References and Notes

1. A. B. Pardee, *J. Biol. Chem.* 179, 1085 (1949).
2. H. A. Krebs, *Biochem. J.* 48, 349 (1951).
3. W. B. Draper and R. W. Whitehead, *Anesthesiology* 5, 262 (1944); G. G. Nahas and H. L'Allemand, *J. Appl. Physiol.* 8, 468 (1956).
4. M. H. Holmdahl, *Acta Chir. Scand. Suppl.* 212 (1956).
5. This compound is commonly known as "tris-hydroxymethylaminomethane" or "tris buffer."
6. The CO_2 produced was calculated on the basis of oxygen uptake when $R = 0.8$.

26 September 1958

Synchronization of Unit Activity in the Cerebral Cortex

Abstract. Simultaneous recording with micropipette electrodes from different units in the cerebral cortex revealed that units seldom fired synchronously. However, there was a temporal relationship in unit firing even when the cortex was "aroused." This relationship was most apparent when strychnine and stimulation were applied to a sensory nerve of an animal asleep or under deep anesthesia.

In a discussion on the electrical activity of the cerebral cortex, Adrian (*1*) stated that "groups of nerve cells very often tend to act in unison when there is nothing to prevent them." Random afferent messages received at the cortex resulted in a breaking down of the synchronous activity of the nerve cells. If the afferent messages were simultaneously received, or if strychnine or some other chemical agent was applied, groups of nerve cells would again respond in unison. This notion was derived from, and subsequently supported by, observations on the waves of potential recorded from isolated structures or fragments of nervous tissue (*2*) and from the cortex of experimental subjects (*3, 4*).

Recently, microelectrodes were used to record unit spike discharges which presumably originated from single nerve cells. Under certain conditions the waves of potential occurred independently of the unit spike discharges (*5, 6*), indicating that they do not necessarily represent envelopes of spikes (*5*). Although observations from these experiments with microelectrodes sometimes suggest the presence of synchronization of unit discharges, especially subsequent to the application of strychnine (*7*), the activity of different cortical units was not simultaneously investigated.

This report concerns the activity of cortical neurons simultaneously recorded with two micropipette electrodes inserted into the somatosensory cortex of cats. The tips of the microelectrodes were estimated to be less than 0.5 mm apart. When a microelectrode picked up spike activity, it was left undisturbed while the other microelectrode was used to study similar activity of other nerve cells within a sphere approximately 1 mm in diameter. Cats were prepared either with a transection between the superior and inferior colliculi (*4*) or with intraperitoneal injection of thiopentone sodium. Stimulating electrodes were placed on a peripheral sensory nerve contralateral to the exposed somatosensory cortex. Toward the end of each experiment, strychnine solution was applied to the area of the cortex where the electrodes were inserted.

The "spontaneous" discharges of the cortical units recorded from Bremer cats and from cats under deep general anesthesia were remarkably similar. They occurred in bursts, each consisting of five to ten short trains of spikes; the intervals between the trains measured from 100 to 400 msec (Fig. 1, *A*). The spike trains recorded from any given pair of units appeared almost simultaneously, with discrepancies varying from 2 to 40 msec. Recordings from cats under light general anesthesia showed many units discharging also in bursts, but the temporal relationship between the bursts from different units was less clear. At times, rythmic bursting activity was recorded from one unit while random discharges were obtained from the other unit. While the animal was waking, bursting activity became less frequent, and when the tail of the cat was pinched, continuous discharges of spikes were recorded. However, a close examination of the records, such as that shown in Fig. 1, *B*, revealed that although synchronous discharges of the two units were scarcely present, there was a tendency for the discharges of the units to pause at about the same time and for the periods to be of similar length (as indicated by the dots in the record).

Stimulation of the peripheral nerve elicited responses with initial spike latencies at intervals either between 5 and 10 msec or between 20 and 30 msec (Fig. 1, *C* and *D*). Those occurred at intervals of 5 to 10 msec and sometimes recurred at intervals of 20 to 30 msec (Fig. 1, *E*). Application of strychnine caused, in most instances (52/60), repetitive discharges in nearly synchronous trains, with discrepancies of 1 to 8 msec in the initiation of the first spike discharge in the trains (Fig. 1, *F*). On some occasions (8/60) the repetitive discharges of one unit were not accompanied by repetitive discharges of the other (Fig. 1, *G*).

The observations cited above, therefore, provide direct evidence to support the notion originally proposed by Adrian (*1*). There are, however, some limiting considerations. (i) Units within a sphere of 1-mm diameter seldom fire at precisely the same instant. (ii) When the cortex is "aroused," the unit activity is said to be "desynchronized," but a relationship between the discharges of the units still exists. (iii) Evoked spike re-

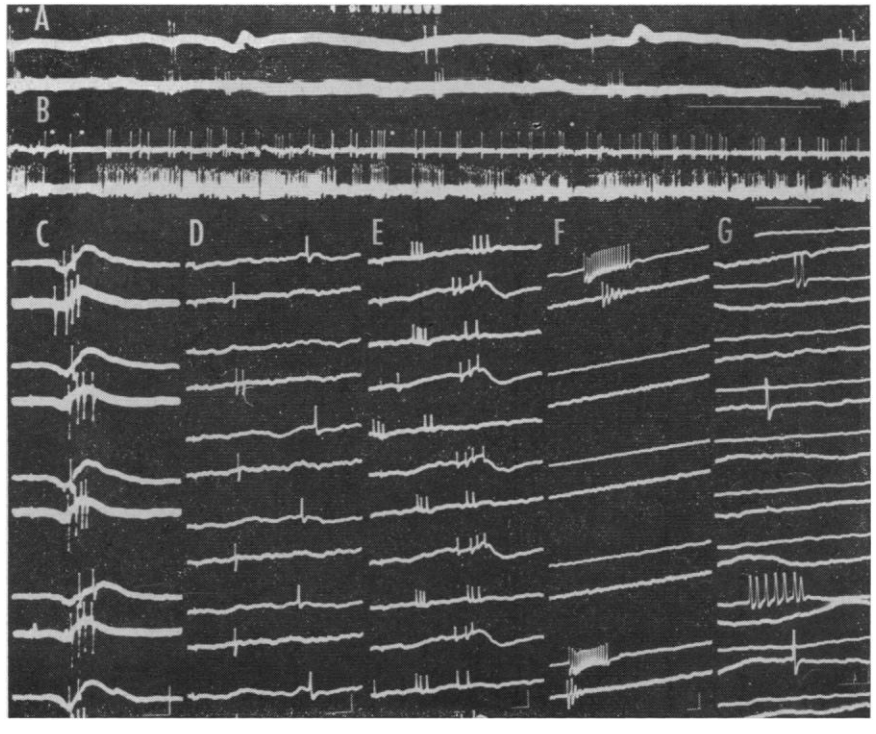

Fig. 1. Synchronous discharges of nerve cells in cerebral cortex: *A*, Discharges subsequent to Bremer section between superior and inferior colliculi; *B*, discharges in response to tail-pinching when cat was waking up from general anesthesia; *C, D, E*, responses to peripheral sensory nerve stimulation; *F, G*, trains of spike discharges following local application of strychnine. Upward deflection represents positivity. Horizontal bars represent 200 msec in *A* and *B*, 5 msec in *C* through *G*. Vertical bars represent 2 mv.

sponses of a given unit to sensory volleys scarcely vary in their latencies, but responses of some units occur about 20 msec following the responses of other units or recur about 20 msec after their initial responses. (iv) Application of strychnine causes repetitive discharge in nearly synchronous trains of approximately 85 percent of, but not all, the cells.

CHOH-LUH LI
National Institute of Neurological Diseases and Blindness, National Institutes of Health, Bethesda, Maryland

References

1. E. D. Adrian, *Proc. Roy. Soc. Med.* 29, 197 (1935).
2. ——— and B. H. C. Matthews, *J. Physiol. (London)* 65, 273 (1928); E. D. Adrian, *ibid.* 75, 26 (1932); F. Bremer, *Comp. rend. soc. biol.* 118, 1235 (1935); B. Libet and R. W. Gerard, *Proc. Soc. Exptl. Biol. Med.* 38, 886 (1938); ———, *J. Neurophysiol.* 4, 153 (1939).
3. E. D. Adrian and B. H. C. Matthews, *Brain* 57, 355 (1934); H. H. Jasper, *Cold Spring Harbor Symposia Quant. Biol.* 4, 320 (1936); G. Moruzzi and H. W. Magoun, *Electroencephalog. and Clin. Neurophysiol.* 1, 455 (1949).
4. F. Bremer, *Compt. rend. soc. biol.* 127, 355 (1938).
5. C. L. Li, H. McLennan, H. H. Jasper, *Science* 116, 656 (1952).
6. V. E. Amassian, *Electroencephalog. and Clin. Neurophysiol.* 5, 415 (1953); V. B. Mountcastle, P. W. Davis, A. L. Berman, *J. Neurophysiol.* 20, 374 (1957); R. Jung, *Electroencephalog. and Clin. Neurophysiol.* 5, Suppl. 4, 57 (1953); G. Moruzzi, *ibid.* 5, Suppl. 4, 221 (1953).
7. C. L. Li and H. H. Jasper, *J. Physiol. (London)* 121, 117 (1953).

15 October 1958

Reliability of Activation Level during Adaptation to Stress

Abstract. This study points out the stability of a quotient expressing the recovery of basal skin resistance (BSR) level. Changes noted in BSR during stress are consistent with the behavior of tranquilized patients and have significance for drug therapy. Information of this type may be quite useful for interpretation and objectivity in a wide range of clinical researches.

To date, studies of the reliability of BSR measures have concentrated on work with normal subjects and tend simply to demonstrate adaptation after repeated exposure to the stimulus. The following study was primarily designed to appraise the reliability of the base-line adaptation of mental patients during stress. Basal skin resistance was the measure chosen since it is inversely related to sympathetic nervous activity or "activation level."

The subjects comprised two groups of 16 patients each, one group composed of 13 on various tranquilizers of the phenothiazine class plus three on Marsilid, an "energizer," and the other group consisting of nondrugged patients. Silver electrodes, stabilized by reversal of polarity every 3.1 sec, were applied to the palms of the patient's hands. The patient reclined on a couch and was instructed to look continuously at a Strobolux which was used to deliver a large field of flickering light from a distance of 7 ft. The Strobolux was turned on after a relaxation period of 10 min. Readings of BSR separated by ½-min intervals were made during the following periods: (i) 0.5 to 1.5 min, the initial resting period; (ii) 9 to 11.5 min; and (iii) 16 to 17 min. After a 3-day interval the procedure was repeated on each patient.

Two test-retest reliabilities were computed by using the following scores which were selected in advance of the data: (i) increase in BSR over the 7-min exposure to flicker, divided by the initial decrease in BSR due to flicker stimulation; (ii) increase in BSR, as above, divided by BSR just after Strobolux stimulation—that is, at 10.5 min.

Although the first of these scores is highly recommended in the literature for measuring the recovery quotient, its use gave insignificant reliabilities. The data strongly suggest that this is due to anticipatory activation during the second session. The use of the second score gave rank order correlations of .72 ($p < .01$) for both drugged and nondrugged groups and a total product moment coefficient of .78 ($p < .01$) for the combined groups. Considering that the second score compounds unreliabilities resulting from changes in adaptation and changes in BSR level at 10.5 min, the reliability is surprisingly high over a 3-day period when the anticipatory effects are taken into account.

A subsidiary experiment, an exploratory attempt at evaluating the validity of BSR measures of activation level, was conducted with data obtained from the above study. Casual clinical observations made by me and my associates on patients under the influence of tranquilizing drugs yielded general agreement to the effect that these patients were manifestly less aroused than those who were not receiving tranquilizing drugs. It was then reasoned that the manifest validity of BSR should be reflected by a higher resistance level for tranquilized than for nondrugged patients. Hence, the three patients on Marsilid were dropped from the drugged group along with three randomly chosen nondrugged patients. The subjects had been so chosen that it was possible to obtain balance or conservative bias with respect to the following characteristics; sex, race, diagnostic category, and manifest agitation (see Fig. 1).

The data were converted to log conductance units in order to approximate a normal distribution. An analysis of variance was made over drug categories for

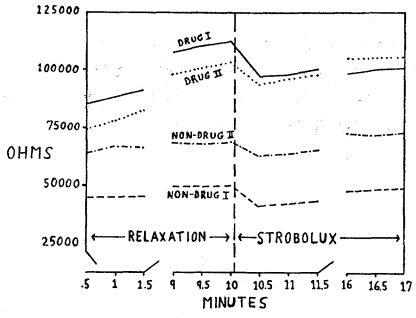

Fig. 1. Average BSR on drugged and nondrugged groups for sessions one and two

the initial resting period and over session number. Interaction and session number were not significant. Drug versus nondrug achieved an F of 9.63 ($p < .01$). A breakdown of this F by two t-tests, one for the first session which was significant at better than the 1-percent level and one for the second session which was not significant, suggested a further influence of anticipatory effects.

The three nondrugged patients were reincluded, and two exploratory hypotheses were tested *a posteriori*. It was found (i) that the change in initial resting level from session one to session two did not differ significantly for drugged or nondrugged groups, and (ii) that the change in BSR over the entire relaxation period was significantly different ($p < .05$) between drugged and nondrugged groups, the former showing a greater increase in BSR.

ARCHIE B. CARRAN
Laboratory of Experimental Psychopathology, Longview State Hospital, Cincinnati, Ohio

28 July 1958

Effect of Chlorpromazine on Salmonella enteritidis Infection in Mice

Abstract. Chlorpromazine increases the susceptibility of mice to infection with *Salmonella enteritidis.*

Goldman reports that infections are numerically among the most frequently encountered complicating factors in the institutional use of chlorpromazine and reserpine (*1*). He states that it is not believed that increased susceptibility to infections is a specific effect of these drugs. Experimental work with different species of animals and different pathogenic organisms has not led to consistent conclusions (*2, 3*). The following experiment was designed to study in a strain of mice the interaction between various dosages of chlorpromazine and the susceptibility to varying inocula of a virulent organism.