Visually Evoked Slow Negativity in Rabbit Cortex.* (25608)

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A negative spike of 15 msec. duration can be evoked by direct activation of cerebral cortex, and a corresponding one (called recruiting response) by serial stimulation of the midline thalamus. In recent work(1,2,3) with D.C. recording we observed a slow negative wave which follows in the wake of each of these primary responses as a separate excitatory process of higher threshold, longer duration (250 msec.), marked propensity for summation upon repetitive stimulation, and longer than usual persistence following the end of a brief series of stimuli. The evidence for separate identity between spike and secondary process made it important to decide if such a late potential could also be evoked by stimulation of one of the paths leading from sensory end organs to cerebral cortex. We selected the evoked visual response as a test case, eliciting it both by optic nerve and light flash stimulation. The slow negativity alluded to had already been observed to follow the primary visual response. Bishop and O'Leary(4) observed it in rabbit cortex using a capacity coupled amplifier, and Goldring and O'Leary(5) saw it in D.C. records obtained by chopping an ink writer trace mechanically. However, in these prior studies its characteristics did not seem sufficiently unique to focus further attention upon it. In the present experiments upon the rabbit the slow negativity is a prominent potential, and accumulating data indicate its similarity to the slow processes previously shown to follow the direct cortical response and the recruiting wave(2,3). Hereafter we describe it and relate it to other electrical events of visual cortical response.

Method. Thirty-two rabbits weighing 1.5 to 2.0 kg were prepared under ether anesthesia after which all wound surfaces were thoroughly infiltrated with 1% Procaine HCl. The animals were then immobilized with Flaxedil and respired artificially. Recording began one hour following discontinuance of ether. In one group of animals a needle insulated to near the tip was inserted into the optic nerve and another having 7 mm tip exposure was placed in the periosteum; nerve stimulus strengths varied between 0.8 and 3.0 V., pulse duration being 0.1 msec. (square wave through isolation transformer). In the other group the retina was activated directly by unfiltered 10 μsec. flashes from a Grass photic stimulator. An artifact for signalling the flash was obtained by leading from the output of a photoelectric cell to jack positions adjacent to those for the recording electrodes. Transcortical records were obtained from visual cortex using non-polarizable calomel electrodes and a D.C. amplifier, oscillograph and camera.

Results. Between threshold and maximal response to direct nerve stimulation the span was 0.9 to 3.0 V. When stimulus strength was raised by steps from a sub-threshold level the first sign of activation noted was a 250 msec. slow negative potential—*slow negativity* (Fig. 1A, 4). At somewhat above threshold for the slow negativity an earlier small positive deflection appeared, signalling initiation of the primary visual response (Fig. 1B, 1). That positive could also be seen with lower stimulus values but was then impossible to distinguish as a specific response component from similar pips which appeared spontaneously in the record of cortical activity (Fig. 1A, 1?). With further increase in stimulus strength the positive phase of primary response (component 1) and the slow negativity (component 4) were noted to grow together in amplitude (Fig. 1B and C), then the negative phase (component 2) of primary response and its ensuing after-positivity (component 3) also developed as stimulus strength increased, (Fig. 1D). Past Fig. 1C (1.3 V.) no further

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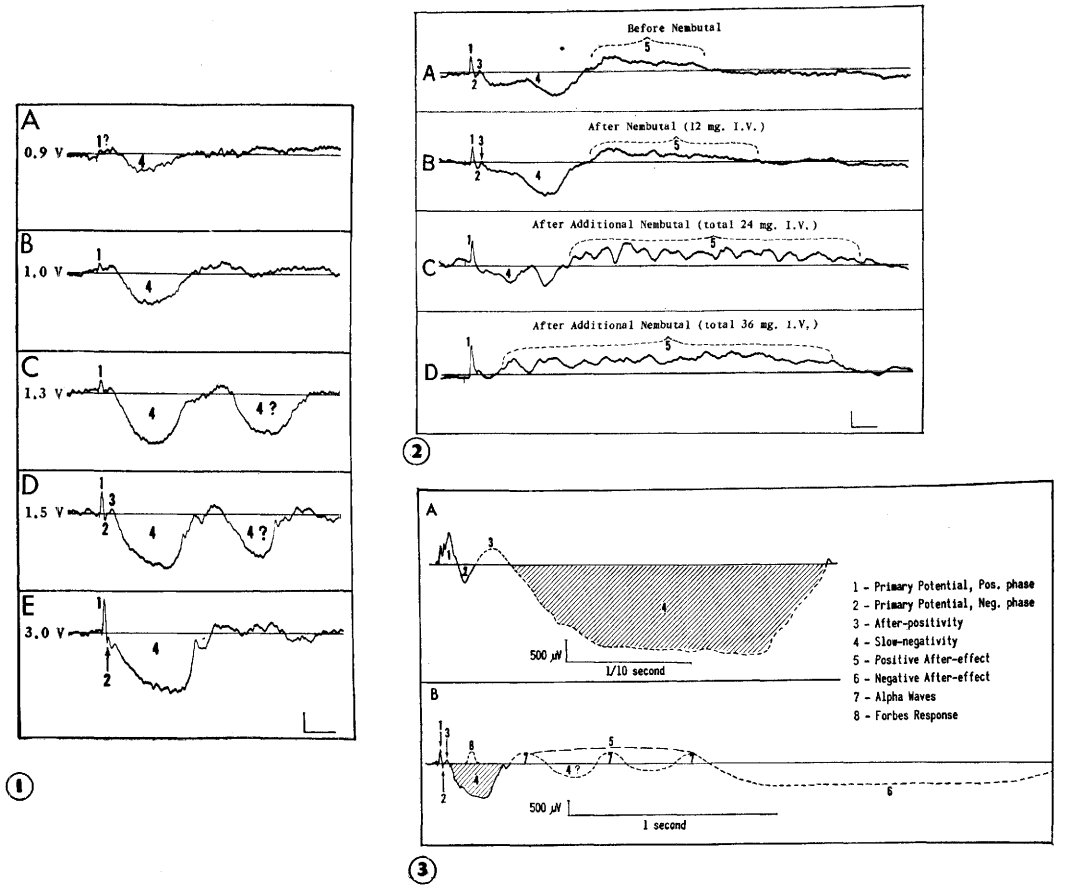

FIG. 1. Visual cortical responses to optic nerve stimuli of increasing strength. Numbers to left of each row refer to stimulus voltage. 1, positive phase of primary evoked potential. 1?, suspected of being positive phase of primary response. 2, negative phase. 3, after-positivity. 4, slow-negativity. 4?, may represent recurring slow negativity. Straight horizontal line in this and subsequent figures is arbitrary baseline against which potential changes are read. Up is positive, down is negative. Cal. key in lower right hand corner: vertical line of right angle = 500 μV; horizontal line = 100 msec. Shock artifacts retouched; otherwise photographs are those of original record.

FIG. 2. Effect of deepening Nembutal anesthesia on optic response evoked by flash stimulus to retina. I.V. = intravenous. 1, positive phase of primary evoked potential. 2, negative phase. 3, after-positivity. 4, slow-negativity. 5, positive after-effect. Cal. key in lower right hand corner: Vertical line of right angle = 500 μV; horizontal line = 100 msec. Shock artifacts retouched; otherwise photographs are those of original record.

FIG. 3. *A.* Evoked primary visual response and slow-negativity diagrammatically represented on time scale sufficiently fast to permit detection of positive spikes on ascending limb of primary positive potential. *B.* Diagrammatic representation of all cortical potentials known to occur with an optic nerve stimulus. Latencies, amplitudes and duration of these potentials and their temporal relationship to each other are those which obtain in actual experimental situation. Figure constructed by schematically adding potentials 4?, 5, 6, 7 and 8 to composite potentials 1, 2, 3 and 4 which is actual record taken from Fig. 1, D.

augmentation of the slow negativity (component 4) occurred even though stimulus strength was raised to 3V., which was maximal for the initial positive phase (component 1). This evidence suggests that whatever excites the slow negativity has a somewhat lower threshold than that of the majority of elements responsible for the primary phase of the response.

The latency of slow negativity varied from one animal to the next but approximated 50 msec. The main factor which contributed to variability appeared to be the after-positivity (component 3) following the negative phase

of the primary response (component 2). If sufficiently well-developed, that after-positivity can cut into the rise of the slow negativity thus lengthening the apparent latency of the latter. In addition, latencies appeared longer when the stimulus was near threshold. However, for any one experiment the latency for slow negativity remained constant for stimuli between half maximal and maximal strength (compare Fig. 1C, D and E).

Occasionally the response to a single nerve stimulus, submaximal for the primary visual response, showed a replica of the slow negativity component following the latter at a short interval (Fig. 1C and D, 4?). However, with maximal stimuli the apparent repetition of the slow negativity usually did not occur. The relation such repetition bears to the rhythmic alpha waves(4,8) which may succeed the evoked response is under study.

A slow negativity component also followed the primary visual response to photic stimulation (Fig. 2A, 4), the duration varying between 250 and 400 msec. That slow negativity, which was evoked by light flash, was followed by an equally enduring slow positive potential (Fig. 2A, 5) and thus differed from the response evoked by a shock to the nerve. We believe this slow positive potential to be identical with the positive after-effect of visual response described previously(6).

Activated by either nerve or flash stimulation the slow negativity was the most susceptible of the components to progressively deepening Nembutal anesthesia. Increments of 12 to 20 mg by successive intravenous injections to a total of 30 to 60 mg caused the slow negativity to disappear gradually. With disappearance it came to be replaced by the long positive after-effect of the primary response. Concurrently the primary response itself might increase somewhat in amplitude (Fig. 2, B through D).

Experiments to define the characteristics of the slow negativity are in progress. Thus we have shown slow negativity to summate in response to low frequency light flashes but (so far) not to a succession of nerve stimuli, to originate beneath the superficial layer of cortex, and to grow in size with surface applications of gamma amino butyric acid. These also characterize the slow negativities which occur as components of the direct cortical and recruiting responses(2,3).

Discussion. Recorded under optimum conditions slow negativity appears to be a unique feature of evoked response. It is actually a more prominent part of the evoked trace than is the primary component. This is graphically illustrated in Fig. 3A, primary visual potential and ensuing negativity being reproduced schematically upon a scale sufficiently rapid to permit analysis of the faster components of primary potential. It is important that all parts of the visual response do not become evident in any one preparation because of differential susceptibility of the components to anesthetic level; some appear with very light anesthesia, others reveal themselves only during deeper stages. However, a composite (Fig. 3B) can be constructed to reveal the temporal and amplitude relations between slow negativity and other components of visual response. These are identified as follows, with the significant features of each: *1,* positive phase of primary response assigned previously to activity in cell bodies and basal dendrites of deeper cortical layers(7,8); *2,* negative phase of primary response, presumed to signal antidromic activation of apical dendrites; it has a greater sensitivity to anesthesia than does the positive phase(7,8); *3,* after-positivity following the negative phase, a poorly understood part of the potential-complex having variable size and duration; *4,* slow negativity, seen only under light anesthesia; *5,* positive after-effect, seen best under moderately deep barbiturate anesthesia, during hypoxia or after repetitious episodes of convulsive activity(5); *6,* long-lasting negative after-effect usually associated with cortical activation(5); *7,* recurrent alpha waves(4) or so-called physiological after-discharge(8); *8,* Forbes "secondary" response, seen best under deep barbiturate anesthesia; it may also be recorded in the unanesthetized animal(9).

Summary. Visual cortex responses to optic nerve and retinal stimulation were studied by D.C. recording upon slow time line. A prominent slow negative wave (250 to 400 msec. duration), slow negativity, occurred in the wake of primary visual response. Evidence

indicates that when activated by nerve stimulation it has a threshold somewhat lower than that of primary response. Under moderately deep Nembutal anesthesia, slow negativity (evoked by optic nerve or light flash stimuli) disappears and is replaced by a longer lasting positive after-effect. The slow negativity described under these conditions is believed to have an origin in the cortex identical with corresponding slow negative waves evoked by direct surface and midline thalamic stimulation. In Fig. 3 it is placed schematically with relation to other components of visual cortical response previously described elsewhere.

1. Goldring, S., O'Leary, J. L., *EEG & Clin. Neurophysiol.*, 1957, v9, 577.

2. Goldring, S., O'Leary, J. L., Huang, S. H., *ibid.*, 1958, v10, 663.

3. Goldring, S., O'Leary, J. L., Winter, D. L., Pearlman, A. L., PROC. SOC. EXP. BIOL. AND MED., 1959, v100, 429.

4. Bishop, G. H., O'Leary, J. L., *Am. J. Physiol.*, 1936, v117, 292.

5. Goldring, S., O'Leary, J. L., *EEG & Clin. Neurophysiol.*, 1951, v3, 329.

6. ———, *J. Neurophysiol.*, 1951, v14, 275.

7. Bishop, G. H., Clare, M. H., *ibid.*, 1952, v15, 201.

8. Bremer, F., *Physiol. Rev.*, 1958, v38, 357.

9. Brazier, M. A. B., *Acta Physiol. et Pharmacol. neerl.*, 1957, v6, 692.

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New Type Concentric Stimulating and Recording Electrode for Electroencephalography and Oscillography. (25609)

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Multipolar electrodes for chronic or acute implanting within the nervous system of experimental animals have always presented problems to investigators of bio-electric phenomena. Some of these problems are: 1) Multipolar metal, glass or twisted wire concentric electrodes are difficult to fabricate because of the problems of insulating one pole from another. Secondly, breakage, shorting and high impedance are common in all of the above types of electrodes. 2) Further, in constructing the concentric electrode of "non-micro" types of more than 2 poles, the diameter of the whole electrode increases in size in such proportions as to be impossible to use in animals with relatively small brains. To overcome some of the above difficulties, a new type of multipolar concentric electrode was developed which employed coats of silver printed circuit paint alternating over coats of insulating material.

Materials. The following materials are necessary for construction of the silver paint type concentric electrode. 1) Straight surgical or hypodermic needle stock of any desired diameter which will give proper rigidity for insertion into nervous tissue by means of stereotaxic devices. 2) Pure silver printed circuit paint. This can be obtained from any electronic parts dealer. 3) Silver solder (No. 430) of the type made by the All-State Welding and Alloys Co., White Plains, N. Y. 4) All-State flux (non-acid) for ferrous and non-ferrous alloys. 5) Insulating baking varnish which resists acids, alkalies, solvents and degreasers. The use of "Epoxylite" made by the Epoxylite Corp., El Monte, Calif. was found to be the best. 6) Lead wire of the miniature variety such as "Tensolite Miniature Wire" manufactured by the Tensolite Insulated Wire Co., Tarrytown, N. Y.

Methods. 1) Arbitrary lengths of steel needle stock were cut to any practical length. Actual lengths were determined later by the depth of structures in the brain stem to be stimulated or recorded from (See Step 4 below). Length and diameter used by the authors for insertion into the brain stems of

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