occurred a few seconds after the strength of the stimulus was reduced to the threshold value. Incidentally, the spontaneity could usually be stopped by again increasing the voltage. Also, the threshold for electrical stimulation fell during and shortly after a period of high-voltage stimulation. The similarity of the responses to strong stimulation and the effects of adding epinephrine or norepinephrine is striking. Finally, large amounts (150 μg/cm^3) of the sympatholytic drug dibenamine abolished or minimized the augmentation in both the atria and the papillary muscle.

It has been tentatively concluded that acetylcholine is the depressor substance and that one of the epinephrine compounds is the potentiating substance. The relative amount of each substance released will determine whether depression or potentiation will predominate. Thus, the lack of a significant depressor effect in the papillary muscle is explained by a relative absence of acetylcholine. In the atria, released acetylcholine overwhelms the concomitant release of the potentiating substance.

It is obvious that this phenomenon should be considered in interpreting the results of experiments which involve electrical stimulation of cardiac tissue. In pharmacological studies on isolated muscles, at least, it is quite possible that certain drugs may exert their effects by altering the threshold for the release of these substances. Further, if different areas of the heart contain different amounts of the two substances, as suggested here, uniformity of results with different tissues could hardly be expected.

More significance might be attached to these results if it could be demonstrated that these substances are released in the spontaneously beating heart strip or in one stimulated by point electrodes at threshold voltage. This seems a likely possibility in view of the fact that acetylcholine and the epinephrines are released in the spontaneously beating perfused heart (*4*). If these substances are released with each normal contraction, a number of previously described phenomena might be explained. For example, the treppe phenomenon and post-stimulation potentiation could well be explained on this basis (see *6*). Also, the opposite effect ("negative" treppe) seen in the rat ventricle could be due to a relative absence of the potentiating substance. Indeed, preliminary studies indicate a crude correlation between the magnitude of the high-voltage potentiation and the extent of the treppe phenomenon and of post-stimulation and extrasystolic potentiation (*7*).

WILLIAM J. WHALEN

Department of Physiology, School
of Medicine, University of
California, Los Angeles

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4 November 1957

Long-Term Recording from Single Neurons in Brain of Unrestrained Mammals

Much of our knowledge of the activity of single neurons in the central nervous system has been concerned with the study of phenomena of short time course —milliseconds to hours—and has involved the use of anesthetized animals, animals with brain lesions, or animals restrained by curarization. Some information is beginning to appear on the activity of single neurons in unanesthetized normal animals, but this is limited to activity of, at most, a few hours for the same neuron (*1*).

It has been found possible to record discharges of single neurons for periods of a week or more by implantation of several stainless-steel wires, 80 μ in diameter, with insulation exposed at the cross section of the tip. The animal in use is the California ground squirrel, *Citellus beecheyi,* which is being used in a study of brain mechanisms in hibernation.

The implantation technique is fully described elsewhere (*2*), and since it involves many details necessary for the particular measurements made in hibernating squirrels, only the details pertinent to this report are described here. The anesthetized squirrel was placed in a specially designed stereotaxic instrument, and holes were drilled and tapped in the skull for four 0-80 stainless-steel machine screws; smaller holes (approximately 340 μ in diameter) were drilled at desired sites for the 80-μ stainless-steel insulated wires. The single 80-μ wires were lowered into the brain through the latter holes with the aid of a manipulator or, for short distances, merely by hand. A dental cement was applied around the base of the electrode and allowed to run onto one of the screws; after the cement had hardened, the electrode holder was loosened and withdrawn. Ordinarily, four to six of these particular electrodes were implanted in the brain of each animal. About 2 mm of the free end of the 80-μ wire was carefully stripped of its insulation and a No. 28 gauge color-coded flexible lead was soldered to it. Several more layers of the dental cement were applied until the solder junction was firmly imbedded. The leads were all brought together, tied at intervals, and passed through a flexible plastic tube, which was then imbedded in cement at its base.

Connection to the unanesthetized, unrestrained squirrel was made by merely plugging in the appropriate leads; these ran out of the animal's cage, and handling of the animal was not involved. Conventional amplifying and recording equipment was used, and the potentials at the tip of the electrode were referred to one of the screws on the skull, which was grounded. With the method of connection used it has been possible to study unit patterns during intervals when the squirrel was falling asleep, waking, and in the alert state.

Figure 1 illustrates the discharge of a unit with a predictable pattern when the squirrel is alert and, in this case, curled up in its nest. The room was dark and the squirrel had been made immune to camera noises by puncturing of both eardrums and plugging of the external meati with cotton at the time of electrode implantation. Three long impulse trains of consecutively shorter duration are shown, with relative silence between trains. Each train is further characterized by a high-frequency outburst close to the start of the train. The slow waves have been filtered out; they are normally

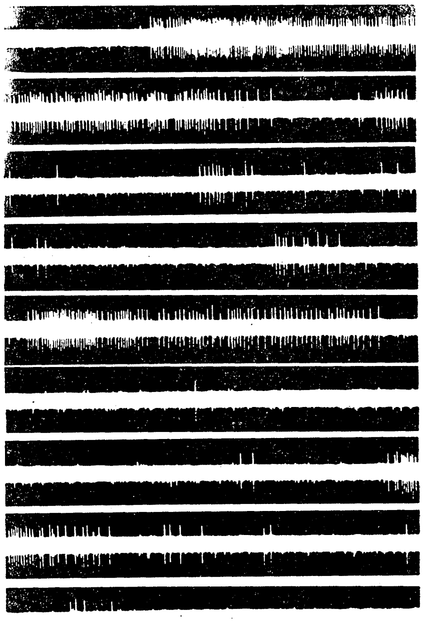

Fig. 1. Pattern of a unit in the mesencephalic reticular formation of an alert, deafened squirrel, resting in the dark, recorded on the eighth day after implantation of the electrode. Time for each strip is 4.6 sec; spikes average 60 μv; time constant, 2 msec.

large enough in amplitude to mask the spikes.

The single fast sweeps shown in Fig. 2 are from a different squirrel and illustrate some of the spike wave forms encountered at a recording site and their persistence some 4 days later. The constant wave form and relatively constant amplitude of the matching pairs support the thesis that these are the action potentials of single and identical neurons.

Studies have so far been limited to the cells of the mesencephalic reticular formation, which are among the largest in the brain; the technique in its present form may not be applicable to all parts of the nervous system.

An observation of interest is the presence of some cells in this region which are predominantly active during sleep, with only short low-frequency bursts or no activity during the alert state. Activity evoked by visual and tactile stimuli can be recorded from this region.

The difficulty of determining the significance of a unit discharge evoked by some peripheral stimulus is obvious. For example, a single flash of light can be observed to evoke the discharge of some relatively silent units in the mesencephalic reticular formation and also to further desynchronize the cortex, alert the olfactory bulb, speed up the heart, and increase muscle tone. It would be difficult to categorize these units as being related to any of these components of the animal's total behavior because of the many variables of similar time course which are changing and are not being recorded. It is quite possible that the unit evoked may not be even indirectly connected with any of these components.

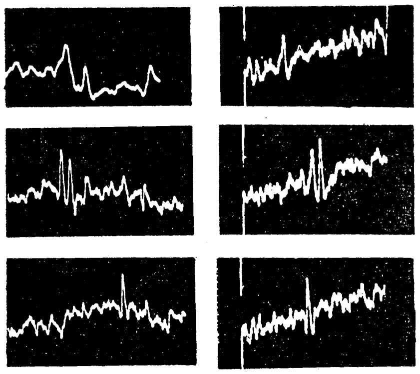

Fig. 2. Comparison of wave forms of similar spikes from one locus in the mesencephalic reticular formation, recorded 4 days apart (recordings in column at right were made 4 days later than those at left). This locus has three distinct spikes, each with a wave form which did not vary over hundreds of observations; a negative diphasic with a preliminary exponential inflection on the rising phase (top, see *3, 4, 5*); a larger negative diphasic with a tendency to fire in pairs (middle); a triphasic spike (lower). The spikes seem to fire independently of each other. Negativity, up; time of each sweep is 8 msec except for upper left, which is 4 msec; amplification of recordings in column at right is 1.3 times that on left; time constant (left), 200 msec, (right), 2 msec.

In conclusion, it is felt that techniques which allow the study of the behavior of neurons over a period of days are of potential value in understanding long-term phenomena in the central nervous system, including learning, memory, and recall; these techniques are now available (*6*).

FELIX STRUMWASSER*
Department of Zoology, University of California, Los Angeles

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* Present address: National Institute of Mental Health, Bethesda, Maryland.

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A Study of Grain Contacts in Granitic Rocks

In order to determine whether a concurrently crystallizing or previously crystallized mineral grain in a granitic rock affects the development of neighboring crystals, a study has been made of the contact relationships of minerals in thin sections of various granites. The study is based on the presumption that, if the different minerals in granites are randomly and uniformly distributed, then the percentage of contact area of a mineral *A* that is in contact with any other mineral *B* should be proportional to the modal percentage of mineral *B* in the rock. In such cases of proportionality, it may be presumed that minerals did not affect the development of neighboring grains.

For all possible pairs of minerals in the granites studied, the following ratio was measured: percentage of total contact length of all grains of mineral *A* occupied by mineral *B*/modal percentage of mineral *B*. The modal percentages were measured by point counting, and the various contacts were measured by retracing the traverses used in point counting and counting the number of times each possible contact (for example, a quartz-plagioclase contact) was crossed. Grain contacts along which albite, chlorite, or other presumably secondary minerals were concentrated were counted as contacts between the two primary minerals on either side of the secondary material.

A total of 31 granitic, quartz monzonitic, and granodioritic rocks were studied. Samples were obtained from a wide range of localities; they included Southern California batholith; intrusions in the Front Range (Colorado), intrusions in the Sierra Nevadas (California), the Idaho and Boulder batholiths, and the White Mountain, New Hampshire, and Oliverian series of New England. The average composition of these rocks is 32.3 percent quartz; 27.7 percent potassium feldspar; 32.6 percent plagioclase; 6.6 percent biotite; minor hornblende (in a few samples); and rare magnetite, zircon, sphene, apatite, and muscovite.

The results are shown in Table 1. The numbers in this table are the geometric means from all samples studied of the ratio: percentage of contact length of mineral *A* in contact with mineral *B*/modal percentage of mineral *B*. In a few samples either potassium feldspar, plagioclase, or biotite was absent, but all means represent at least 28 samples.

As shown by Table 1, many of the ratios are close to one. Statistical *t* tests of the logarithms of the ratios from each sample confirm, at the 99-percent confidence level, that the potassium feldspar-potassium feldspar and plagioclase-plagioclase ratios are less than one. None of the other ratios involving quartz, potassium feldspar, or plagioclase are demonstrably different from one. The percentage of contacts of all minerals with biotite (as the mineral *B* in Table 1) are greater than one, probably because the irregular shape of the biotite causes it to have a large surface area for its volume.

Presumably ratios close to one in Table 1 signify that the minerals involved have had little or no effect on one another's crystallization. In the case of potassium feldspar, a low ratio with other potassium feldspar grains probably indicates that growth of one feldspar crystal prevents nucleation of a similar crystal in the neighborhood. This same explanation might also apply to the low plagioclase-plagioclase ratio, but it is

Table 1. Geometric means of the ratio: percentage of contact length of mineral *A* in contact with mineral *B*/modal percentage of mineral *B*.

Mineral *A*	Mineral *B*			
	Quartz	Potassium feldspar	Plagioclase	Biotite
Quartz	0.84	0.99	0.95	1.60
Potassium feldspar	1.21	0.45	1.15	1.29
Plagioclase	1.04	1.06	0.72	1.63
Biotite	1.09	0.66	0.81	1.20