours (Fig. 2) are due to different experimental conditions. Our data on the susceptibility of the generation of this response to the excitatory state of the brain, and its dependence on stimulus strength cannot decide between these alternatives. There are, however, some further properties that the first and second surface-negative responses share: they have the same conduction velocities, the same extent of spread (measurable to within 500 μ) at any stimulus strength, and the same property of reinforcement or re-initiation (Fig. 7 B). Furthermore the stimulus-response curves usually reach maximum at the same stimulus strengths as those for the first response (Fig. 7 A). If the response is caused by interneurons then they must be situated within 500 μ of the type A cells innervating them: otherwise their independent responses would have been recorded in the present experiments.

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