decreases, tumor nucleotide increases, reaching a maximum at about the 8th day after implantation, followed by a rapid fall. This fall appears to be correlated with the tendency (beginning about the 10th day of tumor growth) for the blood nucleotide level in tumor-bearing mice to return to normal. 3. The intravenous injection of adenylic acid into normal mice causes a transitory rise in blood ATP. With a dose of 4 mg, this increase is in excess of that in the total purine. A similar increase in blood ATP occurs after the injection of AA into the blood stream of tumor-bearing animals. The tumors of such injected animals show a lowered level of AA, ATP, and total purine, but an elevated level of ADP as compared with uninjected controls.

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Single Pyramidal Fiber Responses to Electrical Stimulation.* (20111)

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In an earlier study of the responses of spinal motor neurones following selective activation of pyramidal fibers, an explanation of the findings was based upon the assumption that the pyramidal fibers responded once to each electrical pulse and that there was numerical agreement between the number of pyramidal shocks and the number of impulses initiated in each of the responding fibers(1). Two deviations from the numerical equivalence were considered possible. Some pyramidal fibers may have behaved like certain fibers of peripheral sensory nerves and responded repetitively to single shocks of long duration(2,3). Other pyramidal fibers, due to their presumed longer refractory periods, may have been unable to follow the higher stimulation frequencies, with the resulting occurrence of a response deficit.

It was the purpose of this study to test this assumption by recording responses from single pyramidal fibers activated by pulses of the parameters used previously.

Methods. The experiments have been performed upon cats and macaques in surgical anesthesia as a result of the administration of diallylbarbituric acid in urethane solution. In some instances movement was prevented through the use of d-tubocurarine coupled with artificial ventilation at a level roughly equivalent to the level of ventilation established by the preparation before curarization. The dorsal surface of the medulla oblongata was exposed through an enlarged foramen magnum and the spinal cord was exposed by laminectomy at the desired level. *Stimulating pulses* were controllable in all dimensions and were triggered by the oscillograph sweep generator. The rectangular pulses were applied to the preparation through the mediation of a Grass Stimulus Isolation Unit which slowed the rise and decay times to a degree insignificant for the purposes of this study and which permitted the maintenance of a steady voltage at the stimulating electrodes throughout the duration of the pulse. The current through the stimulating electrodes was measured with the aid of a monitoring oscillograph. The stimulating pulses were applied to the preparation through two forms of stimulating electrodes. Orthodromically conducted volleys were initiated at the level of the pyramid through concentric bipolar electrodes oriented stereotactically. Antidromically conducted volleys were initiated at appropriate cord

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levels through pairs of fine insect needles thrust into position in the lateral column. The needles were insulated except at the tips, held parallel and 1-2 mm apart by a small cardboard spacer. *Recordings* were made photographically from a cathode ray oscilloscope activated by a capacitance-coupled pre-amplifier. The recording electrodes were 12.5 micron insulated alloy wires used either singly or cemented together to form bipolar pairs(4). These could be handled with plastic-tipped forceps and used to explore for suitable positions from which to record single fiber responses. *Impulses recorded from microelectrodes* in the region of the pyramidal decussation as a result of stimulation in the spinal cord could have been the result of activation of systems other than the corticospinal system. In experiments involving antidromic activation, this possibility was controlled in the following way. Bipolar concentric recording electrodes were introduced into the pyramid. The contralateral lateral column was then explored, using the bipolar stimulating needle electrodes with the tips oriented cephalocaudally. At lower cord levels it was found that the stimulating electrodes must be placed with great precision in order to initiate a response which could be recorded from the bipolar concentric electrodes in the pyramid. Movement of the stimulating electrodes through a distance of a millimeter or less was sufficient to eliminate the pyramidal response. Using this type of control continuously as a monitor for the remainder of the experiment, it was found that the single fiber responses recorded from the microelectrode over a second channel always fell within the temporal limits of the summated pyramidal response.

Results. Numerous unsuccessful attempts were made to record responses in single pyramidal fibers after orthodromic conduction. It was not at all difficult to record summated volleys from the corticospinal tracts at cord levels after stimulation of the bulbar pyramid. The failure to record single fiber responses apparently depended upon two sources of difficulty. In the spinal cord the fibers of the lateral corticospinal tracts form a fairly compact bundle. That this is true, even at lumbar levels where the number of fibers is relatively small, is attested to by the fact that the recording electrode may enter and leave the regions giving rise to summated volleys with movements of less than a millimeter. When such a compact group of fibers is activated synchronously, the 12.5 μ electrode does not have sufficient resolving power to isolate responses from single members of the population. In addition, confusion may arise from the fact that the lateral corticospinal tract lies in close approximation to cells of the spinal gray matter which respond to corticospinal impulses(5). In those instances in which single unit records were derived from spinal cord placements, later histological examination of electrode positions confirmed the suspicion that such records were probably derived from cells of the spinal gray rather than from fibers.

An attempt was then made to circumvent these two difficulties by recording from pyramidal fibers after antidromic conduction from spinal cord levels to the level of the pyramidal decussation. With this form of experiment the possibility of recording from synaptically activated cells would be greatly reduced. The intermingling of fibers from the two sides coupled with the longitudinal dispersion of the decussating fibers would reduce the concentration of the active population at any one locus and afford a better opportunity for selecting a single responding fiber.

Responses in single pyramidal fibers have been recorded after antidromic conduction in seven cats and one macaque. The conduction velocities of all 14 of the fibers studied have fallen in the range from 35 to 75 meters per second. Although it is impossible to estimate the diameters of these fibers from their conduction velocities with any degree of accuracy (6), it is probable that they fall into the group of medium-to-large pyramidal fibers and very doubtful that any of the numerous small pyramidal fibers are represented in this group.

Illustrations of responses typical of such fibers are presented in Fig. 1. At this single placement in the pyramidal decussation, activity was recorded from two different fibers. The indicated conduction velocity for the larger, faster response is just short of 55 m.p.s., while that for the smaller, slower response is 38 m.p.s. With a current intensity 5 times

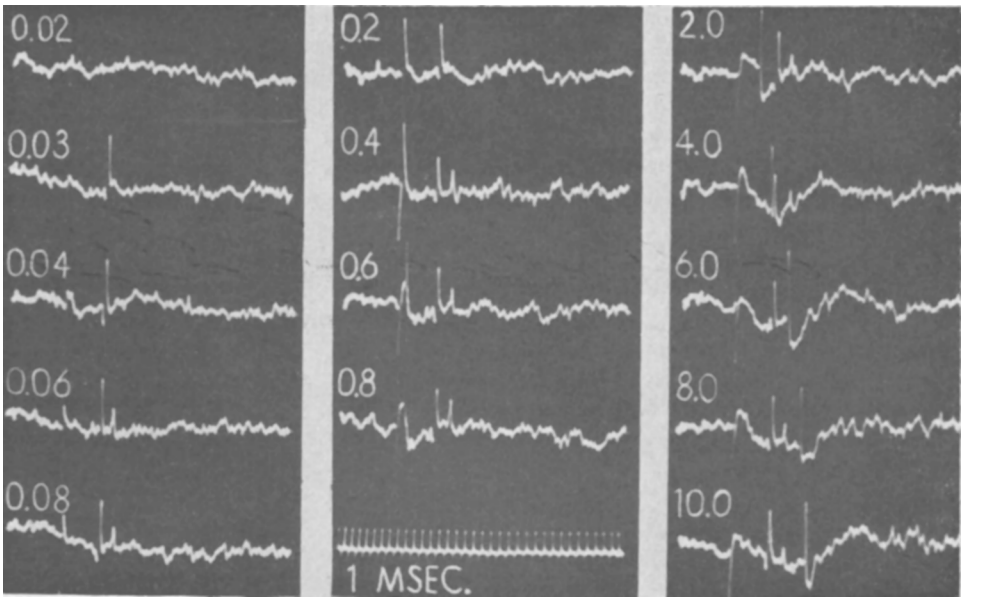

FIG. 1. Single pyramidal fiber responses in the cat recorded from the pyramidal decussation following stimulation of lateral corticospinal fibers at the level of L6. The current intensity was 5 times the rheobase for the faster of the two fibers responding. The duration of the stimulating pulse is indicated for each trace. The faster of the two fibers responded first at a duration of 0.03 msec.; the slower responded first at a duration of 0.06 msec. The "off" shock artefact first becomes clearly evident at 0.2 msec. and is seen at successively later positions in the following traces. At 4.0 msec. it almost overlies the response of the faster fiber and at 6.0 interfered with the recording from the slower of the two fibers.

greater than rheobasic strength, the faster of these two fibers responded first to a pulse of 0.03 msec. duration. As the duration of the stimulating pulse was increased, no indication of repetitive firing on the part of this fiber is evident from the record. The response of the second, slower fiber first became evident at a pulse duration of 0.06 msec. That this is not a second response from the same fast fiber is an opinion based on the lower amplitude of the response, on the uniformity of its latent period throughout the series, on the all-or-none nature of the responses and on the fact that the configuration did not repeat even though the duration of the pulse was increased beyond the illustrated 10 msec.

Four of the single fibers from which records were made showed responses initiated by the "off" transient of the stimulating pulse. This form of repetitive activity was seen only when the pulse duration was in excess of 4.0 milliseconds. No off-responses were recorded at shorter pulse durations.

When tested with pulse durations of 0.5 msec. all of the fibers studied responded faithfully and without response deficits to frequencies of stimulation up to 500 per second.

Discussion. It might be considered dangerous to base conclusions on results involving antidromically conducted impulses since this is an abnormal direction of conduction. However, there is no evidence that excitation and conduction characteristics undergo any alteration along the length of a nerve fiber as long as its structural characteristics remain uniform. It has been found that the conduction velocity of this system of fibers is uniform over its extent in the white matter of the spinal cord(6). On the other hand, the formation of collaterals constitutes the most probable explanation for observed changes in conduction velocity in the dorsal column system of fibers(7). It is therefore considered reasonable to assume that characteristics defined on the basis of antidromic conduction bear a close resemblance to the normal.

The possibility of repetitive responses on the parts of nerve fibers activated by long

duration pulses must be taken seriously in the light of the findings of Skoglund and others (2,3) that peripheral afferent fibers show repetitive responses to rectangular and to linearly increasing currents at intensity levels which are not far in excess of the rheobase. It is not clear whether the likelihood of repetitive firing is equally great for both pulse forms. Neither is it clear whether the probability of repetitive firing is different for fibers of different structural characteristics.

The results of the present study justify the assumption of a one-to-one relationship between stimulus to and response of single pyramidal fibers within the limits of the stimulus parameters used in the previous investigation. Unfortunately, the evidence presented can be applied only to fibers conducting at velocities in excess of 35 meters per second. These are in all likelihood those fibers which have diameters above the median value. Thus we must remain in ignorance about the behavior of the great number of smaller fibers which are found in the medullary pyramid.

Summary. 1. Responses of single pyramidal fibers to stimulation with rectangular electrical pulses of varying parameters have been studied in the cat and the macaque. 2. Those fibers conducting at velocities in excess of 35 m.p.s. do not respond repetitively to pulses of less than 4.0 msec. in duration. Some fibers have shown off-responses to pulses in excess of this duration. 3. All fibers studied have followed repetitive stimulation up to frequencies of 500 per second without response deficit.

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Electron Micrographs of Motor End-Plates.*† (20112)

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The purpose of this paper is to report some preliminary observations on the motor end-plates as seen in electron micrographs. The present concept concerning the nerve muscle relationship at this point is that there is no direct connection between them. Impulses are thought to be transmitted from nerve to muscle at this site by a humoral substance, inorganic ionic changes, or by the action of end-plate potentials(1). However, the possibility of some more or less direct morphological relationship existing between nerve and muscle at this juncture, such as the "periterminal net" of Boeke(2), while discredited, has never been disproved(3).

Material and methods. The material for this study consists of the motor end-plates of the intercostal muscles of the rat. The gold chloride method used for the demonstration of the end-plates was that described by Warren(4). Further treatment of the tissue for electron microscope study consisted of bleaching the gold impregnated pieces of muscle and associated end-plates in a solution of 0.5% potassium cyanide in 50% ethanol. This process was watched under the dissecting microscope so that it could be stopped at the

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