thermore, ability of ECHO-13 to hemagglutinate human group O erythrocytes at 4°C and 25°C, but not at 37°C, is characteristic of ECHO types 3, 6 and 11(13); as noted above these latter 3 virus types are included in Hsiung and Melnick's proposed group A.

Summary. 1) The originally distributed ECHO-13 prototype virus, Hamphill 2-188-20 passage 7, is a mixture of ECHO virus types 1 and 13. ECHO-1 was found in higher titer than ECHO-13 during passage and only the former was isolated at terminal dilution. It was necessary to neutralize ECHO-1 virus with antiserum to demonstrate the presence of ECHO-13 in this mixture and this apparently did not alter its antigenic properties. ECHO-13 virus was successfully reisolated in pure form from the original rectal swab eluate after 4 years storage. 2) Plaque purified strains of reisolated 2-188-20 virus and a Del Carmen 11-4-1 virus isolate were examined as possible ECHO-13 prototypes. The plaque purified 11-4-1 strain produced a broader spectrum antiserum in monkeys in early test bleedings and produced a higher infectivity titer in MKCC. It has been accepted as prototype ECHO-13 by the Committee on Enteroviruses. 3) The biologic properties of ECHO-13 virus in certain animals, chick embryos, cell culture and cell culture fluids are described. A clinically inapparent meningoencephalitis occurred in inoculated monkeys.

1. Comm. on ECHO Viruses, *Science,* 1955, v122, 1187.

2. Hammon, W. McD., Ludwig, E. H., Pavia, R. A., McCloskey, L., W., Sather, G. E., *Ann. N. Y. Acad. Sci.,* 1957, v67, 304.

3. Comm. on Enteroviruses, *Am. J. Pub. Hlth.,* 1957, v47, 1556.

4. Hammon, W. McD., Yohn, D. S., Ludwig, E. H., Pavia, R. A., Sather, G. E., McCloskey, L. W., *J.A.M.A.,* 1958, v167, 727.

5. Reed, L. J., Muench, H., *Am. J. Hyg.,* 1938, v27, 493.

6. Manson, L. A., Rothstein, E. L., Rake, G. W., *Science,* 1957, v125, 546.

7. Hsiung, G. D., Melnick, J. L., *Virology,* 1955, v1, 533.

8. Stulberg, C. S., Page, R. H., Berman, L., PROC. SOC. EXP. BIOL. AND MED., 1958, v97, 355.

9. Salk, J. E., Ward, E. N., *Science,* 1957, v126, 1338.

10. Gerber, P., Hamre, D., Loosli, C. G., *J. Exp. Med.,* 1956, v103, 413.

11. Wigand, R., Sabin, A. B., *Fed. Proc.,* 1958, v17, 538.

12. Hsiung, G. D., Melnick, J. L., *J. Immunol.,* 1957, v78, 137.

13. Goldfield, M., Srihongse, S., Fox, J. P., PROC. SOC. EXP. BIOL. AND MED., 1957, v96, 788.

Received December 19, 1958. P.S.E.B.M., 1959, v100.

Identification of a Prolonged Post-synaptic Potential of Cerebral Cortex.* (24651)

SIDNEY GOLDRING, JAMES L. O'LEARY, DAVID L. WINTER AND ALAN L. PEARLMAN
Division of Neurosurgery and Beaumont-May Inst. of Neurology, Washington University School of Medicine, St. Louis, Mo.

Our prior observations upon cerebral cortex using d.c. recording(1,2) indicate that a long-lasting surface negativity (150-300 msec. duration) develops in the wake of the evoked dendritic potential of negative polarity described by others(3,4). Chang(4) likewise observed that a negative wave could follow the dendritic potential evoked by a single stimulus. Following one surface stimulus the slow negativity we are to describe was observed to be partially submerged by a simultaneously occurring slow positivity (positive after-effect), the signs of the 2 potentials giving the appearance of summing algebraically. However, with serial stimulation (6-20/sec.) the slow positivity disappears uncovering the slow negativity which then increases in amplitude through summation. With such serial stimulation the slow negative responses to the successive shocks also fuse to provide a smooth d.c. change which can outlast a one sec. stimulus

* Aided by grant of U.S.P.H.S. and the Allen P. and Josephine B. Green Fn.

period by 1-3 sec. Formerly we called this slow negativity a negative after-effect and viewed it as resulting from a repolarization of dendritic elements as they recover from the preceding excitation (*i.e.*, from the dendritic potential, 1). Thus we linked the slow negativity with the dendritic potential as a sequent in the excitation-recovery cycle. However, further investigation indicates that the late wave is an independent excitation process separate from that of the primary potential. This conclusion is based upon threshold differences between primary potential and slow negativity, upon differences in the vertical distribution of the 2 potentials in the cortex as they are activated together by a sufficiently strong surface cortical stimulus, and upon their different sensitivities to certain drugs.

Method. The studies reported were done upon rabbit's frontal cortex, using 25 animals. Cat's anterior suprasylvian cortex gave corroborative results. The animals were prepared under ether anesthesia with procainization of wound surfaces. Thereafter, flaxedil and artificial respiration were substituted. Blood pressure and pulse were monitored continuously with a Sanborn electromanometer. Calomel electrodes and a d.c. amplifier and oscillograph permitted undistorted recording of the slower potentials. Monopolar recording was employed placing a critical electrode upon the cortex and a reference one upon the frontal periosteum. The stimulating electrode was a tripolar one placed within 0.5 mm of the critical recording one and composed of the points of 3 insulated 100 μ wires arranged to form an equidistant triangle. Tip separations were 75 μ. These wires were led to the stimulator through a circuit(5) which controlled shock artifact. A Grass stimulator was employed, the stimulus being 3-15 V. at 0.01 msec. duration.

Results. Under these experimental conditions a single threshold stimulus evoked the primary negative potential followed by a surface-positive after-effect. That after-effect grows in amplitude with growth of the dendritic potential as stimulus strength is increased from 3-10 V. (Fig. 1 *A*). Ordinarily at 10 V., but variable from one animal to another, the surface positivity commences to be submerged by a rapidly developing slow negativity. The stimulus necessary to elicit the latter is maximal or supramaximal for the preceding dendritic potential (compare traces, Fig. 1 *A*, 12 and 15 V.). This is the slow negativity which we have observed to summate upon serial stimulation.

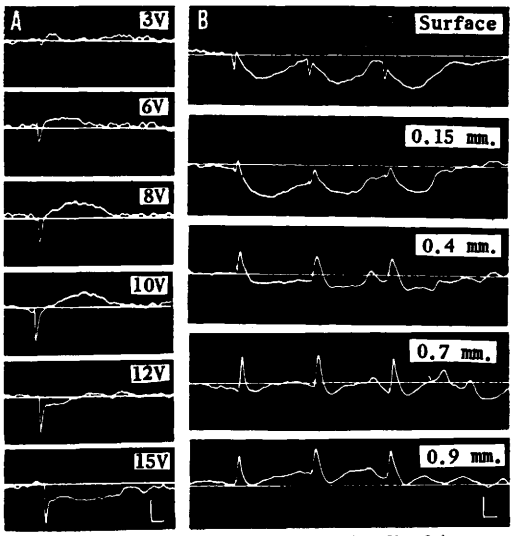

FIG. 1. *A*, cortical responses to stimuli of increasing strength. *B*, serially evoked responses to direct cortical stimulation (6/sec.) as cortical recording electrode is lowered through cortex. Note that primary potential is clearly reversed at 0.15 mm, whereas slow negativity does not show complete reversal until depth of 0.9 mm is reached. Straight line = baseline. Positive up. Vertical cal. line = 500 μV; horizontal, 30 msec.

For Fig. 1 *B*, a saline-filled pipette, having an outside diameter of 100 μ and led from a calomel half-cell, was inserted through the surface cortical layer. The tip was lowered in 0.1 mm fractions (or less) while recording the responses to serial stimulation at 6/sec. The polarity of the potential which we have called *slow negativity* was found to reverse more deeply (0.7 to 0.9 mm) than that of the preceding dendritic one (0.15-0.4 mm).

Pharmacological selectivities also aid in differentiating the 2 components and are well exemplified by the effect of chloral hydrate upon them(6). Fig. 2 *C* and *D* illustrate the potential complex composed of dendritic potential and slow negativity as it is elicited with serial stimulation at 15 V., before and after intravenous administration of a total of 500 mg of chloral hydrate. The summation of slow negativity which occurs upon 20/sec.

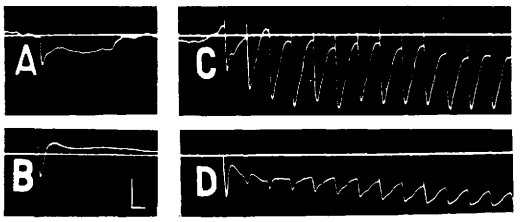

FIG. 2. *A*, cortical response to single stimulus (15 V). *B*, same after intrav. inj. of 150 mg chloral hydrate. *C*, serially evoked responses to direct cortical stimulation (20/sec.). *D*, same as *C*, after intrav. inj. of 500 mg chloral hydrate. Cal., as in Fig. 1.

stimulation becomes exaggerated after the injection (compare Fig. 2 *D* with *C*). By contrast, at the same stimulus frequency the chloral hydrate effects a reduction in the amplitudes of the successively evoked dendritic potentials past the first response of a series.

Fig. 2 *A* and *B* illustrates another effect of chloral hydrate. This one appears following intravenous administration of lesser amounts of the drug (Nembutal behaves similarly). With 150-200 mg injections the slow negativity of Fig. 2 *A* is replaced by an augmented positive after-effect. However, that the slow negativity is not lost is indicated by the downward dip in the positively directed deflection which follows the dendritic potential in Fig. 2 *B*. Although with an injection of this amount the negativity persists, it is obscured through algebraic summation with the augmented after-positivity described above. The additional injection of chloral hydrate to 500 mg again reduces the positive after-effect. It is important that the after-positivities illustrated in Fig. 2 *B* and 1 *A* do not summate upon serial stimulation. For this reason as well as for its identity in threshold with the dendritic potential we still view the slow positivity as an after-effect and not as a separate excitatory process.

Discussion. Evidence drawn from pharmacological selectivity as illustrated in Fig. 2 *D*, threshold differences (Fig. 1 *A*), and differences in depth of origin in the cortex (Fig. 1 *B*), support the conclusion that the dendritic potential and the slow negativity which follows in its wake are different processes. Responses indicative of 3 post-synaptic excitation processes of cortex have been identified by Tasaki, Polley and Orrego(7): axonal responses, duration 1 msec., cell body responses 1.5-3. msec., and dendritic response, 15 msec. We suggest that the 150-300 msec. slow negative wave which we describe represents still another post-synaptic phenomenon. The fact that the stimulus used is a very local one and recording is accomplished within 0.5 mm of the stimulus site argues against an origin by fusion of many temporally dispersed short-lasting processes of variable latencies. The fact that the slow negativity exhibits graded response qualities suggests a dendritic source (3). No other possibilities are apparent at this time.

A unique feature of the slow negativity we describe is its summation during serial stimulation and the continuance of the disturbance past the end of a stimulus period (1-3 sec.) The last indicates singularly slow recovery. Both of these characteristics are evident when the slow negativity is excited from midline thalamus(8). This suggests that the activity of which it is the sign plays a definite role in cortical functioning.

Summary. On the basis of threshold differences, depth of origin in cerebral cortex and pharmacological selectivity, we conclude that 15 msec. negative potential assignable to activity in apical dendrites and ensuing 150-300 msec. slow negative wave are separate neural processes. Our evidence suggests that the slow negativity seen in the wake of dendritic potential is a sign of an independent post-synaptic process having unusually long time course.

1. Goldring, S., O'Leary, J. L., Huang, S. H., *EEG and Clin. Neurophysiol.*, 1958, v10, 663.

2. Goldring, S., O'Leary, J. L., King, R. B., *EEG and Clin. Neurophysiol.*, 1958, v10, 223.

3. Clare, M. H., Bishop, G. H., *J. Neurophysiol.*, 1955, v7, 85.

4. Chang, H. T., *ibid.*, 1951, v14, 1.

5. Landau, W. M., *EEG and Clin. Neurophysiol.*, 1956, v8, 445.

6. Goldring, S., Metcalf, J. S., Huang, S. H., Shields, J., O'Leary, J. L., *J. Nerv. and Ment. Dis.*, Jan. 1959.

7. Tasaki, I., Polley, E. H., Orrego, F., *J. Neurophysiol.*, 1954, v17, 454.

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

Received December 22, 1958. P.S.E.B.M., 1959, v100.