THE EFFECTS OF APPLIED POLARIZATION
ON EVOKED ELECTRO-CORTICAL
WAVES IN THE CAT

by

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INTRODUCTION

Alpha waves, cortical spindles, the repetitive after-discharge, recruiting, and augmenting waves are cyclic potential changes which have in common a frequency of 8--12/sec. and a prominent negativity when recorded at the cortical surface. Numerous studies have been performed on these potential phenomena but in many cases the emphasis has been on the rhythmic characteristics rather than the mechanism of production of the waves themselves.

The alpha rhythm, prominent in the electroencephalogram (EEG) of a normal relaxed subject, was first described in 1929 (1). It is "blocked" by various types of sensory stimulation. Individual alpha waves are roughly sinusoidal, with a wave length of approximately 100 msec. They are widely distributed over the cerebral cortex and one portion may produce alpha waves which are out of phase with adjacent areas of the cortex. The basic mechanisms underlying the production of the cortical waves themselves are unknown, nor is the basis of the rhythm understood. It is likely that the great interest in other cyclic potentials recorded from the cerebral cortex is due primarily to a desire to understand the mechanisms underlying the production of the alpha phenomenon.

Most investigators assume the cortical spindle to be a form of activity similar to the alpha wave of the normal subject (2,3,4) although this is not definitely known. Spindle waves are characteristic of the EEG during barbiturate anaesthesia, in the isolated brain (5), and in animals with lesions of the brain stem reticular formation (6). These potential changes occur in bursts. They are initially small, with a progressive increase then decrease in magnitude from beginning to end of the train. Activity between bursts is of high frequency and low amplitude and at least superficially appears similar to that seen in the EEG during blocking of the alpha rhythm by sensory stimulation. Many individual spindle waves have an initial positivity preceding the characteristic large negative deflection (7). The bursts are scattered widely over the cortical surface and various areas of the cortex spindle out of phase with one another. As is the case with the alpha wave, variability in the individual wave forms makes their study somewhat difficult and most of the investigations of the spindling phenomenon have been involved with a study of the rhythm.

Cyclic waves which follow a primary response have been described by numerous investigators and are usually known as repetitive after-discharge (8,9,10,11). The experimental conditions favoring the production of this response are not well known, and the waves are not found in all preparations in which the primary response is seen. Most authors do not describe individual waves in the afterdischarge, but their records reveal predominately negative potentials which progressively decrement for 1--2 seconds after the stimulus. They are limited to the cortical projection area of the particular sensory relay system stimulated.

Recruiting and augmenting responses are thalamically evoked potentials and are convenient for expermental study of both cortical rhythm and of individual wave characteristics because of their consistency from wave to wave, train to train, and animal to animal. It is possible that information regarding mechanisms of production of these potential flustuations will eventually lead to an understanding of the nature of spontaneous electro-cortical waves.

Recruitment was first described by Dempsey and Morison (12,13,14). During the systematic exploration of the thalamus of the cat with stimulating electrodes, electrical stimuli applied to an area in the medial thalamus were found to evoke cortical responses which after the second or third stimulus at the critical 8--12/sec. frequency would increment with successive shocks up to a maximum. When the stimulus train was continued for several seconds, the responses would decline for several seconds only to increment again, a phenomenon labeled "waxing and waning". Each recruitment wave followed the thalamic stimulus after 20--40 msec. and lasted 30--50 msec. Generally the wave was monophasic and surface negative, occasionally diphasic with a late positive deflection. These waves were distributed over the entire exposable cortical surface but were especially prominent in the cortical association areas, g. proreus, the middle suprasylvian g. and the posterior suprasylvian g. In searching for a possible anatomical substrate for this phenomenon the suggestion was made that the responses were due to activity evoked at the cortex from stimulation of non-specific afferent fibres which made diffuse cortical connections. Non-specific afferent fibres were first described by Lorente de No (15). Subsequent studies of the recruiting phenomenon have led to the concept of a medially located thalamic projection system which is quite separate from the well-known sensory and elaborative projection systems. This anatomic system is known commonly as the diffuse projection system and incorporates the intralaminar and midline thalamic nuclei. The anatomical association between the diffuse projection system and non-specific cortical afferents remains to be conclusively established.

Augmentation was the term given to cortical responses evoked by repetitive stimulation of the ventrolateral thalamus, internal capsule and medial lemniscus

(10,16). The response to the first stimulus in the train was the classical diphasic primary response. Subsequent responses incremented to a maximum after the third or fourth stimulus. The primary response lasted about 15 msec. and was unchanged throughout the repetitive train. The true augmenting wave was a second diphasic deflection whose initial positive deflection fell at the peak of the primary response negativity, corresponding to a latency of 5--10 msec. The augmenting negativity lasted 30--50 msec. Augmenting responses and the primary response were distinguishable because thalamic placements could be found where one or the other could be produced individually with threshold stimuli, because the primary response could follow frequencies up to 50/sec, while augmentation was limited to frequencies below 15-20/sec., and because the primary response was independent of the repetitive after-discharge while augmentation was blocked by a simultaneous repetitive after-discharge. Augmentation in this case was limited to the sensori-motor cortex in an area which was slightly larger than the area giving rise to a primary response evoked from the same thalamic placement.

Recruiting, and to a lesser extent augmentation, have been studied in numerous subsequent investigations. The original investigators felt that recruiting and spindles were closely related phenomena and represented activity in the same neuronal system (12,13,14). This comparison has been emphasized in numerous subsequent investigations (2,17,18,19,4). Recently, however, it has been shown that augmenting and spindling waves have similar effects on the responsiveness of pyramidal tract neurones, while recruiting responses did not alter the responsiveness of the efferent system (7). Since both augmenting and recruiting responses have certain characteristics in common with spindling, it would suggest that a direct comparison of recruiting and augmenting responses should be undertaken.

A review of the literature in reference to recruiting and augmenting indicates that direct comparisons of the characteristics of these responses have not been frequently made. Most of their similarities and dissimilarities can only be inferred by a comparison with a third phenomenon such as cortical spindle waves or repetitive after-discharge. Because of the dearth of direct comparative studies, the effects of electrical polarization of the cortex from which these potentials are recorded was undertaken with the hope that some information regarding the cortical substrate of both phenomena would be forthcoming. Some reasons for the selection of polarization as an empirical conditioning procedure will be discussed in a later section.

A summary outline of the observations which emphasize either directly or indirectly the dissimilarities and similarities of these two phenomena has been prepared in the hope that it will make clear the need for more direct study of these evoked electro-cortical waves.

A. Observations which emphasize the dissimilarities of recruiting and augmenting.

1. Interactions with spontaneous spindles.

Numerous deductions have been made in regard to the independence of cortical waves on the basis of failure to demonstrate occlusion. It is assumed that a population of neurones which is capable of responding to one of several routes of presynaptic activation with the production of a potential wave can not simultaneously respond maximally to activation by more than one pathway at a time. The potential waves produced by the two different presynaptic routes are said to undergo occlusion when they can not be simultaneously evoked. On the other hand if two separate populations of neurones are involved and are simultaneously activated, the potential waves representing the activity of both these two populations will be recognizable.

Stimuli applied to nuclei of the diffuse projection system at a frequency less than the prevailing frequency of the cortical spindle bursts were ineffective in eliciting recruiting responses and the stimulus artifacts fell randomly among the spontaneous waves. When the frequency of stimulation was greater than the prevailing burst frequency, simultaneous recruiting and spindle waves resulted in the complete occlusion of one or the other. When either wave just preceded the other, the second was partially or completely occluded (16).

Augmenting waves on the other hand were identifiable regardless of the presence or absence of a spontaneous spindle wave, indicating a lack of occlusion (10). In the examples presented in this study however, the augmenting waves consisted entirely of surface positive deflections, leaving open the question of a possible occlusion between augmenting negativity and the spontaneous spindle waves.

2. Interaction with repetitive after-discharge.

Recruiting responses were identified during repetitive after-discharge and no evidence of occlusion could be demonstrated between these two cyclic phenomena (10).

Augmenting responses and the repetitive after-discharge evoked in the sensori-motor area of the cat, however, did show evidence of mutual occlusion. Only primary responses could be identified during a repetitive after-discharge while primary responses evoked during the augmenting response were not followed by repetitive after-discharge.

3. Effects of single stimuli applied to the thalamic areas giving rise to recruiting and augmenting responses.

Single shocks applied to the medial thalamic areas in barbitalized preparations, the isolated brain, or animals with lesions of the brain stem reticular formation gave rise to widespread cortical bursts which were indistinguishable from spontaneous spindle bursts (13, 20, 3, 4). This phenomenon has been labeled spindle tripping (21).

Single shocks applied to the ventro-lateral thalamus produced repetitive after-discharge, which like augmentation was limited to the sensori-motor cortex (10, 11).

The repetitive after-discharge and the spontaneous spindle burst represent different and independent forms of activity in the eyes of some investigators because no occlusion took place during studies of interaction of these two phenomena (11, 12, 2). Repetitive after-discharge was detected in n. ventralis posterolateralis while the medial thalamic nuclei were silent and the converse was true of spontaneous burst activity (10). High frequency stimulation of medial thalamic nuclei was found to abolish spontaneous spindle burst activity leaving a simultaneously evoked repetitive after-discharge unaffected (10), but this was not confirmed when the repetitive after-discharge was evoked alone, i.e. high frequency stimulation of intralaminar nuclei abolished the repetitive after-discharge in the sensori-motor cortex (3). Nevertheless the preponderance of evidence suggests that repetitive after-discharge and spontaneous burst are representative of different thalamo-cortical mechanisms, and the similarities between recruiting and spindles and augmenting and repetitive after-discharge respectively in these earlier papers offer some indirect evidence for the independence of the augmenting and recruiting phenomena.

4. Surface distribution of potentials.

Since Dempsey and Morison described recruiting potentials over the entire exposable cortex, two opinions have arisen regarding this point. The disagreement is manifest as a difference in cortical distribution but is more intimately related to two different views on the nature of the thalamic response to recruiting stimuli.

Magoun and his co-workers (21, 23, 24) found that recruiting responses were limited to the association areas of frontal, cingulate, orbital, and posterior suprasylvian cortex with complete sparing of the primary sensory receiving areas. In the thalamus recruiting responses were recorded in all thalamic nuclei of the diffuse projection system plus the association nuclei n. lateralis posterior, pulvinar, and n. dorsalis medialis, with sparing of the primary relay nuclei. The latency of responses recorded at the cortex was the same regardless of which portion of the diffuse projection system was stimulated although the anterior portion of the medial thalamus was found to be the most responsive and excitable portion of the system. It was proposed that the nuclei of the diffuse projection system responded as a unit to stimulation of any nucleus within it.

Fibres mediating this response left the thalamus principally by way of the respective thalamic association nuclei with the result that only the corresponding cortical projection of these nuclei responded with recruiting responses.

On the other hand, Jasper and associates (20, 22, 25, 3) have observed that recruiting responses may be demonstrated in all areas of the exposable cortex when the level of barbiturate anaesthesia is deep enough in confirmation of the original observations. Furthermore, recruiting responses have been recorded in various association areas of the cortex after destruction of the corresponding thalamic association nuclei. A number of lines of evidence point to a crude topographical organization of the midline and intralaminar nuclei of the thalamus, suggesting that the mass response of the diffuse projection system found by Magoun et al (21, 23, 24) might have been due to the use of stimulus electrodes which were too large and stimulus intensities which were too high. Tripped spindles appear earlier in the anterior portions of the cerebrum with stimulation of the anterior and medial portions of the diffuse projection system, while dorso-lateral portions of the system gave rise to tripped spindles which arose first in the parieto-occipital cortex. When stimulating electrodes with tip separations of 150 microns were used, localized recruiting responses could be evoked which corresponded to the cortical topography mentioned above. Local abolition of cortical spindles could be produced with high frequency stimulation of various portions of the diffuse projection system. The concept of a topographical organization of the medial thalamus was further suggested by the demonstration of DC shifts after high frequency stimulation of the mid-line nuclei which correlated closely with the distribution of recruiting responses and were limited to the frontal areas of the cortex (26).

Thus the preponderance of evidence favors the view that the recruiting response can be recorded from all portions of the cerebral cortex and that activity ascends over pathways that are independent of the association nuclei of the thalamus. With proper conditions a topographical organization of the thalamus can be demonstrated.

Augmenting responses have been recorded from repetitive stimulation of the sensory relay nuclei of the ventro-lateral thalamus and from n. ventralis lateralis, and the area from which an augmenting response could be recorded was greater than that giving rise to primary responses from a given thalamic electrode placement (10, 7). It was, however, still limited to the primary cortical projection, in this case, the sensori-motor area. Augmenting responses have been recorded also from the ectosylvian gyrus during repetitive stimulation of the medial geniculate nucleus (25) and from the parietal cortex during stimulation of n.

lateralis posterior (4).

Therefore, recruiting and augmenting responses differ in their cortical distribution, but the distributions do overlap in certain regions, i.e. the frontal and parietal areas of the cortex.

5. Depth distribution of recruiting and augmenting potentials.

Recruiting potentials have been recorded at various depths of the cerebral cortex by Li et al (19) and the responses have differed in the depths depending on the cortical recording site. The potential which is most characteristic of the surface response, the negative wave, was reversed to become a deep positive deflection over a depth of cortex which varied 0.4--1.5 mm. in their series. Spontaneous spindles behaved similarly and in many cases the depth of reversal was identical for both waves in a given preparation. A more careful study (27) has shown that the surface negative wave is converted to a deep positive wave in a slightly different manner than that previously described. In experiments in which recruiting responses were uncontaminated by stimulation of specific projection fibres, the conversion of the recording from a surface negativity to a deep positivity was limited to the superficial layers of the cortex. Evidence was found also for the presence of two patterns of depth potential distribution during spontaneous spindle waves and one of these patterns resembled that seen during recruiting responses.

Augmenting responses differed rather markedly from recruiting responses in regard to the depth distribution of potential changes. The surface positive component of these waves was attributed to activity beginning deep in the region of the terminations of specific thalamo-cortical afferents, while the surface negative component was ascribed to the appearance of this activity at the cortical surface after upward movement through the cortex. In this same study a second variety of spindle wave was shown to have a depth distribution of potential change with this same pattern (27). The augmenting responses differed little from descriptions of the depth distribution of potentials during a primary response (28, 29), except, of course, for the difference in the temporal relations of the two waves.

6. Effect of removal of cortical grey matter.

After complete excision of the sensori-motor cortex, the recruiting response was found to be present in the subadjacent white matter, although it was converted to a monophasic positive wave (30). This alteration was not confirmed by another investigator who found the recruiting responses completely unaltered by removal of the cortex (25).

Augmenting responses evoked by stimulation of the medial geniculate body were completely abolished from the ectosylvian gyrus (25).

7. Summary.

The evidence for the independence of recruiting and augmenting is based on several early investigations which relied greatly on studies of interaction with other cyclic cortical potential waves. Recruiting and spontaneous spindles were relegated to a common mechanism, while augmenting and the repetitive after-discharge were equated. The independence of repetitive after-discharge and spontaneous spindles on the basis of failure to show mutual occlusion suggests that recruiting and augmenting themselves represent independent forms of neuronal activity. The depth distributions of potential during recruiting and augmenting responses were definitely different from one another. However, two patterns of distribution were seen during spontaneous spindle waves, one resembling recruiting, and the other resembling augmenting. This would suggest that certain qualifications must be made when it is stated that spindle waves are similar to recruiting responses. Lastly, removal of the cortical mantle destroys the augmenting responses recorded at the surface, while evidence of recruiting responses have been seen even after its removal.

B. Observations which suggest that recruiting and

augmentation are similar.

1. Similarities in wave form.

As mentioned previously, both waves have in common a large cortical negative wave which increases in magnitude to a maximum after several stimuli. This characteristic has been used as the basis for the inference that both responses are manifestations of activity in the same neuronal structure (4). Augmentation is always associated with an initial positive deflection. On occasion a very small initial positive wave may precede the recruiting response. Either wave may or may not be followed by a late positive deflection.

2. Effects of high frequency stimulation of the reticular activating system of the brain stem.

Reticular stimulation abolished the major portion of the recruiting responses at the cortex in the isolated brain (17) and in the olfactory bulb (31). Similar stimulation did not influence the primary response in any way but abolished or prevented the development of the incremental negative wave of the augmenting response (32).

3. Effects of high frequency stimulation of thalamic recruiting and augmenting sites.

A DC shift could be recorded in the sensori-motor cortex after high frequency stimulation of either the midline thalamic nuclei or the ventro-lateral thalamus. The distribution of the steady potential was correlated directly with the distribution of the respective recruiting or augmenting responses evoked in the same area (26).

4. Activity relayed down the pyramidal tract.

Spontaneous spindle waves were associated with a relayed volley (33) which could be recorded with a gross electrode in the pyramidal tract of the medulla and was correlated with the initial portion of the spindle wave recorded at the cortical surface (7). A similar pyramidal wave was seen during augmentating waves and was correlated with the initial surface positive portion of the surface response. It is questionable whether a gross relayed pyramidal volley is present during the recruiting response evoked from stimulation of the midline thalamic nuclei. Very small deflections were occasionally seen to be temporally related to the recruiting responses, but controls suggested that these potentials may have arisen outside of the pyramidal tract (7). In recruiting responses elicited from the intralaminar nuclei, a gross relayed volley was demonstrated in most of the records published by Arduini and Whitlock (18). However the recruiting waves evoked in these experiments had a prominent initial positive deflection and the possibility that there was simultaneous stimulation of the adjacent n. ventralis lateralis can not be eliminated. It is also possible that fibres of passage from specific thalamic nuclei are stimulated simultaneously when recruitment is evoked from the intralaminar nuclei, since specific fibres pass through the lateral and anterior portions of the diffuse projection system (34).

Activity in single pyramidal tract fibres was correlated with pyramidal and cortical spindle waves (35) and also with thalamically evoked recruiting responses (18), but the same objection may be raised here about the possibility of some sort of mixed augmenting and recruiting response with stimulation of the intralaminar nuclei. Activity in single units has not been examined during augmenting responses, but in view of the large pyramidal volley it is reasonable to expect that a pattern of single unit responses will be found that is similar to spontaneous spindle waves.

5. Interaction of recruiting and augmentation potentials.

When an augmenting response was timed to fall during various phases of a recruiting response, partial occlusion of the negative components was demonstrated. Depression of the negative component of one response was particularly marked when elicited during the late positive deflection of the preceding response. Pyramidal relayed volleys during augmenting waves were enhanced when the augmenting wave was evoked during a recruiting wave, while depression of the relayed volley occurred during the late positivity of the recruiting response (36).

6. Summary.

Suggestions that recruiting and augmenting responses may represent similar mechanisms are afforded by the observations of similarities in wave form and by the fact that both phenomena are abolished by stimulation of the reticular formation of the brain stem. A DC shift is recorded in frontal cortex high frequency of either midline or specific thalamic nuclei. The evidence for the relay of activity down the pyramidal tract during augmenting and spindling is convincing, but studies which demonstrated a similar relay of activity during recruiting responses are open to some criticism. Finally, direct interaction of recruiting and augmenting reveals mutual occlusion of the negative components of each response.

C. Mechanism of production of recruiting and augmenting responses.

In view of the extensive literature on recruiting and augmenting, a brief review of the hypotheses dealing with the mechanism of production of these responses might be helpful.

The original investigators (12, 13, 14) felt that these responses represented activity in neuronal systems which were independent at both thalamus and cortex.

They suggest that the recruiting response is mediated by non-specific thalamo-cortical afferents which originate in the midline and intralaminar nuclei. The augmenting response is dependent upon specific thalamo-cortical afferents but involves a thalamic pool of interneurones which through reverberating circuits at the thalamic level account for the phenomenon of augmentation.

Brookhart and Zanchetti (7) suggest that the recruiting and augmenting responses may have in common a cortical pyramidal cell, their differences ascribable to a different level of termination of thalamo-cortical fibres on the cortical neurone. Corticipetal fibres involved in the recruiting response may terminate on apical dendrites while fibres mediating spindling and augmentation may terminate either directly or via an intercurrent Golgi II cell on the basal dendrites and cell body of the same neurone.

Bishop and Clare (37) have studied the primary response at the cortical level and feel that a large part of the response is due to a conduction of a wave of depolarization up the apical dendrites resulting in a surface positive-negative deflection. The wave begins at the level of termination of specific thalamo-cortical afferents in layer IV. Recently the view has been taken that other cortical responses, including augmenting and recruiting, which are characterized by a prominent surface negative wave represent responses of the apical dendrites of cortical pyramidal cells (4). This constitutes an expansion of the idea that augmenting and recruiting are different only in the nature of the termination of the corticipetal fibres involved in the particular response.

D. Statement of the problem.

It is obvious that studies directly comparing the augmenting and recruiting responses are few indeed, and in view of the hypotheses suggesting a common cortical structure might be involved in both responses, an experimental procedure which would be expected to influence these responses at the cortical level was required.

Electrical polarization of the cortex seemed an appropriate choice as a conditioning procedure for the comparison of these evoked potentials for three reasons. The ease with which the polarization could be localized to the cortical areas from which the responses were recorded was the first major factor in this selection. Secondly, certain investigations reported in the literature indicated that steady potentials occurred spontaneously in central nervous system structures (38, 39, 40). Lastly, studies of nervous activity in the presence of applied polarizing currents have demonstrated that various potential phenomena could be influenced by this procedure. The action potential of peripheral nerve was increased in amplitude under the anode and decreased or blocked under the cathode when steady currents were permitted to flow through the nerve (41). A proportional relation was found between the membrane potential and the post-synaptic potential recorded with intracellular electrodes in a ventral horn cell when the membrane potential was altered by direct polarizing currents flowing across the cell membrane (42). Large diphasic caffeine waves in the isolated frog cortex showed characteristic alterations in the presence of polarizing currents. Surface positive polarization resulted in a decrease or abolition of the initial positive component and enhancement of the negative deflection, while currents flowing in the opposite direction resulted in exactly the reverse effect (38). Polarization of the cortex giving rise to primary responses produced somewhat similar findings. When the surface was positive, the negative components were greatly enhanced and the initial positive deflection was diminished or abolished. Surface negative polarizing currents greatly augmented the initial positive deflection and decreased or abolished the surface negative component (43).

In view of these considerations, it seemed justifiable to predict that polarization of the cortex during the production of recruiting and augmenting responses would give rise to certain alterations in the evoked potentials. It may be assumed that if these responses are due to activity in the same or similar cortical structures, they would very likely respond to conditioning by polarizing currents in a similar manner. On the other hand, if the production of the recruiting and augmenting responses depended on the activity of different cortical structures, it could be anticipated that the responses would differ in their response to conditioning by polarizing currents.

METHODS

Twenty-one cats free of gross neurological disease and each weighing at least 2.5 kg. were used in the various phases of this study. The animals were given 0.6 mg. atropine sulfate intraperitoneally about twenty minutes before the experiment began. Ether anaesthesia was induced by mask and maintained by open drip on a gauze pad over the end of a tracheal cannula. A polyethylene catheter was placed in the femoral vein for the injection of drugs. The head of the cat was then fixed in a suitable stereotaxic instrument and the cranium exposed. The frontal sinus was opened and the thin sheet of bone forming its posterior wall was carefully removed until the cortex around the cruciate sulcus was brought into view. The anterior and posterior sigmoid gyri were included in this exposure, the two together constituting what is generally known as the sensori-motor cortex in the cat. Suitably placed trephine openings were made over the apex of the skull for the admission of diencephalic stimulating electrodes. 0.5 cc. 1% procaine HCl was infiltrated around the Gasserian ganglion on each side and the skin edges of the scalp incision were injected with an additional 0.5 cc. This local anaesthesia was repeated at periodic intervals throughout the experiment.

At this point in the procedure, ether was discontinued and 1 mg. decamethonium bromide was administered. Artificial respiration was maintained with a positive pressure respiratory pump. Additional doses of the immobilizing agent were given throughout the day as needed. Subsequent steps in the preparation for the experiment required approximately one hour so that the effects of ether anaesthesia were dissipated before any recording was done.

Wherever possible the animal was protected from excessive cooling by liberal use of an electric pad and by maintaining the room temperature between 80 and 90 degrees F. The cortex itself was protected by a film of warm mineral oil at all times except during periods of actual recording. Additional protection was afforded by the practice of recording transdurally whenever possible. In spite of these measures, a deterioration of the preparation was often found after several hours, marked by an increase in the stimulus intensities required to evoke electro-cortical waves and a change in the contour of the waves recorded at the cortical surface.

Steel concentric electrodes were used for stimulation of the thalamus. The electrodes were insulated except at the tip, and the two poles were separated by a distance of less than 1 mm. The electrode was located in the appropriate thalamic area with the aid of the stereotaxic instrument and final selection of a placement was based on observation of the evoked cortical response. The possibility of eliciting mixed recruiting and augmenting responses during stimulation of intralaminar portions of the diffuse projection system has been mentioned previously. Recruiting responses were evoked from the midline thalamic nuclei exclusively, since anatomical studies reveal that they project specifically only to portions of the rhinencephalon and limbic lobe (34). Thus specific fibres projecting to frontal cortex are not apt to be stimulated in the midline nuclei and the more medial placement makes excitation of the specific thalamic nuclei by electrical spread of stimulating current less likely. Augmenting responses were elicited from the ventro-lateral thalamic nuclei, n. ventralis lateralis, n. ventralis posterolateralis or n. ventralis posteromedialis.

Thalamic stimuli consisted of square waves produced by electronic stimulators and led to the thalamic stimulating electrode through an isolation transformer. The pulse duration, pulse amplitude and the pulse repetition rate could be independently controlled. In all experiments, stimulating pulses of less than 1 msec. and of submaximal intensity were used, and the most effective repetition rate almost without exception was 6--8/sec. Stimulating current intensity was measured by recording the IR drop across a 100 ohm resistor placed in one of the output leads of the isolation transformer and the value computed from Ohm's Law.

Electrodes for recording over unexposed cortex consisted of steel phonograph needles imbedded firmly in bone of the skull. Non-polarizable Ag-AgCl wire electrodes were utilized for recording directly from the dura of the sensori-motor cortex. Indifferent and ground leads were placed in the flesh of the ear or scalp.

Two recording systems were used. For placement of the thalamic electrode an eight channel electroencephalograph was utilized. EEG recording made possible an estimation of the general cortical distribution of evoked responses and also facilitated observations on the contour of the individual wave forms until the best thalamic stimulating site was located.

For permanent recordings and a more accurate representation of electro-cortical waves, the potentials were led to a capacity coupled amplifier and displayed on two cathode ray oscilloscopes. The responses were recorded photographically from one oscilloscope while the other was used as a visual monitor. In certain cases, a second recording channel was used for control purposes. Generally the second channel recorded activity from an electrode placed in the pyramidal tract or from the cortex contralateral to the area being subjected to conditioning by polarizing currents.

In several early experiments, it was considered necessary to balance the steady potential difference which was produced between the input leads to the pre-amplifier during the flow of polarizing current. This compensation was furnished by a cathode follower which had a battery and potentiometer attached for adjusting the steady potential difference between its output leads. The cathode follower itself was placed in the recording circuit only because of the attached compensating circuit. It was soon found that alterations in the wave forms produced by polarization were the same without this voltage compensation and it was not used for the remainder of the experiments.

Polarizing currents were applied to the preparation through non-polarizable Ag-AgCl electrodes immersed in a barrel of glass tubing containing saline. A final contact was made by saline soaked wool wicks. Frequent aspiration of the excess saline solution from the recording area was necessary. The surface polarizing wick was placed carefully around the cortical recording electrode, and its location was critical. Direct currents did not alter the evoked responses when the wick was placed over areas of the cortex away from the recording electrode. The indifferent polarizing electrode wick was generally placed against the hard palate although its location was not critical and alterations in evoked responses could be just as effectively produced when the wick was in the cervical incision or in the occipital region.

Polarizing currents were supplied from a battery driven circuit containing a potentiometer for varying the current intensity and a milliammeter for monitoring purposes.

Currents up to 3.0 mA were available, but in practice the current intensity seldom exceeded 1.5 mA. The direction of flow of current was described according to the polarity of the different polarizing electrode and hereafter is abbreviated SP (surface positive polarization) and SN (surface negative polarization). Evoked potentials recorded with the polarizing wicks in place and direct current flowing are termed "conditioned" responses, while responses recorded in exactly the same way without polarization are known as "unconditioned" responses.

Film records of the data were analyzed after suitable development and enlargement. The experiment was not designed for a proper statistical analysis but certain small sample statistical determinations were possible. Measurements of the latency and amplitude of all the unconditioned responses from a given cortical recording electrode placement were measured and the standard deviation estimated from the range using a factor based on the number of samples (44). The mid-range constituted an assumed mean. Conditioned samples were compared with this statistic. Since the conditioned samples can be considered to have a mean and standard deviation at each level of polarizing current, and since only one sample of a conditioned response was obtained at each level giving us no indication of the variation, a single conditioned response whose measured parameter falls outside the estimated S.D. of the unconditioned responses could not be considered significant. An alteration was considered significant when the measured parameter of the conditioned response fell consistently 2 S.D. or more from the mid-range of the unconditioned parameter and was altered in the same direction in all the experiments in proportion to the intensity of the polarizing current.

At the termination of the experiment, the brain of the animal was perfused with 10% formalin and left overnight with the stimulating electrodes in situ. After suitable fixation, histological confirmation of the placement of the thalamic electrode was made from the carbol-thionin sections.

RESULTS

A. Unconditioned recruiting and augmenting responses.

1. Recruiting.

Repetitive electrical stimuli applied to the midline thalamic nuclei produced recruiting responses which were recorded from the anterior sigmoid gyrus. The response to the first shock was small or absent, but with recurrent stimuli a negative deflection was produced which appeared 15--25 msec. after each stimulus artifact. This response incremented with successive stimuli at the critical 8--12/sec. frequency and frequently reached amplitudes of 750 microvolts after 2--5 stimuli. The surface negative wave, which in some experiments was all that was seen in response to midline thalamic stimulation, is designated RN (recruiting negativity) in this report. On occasion an initial positive deflection was seen after a latency of 10--15 msec. This component will be designated RP (recruiting positivity). It seldom exceeded 50 microvolts in amplitude in a good preparation. Another variable component of individual recruiting responses was a late positive deflection following RN and continuous with it. It generally was variable in amplitude and duration but fell within the range of 20--60 msec. and 20--100 microvolts respectively. This component is designated RLP (recruiting late positivity) for purposes of description. An example of a train of these responses is illustrated in Figure I-A.

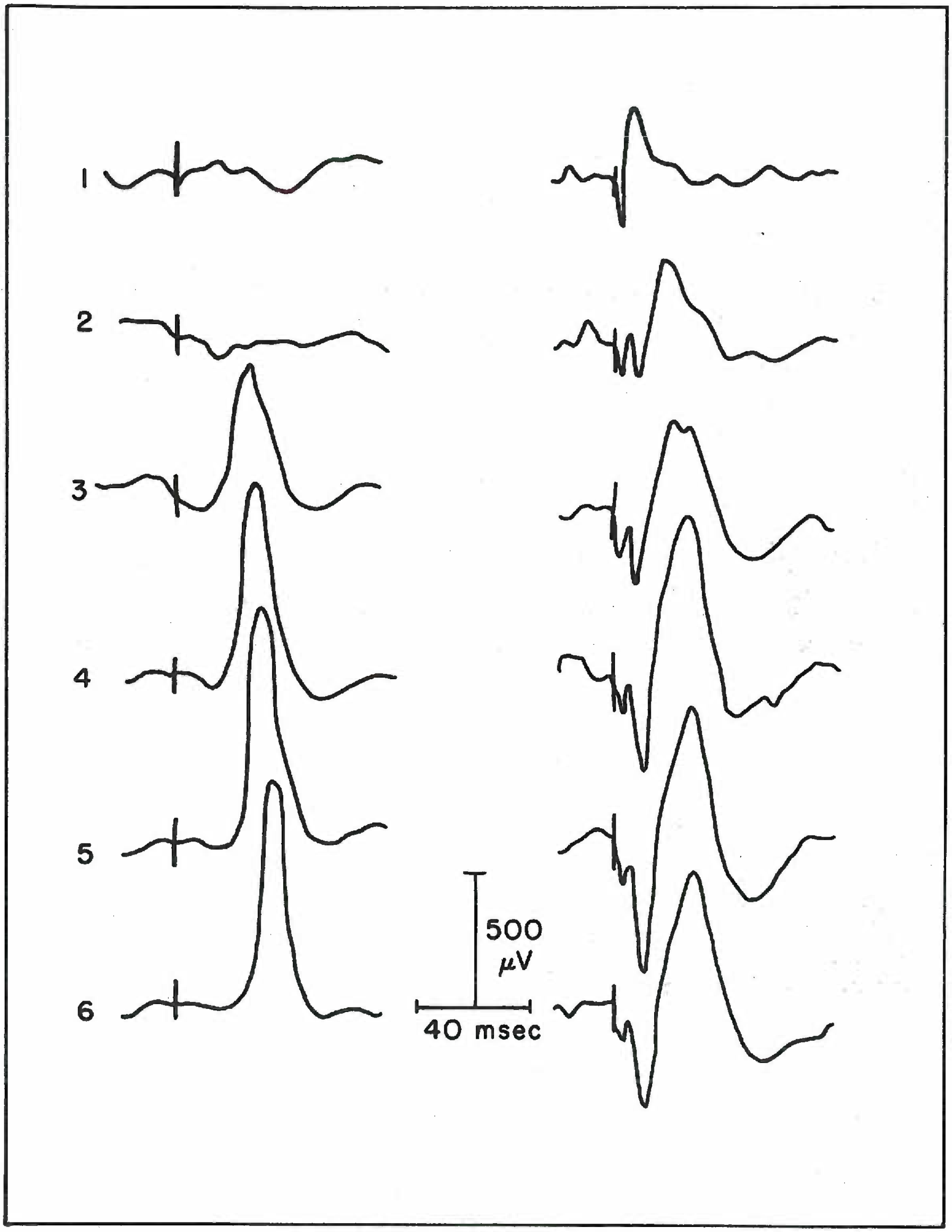
2. Augmentation.

Augmenting responses were evoked by repetitive stimulation of the specific sensory nuclei of the thalamus, n. ventralis posteromedialis and n. ventralis posterolateralis or the motor relay nucleus n. ventralis lateralis. The response to the first thalamic stimulus was the well known primary response. On occasion this primary response was followed by a small 15--20 msec. negative wave which was considered to be part of the augmenting phenomenon. Repetitive stimuli continued to evoke primary responses which were recognized as small notches superimposed on the larger incremental augmenting responses. In some experiments the primary response was diminished with repetitive stimulation, while in others it appeared to remain about the same throughout the train. Beginning with the second shock, an incremental positive and negative component were added to the potential complex. The positive wave, hereafter designated AP (augmenting positivity), peaked at the apex of the negative component of the primary response, lasted 10--20 msec., and increased in amplitude up to several hundred microvolts. The succeeding negative component of the augmenting response, AN (augmenting negativity), generally lasted 30--50 msec., and it also incremented to an amplitude of several hundred microvolts. AP and AN were

FIGURE 1

A. Configuration of typical unconditioned recruiting responses. The tracings were made from oscillograph records of the first six responses in a train, derived from a monopolar electrode on the anterior sigmoid gyrus. There was no response to the first and second thalamic stimuli and the incrementation of recruiting negativity (RN) began after the third shock. Initial positivity (RP) and late positivity (RLP) were inconstantly present even in the same train. In this and following figures upward deflections represent negativity of the different electrode with respect to the reference electrode. (3 - 27, 0.8 msec., submaximal stimuli to n. centralis medialis)

B. Configuration of typical unconditioned augmenting responses. Tracings of the first six responses in a train were recorded with a monopolar lead from the anterior sigmoid gyrus. Response 1 is a primary response. Note the development of the incremental initial positive component (AP) and negative component (AN) from response 2 - 5. The initial positive component of the primary response is diminished with subsequent shocks. The late positivity (ALP) is prominent in this train. (7 - 17 - A, 8/sec., 0.1 msec., submaximal stimulus intensity to n. ventralis lateralis)


1
2
3
4
5
6
500
µV
40 msec

the invariable components of the augmenting response. They frequently reached their maximum after the second or third thalamic shock, but the tendency was for AP to become maximal earlier in the train than AN. A third component which was seen in some experiments was a late positive deflection following AN, abbreviated for descriptive purposes ALP (augmenting late positivity). This response, when present, generally lasted 20--60 msec. and rarely exceeded 250 microvolts.

A train of unconditioned augmenting responses is illustrated in Figure I-B.

B. Responsiveness of recruiting and augmenting responses to polarizing currents.

It has been stated previously that the conditioning current intensity was not considered a valid criterion of comparison between individual experiments. Nevertheless, viewed in toto the experiments revealed that a definite difference in the susceptibility to alteration by polarization existed between these two cortical waves. This susceptibility to alteration by conditioning direct currents was termed responsiveness. Table I is a tabulation of the polarizing current intensities of several recruiting and augmenting experiments at which the maximal amplitude of the surface negative components during SN were 20% or less of average amplitude of the fully developed unconditioned

TABLE I

Responsiveness of Electro-cortical Waves

	Recruiting	Augmenting
Average Intensity SN producing negative component 20% of UC value	0.96 mA	0.27 mA
Range	0.75 - 1.0 mA	0.2 - 0.3 mA
Number of Experiments	4 (1 greater than 0.5 mA)	5

responses. In one recruiting experiment, SN was carried only to an intensity of 0.5 mA at which level the RN was 45% of its unconditioned value. In two of the experiments included in this table, the recruiting and augmenting responses were recorded alternately from the same cortical electrode. The difference in the average polarizing current intensity which produced an 80% reduction in amplitude in the two responses, 0.27 mA for augmenting responses and 0.96 mA for recruiting responses, emphasizes numerically an observation which was made many times during the course of these experiments.

C. Effects of surface positive polarization.

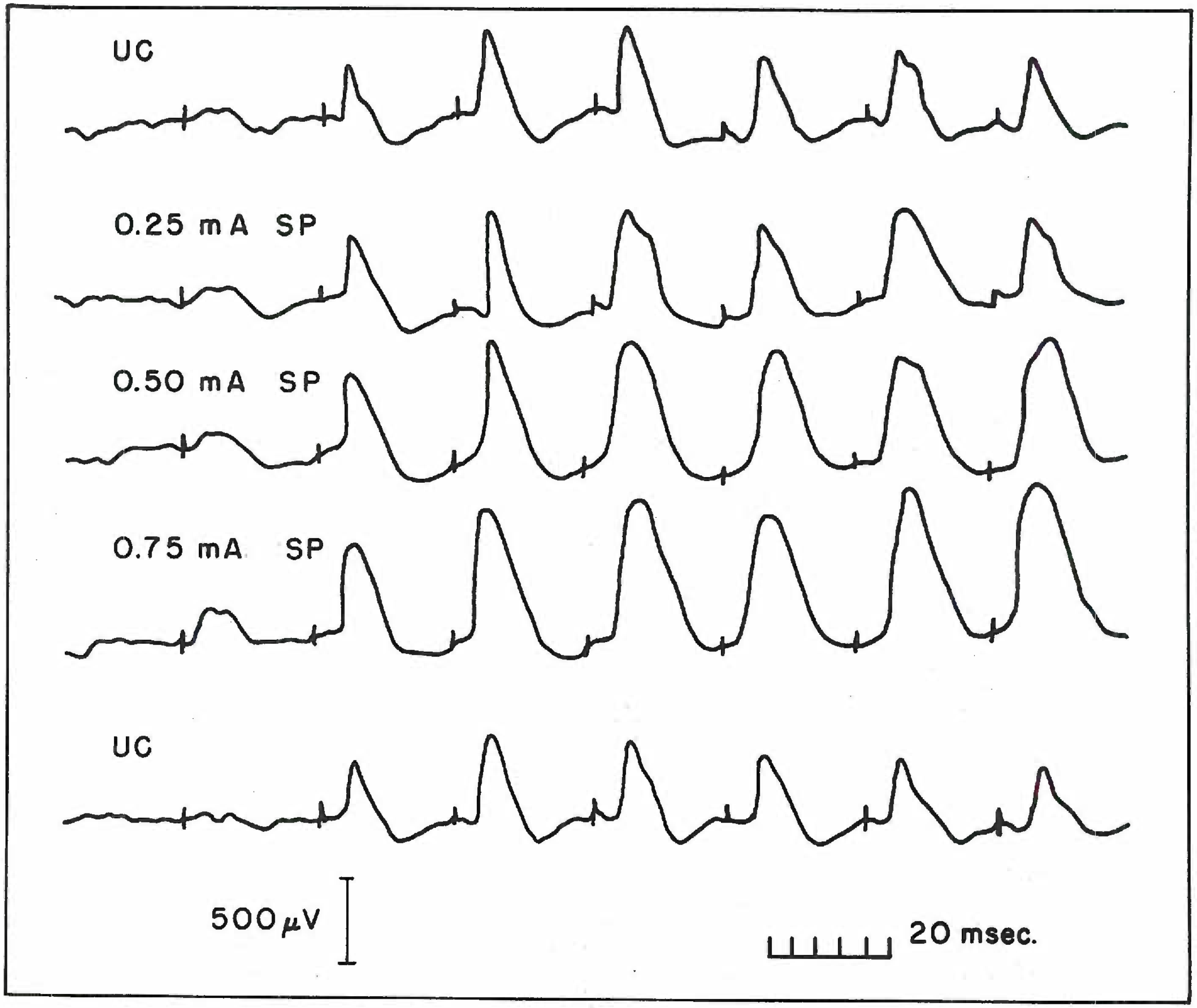
1. Recruiting.

The changes produced by progressive SP are illustrated in Figure 2. There was a progressive enhancement of the individual RN with each succeeding level of polarizing current intensity. This enhancement was made up of increases in both amplitude and duration of RN in most experiments, although the duration changes were difficult to assess in some cases because of the presence of an RLP.

In most recruiting experiments several stimuli were required before the responses reached a maximum amplitude and little or no response is seen after the first shock. SP frequently revealed a response to this stimulus, even though in most cases the number of stimuli required

FIGURE 2

Effects of surface positive polarization (SP) on configuration of recruiting responses. Responses 2 - 7 are illustrated in each train. Top and bottom trains were unconditioned (UC), remainder of trains were recorded during increasing intensities of SP. Note the increase in amplitude and duration of RN, which was related to the increase in polarizing intensity. All trains reached maximum amplitude after the same number of thalamic stimuli. (7 - 3, 8/sec., 1.0 msec., submaximal stimuli to n. centralis medialis, recorded from anterior sigmoid gyrus)


UC
0.25 mA SP
0.50 mA SP
0.75 mA SP
UC
500µV
20 msec.

for the responses to reach a maximum in a given train was not altered over the unconditioned trains.

In view of the demonstration of conduction velocity alterations in axon action potentials (41) and cortical caffeine waves (38) during the flow of direct currents, careful measurements were made on the latency of the peaks of both recruiting and augmenting waves. Peak latencies were chosen rather than latency to the onset of the various components because of the greater ease of accurate measurement and because of the assumption that the evoked waves are composites of several potential components. On this premise it is reasonable to conclude that a peak represents a predominance of a certain cortical activity and offers the best point for measuring alterations during conditioning procedures.

The tabulation of the data on latency measurements of the unconditioned RN peaks in Table II confirmed in general the tendency of recruiting responses to peak progressively later from the beginning to the end of the train (45). In some experiments this tendency was much more marked than others and in one experiment the difference was nearly 20 msec. between response 2 and response 7. On the other hand, one experiment which showed no cortical potential till the 5th thalamic shock showed no difference in latency between the 5th and the last response.

TABLE II

Latency of RN Peaks

Response	UC		Surface Positive			Surface Negative			
			0.3 mA	0.5 mA	1.0 mA	0.3 mA	0.5 mA	1.0 mA	
	M R (msec.)	S.D. (msec.)	(S.D. from M R)			(S.D. from M R)			
2	42	2.6	-0.78	2.3	0	0.77	-1.5	---	3 - 27
3	44	3.9	-0.51	0	-1	0	-1	-1.5	
4	44	2.6	1.5	2.3	0	2.3	-0.77	-1.5	
5	48	3.9	1.5	1.5	-1	2	-1.3	-1.5	
6	47	3.3	0.9	0.9	0.3	0.9	-0.3	-2.1	
7	49	4.6	1.3	0.22	-0.22	1.3	-0.22	-1.9	
			0.4 mA	0.6 mA	0.8 mA	0.4 mA	0.6 mA	0.8 mA	
2	37.5	3	0.16	0.16	0.83	-1.8	-2.5	---	7 - 16 - A
3	35	0.8	3.8	3.8	6.2	-2.2	-1	-2.2	
4	37.5	1.9	1.8	1.8	3.4	-0.79	-1.8	-0.79	
5	42	1.6	1.2	-2.5	3.7	-0.62	-1.8	-1.2	
6	42.5	1.9	1.3	4	4	-0.26	-1.1	-1.1	
7	42	3.2	-0.62	2.5	1.2	-0.62	-0.62	-2.5	

TABLE II (continued)

Latency of RN Peaks

Response	UC		Surface Positive			Surface Negative			
			0.5 mA	0.75 mA	1.0 mA	0.5 mA	0.75 mA	1.0 mA	
2	31	2.2	-1.3	0.45	0.45	-0.45	-1.3	-0.45	
3	35	2.2	0.45	2.3	1.3	-0.45	-1.4	-0.45	
4	37	0.74	-1	1.2	1.2	-1	-1	4	7 - 3
5	37	0.74	4.1	4.1	1	-4	-4	-4	
6	37	0.74	1	4.1	4.1	-4	-1	-4	
7	38	1.5	0	0	0	-2.6	-4	-2.6	
			0.06 mA	0.3 mA	0.5 mA	0.06 mA	0.3 mA	0.5 mA	
2	31	2.1	0.9	-0.48	0.9	-0.48	-0.48	-0.48	
3	36	2.8	-0.36	-0.72	1.1	-1.4	-2.1	-1.4	
4	41.5	2.5	0.2	0.2	0.2	-1.8	---	---	7 - 24
5	45	1.4	-0.7	0	0	-2.1	0	-1.4	
6	49.5	2.5	-0.6	0.2	-0.6	-2.6	-0.6	-1.8	
7	50.5	1.7	-0.29	-0.29	-2.6	-1.5	-0.29	-2.6	

TABLE II (continued)

Latency of RN Peaks

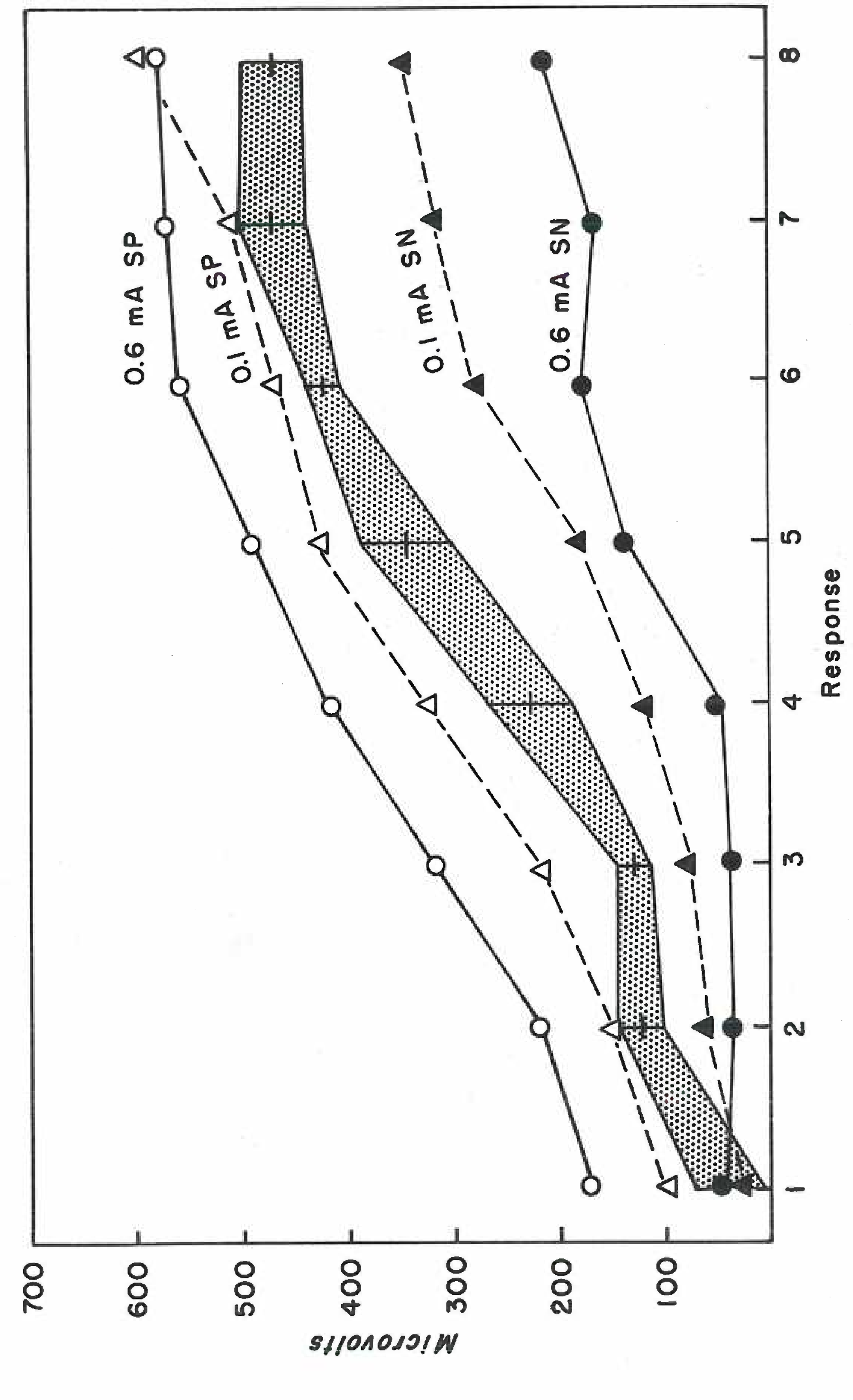
Response	UC		Surface Positive			Surface Negative		
			0.5 mA	0.75 mA	1.0 mA	0.5 mA	0.75 mA	1.0 mA
5	41	2.6	1.1	-0.38	0.38	0.38	---	---
6	39	2.6	1.1	0.39	0.39	1.3	-0.39	---
7	39	0.74	1.3	4	1.3	-1.2	1.2	-1.2
8	39.5	2.1	0.24	-0.71	1.2	0.71	1.2	0.24
9	40.25	2.0	1	0	0	1	0	-1.7
10	40	1.7	1	0	2.3	-2.1	-0.5	0

In Table II the latency of conditioned recruiting response peaks have been computed in units of S.D. from the mid-range of unconditioned responses. A minus figure in this and other tables containing latency measurement data signifies a decrease in the latency of that peak from the mid-range of the unconditioned values. The majority of the conditioned values (84.5%) were less than 2 S.D. from the mid-range of the unconditioned response values. Of those samples showing a change greater than 2 S.D., 13% represented an increase in latency and 2% a decrease in latency. Another significant factor is the lack of relation between the conditioning current intensity and the magnitude of deviation in the latency. In many of the responses showing a change in latency greater than 2 S.D., a corresponding response at a higher level of polarizing current did not produce a proportional increase in the change in latency. These data are difficult to interpret but the most likely inference would be that SP has not altered significantly the peak latency of the RN. It seems reasonable to assume that if enough samples of recruiting trains were measured at each level of conditioning current intensity, the mid-range and variation of the conditioned samples would be similar to the parameters of the unconditioned responses. The design of the experiment did not permit the accumulation of this data, so that no confirmation of this suggestion can be made.

Although both amplitude and duration of RN were increased during SP, the amplitude can be more easily determined with accuracy. Unlike the effect on the latency of the RN peaks, the amplitudes of this component responded in a characteristic and predictable manner to SP. The results of measurement of the RN amplitudes of a typical recruiting experiment during conditioning are plotted in Figure 3 (open symbols) and compared with the unconditioned parameters from the same experiment. The slow progressive increment in the unconditioned RN is illustrated in this figure, the responses in this instance reaching a maximal amplitude at response 7. SP produced an increase in the amplitude of each response throughout the train and the increase was proportional to the intensity of the polarizing current. The amplitudes of the conditioned responses were increased over the unconditioned values to about the same degree throughout the train. This is evident from the parallel courses of the lines representing amplitudes of both unconditioned and conditioned responses. Although only two intensities of polarizing current have been displayed in this and succeeding figures for reasons of clarity, the proportional relationship between increase in individual response amplitude and conditioning current intensity was maintained at all levels of current intensity up to the maximum used for each experiment.

FIGURE 3

Effects of polarization on the amplitude of RN. Amplitude in microvolts is represented on the ordinate, response number on the abscissa. The hatched figure represents the parameters of unconditioned responses. The length of the vertical bar at each response represents an amplitude of 2 S.D., an estimate of the variation of unconditioned values. Mid-range amplitude of the unconditioned responses is marked by a horizontal line on the vertical bar at each response. Open symbols indicate values during SP, closed symbols, surface negative polarization (SN). Note the proportional relation between polarizing current intensity and amplitude of each response and also the parallel course of the curves representing unconditioned and conditioned values. (7 - 24, 8/sec., 1.0 msec., submaximal stimuli to n. centralis medialis, monopolar recording from anterior sigmoid gyrus)


0.6 mA SP
0.1 mA SP
0.1 mA SN
0.6 mA SN
Microvolts
700
600
500
400
300
200
100
Response
1
2
3
4
5
6
7
8

2. Augmentation.

Augmenting responses were altered by polarizing currents in a manner which at first glance seemed more dramatic. The greater responsiveness of augmenting leads to this impression, but the most significant factor was the fact that simultaneous changes took place in both the AP and AN during the flow of polarizing current. Figure 4 illustrates the alterations produced by SP during trains of typical augmenting responses. The AP was diminished while the AN was enhanced by increasing levels of polarizing current. Expressed in another way, the net result during SP was an increase in surface negativity. In responses where there was no observable potential after the first shock to suggest the presence of augmentation, SP did not produce an augmenting potential.*

The latency to the peaks of AP and AN were measured in five experiments and the data are presented in Table III. The latency of the unconditioned AP in some experiments was short in the initial responses but in every case reached its maximal value by the third response. The latency of the unconditioned AN peaks remained constant in contrast to the change in latency of RN seen in most

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* No systematic observations were made on the primary response during polarization except to confirm the observation that SP decreased the initial surface positive component and enhanced the surface negativity while SN effects were the reverse (43).

FIGURE 4

Effects of SP on the configuration of augmenting responses. Responses 1 - 6 are illustrated in each train. Top and bottom records were unconditioned (UC), the other trains were recorded at the indicated values of SP. Note the presence of an augmenting potential after the first shock. AP incremented to a maximum earlier in the train than did AN. There was no ALP in this experiment. There was enhancement of AN and diminution of AP which was proportional to the polarizing current intensity. The net effect was an increase in negativity during SP. (7 - 17 - B, 8/sec., 0.05 msec., submaximal stimuli to n. ventralis lateralis, recording from anterior sigmoid gyrus)

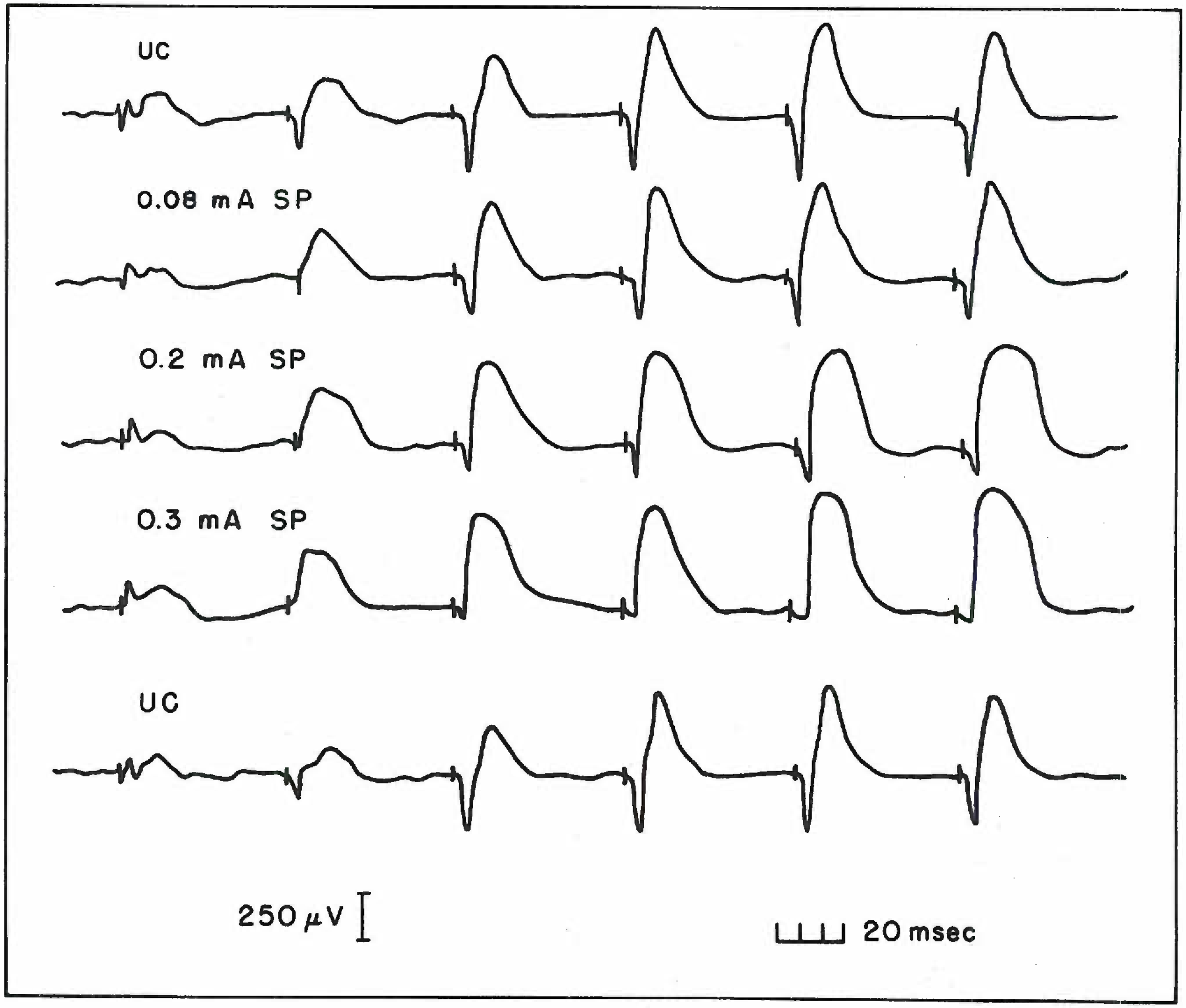

UC
0.08 mA SP
0.2 mA SP
0.3 mA SP
UC
250 μV
20 msec

TABLE III

Latency of Augmenting Components During SP

Response	A P					A N					
	UC		0.08 mA	0.1 mA	0.3 mA	UC		0.08 mA	0.1 mA	0.3 mA	
	M R (msec.)	S.D. (msec.)	(S.D. from M R)			M R (msec.)	S.D. (msec.)	(S.D. from M R)			
1	(3.5)	1.2	-0.42	0.42	-0.42	34.5	4.3	-1.3	0.8	-3.5	
2	7.5	3	1.1	-1.1	-1.1	37	5.3	-1.3	-2.5	-5.4	
3	12	1.5	-0.67	0	-2	35.5	2	-1.7	-3.8	-4.4	7 - 17 - A
4	11.5	1.8	0.28	0.84	0.28	33	2.3	-1.3	-2.6	-3.9	
5	12.5	1	0.5	-0.5	1.5	32	1.8	-1.1	-1.1	-2.3	
6	12.5	1.8	1.4	-0.28	0.28	33	0.8	-1.3	-1.3	-1.2	
1	(3.4)	0.5	-1	-1	0	32	7	-0.42	-0.14	-4	
2	7	3	-0.34	-1	-1	33	7	-0.14	-1	-1.8	
3	11	1.1	0	0	-1	34.5	2	-0.1	-0.1	-4.2	7 - 17 - B
4	11	1.1	0	-1	-1	33	1	0	-3	-3	
5	11	1.1	-1	1	0	33	1	1	-3	-1.4	
2	14.5	0.37	-1	-1	-3	40	4.5	-0.45	-1.8	-5.1	
3	14.5	0.37	-1	1	-2	41.5	2.6	-3.7	-3.3	-9	
4	14.5	0.74	-1	-1	-1.9	38	2.2	-1.8	-2.3	-3.6	7 - 24
5	15	0.37	-1	0	-1.2	37	0.74	-1.3	-2.7	-~~1~~3.0	
6	15.5	0.37	-1	-1	-1.8	37.5	1.9	0.26	-0.26	-1.3	
7	15.5	0.37	-1	-1	-1.9	38	1.5	0	0	-1.8	

TABLE III (continued)

Latency of Augmenting Components During SP

Response	UC		A P 0.03 mA	0.1 mA	0.3 mA			A N 0.03 mA	0.1 mA	0.3 mA	
2	13.3	1.1	1.3	1.3	1.3	30	4.3	1.2	-0.39	1.2	
3	20	4.3	-0.46	---	0	37.5	4.3	---	-1.7	1.2	
4	21	3.3	-0.39	-0.39	-0.39	40	4.3	1.1	0	2.3	
5	23	2.3	-1	---	-1	51.3	3.2	1.1	-3.6	-0.47	7 - 5
6	21	3.3	-0.39	---	-0.39	53	2.2	1.1	-5.7	-1	
7	23	2.3	0	---	1	53	2.2	1	-1.1	---	
8	21	3.3	0.22	---	1.1	53	2.2	---	1	-1	
9	23	4.3	-0.59	---	0.59	50	4.3	1.2	1.2	-0.59	
			0.25 mA	0.5 mA	0.75 mA			0.25 mA	0.5 mA	0.75 mA	
1	(4.5)	0.43	---	---	---	17	0.86	---	-10	-11	
2	9	0.86	0	---	---	18	1.7	-1.7	-1.1	-3.5	
3	9	0.86	0	---	---	10.5	0.43	-0.35	-1	-1	
4	10.5	1.4	-0.35	---	---	18	1.7	-0.59	0	-1.2	4 - 21
5	11	0.86	-2.3	---	---	18.5	3	-0.83	-0.83	-0.5	
6	10	1.7	0	---	---	18	1.7	-0.59	-0.59	-0.59	

unconditioned trains.

AP peak latencies were not significantly altered by SP. AN peaks, however, were consistently earlier during the initial few responses of the conditioned trains, particularly at the higher levels of direct current intensity. In four of the five experiments compiled in Table III, this effect is seen as a marked decrease in the latency of AN. The latency measurements from experiment 7-24 have been plotted in Figure 5 to demonstrate this alteration. The hatched portion of the figure represents the parameters of the unconditioned AN peak latencies. The width of the hatched figure for each response represents the variation in latency of the unconditioned responses (2 S.D.). During a moderate degree of polarization (0.1 mA) the AN peaks of the first few responses in the train tended to fall earlier than the unconditioned value, though the decrease in latency was not significant according to the standard adopted earlier. At the higher level of polarizing current intensity (0.3 mA) there was a striking decrease in the latency of AN which progressively fell with successive responses to insignificant levels near the end of the train.

A closely related change from beginning to end of the conditioned trains was the successive growth in amplitude of AP. In other words, there was a correlation between the size of the AP and the latency of the peak of

FIGURE 5

Alterations in latency of AN during SP. Response number is on the ordinate, latency to the AN peak on the abscissa. The hatched figure represents the parameters of the unconditioned responses. The horizontal bar at each response represents a variation of 2 S.D. The mid-range is indicated as a short vertical marker on each bar. Note that the mid-ranges of responses 2 - 7 did not vary greatly from the beginning to the end of the train. SP decreased the latency of the initial responses in the train, but late response peaks were unchanged. (u - 24, 8/sec., 0.1 msec., submaximal stimuli to n. ventralis posteromedialis, recording from anterior sigmoid gyrus)

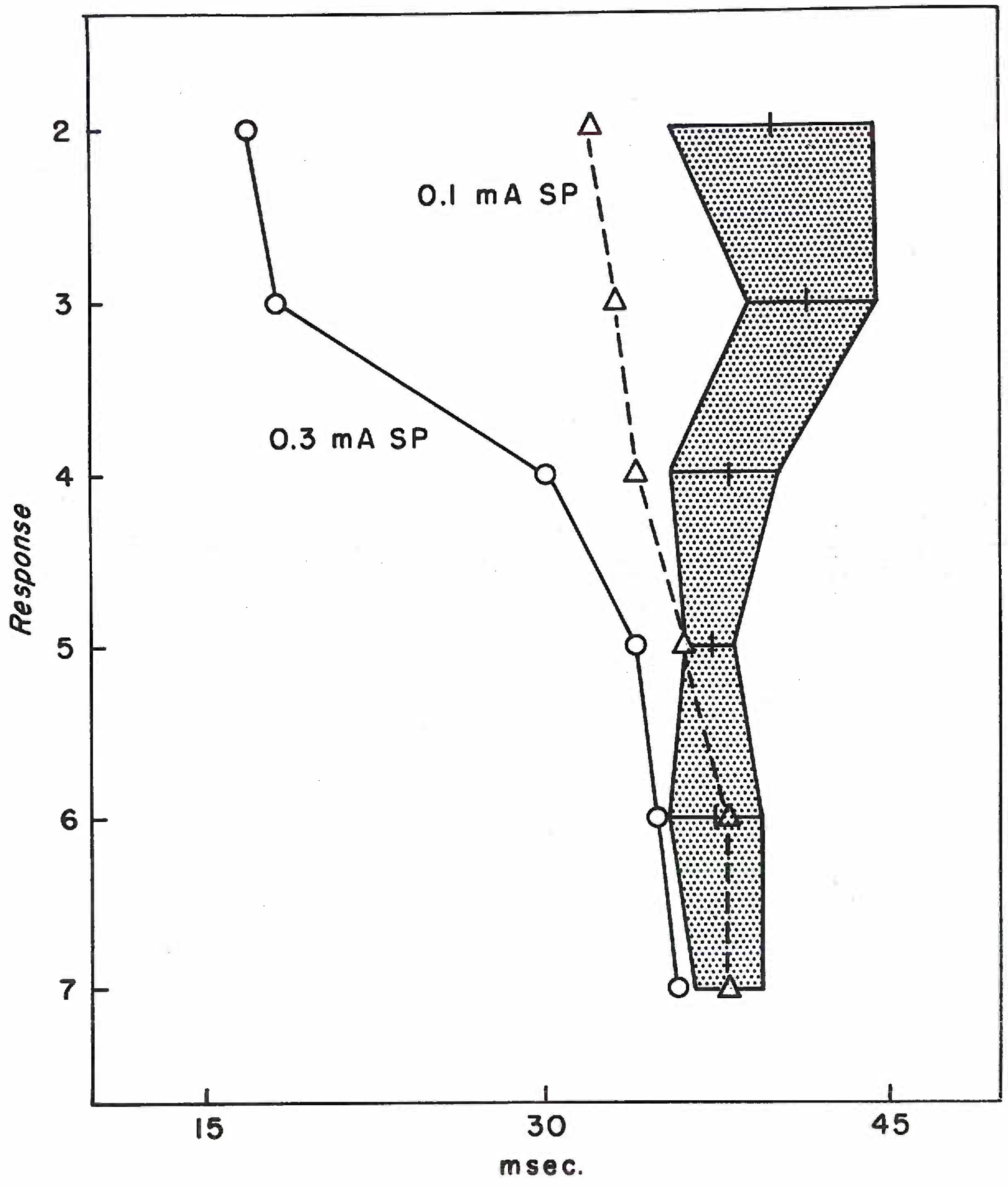

0.1 mA SP
0.3 mA SP
Response
2
3
4
5
6
7
15
30
45
msec.

TABLE IV

Relationship of A P Amplitude and A N Latency, 7 - 24, 0.3 mA S P

Response	Amplitude AP (μV)	% of $\bar{\bar{x}}$ #4 - 7	Latency AN (msec.)	% of $\bar{\bar{x}}$ of #4 - 7
2	40	18	16	48
3	80	37	18	54
4	200	92	30	89
5	220	101	34	102
6	230	105	35	103
7	220	101	36	107

Average ($\bar{\bar{x}}$) #4 - 7
217.5 μV

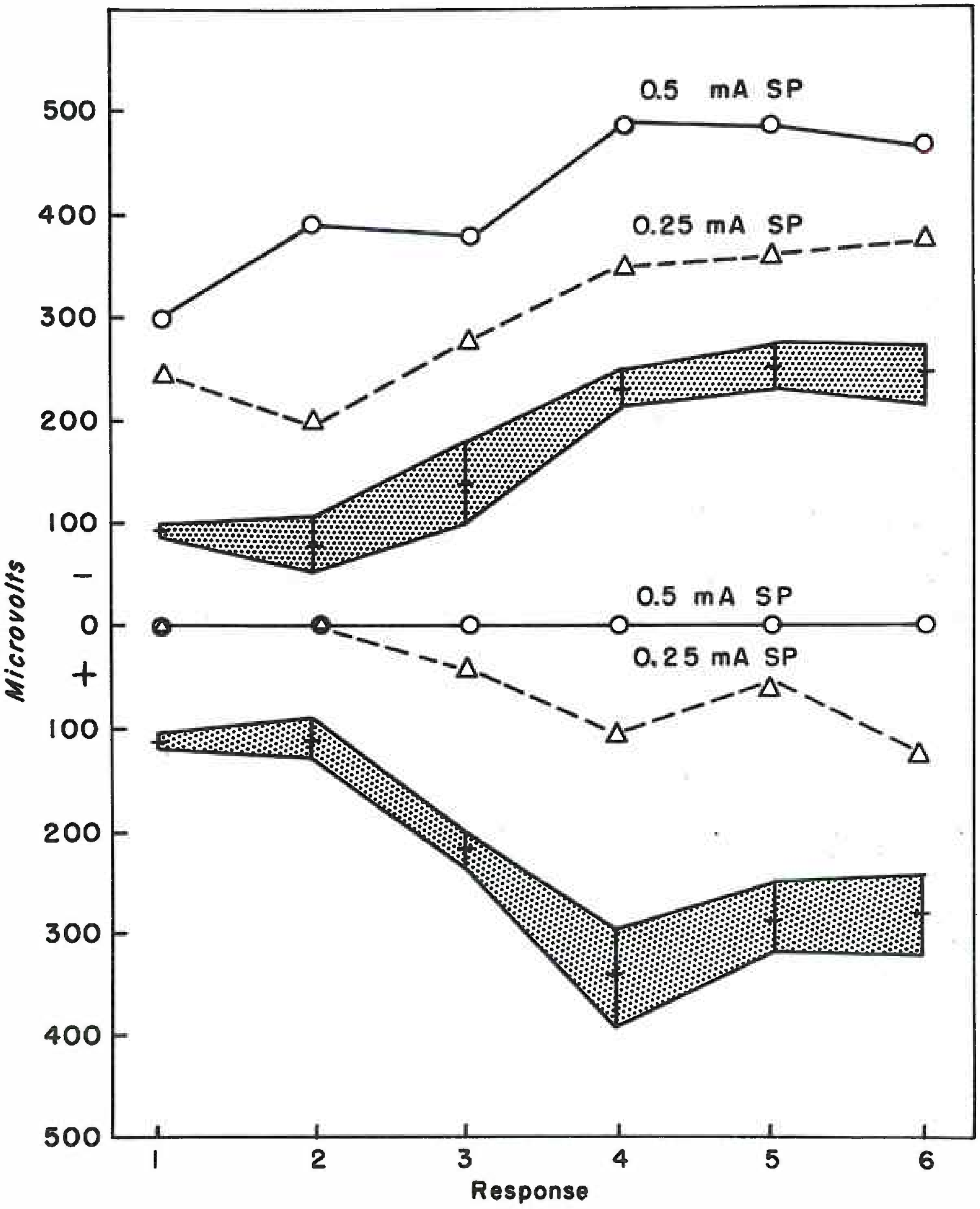
Average ($\bar{\bar{x}}$) #4 - 7
33.5 msec.

the AN at higher intensities of SP. There was no such correlation between AP amplitude and AN peak latency in the unconditioned responses, as is obvious from the stable value for unconditioned AN peaks throughout the train illustrated in Table III and in Figure 5. The relationship between conditioned AP amplitude and the latency of AN during polarization at 0.3 mA is demonstrated in Table IV. The data are computed also in per cent of an average value of voltage or latency of those responses which have reached a stable value in the train. The data in this table are characteristic of the findings in three experiments. In two other experiments, each of which showed the great decrease in AN peak latency in the initial responses in the train, the AP was completely abolished at this level of SP. The essential validity of the correlation was strengthened, however, by the observation that the initial portion of AN had less slope in the later responses in the train than in the initial responses. This suggested that AP was present in the later responses, even though the net potential difference recorded at the surface was negative.

SP affected the amplitude of augmenting responses according to the relation demonstrated in Figure 6. The upper hatched portion of the figure represents the measurements of unconditioned AN peaks. The lower hatched portion

FIGURE 6

Effects of SP on the amplitude of the components of augmenting responses. Amplitude in microvolts is on the ordinate, response number on the abscissa. The lower hatched figure represents the amplitudes of the unconditioned AP, the upper hatched figure the parameters of unconditioned AN. The width of the hatched figure has the same significance as outlined in previous figures. Note the difference in the number of stimuli required for AP and AN to reach maximum amplitude in the train. During conditioning, there was a change in amplitude of both components which was proportional to the polarizing current intensity. The net effect of SP was to increase the negativity during each response. At 0.5 mA the AP has been completely abolished. The responses in the other trains reach their maximum value after the same number of stimuli. (4 - 21, 6/sec., 0.2 msec., submaximal stimuli to n. centralis medialis, recorded from the anterior sigmoid gyrus)



0.5 mA SP
0.25 mA SP
0.5 mA SP
0.25 mA SP
500
400
300
200
100
−
0
+
100
200
300
400
500
Microvolts
1
2
3
4
5
6
Response

of the figure represents the same measurements of the unconditioned AP peaks. The width of the band plotted for each response represents an amplitude of two S.D.'s estimated from the range of the unconditioned values. The values for the unconditioned responses emphasize the point mentioned previously that AP frequently reached its maximum earlier in the train than did AN. The proportional relation between the intensity of polarizing current and the change in peak amplitude for each response in the train is emphasized in this figure. The conditioned trains tended to reach their maximum value at the same time as the unconditioned trains. The AP was completely abolished at a current intensity of 0.5 mA. The results illustrated in this figure are quite typical of augmenting experiments during SP, with the qualification that the actual intensity of polarizing current at which complete abolition of AP occurred varied from experiment to experiment.

3. Summary.

SP affected the negative component of both responses in a similar fashion, the net result being an increase in amplitude which was proportional to the polarizing current intensity. The enhancement of AN was associated with a corresponding diminution in AP. The latencies of RN and of AP during SP were unpredictable, and, in view of the shortcomings of the statistical design of the experiment, were not significantly altered. AN reached its peak significantly earlier in the initial responses in the train and its latency change was correlated with the amplitude of the AP during the higher levels of polarizing current.

D. Effects of surface negative polarization.

1. Recruiting.

The changes in recruiting responses conditioned by SN differed in several respects from the changes accompanying SP. The alterations produced in RN consisted of a progressive reduction in amplitude and duration during conditioning with SN. This is illustrated in Figure 7. A concomitant change seen in all the recruiting experiments was the development of RLP with increasing current intensities. In three experiments, a small unconditioned RP was present, but, due to the irregularities of its appearance even in the same train of responses, it was not subjected to a careful analysis. During SN, however, RP was frequently seen and was often closely related to the enlargement of RLP. A careful study of all the conditioned recruiting responses resulted in the distinct impression that SN, by reducing the amplitude and duration of RN, permitted the registration of an underlying positive wave of which RP and RLP were component parts. Additional examples of this change in wave form are presented in Figure 8. These samples suggest that conditioned responses

FIGURE 7

Effects of SN on the configuration of recruiting responses. Responses 1 - 7 are illustrated in each train. Top and bottom trains were unconditioned, the remaining trains were recorded during the indicated intensity of polarizing current. Increasing levels of SN decreased the amplitude and duration of RN. Concomitantly, the RLP was increased, and in some responses, the RP. Both conditioned and unconditioned trains reached maximum amplitude at response 7. (7 - 24, 8/sec., 1.0 msec., submaximal stimuli applied to n. centralis medialis, recording from anterior sigmoid gyrus)

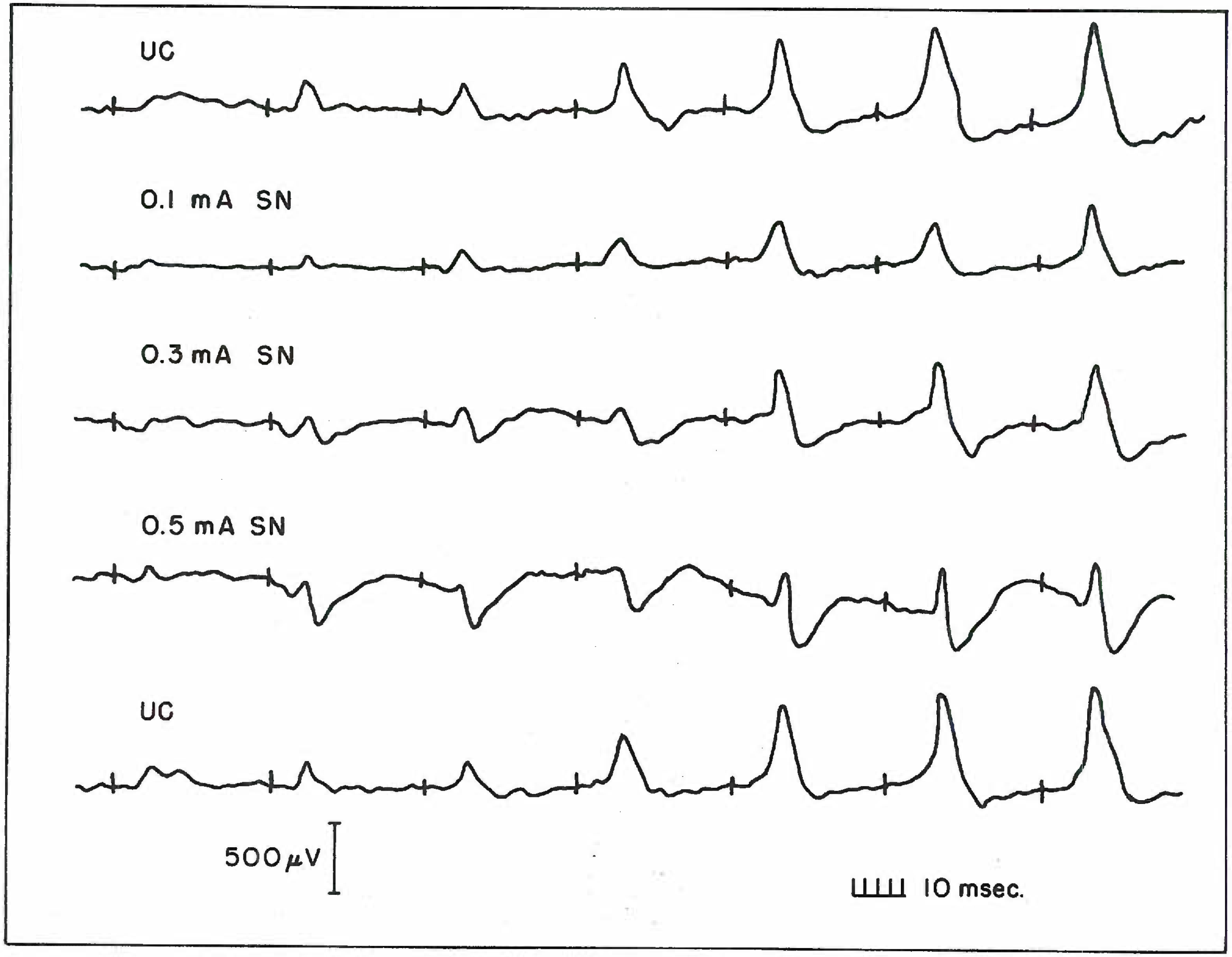
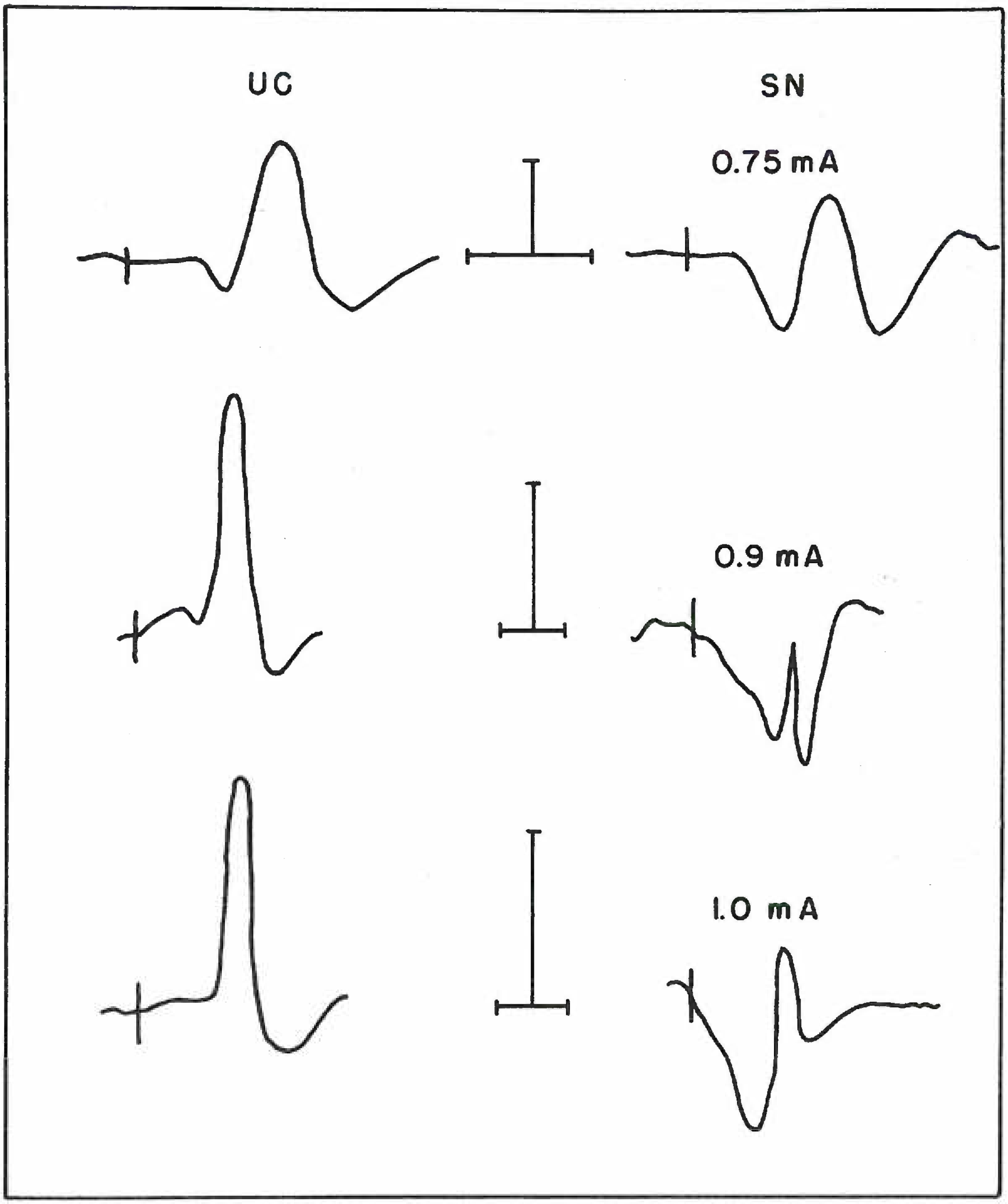

UC
0.1 mA SN
0.3 mA SN
0.5 mA SN
UC
500 μV
10 msec.

FIGURE 8

Unconditioned recruiting responses with the corresponding response during SN. Note the decrease in latency to the onset of RP and the contours which suggest that RP and RLP are parts of the same positive wave during SN. The positive wave (RP and RLP) may be in phase with RN, as in the upper figure, or out of phase, as in the lower figures. Calibrations represent 20 msec. and 500 microvolts. Upper tracings (4 - 21, 8/sec., 1.0 msec., submaximal stimuli to n. centralis medialis, recording from anterior sigmoid gyrus, response 10). Middle tracings (3 - 27, 8/sec., 0.8 msec., submaximal stimuli to n. centralis medialis, recording from left anterior sigmoid gyrus, response 7). Lower tracings (same experiment as above, recording from right anterior sigmoid gyrus, response 7).


UC
SN
0.75 mA
0.9 mA
1.0 mA

began soon after the stimulus artifact and that the apparent long latency of the unconditioned recruiting responses might in reality be due to a period of zero potential change during which the negativity of local depolarization is balanced by the simultaneous occurrence of a distant sink which, acting by itself, would produce surface positivity. Occasionally it was noted that SN revealed a small positive response following the first thalamic stimulus and which corresponded in time with the RP. This response incremented and became continuous with RLP with succeeding stimuli. The RN then developed in this positive trough. This observation lends credence to the idea that RP and RLP were portions of the same potential wave and that the RN and the positive components revealed during SN may in certain cases be separated from one another.

An analysis of the RN peak latencies during SN revealed results analogous to those found during SP. These data are presented in Table II. Approximately 80% of the conditioned samples measured fell within 2 S.D. of the mid-range of unconditioned RN peaks. Of the remaining 20%, 2.5% were positive, representing an increase in the latency, while 17.5% of the samples were more than minus 2 S.D. from the mid-range of the unconditioned values. There was the same lack of relation between the conditioning current intensity and the degree of change in latency as was seen in SP. Again the most likely conclusion must be that the RN peaks are not significantly altered by polarization.

The decrease in the amplitude of RN during progressive SN is illustrated by the filled symbols in Figure 3. In all responses except the first, the RN is significantly decreased from the unconditioned value and to a degree that is proportional to the conditioning current intensity. The apparent failure of SN to influence the first response in this particular experiment represents an exception to the other four experiments analyzed in this way. The amplitudes of RN peaks throughout the train tend to increase to the same degree that the unconditioned response amplitudes increase. Once again, it is apparent that polarization did not alter the number of stimuli required for the attainment of maximum amplitude in each train.

2. Augmentation.

Augmenting responses showed alterations during SN which in certain respects were the reverse of those seen during SP. The AP was enhanced in amplitude and duration while the AN was decreased, both alterations bearing a relation to the intensity of the polarizing current. These alterations are illustrated in Figure 9. The net effect of SN on the augmenting responses was an increase in the total positivity, or alternately, a net decrease in the

FIGURE 9

Effects of SN on the configuration of augmenting responses. Responses 1 - 6 are illustrated in each train. The tracings are arranged as in Figure 4. Increasing intensities of SN enhanced AP and diminished AN. The net effect was an increase in the amount of positivity, or alternately a decrease in the negativity recorded in each response. SN did not change the number of stimuli required for the responses to reach a maximum in each train. (7 - 17 - B, same stimulus parameters and recording site as in Figure 4)

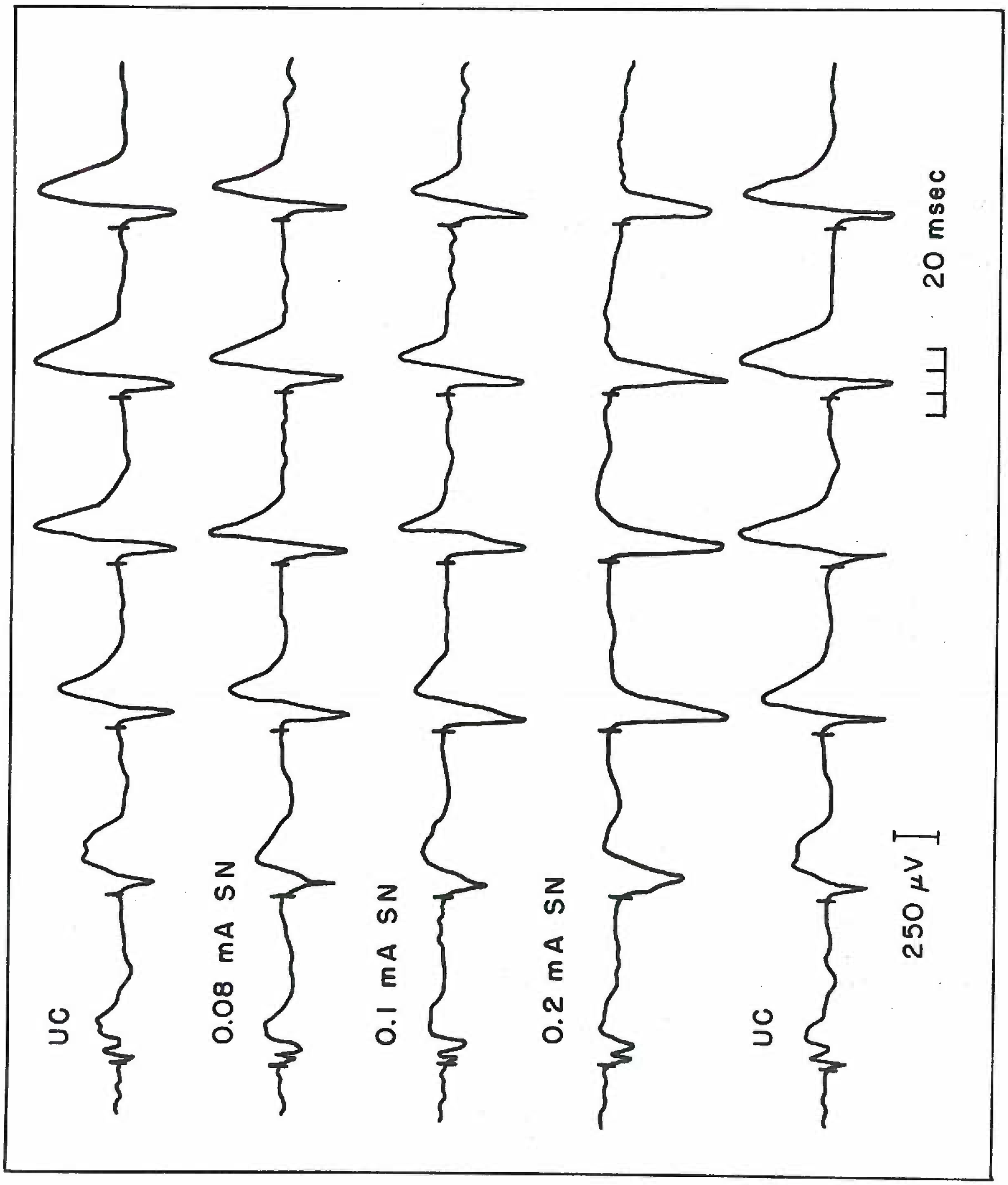

UC
0.08 mA SN
0.1 mA SN
0.2 mA SN
UC
250 μV
20 msec

TABLE V

Latency of Augmenting Components During SN

			A P					A N			
Response	UC		0.08 mA	0.1 mA	0.3 mA	UC		0.08 mA	0.1 mA	0.3 mA	
	MR (msec.)	S.D. (msec.)	(S.D. from MR)			MR (msec.)	S.D. (msec.)	(S.D. from MR)			
1	(3.5)	1.2	0.42	0.42	0.42	34.5	4.3	1.2	---	1.2	
2	7.5	3	0.5	0.5	2.1	37	5.3	-0.19	0.57	1.1	
3	12	1.5	-0.67	-1.3	0	35.5	2	0.25	2.2	---	7 - 17 - A
4	11.5	1.8	-0.28	-0.28	0.84	33	2.3	0	-0.43	---	
5	12.5	1	2.5	1.5	1.5	32	1.8	-0.55	0	---	
6	12.5	1.8	-0.28	0.28	1.4	33	0.8	-1.2	2.5	---	
1	(3.4)	0.5	1	-0.45	1	32	7	0.29	1	1	
2	7	3	1	1	1	33	7	0.14	1.1	1	
3	11.1	1.1	1	-2.7	-1	34.5	2	0.5	3	---	7 - 17 - B
4	11	1.1	0	-1	-1	33	1	-1	1	---	
5	11	1.1	-1	0	0	33	1	-1	0	---	
2	14.5	0.37	2.4	1	2.4	40	4.5	---	0.48	---	
3	14.5	0.37	1	-1	---	41.5	2.6	0.58	-2.1	---	
4	14.5	0.74	2	2	2	38	2.2	---	0.9	---	
5	15	0.37	1	0	1	37	0.74	-1.3	1.3	---	7 - 24
6	15.5	0.37	1	-1	2.2	37.5	1.9	0.26	1.3	---	
7	15.5	0.37	1	1	2.3	38	1.5	0	1.8	---	

TABLE V (continued)

Latency of Augmenting Components During SN

			A P					A N			
Response	UC		0.03 mA	0.1 mA	0.3 mA	UC		0.03 mA	0.1 mA	0.3 mA	
2	13.3	1.1	1.3	-0.73	6.1	30	4.3	0	-1.2	---	
3	20	4.3	0.46	1.1	1.1	37.5	4.3	0.58	-0.58	---	
4	21	3.3	0.39	---	1.2	40	4.3	1.1	1.1	---	
5	23	2.3	-1	1	0	51.3	3.2	-1.1	1.1	---	7 - 5
6	21	3.3	-0.39	-0.39	0.39	53	2.2	1.1	-1.1	---	
7	23	2.3	1	-1	1	53	2.2	-1.1	1.1	---	
8	21	3.3	1.1	1.1	0.3	53	2.2	1	-1	---	
9	23	4.3	0.59	0.59	0	50	4.3	0.58	0	---	
			0.25 mA	0.5 mA	1.0 mA			0.25 mA	0.5 mA	1.0 mA	
1	(4.5)	0.43	1	-1	1	17	0.86	1	1	1	
2	9	0.86	1	0	1	18	1.7	-1.1	-1.1	-1.1	
3	9	0.86	---	1	-1	11.5	0.43	-0.35	1	-1	
4	10.5	1.4	---	-1.7	-0.35	18	1.7	-1.2	-1.2	-1.2	4 - 21
5	11	0.86	0	-1	-1	18.5	3	-0.83	-0.83	-0.83	
6	10	1.7	0.59	0	-0.59	18	1.7	-1.3	0	0	

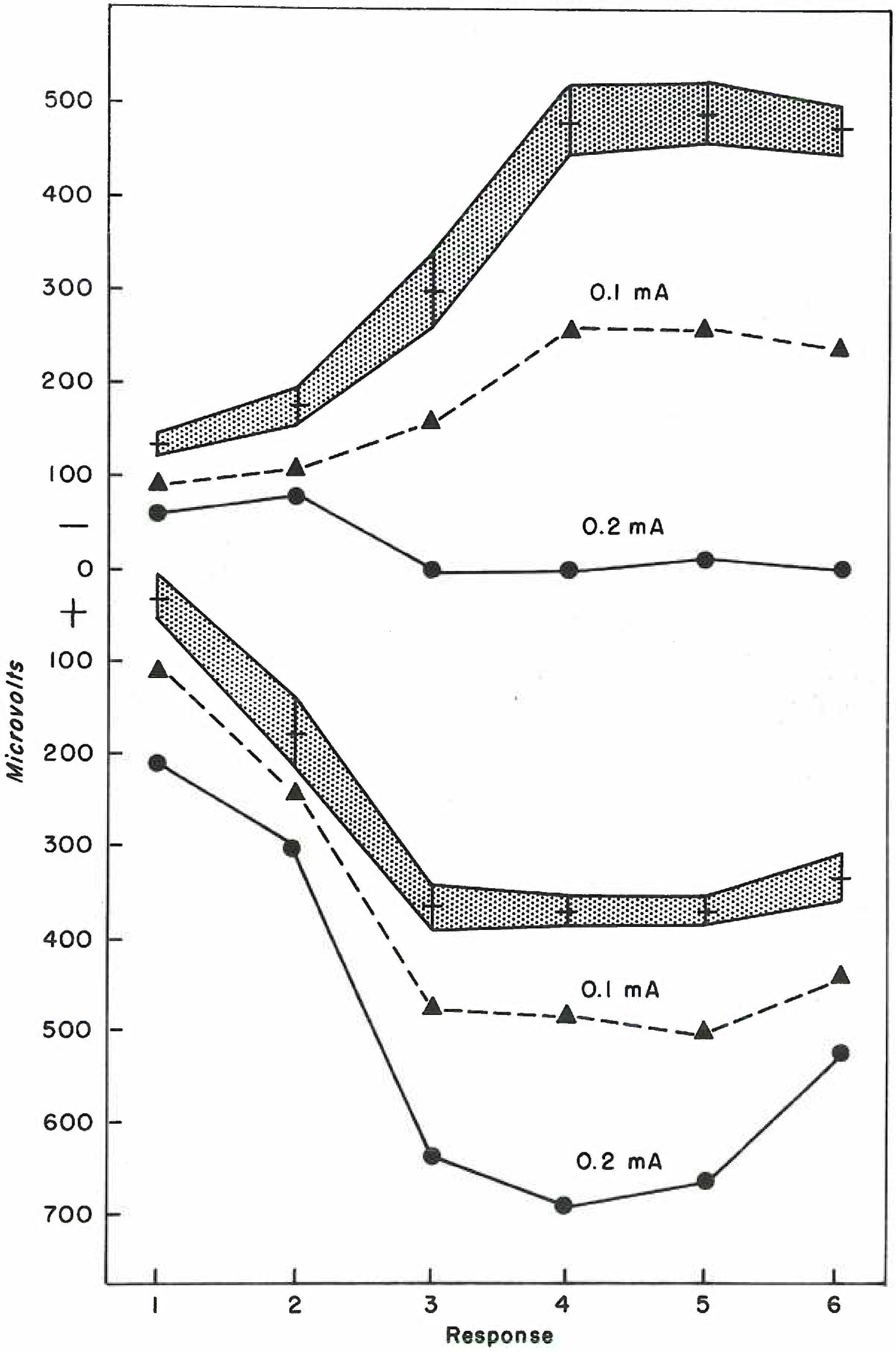
negativity of the augmenting responses.

With a few exceptions, the latency of the AP and AN peaks was not changed during SN. The data on measurement of augmenting peaks at various levels of conditioning current intensity are included in Table V. In 6.5% of the samples in Table V, AP was significantly greater than the mid-range of the unconditioned response latencies and some of these represented increases in latency, others, decreases. In 4% of the conditioned responses AN peaks had latencies outside the level of significance, some of them representing an increase in latency, others representing a decrease. There was no relation between stimulus intensity and the degree of change in latency in those instances where conditioning produced a change greater than 2 S.D. from the mid-range.

Figure 10 illustrates graphically the changes in amplitude produced at two levels of direct current intensity. The figure is typical of all the augmenting responses in this series of experiments. The upper hatched portion of the figure represents the mid-range and standard deviations of unconditioned AN while the lower hatched portion of the figure represents the same parameters of unconditioned AP peak amplitudes. The AN peaks reached their maximum amplitude later in the train than did AP peaks in conformance with previous data. SN increased the amplitude

FIGURE 10

Effects of SN on the amplitude of the components of augmenting responses. The figure is arranged as in Figure 6. This figure illustrates the tendency of AP to reach its maximum earlier in the train than AN. There was a diminution in the amplitude of AN and an increase in AP which was proportional to the polarizing current intensity. The net effect of SN was to increase the positivity recorded in each response. Note that at 0.2 mA, AN has been virtually abolished. With this exception, the conditioned trains reach a maximum after the same number of stimuli as do the unconditioned trains. (7 - 17 - B, analysis of experiment illustrated in Figure 9)



500
400
300
200
100
—
0
+
100
200
300
400
500
600
700
Microvolts
0.1 mA
0.2 mA
0.1 mA
0.2 mA
1
2
3
4
5
6
Response

of AP and decreased the amplitude of AN in each response to a degree that was proportional to the intensity of the polarizing current. The parallelism between the lines connecting the amplitudes of the conditioned responses and the general contour of the unconditioned response peak amplitudes is again apparent, and the observation that polarizing currents did not alter the number of stimuli required for the responses to reach their maximum in the train is seen to be applicable to SN polarization of augmenting responses.

3. Summary.

SN diminished the negative component of both recruiting and augmenting responses. The positive component of augmenting was concomitantly increased, while an enhancement of RP and RLP was seen in recruiting responses. Viewed in another way, SN diminished the degree of negativity recorded during both types of evoked potential. Certain observations during recruiting responses suggested that RP and RLP were parts of the same positive potential wave and that diminution of RN exposed this wave in its more or less pure form.

E. Stimulus intensity of threshold thalamic shocks during polarization.

In one recruiting and one augmenting experiment the stimulus intensity at the thalamic stimulating electrode necessary to evoke threshold responses was measured. The threshold intensity was considered that current which produced an observable incremental cortical response with repetitive stimuli. The results of these measurements are shown in Table VI. This analysis revealed that polarizing currents did not alter the thalamic threshold for the production of a cortical response, even though once a threshold intensity was reached the individual cortical responses might be larger or smaller than the responses evoked in the absence of the flow of polarizing current.

F. Effects of polarization on the relayed pyramidal volley of augmenting responses.

In a number of experiments, a concentric recording electrode was placed in the pyramidal tract at the level of the pons, making possible the simultaneous recording of the surface potentials and the pyramidal relayed volley. The potential recorded in the pyramidal tract during augmentation was a monophasic positive wave which began 5--8 msec. after the thalamic stimulus artifact and persisted for the duration of AP. Occasionally, the positive potential was followed by a second small positive or negative deflection which coincided temporally with the AN recorded at the surface.

The pyramidal relayed volley was unchanged by cortical polarization in all experiments in which such

TABLE VI

Thalamic Threshold Stimulus Intensity During Conditioning

Recruiting (7 - 16 - A) (Stimulus intensity in mA)			(Augmenting (7 - 15) (Stimulus intensity in mA)		
Polarizing Current (mA)	SP	SN	Polarizing Current (mA)	SP	SN
0.04	0.28	0.25	0.04	0.07	0.07
0.08	0.30	0.28	0.08	0.09	0.09
0.10	0.30	0.30	0.20	0.07	0.09
0.20	0.30	0.27	0.50	0.12	0.08
0.40	0.27	0.27	1.00	0.13	0.08
0.60	0.24	0.30	2.00	0.09	0.08
1.00	0.28	0.32	----	----	----

Recruiting:
Pulse duration: 0.5 msec.
Range UC: 0.25--0.32 mA

Augmenting:
Pulse duration: 0.1 msec.
Range UC: 0.06--0.12 mA

recording was utilized, even though the corresponding cortical response might be markedly altered. Severe cooling or severe mechanical trauma to the cortex did diminish and occasionally abolish the relayed volley. The augmenting responses recorded during these procedures produced large monophasic positive potentials which resembled, in most respects, the augmenting responses produced during SN.

Unconditioned recruiting responses were generally not accompanied by a pyramidal relayed volley and none was produced by polarization of the cortex.

In spite of the consistent absence of any alteration in the pyramidal relayed volley during polarization, this negative result must be considered tentative until further control procedure and a more thorough study of the origin of the pyramidal relayed volley are performed.

G. Alterations produced inconstantly by polarizing currents.

1. Effects of SP on ALP and RLP.

The late positive deflection was increased in amplitude in both recruiting responses in certain experiments. This increase particularly during augmenting responses was occasionally quite marked, and the ALP in these cases continued up to the succeeding response in the train. The amplitude of the increase was proportional to the intensity of the polarizing current and was most prominent in those experiments which had a fairly prominent RLP or ALP. The conditions favoring the production of this phenomenon were not studied in detail.

2. Late negative wave during SN of augmenting responses.

In four of six experiments on augmenting responses, the ALP was reduced with SN and a late negative slow wave developed which was clearly separated from the AN. This wave was of low amplitude, beginning 80--100 msec. after the thalamic stimulus artifact and frequently persisted until the succeeding stimulus artifact. The contour of this deflection is seen in the 4th response, at 0.2 mA SN, Figure 9. The conditions favoring the production of this deflection remain obscure.

DISCUSSION

The pertinent observations in regard to the influence of cortical polarizing currents on recruiting and augmenting waves can be summarized briefly. There is a definite difference in the responsiveness of recruiting and augmenting waves to alteration by direct currents. Choosing an arbitrary standard, the augmenting negativity was depressed by current intensities less than one third those required for similar reduction in the recruiting negativity. The negative components of both responses, which present many similarities in the unconditioned state, were found to respond qualitatively in the same manner to the influence of electrical polarization. SP increased, SN decreased the amplitude and duration of the negative components of both responses. Augmenting responses were marked by a prominent initial positive component which was affected in a manner opposite to the augmenting negativity, SP decreasing its magnitude and SN increasing its magnitude. There was no comparable initial positivity in recruiting responses recorded at the cortical surface. However, during SN, an initial and a late positivity were substantially increased in size and appear to be portions of the same positive deflection. Thus it is apparent that the net effect of SN was to decrease the amount of surface negativity in both responses, while the net effect of SP was to increase the amount of surface negativity in both responses. The latency of the peaks of both responses were, in the main, not significantly changed by cortical polarizing currents. SP did significantly decrease the latency of the peak of the augmenting negativity in initial responses in the train, but as the augmenting positivity incremented to a maximum amplitude, this change in peak latency fell to levels which were not significantly different from the unconditioned augmenting negativity. The number of stimuli required for responses to reach maximal amplitude in a train was unchanged by the flow of polarizing currents. No alteration was observed in the parameters of the pyramidal relayed volley during cortical polarization. Lastly, there was no change in thalamic threshold stimulus intensity during the flow of polarizing currents.

It seems unlikely that polarizing currents alter the characteristics of the recording system used in these experiments. Non-polarizable recording electrodes were used in the vicinity of the different cortical polarizing electrode and the wick was never permitted to touch the cortical pick-up. Of even more significance was the observation that contour of the conditioned responses was the same when recording was done in such a way as to present evoked responses to the pre-amplifiers at a zero DC level.

The difference in responsiveness of the two responses studied in these experiments, though certainly prominent, is not considered evidence for the idea that recruiting and augmenting are manifestations of activity in basically different structures in the cerebral cortex. There are two possible explanations for this difference in susceptibility to alteration by direct current conditioning.

The first consideration is one of quantity. Are there more elements responsive to polarization taking part in one response than in the other? Unfortunately the data give no information which might help us weigh this possibility. The fact that unconditioned augmenting responses reach their maximum earlier than recruiting responses can not be considered evidence for a greater density of responsive elements in the former, because the eventual amplitude reached in both responses is in the same range, 250-1000 microvolts. On the other hand, the similarity of the maximum amplitude can not be considered evidence against the possibility of a greater density of responsive elements in augmenting responses, because numerous nervous structures are capable of undergoing graded responses (28, 46, 47, 48). Thus, fewer recruiting elements could conceivably be undergoing a greater change with the result that the final amplitude of the response in both instances might be the same. There is no information regarding the magnitude of the afferent volley in either response, nor have we an index of any evoked corticifugal activity during recruiting to compare with the volley relayed down the pyramidal tract during augmentation.

In the absence of any evidence for or against the idea of a quantitative difference in the elements responding to two types of thalamic stimulation, what qualitative factors might account for the difference in responsiveness to polarization? The most pertinent information in this regard indicates that there are two separate pathways to the elaboration of the final surface negative response. Careful depth recordings in the cortex reveal that augmenting responses originate in cortical layer IV. Recruiting on the other hand, when careful controls eliminate the possibility of simultaneous activity in specific thalamo-cortical fibres, is characterized by the presence of a sink which is restricted to the most superficial reaches of the cortex (27). The most likely inference to be derived from these data is that the negativity of both recruiting and augmenting responses represents the activity of similar structures, activated in different ways. For example, the augmenting negativity may represent the responses of superficial aspects of apical dendrites activated antidromically, analogous to the antidromic conduction of activity in apical dendrites during the primary response (37, 29), while recruiting responses may represent the activity of apical dendrites activated by superficial local synaptic depolarization. Again, the data do not reveal any ultimate explanations for the observed differences in responsiveness of these phenomena, nor do they offer any evidence for or against the supposition that the difference in responsiveness is related to the difference in the pathway by which the responses are evoked.

Granted that there are unexplained differences in the responsiveness of recruiting and augmenting to polarizing currents, the possible mechanisms of production of alterations in the contour of these responses require some comment.

Bishop (43) has proposed a scheme on strictly theoretical grounds which presumes that potential waves recorded at the cortical surface are constituted of the summated potentials of individual neuronal discharges. During polarization, these discharges would be altered in amplitude and/or polarity in a manner analogous to the behavior of short lengths of polarized axon. The explanation does not seem applicable to these experiments because of differences in recording technique and because no such alterations were produced in the contour of the action potentials of spontaneously active cerebellar units during the flow of direct current (49) or on spontaneously active cortical units recorded during the flow of direct currents.

A second possible mechanism by which the contour of the evoked potentials might be altered is a change in the number of unitary discharges making up the potential. Numerous studies have indicated that direct currents increase the number of neuronal discharges from single cells (49, 50, 51, 52, 53). However, there are two principal reasons why a change in the number of unitary discharges during polarization is considered an unlikely explanation for these results. In the first place, an absence of change in the thalamic threshold for the production of an incremental response argues against any increase or decrease in the number of unitary discharges during conditioning by direct currents. If an actual change in the quantity of responsive units during polarization occurred, a corresponding change in stimulus intensity would be required for the production of an observable cortical response. Secondly, it was observed on numerous occasions that the size of the relayed pyramidal volley during the production of augmenting waves was unchanged by polarization of the cortex, regardless of the intensity of the polarizing current. During recruiting responses, polarization of the cortex did not produce any relayed pyramidal volley when, as in most cases, there was none in the unconditioned response.

A third possible explanation for the changes produced by electrical polarization of the cortex may be based on the assumption that cortical waves are constituted of summated membrane depolarizations of a graded character. Instances where polarizing currents alter the magnitude of individual membrane changes have been mentioned previously (41, 42). It has been suggested that certain nervous structures are capable of undergoing activity of a graded nature in contrast to the classic prototype of nervous activity, the all-or-nothing response or action potential (47). These tissues respond in direct proportion to the intensity of the stimulus and are characterized by a lack of an absolute refractory period which means that steady stimuli may result in a membrane response which is maintained at a constant level for the duration of the stimulus. The lack of evidence for an increase in the actual number of responsive units during polarization plus the direct relation between the current intensity and the amplitude of the negative components of both recruiting and augmenting responses suggest that some structure capable of graded responses may be involved in the production of these alterations. Thus it is proposed that the qualitative similarity in the effects of polarizing currents on the negative component of the evoked potentials implies that a similar cortical structure is involved in the production of both these potentials, and the indications are that this cortical structure is one which responds to excitation in a graded fashion.

There are a number of observations which suggest that this structure is located in the superficial reaches of the cortex.

It has been known for many years that an electrode placed in an area of neuronal activity will be negative to neurologically inactive tissue. Therefore, it may be assumed that some sort of nervous activity is present in the vicinity of the surface electrode during both responses. The influence of polarizing currents will be greatest at the point where the current density is the greatest. This obviously is at the cortical surface near the recording electrode. An additional observation which emphasizes this point is the finding that the position of the indifferent polarizing electrode is not critical as far as producing alterations in the wave contours is concerned.

Further convincing evidence that most of the effects of polarization are at the surface is based on the observation that surface depressants mimic the action of SN of the cortex. Veratrine applied topically produced a steady negative potential at the cortical surface and evoked primary responses were predominantly positive (54), thus bearing an analogy to the effects of SN. Cocaine reduced recruiting responses to positive waves which were unchanged by complete ablation of the cortex (30) and the result of procaine and metycaine applied to the surface was similar (23). Moderate cooling of the surface of the cortex reduces both augmenting and recruiting responses to large positive deflections. In experiments in which a recording electrode was placed in the pyramidal tract, simultaneous recording of the surface augmenting potentials and the pyramidal relay indicate that the depressant effect on the AN occurred above the cortical layer IV because the relayed response was unchanged (26). The functional integrity of the thalamo-cortical afferents and the efferent neurones in layers IV and V must have been intact. Recruiting responses elicited in the same preparation were affected in the same way, again localizing the effects of cooling to the superficial cortex (26). Mention was made previously of the observations that polarizing currents did not alter the pyramidal relayed response, even though the corresponding cortical response during SN was predominantly a large positive deflection. Lastly, the effects of deterioration of the preparation from drying or cooling or of mechanical trauma to the cortical surface during the experiment resulted in the conversion of the evoked potentials to large positive deflections. On several occasions it was observed that SP applied to one of these deteriorated preparations resulted in the production of responses which had a negative component similar to normal unconditioned responses and in some cases the responses appeared exactly the same.

When the surface of the cortex was subjected to the action of an excitatory agent, opposite changes were produced in the evoked responses. The predominant effect of topical strychnine on the contour of evoked waves was an increase in the amplitude of the negative component of both recruiting (23, 55) and augmenting (55) responses.

The evidence therefore seems very convincing that the alterations produced by polarizing currents are closely related to changes produced in the upper reaches of the cortex.

The net effect of SN is a decrease in the amount of negativity recorded during both recruiting and augmenting responses. These alterations seem best explained on the basis of a persistent partial depolarization of the elements producing the surface negative components of the responses. If such partially depolarized elements are excited by one pathway or another, the change in membrane potential would be smaller in magnitude than that occurring in the unconditioned state.

It will be recalled that SN results not only in a reduction of the surface negative component of both evoked responses, but also results in a growth of the surface positive components (AP, RP, RLP). In the case of the augmenting response, the initial surface positivity is undoubtedly the reflection of depolarization occurring in layers IV and V of the cortex (27). The patterns of potential change occurring deep within the cortex during recruiting waves point to the existence of a zone of depolarization in some unknown subcortical locus (27, 30). It may be that SN actually increases the magnitude of these events, thus increasing the surface positive components of the evoked responses. However, such a supposition is not essential to the explanation of the increased magnitude of the surface positive components, since changes of surface potential represent resultants of all simultaneous events. Thus, it appears more likely that the increased amplitude of the surface positive components of the evoked responses simply represents an absence of concurrent surface negativity. According to this view, the reduction of the surface negative component merely reveals the existence of a surface positive component which was previously hidden or obscured.

SP increases the amplitude and duration of the negativity recorded during both augmenting and recruiting responses. The most reasonable supposition would be that the membranes responsible for the negative components become hyperpolarized during the flow of the conditioning current. Thus, when these membranes are activated over any pathway, the total shift of membrane potential would be greater than that occurring in the unconditioned state.

The simultaneous reduction in the amplitude of the surface positive components of the responses could again be a manifestation of a changing resultant.

The data on measurement of the latencies of the peaks during conditioning by polarizing currents is difficult to evaluate because of the inadequate design of the experiment from a statistical point of view. Taken as a whole, however, the experiments suggest that there is no change in the latency of the peaks during conditioning with the single exception of the augmenting negativity during SP. SP does produce a significant decrease in the latency of the negative peaks during the first few responses of augmenting trains. If it is assumed that the time course of the wave components is unchanged by polarization, this alteration does not fit the hypothesis. If one assumes that the time courses are altered, any change in the peak latency could be explained. There are no reliable data which give any information in regard to the effects of polarization on the time courses of these components.

The absence of any tendency in the trains to reach maximal amplitude earlier or later during conditioning requires a brief comment. The incremental characteristics of these phenomena are unaffected by polarization. In view of the evidence for the superficial locus of elements affected by polarizing current, this finding suggests that the mechanism for successive incorporation of cortical units giving rise to the negative components of the responses lies either deep in the cerebral cortex or in a subcortical structure. It has been proposed by a number of investigators that activity in closed neuronal circuits underlies the incrementation seen in a number of electrocortical waves including augmenting and recruiting responses (3, 14, 23). Thus thalamic neurones are facilitated by corticifugal activity from the preceding evoked response at the same time that an additional thalamic stimulus is applied, resulting in a progressively greater evoked cortical response. One might anticipate then that an alteration of an evoked cortical response with polarizing current might produce an alteration in the subsequent cortico-thalamic volley which then should be manifest as a change in the number of stimuli required for the responses to reach their maximum in the conditioned trains. Although this suggests that the concept of thalamo-cortical reverberating circuits is not tenable, other explanations could account for this apparent inconsistency. The cortical components of the reverberating circuit may lie deep in the cortex and, like the pyramidal tract efferents, be unaffected by polarizing currents. The negative components of recruiting and augmenting may represent activity in structures which are not directly involved in the thalamo-cortical circuit. Unfortunately the data do not suggest any reasonable explanation for the failure to alter the incremental characteristics of these responses.

On several occasions, the apical dendrites of cortical pyramidal cells have been mentioned as a possible structural substrate for at least the negative components of both recruiting and augmenting responses. Apical dendrites are in some respects excellent candidates for the structure which is common to both phenomena. The superficial layers of the cortex are densely packed with the terminal arborations of the apical dendrites (56). Synaptic contact on the surface of the pyramidal cell is made in two regions, the so-called para-dendritic endings on more superficial dendritic structures, and the pericorpuscular endings on basal dendrites and cell body proper (57). This could account for the differences in the responsiveness of the cortico-spinal system during augmenting and recruiting responses if specific fibres terminated in the vicinity of the pyramidal tract efferents and unspecific fibres from stimulation of the midline nuclei made a distant contact on the distal portions of the apical dendrites (7). Mention has been made of the graded response characteristics of apical dendrites (28, 46, 47, 48, 54) and also of the resemblances of the changes produced in these experiments to activity in graded response tissues. It also seems reasonable that a tissue which is capable of undergoing graded responses would be very likely to be responsive to a steady conditioning influence such as direct current. It may be possible that the incremental characteristics of these responses might be dependent upon those portions of the neurone lying more deeply in the cortex and relatively unaffected by the influences on the terminal portions of the apical dendrites. And lastly, the great surface area of the apical dendrites close to the surface should make them especially susceptible to topically applied drugs, to cold, to trauma, and to the influence of polarizing currents.

Unfortunately, it still can not be positively stated that apical dendrites give rise to negative potentials seen in thalamically evoked potentials or of other cyclic potential waves which are marked by a prominent surface negativity. At the present time this speculation seems to fit many of the observations made in regard to these phenomena.

SUMMARY

1. Recruiting and augmenting responses were recorded from the sensori-motor cortex of cats during the flow of electrical polarizing currents. Observations on the responsiveness, wave form, pattern of pyramidal relayed activity, thalamic threshold stimulus intensity and rate of incrementation were made during polarization of the cortex giving rise to both types of electro-cortical waves.

2. Augmenting responses were more susceptible to alteration by electrical polarization than were recruiting waves.

3. The net effect of surface positive polarization was an increase in the amount of negativity recorded in each response. Surface negative polarization produced the opposite effect. These changes were explainable on the basis of increases and decreases respectively in the negative component common to both responses. The qualitatively similar reaction to polarization in both phenomena was considered evidence for the idea that the negative components represent similar forms of activity.

4. The latency of the peaks was unchanged by polarization with the exception of the augmenting negativity during surface positive polarization. In this case,

the initial responses in the train had a decreased latency which was related to the absence of a preceding initial positive component.

5. Polarization produced no change in thalamic threshold stimulus intensity, the pattern of relayed pyramidal activity, or the rate of incrementation during trains of either recruiting or augmenting responses.

6. The results were discussed in detail. It was concluded that the effects of polarization were best explained on the basis of alterations produced in some structure located in the superficial reaches of the cortex. The negative components of both recruiting and augmenting responses were produced by the activity of the same or similar structures.

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