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THE FUNCTIONAL ACTIVITY OF SINGLE UNITS IN THE CENTRAL NERVOUS SYSTEM[1]

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WITH the recognition of the neurone as the ultimate anatomical unit of the nervous system it came to be tacitly assumed that all nervous and mental phenomena are, in the last analysis, explicable in terms of the combined activity of single nerve elements. Individual neurones, however, had, until very recently, eluded isolation as functioning entities, and knowledge of the intimate details of their behavior was therefore lacking. Without this information it was quite impossible to form a satisfactory conception of the elementary principles of nervous activity, and many details of reflex action remained obscure. Single *muscle* fibers, to be sure, had been studied by Lucas, Pratt and others to great advantage, and single axones had been placed under direct observation by using artificial stimulation (pore electrode), but these studies gave little or no information concerning the characteristics of the nerve cell itself. The responses of a single intact neurone, activated within the central nervous system by a natural stimulus, were first placed under direct observation in 1928, and since then notable progress has been made in the analysis of their behavior. The quest of a single neuro-muscular unit has in fact had many of the dramatic features associated with the quest of the single atom, and the success achieved by the physiologist is in most respects quite as remarkable as that of the physicist.

Isolation of the unit was made possible largely by virtue of the electrical response accompanying activ-

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[1] Schiff Foundation Lecture, Cornell University, April 17, 1931.

ity. The potentials developed by such microscopical units are small, but with modern valve-amplification this is a matter of little consequence; a much greater difficulty has been the anatomical isolation of the unit from the myriad of similar structures—nerve cells, nerve fibers, muscle fibers—surrounding it. This special problem is well exemplified by the early work on the voluntary electromyogram. Since every muscle fiber gives rise to an electrical response during activity, numerous and large electrical deflections can be obtained from a muscle, *e.g.*, the human biceps, during voluntary effort. A large number of studies concerning the nature of such electrical variations were carried out with capillary electrometer and later with the Einthoven galvanometer, and the attempt was made by Gotch, Piper, Garten, Forbes, Adrian and others, to infer the characteristics of activity of the individual nerve cells which had thrown the muscles into voluntary activity. In the early literature much of the discussion turned upon the existence of an alleged rhythm of approximately 50 per second which was commonly seen in the voluntary electromyogram (Fig. 1). At best, however, it was an "impure" rhythm, for there were many subsidiary vibrations ("secondary waves") thought to be due to elements out of phase with the majority. The real difficulty lay not here, but in the interpretation of the "primary" (50 per sec.) waves. There was no clear proof that they represented the responses of single units; it was quite possible that rotation of activity occurred among individual elements and that any given neurone might respond at a much lower rate than that indicated by the 50 per second rhythm. I had occasion six years ago to review the subject in some detail, and, in view of these and other considerations, I ventured at that time to make the following prediction:[2] "Not until the responses of individual units can be recorded singly will electrical records give a decisive answer as to rate of discharge of spinal motor neurones. Already, however, (1925) Adrian and Zotterman have succeeded in recording the action currents of a single proprioceptive afferent nerve fibre responding to an adequate stimulus (stretch) applied to its end-organ. In addition to the importance of so great a technical achievement, it also promises that a definitive solution of the long-debated question of the intrinsic rhythm of spinal centers may be reached in the near future." The inference was an obvious one and I can take little credit for its unexpectedly prompt justification, since it has come about through the ingenuity and foresight of other investigators.

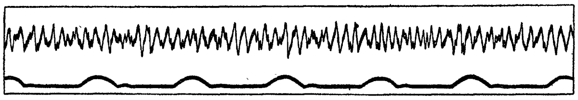

FIG. 1. An electromyogram of voluntary contraction of the flexor muscles of the forearm obtained by Piper. Note the rhythm of approximately 50 per sec. Time 0.20 sec. (H. Piper, ''Über die Ermüdung bei willkürlichen Muskelkontraktionen.'' *Arch. f. Anat. u. Physiol.*, 491–498, 1909.)

While studying the stretch reflex[3] of the red fibered soleus muscle (cat), Denny-Brown[4] observed that on applying very slight degrees of stretch to the tendon a regular sequence of small galvanometer deflections was obtainable from the muscle (Fig. 2). He correctly interpreted these as being due to the activity of the group of muscle fibers innervated by a *single* anterior horn cell of the spinal cord. When the stretch stimulus was slightly increased a second group of action currents usually appeared maintaining a different rhythm from the first, and therefore waxing and waning with the first series of deflections (Fig. 2). It was quite evident that the second series of deflections represented the activity of an additional motor unit. With further stretch more units come in and the electrical deflections ultimately become quite confused and irregular.

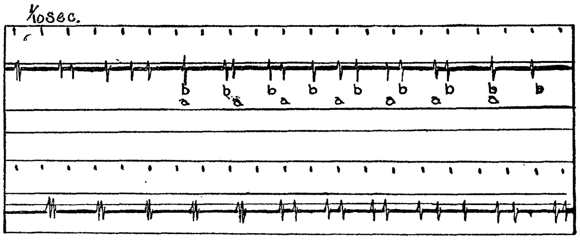

FIG. 2. The electrical response of single units of soleus muscle responding to slight stretch; string galvanometer record unamplified. In A the unit 'a' drops out toward the end of the record and unit 'b' persists. In B the waxing and waning of two units discharging at slightly different rates is clearly seen (Denny-Brown).

Working independently of Denny-Brown, Adrian and Bronk[5] succeeded, at approximately the same time, in obtaining from nerve the action currents of single discharging units. Their observations as to rate of discharge, waxing and waning of discrete rhythms, etc., entirely confirmed, and in some respects

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[2] J. F. Fulton, ''Muscular Contraction and the Reflex Control of Movement,'' Baltimore: Williams & Wilkins, pp. 477–478.

[3] E. G. T. Liddell and C. S. Sherrington, ''Reflexes in Response to Stretch (myotatic reflexes),'' *Proc.* Roy. Soc. B/96: 212–242, 1924.

[4] D. E. Denny-Brown, ''On the Nature of Postural Reflexes,'' *Proc.* Roy. Soc., B/104: 252–301, 1929.

[5] E. D. Adrian and D. W. Bronk, ''The Discharge of Impulses in Motor Nerve Fibers. Part II. The Frequency of Discharge in Reflex and Voluntary Contractions,'' *Jour. Physiol.*, 67: 119–151, 1929.

(to be considered later), considerably extended the work of Denny-Brown. Before describing the details of these important observations, we must pause to discuss the anatomical basis of the so-called "motor unit." It was a matter of some surprise to realize that a string galvanometer, without the aid of valve-amplification, was capable of registering the action currents from such a unit.

THE MOTOR UNIT[6]

Denny-Brown's observation was in harmony with the belief that a motor nerve fiber, through peripheral bifurcation, generally innervates a relatively large number of muscle fibers. However in 1928 very few direct observations were available from which an exact calculation could be made. The early (1873) estimates of Tergast[7, 8] and others had not taken into consideration the existence of a large proportion of sensory fibers in muscle nerves. But in the case of the tenuissimus muscle it was evident from the data of Porter and Hart[9] and Adrian,[10] that as many as 140 to 160 muscle fibers must be innervated by a single motor nerve fiber.[2] This presupposed extensive peripheral dichotomy, the existence of which was made quite clear by the observations of Cooper,[11] who studied the peripheral ramifications of motor nerve fibers in the frog and the cat. She encountered many instances of double branching and one instance of "trichotomy."

The problem of complete enumeration of all of the fibers in a given muscle with a view to determination of the "innervation ratio" has recently been undertaken by D. A. Clark.[12] Using cats whose hind limbs had been desensitized by removal of all appropriate posterior root ganglia (in which therefore complete degeneration of all sensory fibers had occurred), he was able to count the motor nerve fibers accurately, and he developed an ingenious method for enumerating all of the muscle fibers, using two representative muscles, soleus and extensor longus digitorum. For soleus an innervation ratio of 1 to 120 was established and for extensor longus digitorum 1 to 155. This means that when a single anterior horn cell supplying the soleus muscle discharges, on an average 120 muscle fibers are thrown into action. This readily accounts for the facility with which Denny-Brown was able to secure action currents of a single unit.

One of the first questions that presents itself relates to the *tension* value of such a group of muscle fibers. How much tension can a single unit develop? It is obvious that this value will impose an absolute limit to the degree of fractionation of which the central nervous system is capable in respect of the muscle which it controls. Chronologically this particular problem was considered before the ratios of Clark were established, in a paper by Eccles and Sherrington[13] published in June, 1930.

Using deganglionated preparations they measured, by means of an accurate torsion-wire myograph, the total tension developed during a twitch and in a tetanus of a group of representative muscles including soleus, extensor longus digitorum, and gastrocnemius. Afterwards, the motor nerve fibers supplying the muscle in question were enumerated and the value so obtained was divided into the total tension development previously observed. The figures arrived at for the tetanus were surprising and are indicated as follows:

	Gm.	No. units
Gastrocnemius (medial head)	30.1	430
Soleus	9.9	200
Semitendinosus	5.5	630
Extensor longus digitorum	8.6	330
Crureus	10.2	250

For the *twitch,* values of approximately a third to a quarter of this amount were obtained. It is thus evident that a single anterior horn cell of gastrocnemius is capable of controlling as much as 30 grams of tension, being larger the larger the animal. On the basis of Clark's enumeration for soleus and extensor longus digitorum, it was possible to calculate a number of additional values, *i.e.,* weight per muscle fiber, and tension per muscle fiber, as indicated in the following table taken from his paper.[12]

Eccles and Sherrington also made a number of significant observations concerning the dichotomy of motor nerve fibers; thus on enumerating the number of mylinated fibers at various levels between the spinal cord and a given muscle, they observed a considerable

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[6] The phrase "motor unit" was introduced in 1925 by Sherrington who later defined it as follows: "The muscle and its nerve may be thought of as an additive assembly of 'motor units,' meaning by 'motor unit' an individual motor nerve fibre together with the bunch of muscle fibres it innervates."

[7] P. Tergast, "Ueber das Verhältniss von Nerve und Muskel," *Arch. f. Mikros. Anat.*, 9: 36–46, 1873.

[8] Tergast observed one nerve fiber to about three muscle fibers in the eye muscles of sheep, but a ratio of 1: 80 to 1: 120 for the limb muscles of the dog.

[9] E. L. Porter and V. W. Hart, "Reflex Contractions of an All-or-None Character in the Spinal Cat," *Am. Jour. Physiol.*, 66: 391–403, 1923.

[10] E. D. Adrian, "The Spread of Activity in the Tenuissimus Muscle of the Cat and in Other Complex Muscles," *Jour. Physiol.*, 60: 301–315, 1925.

[11] S. Cooper, "The Relation of Active to Inactive Fibres in Fractional Contraction of Muscle," *Jour. Physiol.*, 67: 1–13, 1929.

[12] D. A. Clark, "Muscle Counts of Motor Units: A Study in Innervation Ratios," *Am. Jour. Physiol.*, 96: 296–304, 1931.

[13] J. C. Eccles and C. S. Sherrington, "Numbers and Contraction-Values of Individual Motor-Units Examined in Some Muscles of the Limb," *Proc.* Roy. Soc., B/106, 326–357, 1930.

Muscle	Weight per muscle fibre	Tension per muscle fibre	Tension per nerve fibre	Innervation ratio
	mgm	mgm	grams	
M. soleus	0.122	84.0	9.9	1: 120
M. extensor longus digitorum	0.072	48.5	8.6	1: 165

increase in the more peripheral cross-sections. This is well indicated in their diagram (Fig. 3) of the deafferented nerve to gastrocnemius medialis, observed during 53 mm of its course toward the muscle. At the beginning it had 662 motor fibers and at the distal point examined, 815.

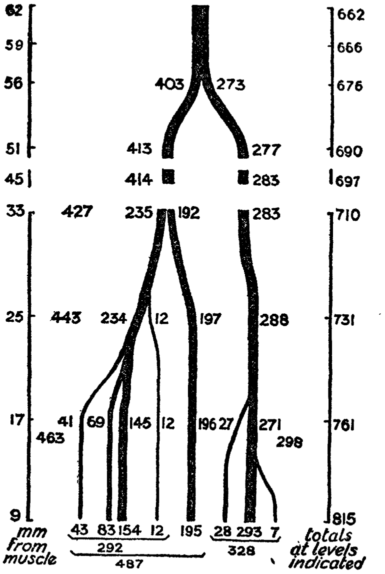

FIG. 3. Eccles and Sherrington's diagram showing their enumerations of fibers in the nerve to gastrocnemius medialis during 53 mm of its course toward the muscle.

Eccles and Sherrington also observed that the motor fibers fell into two groups with respect to their size, a large number of approximately 4 μ and a second group of roughly 14 to 15 μ. Both groups come through the anterior root and were unaffected by removal of the sympathetic ganglion chain. The presumption is that both the large and the small fibers innervate muscle fibers in the usual way through motor end-plates, and the question naturally arises as to the reason for these differing diameters. In studying the incidence of dichotomy Eccles and Sherrington found that the largest fibers were the earliest to divide in their course from spinal cord to muscle and that dichotomy was seldom encountered among the fibers of small diameter except it occur relatively near their ultimate terminations.

They were inclined therefore to believe that the large fibers, through extensive dichotomy, form the largest motor units. The small fibers, forming smaller motor units, serve to make the delicate adjustments necessary for muscular coordination. Eccles and Sherrington also infer that the total area of the large fibers gives an index of the total number of muscle fibers which they supply. Though only 66.3 per cent. in point of numbers, the large group form 92.4 per cent. of the total cross-sectional area. The presumption, therefore, is that the majority of units are large.

Denny-Brown was aware that the tension developed by single units was of the order of magnitude of 1 to 20 gms, but his levers did not permit accurate determination. The average contraction-tension per motor unit for the twitch of soleus in one of Eccles and Sherrington's anatomical estimates was 2.48 gms. With a specially devised eye-muscle myograph (torsion-wire pattern) Eccles and Sherrington[13] were able to obtain stretch reflexes of varying sizes in response to a momentary tap on the table to which the muscle was fixed. A twitch-like response often appeared which was seldom less than *c.* 2.0 gms in tension (Fig. 4), and, if the tap were more intense, larger responses occurred which, on measurement, proved to differ from one another by increments of 1.5 to 2.5 gms; thus in one of their figures showing a series of responses, the tension values were as follows: 0, 0, 2.5, 2.5, 4, 6.5, 6.5, 6.5, 6.5, 7, 8.7, 10.5 gms. From this they conclude (p. 352), "There seems no reason to doubt that the 2.5 gm. responses are twitches of single motor-units, and the 4 gm. responses of 2 units. Continuing the series it seems likely that 6.5–7 gm. is given by 3 units, 815 gm. by 4 units, and 10.5 gm. by 5 units. In this series 2.5 gm. is the greatest tension of a single unit and 1.5 gm. is the smallest. Further observations during the experiment accorded perfectly with these values; in all cases 1.5 or 2.5 gm. was the tension produced by a single unit." Occasionally in their experiments a firm tap

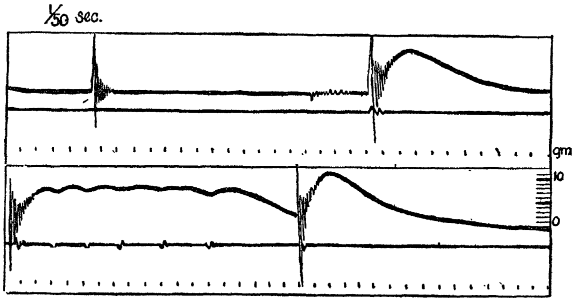

FIG. 4. Simultaneous electrical and mechanical record of units (2 to 3) of the soleus muscle (decerebrate cat) responding to a momentary tap. In the lower record a tetanic response is seen (Eccles and Sherrington).

was *not* followed by a rise of tension (Fig. 4); in such a case there was no electrical response from the muscle, and, as they point out, this serves as an admirable control to the experiment: *i.e.*, there was either a response of *c.* 2.0 gm on the tension record associated with a 1 to 2 mm on the electrical record, or no response in either.

In some of their records *repetitive* responses (Fig. 4) were obtained involving single units, and the greatest tension registered did not exceed 10.4 gm and varied between that value and *c.* 7.0 gm. This is within the range which one would anticipate from the average contraction-tension per motor unit worked out on anatomical grounds (see above).

RATE OF DISCHARGE OF THE ANTERIOR HORN CELL

The most important disclosure from study of single units is their relatively slow rate of discharge. From observations on the voluntary electromyogram, and more particularly from reflex electromyograms in animals (in which responses had been taken *en masse* from the muscle as a whole), it had been inferred that nerve cells may discharge at rates varying from 50 to 500 per sec. It is certainly significant that with isolated units in "tonic" contraction no rhythm higher than 25 per sec. has ever been observed, and the majority have shown rates varying from 5 to 20 per sec.; thus, in Denny-Brown's record (Fig. 2), the first unit was discharging at 7 per sec. and the second at 5.5. In Eccles and Sherrington's tetani of soleus the highest rate seen was 13.7 (Fig. 4). To be sure, these observations were made on soleus, a relatively slow muscle, but the remarkable work of Adrian and Bronk[5] confirms the values obtained, and we now propose to consider this work in detail.

By carefully dissecting a nerve trunk under a binocular microscope, Adrian and Bronk found it possible to transect all but two or three fibers so that only these remained in functional continuity with the nervous system. Leads were then taken from the nerve at points distal to the dissection, and with valve-amplification the responses of individual fibers were readily recorded by means of a capillary electrometer. Various muscle nerves were then examined under different forms of stimulation. During a *flexor* reflex (decapitate cat), evoked by pinching the foot and recorded from the nerve to peroneus longus, the discharge in a single unit was at first very slow, *e.g.*, 5 or 6 per sec., attaining at the end of 1 to 2 seconds a rate of 18 to 20 per sec., again subsiding as the stimulus of the foot was diminished (Fig. 5). In an *extensor* nerve (decerebrate preparation), *e.g.*, that to vastus lateralis, individual units were readily obtained which at rest discharged continuously for long periods at 20 to 25 per sec.; at the height of a crossed extensor reflex the rate might rise as high as 80 to 90 per sec., never above 100. This showed quite clearly that the stronger the stimulus, the more rapid the rate of discharge, and it was evident from this that *rate* of discharge is a highly important factor in the grading of contraction in skeletal muscle. It is a fact of some significance that alterations in rate were more readily demonstrated in extensor muscles than in flexors, for the extensors are called upon for more delicate adjustments of posture and movement than is generally required in the more primitive flexor reactions.

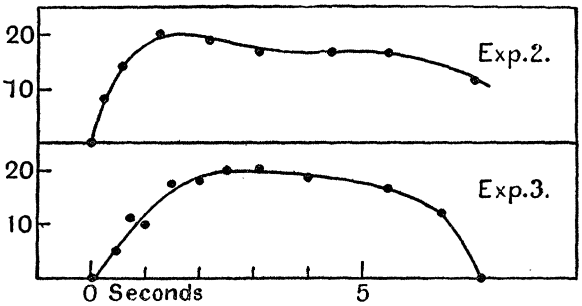

FIG. 5. Adrian and Bronk's curve illustrating the variation in the rate of response of a single unit of peroneus longus during a flexor reflex. *Exp. 2*, decapitate preparation; *Exp. 3*, decerebrate with spinal transection.

By another ingenious device Adrian and Bronk[5] have succeeded in recording single muscle fiber groups in muscles whose nerves were not artificially cut down. They employed the expedient of a concentric needle electrode consisting of a small hypodermic needle into which was inserted a No. 36 gauge enamel wire (193 µ in diameter), the outside of the hypodermic needle forming one electrode and the exposed cut surface of the enamel wire, the other. In this way they suc-

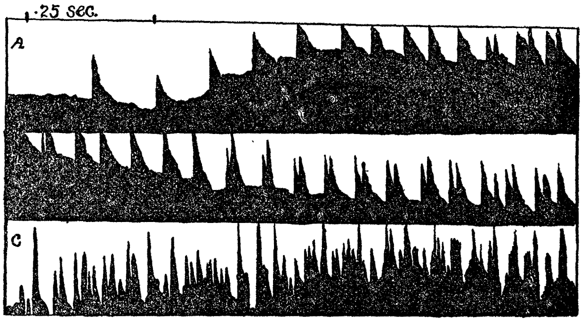

FIG. 6. Record of the development of a voluntary contraction of the human triceps obtained with the concentric needle electrode. In A one unit is responding, at first slowly and then more rapidly; a second unit then appears which in B is seen waxing and waning with the first. In C a large number of units are discharging (Adrian and Bronk).

ceeded in obtaining single and double units during voluntary contraction of human arm muscles (Fig. 6). Not infrequently a contraction began at a rate of 5 or 6 per sec., gradually increasing in magnitude as the contraction became stronger, ultimately reaching 30 or 40 per sec., and occasionally as much as 50. There was no evidence of a predominant 50 per sec. rhythm such as one sees when the muscle mass is examined as a whole (Fig. 1). Once more they demonstrated marked grading of rate during the development of contraction. With this technique they also re-examined certain muscles of the cat, including soleus, confirming Denny-Brown, and they also observed in quadriceps that a "tonic" discharge at a rate of 9 or 10 per sec. might persist for long periods of time without alteration in rate. Denny-Brown had indicated quite clearly that these so-called "tonic" responses were in reality stretch reflexes, for they disappeared when the muscle was caused to relax. Though its rate during a stretch reflex is usually remarkably constant, it may be diminished by application of a weak inhibitory stimulus (Denny-Brown), and I have several times seen soleus units slow down before dropping out of action on turning the head of the preparation away from the recording muscle, a manoeuvre which diminishes the resting tonus in the extensor muscles on that side (Magnus and de Kleyn).

With these characteristics of discharge in mind it is apparent that if more than a few fibers are brought into action, each one discharging asynchronously at a variable rate, the electrical result will be a complex series of deflections which would utterly defy analysis. Such records are readily obtained on gradually increasing a stretch reflex; first one unit, then another, later three or four come in, and ultimately a number so large that the electrical record is meaningless. The important outcome of the analysis of the rates of discharge are twofold: (1) Gradation of activity may be achieved, especially in extensor muscles, by variation in rate of discharge; (2) tonic responses are maintained by rates of discharge ranging from 5 to 15 per sec., at which rate a fiber can go on discharging indefinitely, apparently without fatigue.

OTHER CHARACTERISTICS OF THE MOTOR UNIT

Through analysis of the deafferented tibialis anticus muscle of the cat responding reflexly to two suitably timed, single break-shock stimuli applied to one of the afferent nerves of the hind limb, Eccles and Sherrington in a very recent series of studies[14,15,16,17,18] have thrown much new light upon the functional activity of the units involved in the flexor reflex. For convenience of designation we propose to follow their convention of referring to the first stimulus as C_1 and the second stimulus as C_2.

Latent period.—They have confirmed the determinations of Jolly, and Forbes and Gregg for the "central reflex time" of the flexor reflex to C_1 as falling within the range of 2.75 to 4.35σ, the period being briefer the stronger the stimulus. If, however, C_2 falls within 4 to 36σ of C_1 the latency of C_2 is markedly diminished, and they have proved that the diminution occurs at the expense of the central reflex time. In some experiments it became as brief as 0.5σ, of which a small fraction must be due to conduction time within the nervous system, and the writers therefore conclude that the latent period of individual neurones may, in response to a second stimulus, be as brief as 0.2σ.

Refractory period.—Some writers have assumed that the neurone is without a refractory period. The work of Eccles and Sherrington indicates that this is emphatically incorrect. In their analysis of the reflex response of tibialis to two centripetal volleys they found, when C_1 was sufficiently strong, that C_2 produced a response of varying size depending upon the C_1C_2 interval, being least effective at about 14σ after C_1 (Fig. 7). They have brought forward a series of convincing arguments to show that the greater effectiveness of C_2 at intervals less than 14σ

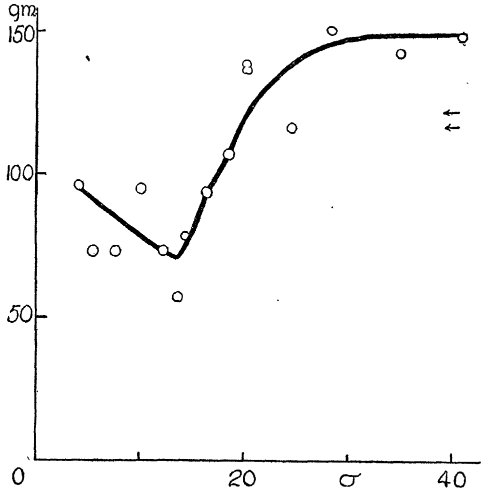

FIG. 7. Curve showing the tension evoked reflexly in tibialis anticus by a second stimulus following at intervals of 4 to 40σ after another stimulus of equal intensity. Note the "minimum" at 14σ.

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[14] J. C. Eccles, "Studies on the Flexor Reflex. III. The Central Effects Produced by an Antidromic Volley," *Proc.* Roy. Soc., B/107: 557–585, 1931.

[15] J. C. Eccles and C. S. Sherrington, "Studies on the Flexor Reflex. I. Latent Period," *Proc.* Roy. Soc., B/107, 511–534, 1931.

[16] *Idem.* II. "The Reflex Response Evoked by Two Centripetal Volleys," *Ibid.*, 535–556.

[17] *Idem.* IV. "After Discharge," *Ibid.*, 586–595.

[18] *Idem.* V. "General Conclusions," *Ibid.*, 596–605.

is due to calling into action units not discharged by C_1 but which had been facilitated by that stimulus ("the subliminal fringe,").[19] Units discharged by C_1 are refractory during the greater part of this period. Following C_1, therefore, two opposing processes go on concurrently in the center: (1) Dissipation of "facilitation" in the neurones of the subliminal fringe, and (2) recovery of excitability in neurones discharged by C_1. This readily accounts for the "minimum" in the response, and the fact that it should occur at 14σ gives a clue to the approximate duration of the refractory period.

The evidence for this interpretation turns largely upon the response of the motor unit to an *antidromic* volley of impulses, *i.e.,* produced by a single stimulus applied to an intact (but deafferented) motor nerve. Eccles[14] has shown that when a motor axon is stimulated in the reverse direction the anterior horn cell is made refractory to centripetal stimuli for a period of 10.5σ, of which 2.5σ represents an absolutely refractory period and *c.* 8σ a relatively refractory period. This new disclosure is one of considerable importance and has thrown quite a new and unexpected light upon the physiology of the neurone. When an antidromic stimulus is applied so as to reach the anterior horn cells between C_1 and C_2 (C_1C_2 interval being less than 14σ, *i.e.,* less than the "minimum") the response to C_2 was largely abolished even though the refractory period (10σ) of the antidromic volley could have had little effect. It is concluded from this that normally the response of C_2 must have depended upon an enhancement of the excitatory state produced in certain neurones by C_1 but not actually discharged by that stimulus. Eccles concludes also that an antidromic volley removes, in subliminally excited neurones, all traces of a preformed central excitatory state and causes the neurones affected to be refractory for a period of 10.5σ. The refractory state so produced is held to be identical with the refractory period following the normal discharge of a neurone. The slight discrepancy between the magnitude of the two values (10.5σ as compared with 14 to 15σ, the relatively refractory period of the reflex arc) is probably due to the greater degree of temporal dispersion of activity incident to stimulation of centripetal volleys.

When an antidromic volley falls during an after-discharge[17] a period of complete quiescence occurs lasting not less than 20 to 50σ which is too long a period to be explained by the central refractory period and must therefore be due to removal of the central excitatory state responsible for the repetitive discharge. In these circumstances all neurones are affected at once and the first sign of activity following the antidromic volley gives evidence of the least interval between successive impulses of the rapidly firing units. When the interval is as great as 50σ it clearly shows that no unit is discharging at a rate greater than 20 per sec. A second corollary is that after-discharge *per se* "depends on the continued arrival of delayed excitatory impulses" rather than on a supraliminal excitatory state. This places the cause of after-discharge further upstream in the reflex arc than the axon hillock of the anterior horn cell, but leaves it still one of the unsolved mysteries of reflex physiology.

Eccles and Sherrington's analysis of the reflex responses evoked by two closely concurrent centripetal volleys indicates that under strong repetitive stimulation from any source the summated rhythm, *e.g.,* the 50 per sec. response in the voluntary electromyogram, is probably due to an asynchronous rotation of units rather than to a group of units discharging at the observed rate. Adrian and Bronk's direct observations on the single unit in voluntary contraction of the human forearm indicate that the rate of discharge is highly variable and that little or no significance can be attached to the rates of discharge previously observed in the voluntary electromyogram.

THE CENTRAL EXCITATORY STATE

The recent experiments of Eccles and Sherrington allow us to reconsider the problem of excitation within the nervous system. They point out that the central excitatory process has many characteristics in common with the so-called local excitatory process in peripheral nerve, "Thus it seems likely," they remark, "that the central excitatory state is a specialised manifestation of the local excitatory state (*cf.* Sherrington, 1921). According to the membrane theory, the latter is a partial depolarisation of the polarised membrane surrounding the axis cylinders of nerve fibres, so on analogy central excitatory state is probably a depolarisation of those parts of the surface membranes of motoneurones on which the excitatory impulses impinge, *i.e.,* the synaptic membranes."

There can be no doubt as to the close parallel between the central excitatory state and the local excitatory process in nerve. They are both due presumably to a local concentration of ions at a previously polarized interface but it seems to me necessary to draw a sharper distinction than Eccles and Sherrington have done between the polarized interface and the action upon it of ions leading to ex-

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[19] D. E. Denny-Brown and C. S. Sherrington, "Subliminal Fringe in Spinal Flexion," *Jour. Physiol.,* 66: 175–180, 1928. See also, C. S. Sherrington, "Some Problems attaching to Convergence." (The Ferrier Lecture). *Proc.* Roy. Soc., B 105, 332–362, 1929; *idem.,* "Quantitative management of Contraction for 'Lowest-level' Coordination." (The Hughlings Jackson Memorial Lecture). *Brit. Med. Journ.,* i, 207–212, 1931.

citation. If the site of accumulation of ions responsible for the central excitatory state were the diffuse peripheral boundary of the nerve cell, which is inherent in their interpretation, I find it very difficult to understand how it is possible for an excitatory impulse reaching the cell at one point to summate with a similar impulse reaching the cell at a distant point; unless there is some special process of local conduction along the surface of the cell, this would be virtually impossible. If, on the other hand, one assumes a site of accumulation of ions common to impulses reaching the cell from every point and that all influence impinges ultimately at this point, the difficulties are minimized. I would urge further that the sharply circumscribed characteristics of refractory period, rate of discharge, etc., presupposes a discrete controlling center within the cell. However, the allocation of the central excitatory state to the region of the synapse has the logical advantage of placing it at the surface of the cell along which conduction is believed to occur. In offering an alternative interpretation, I do so, fully recognizing the inherent objections facing any theory of central excitation at the present time.

CONCLUSION

Single motor units, *i.e.*, anterior horn cells plus the muscle fibers they innervate, have recently been placed under direct observation while responding to a normal reflex stimulus. Details such as the normal rate of discharge, latent period, refractory period, influence of fatigue, etc., have been carefully studied. The work of Denny-Brown, Adrian and Bronk, Eccles and Sherrington have all indicated that the natural rate of discharge of the anterior horn cell is slow, *i.e.*, 5 to 25 per sec., and never more than 80 to 90 per sec. under intense stimulation. A motor unit discharging at 10 per sec. may continue in activity for indefinite periods of time without fatigue. Tonic responses are maintained by such rates of discharge and therefore no special tonic mechanisms need be postulated to explain the absence of fatigue.

An individual anterior horn cell may, through peripheral bifurcation of its axon, command 150 or more muscle fibers, and it may, in consequence, develop during natural tetanus, a tension of 20 to 30 gms (*e.g.*, units of gastrocnemius medialis). In soleus, a red "postural" muscle,[20] the ratio of nerve to muscle fibers is 1 to 120 and the average tension value of the unit 10 gms. Direct observations of the tension developed by single units confirm the values obtained through anatomical averages.

The neurone has a refractory period of 10 to 15σ, which accounts for its normal slow rate of discharge. When an axon is stimulated antidromically[14] the neurone becomes similarly refractory for a period of about 10.5σ and all evidence of a central excitatory state is removed by such a stimulus. The central excitatory state has many properties in common with the local excitatory process.

A RECENT DRIFT IN BIOLOGICAL THOUGHT[1]

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AT the close of the nineteenth century mechanism prevailed. The heavens no longer declared the glory of God but rather the marvelous phenomena that had accidentally transpired within the cosmic test-tube. Even the mind of man was but an epiphenomenon. It was the rattle of machinery. William Keith Brooks, in reaction to this mechanism, was frequently heard to remark, "Yes, my mind may be but the rattle of machinery, but what perplexes me is who hears the rattle?"

To modern physicists, the mechanism that prevailed three decades ago no longer appears to be satisfactory. Millikan closed his presidential address at Cleveland, last December, with the question "Has not modern physics thrown mechanism, root and branch, from its house?" and Jeans has placed a Creator back upon the throne. He says: "Everything points with overwhelming force to a definite event, or series of events of creation. . . . The universe can not have originated by chance out of its present ingredients."

Modern biologists are yet striving to reduce vital phenomena to mechanical terms. Surface phenomena, colloidal phases and molecular changes are invoked, and that properly so, to explain these phenomena. But we must keep in mind that vital phenomena carry us beyond the ponderable. So our scientific efforts will not suffice when we come to consider all that life displays. Even an ameba carries us beyond the realm of science. Men have sought to explain the movement of this unicellular animal as the result of surface tension disturbances, of changes in colloidal states or of molecular changes. An

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[20] D. E. Denny-Brown, "The Histological Features of Striped Muscle in Relation to its Functional Activity," *Proc.* Roy. Soc., B/104: 371–411, 1929.

[1] Address delivered at the Virginia Academy of Science, April 24, 1931.