REFLEX DEPRESSION IN RHYTHMICALLY ACTIVE MONOSYNAPTIC REFLEX PATHWAYS

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Fluctuation of excitability in the spinal cord in one sense has been a source of annoyance to most who have employed monosynaptic reflexes for one purpose or another. At an early stage in the exploitation of monosynaptic reflexes it became usual practice to record a number of responses in any given circumstance and to average the lot in the hope of attaining a degree of precision in measurement. In a general way it was recognized that mean monosynaptic reflex amplitude could be different at different repetition rates, but until Jefferson and Schlapp (9) studied repetition for its own sake, most were content to control whatever was at work by maintaining the repetition rate constant and, perhaps, discarding the initial responses of a series. Whilst thinking in terms of single shocks one was dealing in fact with trains of shocks. Feeling that the only logical distinction between single shock and repetitive stimulation could be made at a frequency which is just sufficiently low that one reflex event leaves no measurable impression upon the next, the present experiments were begun with the lowly aim of finding that frequency. The answer was such as unequivocally to show that any attempt to achieve single shock conditions as well as a reasonable degree of precision in the face of fluctuation is quite impractical.

The experiments to be described with very few exceptions were performed upon decapitate cat preparations. The remainder were anesthetized with chloralose-urethane. Monosynaptic reflexes pertaining to a flexor motor nucleus or an extensor motor nucleus were elicited by afferent stimulation of the distally severed nerves to biceps posterior-semitendinosus or the pretibial flexors, and to triceps surae, plantaris, or flexor longus. Recording was done from the appropriate distally severed ventral root, that being either the seventh lumbar or first sacral.

In all but a few experiments recordings were made with the aid of a Grass camera adjusted for moving film. The oscilloscope sweep was not employed. By suitable adjustment of the sweep controls, however, the beam bright cycle was gated to display only the monosynaptic reflex. The resulting records thus had the appearance shown in Fig. 2.

To express monosynaptic reflex amplitude as a function of frequency some

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100 successive responses at each desired frequency were measured, and the mean value extracted which then was plotted on the ordinates against frequency on the abscissae. Fig. 1 illustrates a typical experiment, so plotted, in which frequency was varied between 3 per minute (0.05 per second) and 50 per second. Reflex amplitude is expressed in per cent of the mean value at a frequency of 3 per minute. This value was chosen because experiment had failed to disclose any dependent variation in mean amplitude at still lower frequencies. Reflex behavior at frequencies higher than 50 per second (*cf.* reference 1) is considered in a subsequent paper (14).

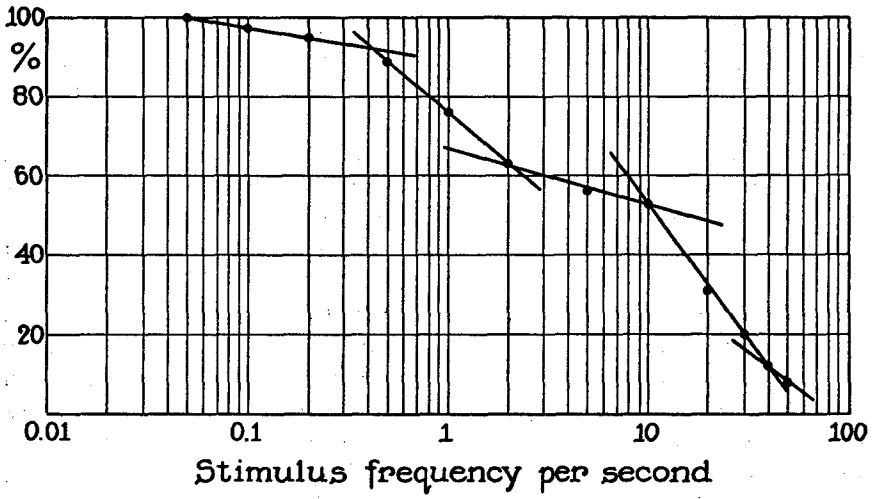

FIG. 1. Relation between afferent stimulation frequency and mean monosynaptic reflex output in the range from 0.05 per second (3 per minute) to 50 per second.

Within the range of frequencies entered in Fig. 1 it is seen that mean monosynaptic reflex amplitude decreased with increasing frequency, itself neither a new nor surprising result. It was not known, however, that the depression of repetition occurred at such low frequencies, since Jefferson and Schlapp (9) had not observed depression with stimulation less frequent than 20 per minute. Now obviously if reflex response is depressed at a certain frequency there must be a period of downward adjustment at the onset of a train of stimuli at that frequency. Because of this fact responses at the onset of a stimulus train either were unrecorded or were discarded in the hope of sampling the steady state condition. Since the significance of the mean monosynaptic reflex amplitude (M) at any given frequency depends upon the establishment of steady state conditions some attention has been directed to finding whether or not this in fact was accomplished.

Establishing the Steady State.—Fig. 2 illustrates the onset of trains of mono-

synaptic reflexes elicited at frequencies varying between 6 per minute (*Q* 10) and 20 per second. By mere inspection it is impossible to say that any period of downward adjustment in amplitude takes place at frequencies lower than 30 per minute (*Q* 2). This is in accord with the observations of Jefferson and

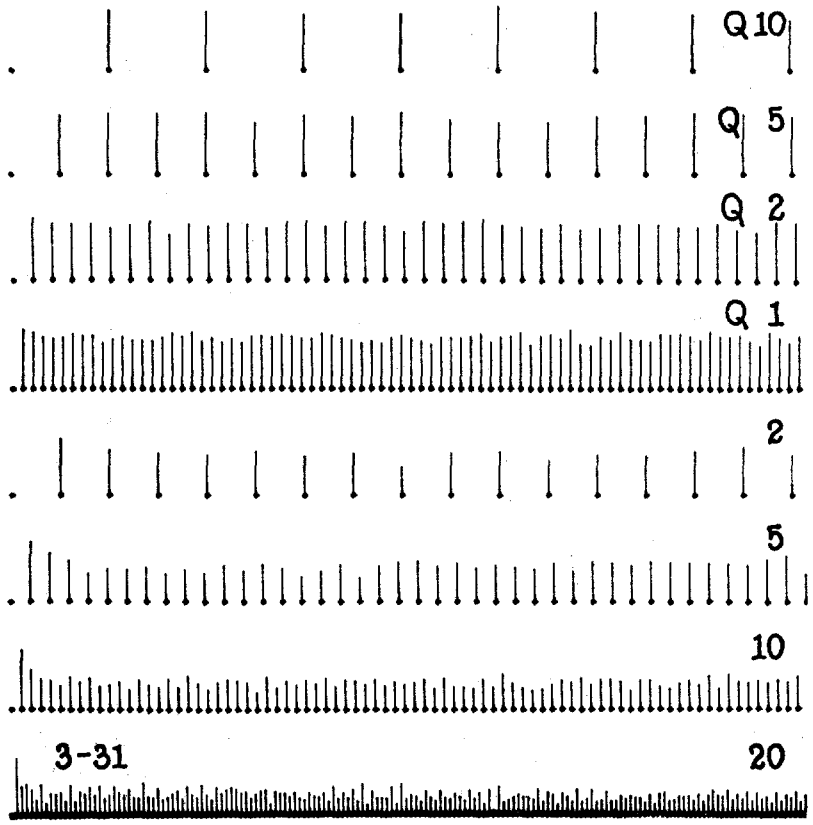

FIG. 2. Onset of trains of monosynaptic reflex volleys at frequencies in the range from 6 per minute (*Q* 10 seconds) to 20 per second to show period of downward adjustment. Film speed for lower four records ten times that for upper four records.

Schlapp (9) who were aware, however, that statistical analysis might reveal depression at lower frequencies of rhythmic stimulation. At higher frequencies than those exemplified in Fig. 2 the initial downward adjustment in amplitude is more dramatic and can be seen, as in the recordings of Eccles and Rall (5), to overshoot the supposed mean steady state value.

Despite the enduring quality of the process underlying depression of response at relatively low frequencies of stimulation the period of adjustment to steady state conditions as far as the eye can tell is rapidly completed. As a

test for the establishment of steady state conditions each series of observations, from which a mean monosynaptic reflex amplitude (M) was extracted, has been divided into two equal component series from which were obtained two mean values M_1 and M_2. Fig. 3 plots M_2 as a function of M_1. The scale of coordinates is arbitrary but consistent in the sense that all values initially were measured in the same units from the photographic records. Absolute amplitude of the mean monosynaptic reflex at a given frequency differed from experiment

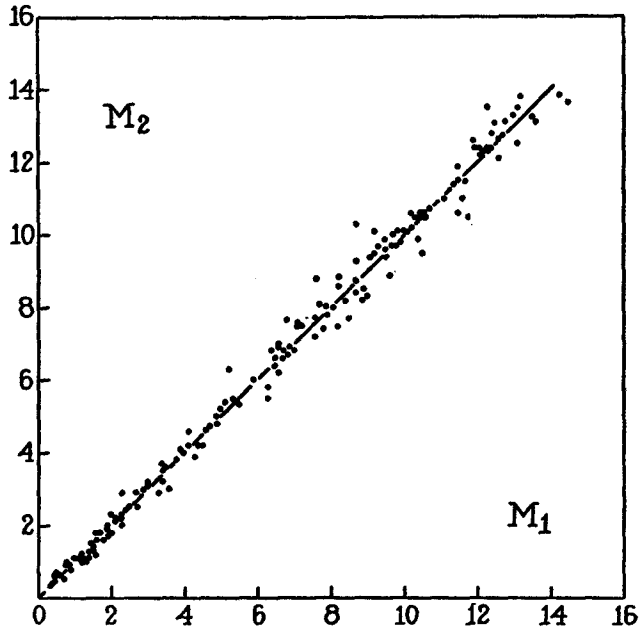

FIG. 3. Each series of monosynaptic reflexes at a given frequency has been divided into two equal component series. Mean monosynaptic reflex amplitude for the second component series (M_2) is plotted on the ordinates as a function of mean amplitude for the first component series (M_1) on the abscissae.

to experiment, as did the amplification employed, but amplification was constant throughout any one experiment. Hence there is no strict relation between the mean values plotted in Fig. 3 and frequency. Nevertheless, in general, the large values represent low frequency responses and the small values high frequency responses. The range of frequencies represented in Fig. 3 is from 3 per minute to 80 per second.

From inspection of Fig. 3 there appears to be no reason to doubt that steady state conditions were established following the initial period of downward adjustment. Two other possibilities existed *a priori*: that iterative monosynaptic reflexes might display a slow increment in amplitude or, alternatively, a slow

decrement. That they did not in the samples is, of course, important from a purely practical point of view. To say that they do not is another matter. It is not unknown for the amplitude of monosynaptic reflexes to drift in one direction or the other during prolonged series of observations. Such changes, however, appear to result from insufficient control of extraneous factors, slight temperature variation being the major known offender, rather than from intrinsic frequency-coupled events.

Relation between Synaptic Drive and Degree of Depression.—The relation be-

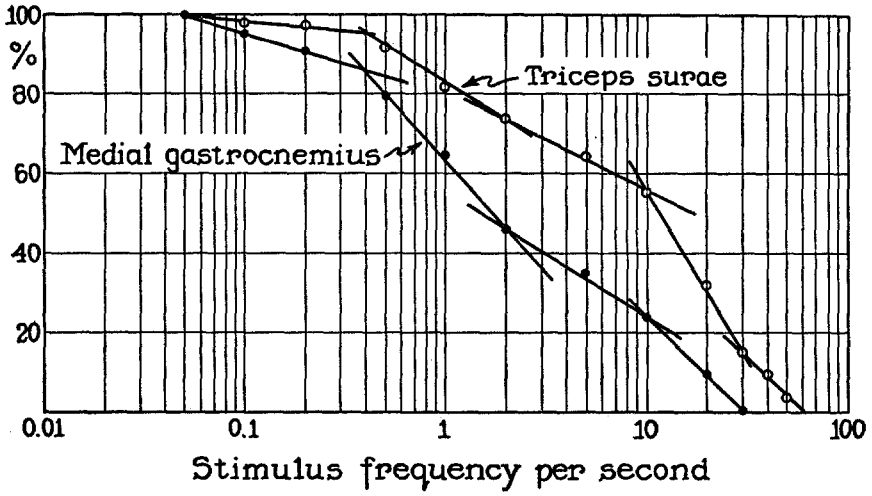

FIG. 4. A comparison of the relation between afferent stimulation frequency and mean monosynaptic reflex output when the entire afferent supply to triceps surae is stimulated and when afferent stimulation is restricted to the medial gastrocnemius component.

tween frequency and amplitude displayed in Fig. 1 is typical. Not unexpectedly, however, degree of depression differs from one experimental situation to another. This is exemplified by the experiment presented in Fig. 4 in which the frequency-amplitude relation was explored initially with afferent volleys in the entire nerve supply to triceps surae and subsequently with afferent volleys restricted to the medial gastrocnemius component. Recording was from the first sacral ventral root that had been tested for content of lateral gastrocnemius motor axons by the use of lateral gastrocnemius afferent volleys. No reflex being present in the resting state, although a small one did appear in the post-tetanically potentiated state, it can be presumed that the reflex elicited by stimulation of the entire nerve pertained essentially, one cannot say exclusively, to medial gastrocnemius. As all other conditions were held constant the important variable was the intensity of synaptic drive upon the moto-

neurons of medial gastrocnemius. In the experimental result depicted in Fig. 4 there is, except for degree of depression, good correspondence between the frequency-amplitude relation of the motor pool at the two intensity levels of synaptic drive.

Magnitude of the monosynaptic reflex elicited from a given motor nucleus, say triceps, by maximal group I afferent volleys may vary considerably from one experiment to the next, a difference that can be accentuated greatly by appropriate manipulation of body temperature. In Fig. 5 are contrasted the frequency-amplitude relations of tricipital monosynaptic reflexes from two

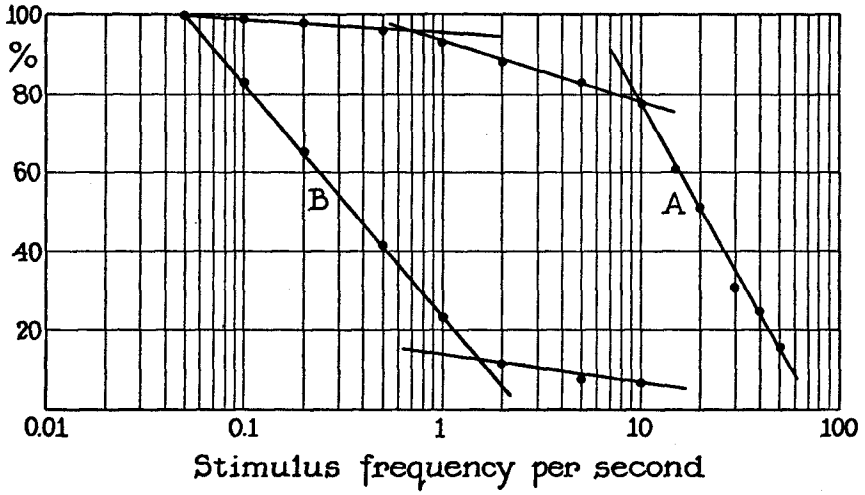

FIG. 5. Relations between afferent stimulation frequency and mean monosynaptic reflex output utilizing (A) a powerful reflex at T = 34°C. and B a feeble reflex at T = 38°C.

preparations one of which, maintained at 34°C., transmitted a powerful reflex, the other of which, maintained at 38°C., transmitted a feeble reflex. The former reflex (curve A) suffers most in the frequency range above 10 per second, although the low frequency depression is distinctly present. By contrast the latter reflex (curve B) comes close to extinction in the range between 1 and 10 per second.

The difference in form between curves 5A and 5B can best be understood with the help of studies upon the behavior, in similar circumstances, of individual motoneurons. To anticipate the findings from study of individual motoneurons (15) it can be said that any monosynaptic reflex includes among its responding member neurons some that are highly resistant to the low frequency depression and others that are highly susceptible. In the first approximation any of the curves in Figs. 1, 4, and 5 can be constructed by varying the ratio between the two sorts of neurons in the discharge zone.

Two Phases of Depression.—A better idea of the course of depression can be gained by plotting on linear coordinates the frequency-amplitude relations of monosynaptic reflexes. In Fig. 6 this is done. Considering the form of the curves presented it seems a just postulate that one is dealing with two processes, one of relatively short duration that influences the outcome only at frequencies in excess of approximately 10 per second and one of enduring quality. Accordingly it is appropriate to speak of high frequency and low frequency depression

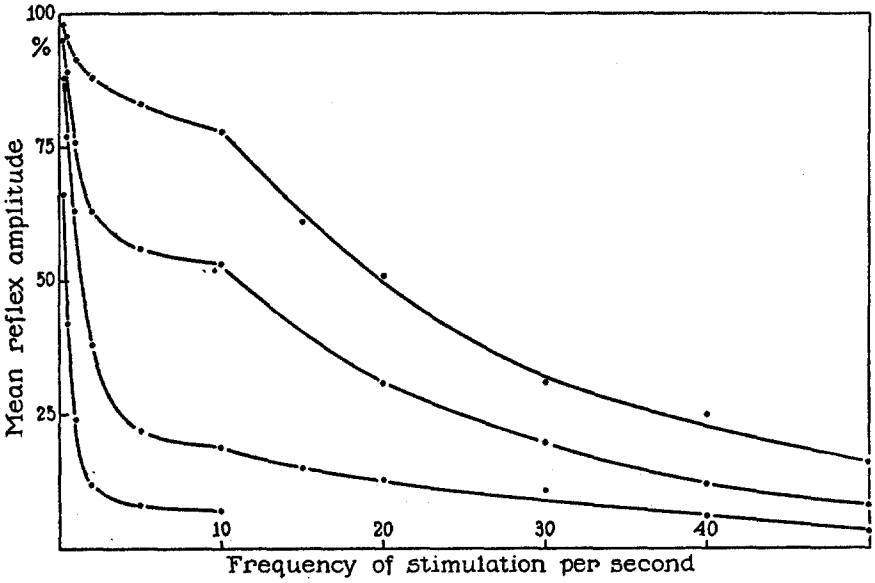

FIG. 6. Linear plots of the relation between afferent stimulation frequency and mean monosynaptic reflex output in four experiments showing differing intensities of depression in the low and high frequency ranges but similarity in the temporal course of depression. Frequency range from 0.2 per second (12 per minute) to 50 per second.

although in assigning the terms it must not be supposed that the now designated low frequency depression does not influence the issue at frequencies higher than 10 per second.

Since the significant discontinuity in the frequency-amplitude curves of Fig. 6 occurs at a frequency of 10 per second one surmises that the high frequency depression is an expression of the influence of the subnormal process in motoneurons.

On High Frequency Depression.—Fig. 7 presents the results of several experiments designed to examine the course of high frequency depression. The method of plotting requires comment. Mean reflex amplitude here is expressed not in terms of frequency but as a function of interval between successive

volleys. This permits a comparison between experiments employing frequency series and experiments employing the conditioning shock-testing shock technique. In order to examine events at the shock intervals of immediate interest and to scale the values from the several experiments amplitude in each at a shock interval of 120 msec. has been designated as 100 per cent and values at other intervals expressed in per cent of that value. The broken line curve charts the course of subnormality as delineated by the conditioning antidromic volley, testing reflex volley technique (12).

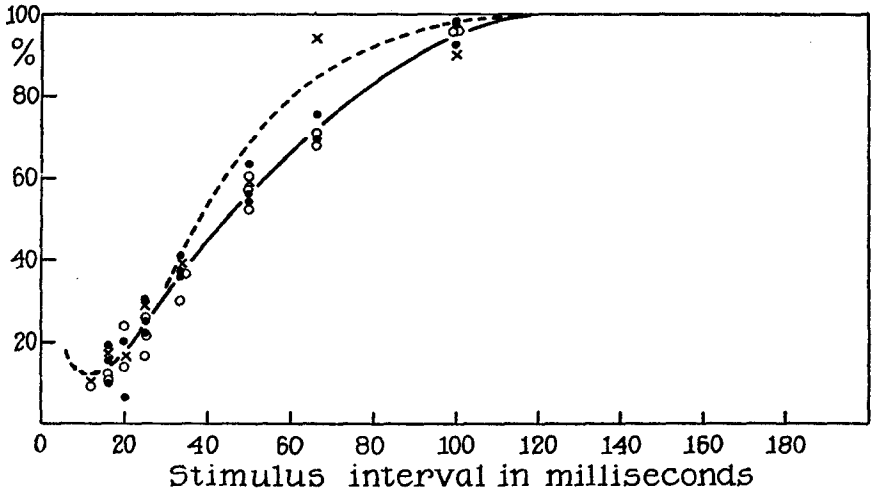

FIG. 7. High frequency depression in flexor and extensor nuclei compared. Mean monosynaptic reflex amplitudes are plotted on the ordinates in per cent of the amplitudes at 120 msec. interval between successive stimuli. The abscissa represents interval between successive stimuli rather than frequency. Results from five experiments are included. Some of the plotted points represent duplicate determinations. The broken line plots course of motoneuron subnormality.

It is clear that the experimental points are very close to the subnormality curve, but it is equally clear that they do not coincide with it. Thus, even if subnormality is the major factor at the shock intervals under discussion, there is yet another factor operating. This, one may suppose is the early part of the process underlying late depression. In view of the experiments of Brooks, Downman, and Eccles (*cf.* reference 4 their Fig. 4 *a*) the point need not be labored except to the extent that comparability of result derived from two-shock analysis and from frequency amplitude series has yet to be established. This question is discussed in connection with Fig. 9.

A more serious question at this juncture is whether the high frequency depression in the steady state is due solely to agencies intrinsic to the monosynaptic pathway, or whether other systems are to some extent contributory. In

fluence by reflex pathways originating in group III fibers can be eliminated from consideration for stimulation did not embrace these higher threshold fibers. However, stimulation necessarily did involve group II fibers and group IB fibers in addition to the monosynaptic afferent group IA fibers. In extensor nuclei the group II fibers, being afferent to a flexor reflex, could contribute to depression but in flexor nuclei would act to mitigate depression. The test, then, for group II afferent fiber contribution is to compare frequency-amplitude relations in flexor and extensor nuclei. This has been done with the result

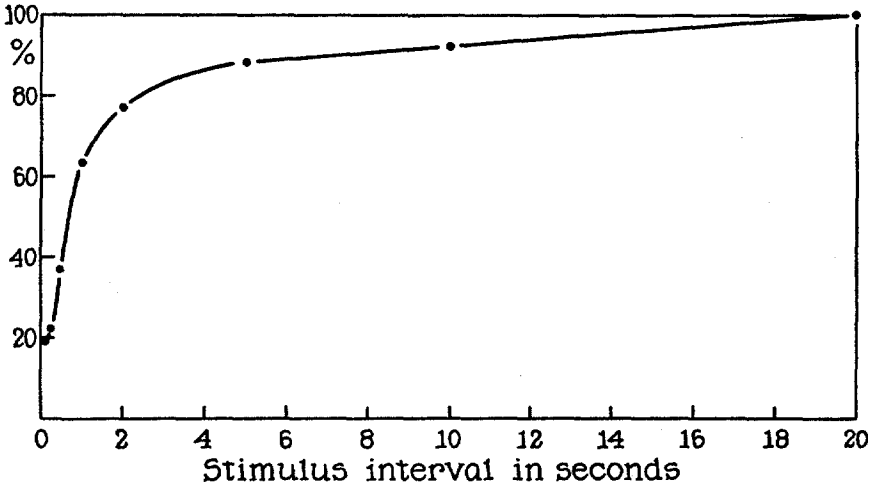

FIG. 8. Time course of low frequency depression obtained by plotting on the ordinates mean monosynaptic reflex amplitude, in per cent of mean amplitude at a frequency of 0.05 per second (3 per minute), as a function of interval between successive stimuli at each frequency studied.

shown in Fig. 7. Open circles represent frequency-amplitude determinations for flexor monosynaptic reflexes, the remaining symbols represent determinations for extensor monosynaptic reflexes. In all five experiments are illustrated.

Since there is no systematic difference between flexor and extensor monosynaptic reflex frequency-amplitude relations in the high frequency depression range one is inclined to discount for that range a significant conditioning role played in the steady state condition by group II flexor reflex connections to motoneurons. It should be noted that Eccles and Rall (5) describe differences during the period of adjustment that could be related to group II action. On the other hand, Jefferson and Schlapp (9) found little distinction between the behavior of flexor and extensor nuclei and even found that addition of sural nerve volleys to gastrocnemius nerve volleys did not change the frequency-amplitude relation of gastrocnemius monosynaptic reflexes.

It is difficult at this stage to rule out participation of the group IB disynaptic

system in the production of the depression of repetition, for in operation this system would be inhibitory to the homonymous motoneurons be they flexor or extensor (10).

Low Frequency Depression.—In order to form a picture of the process that might be responsible for low frequency depression it is useful to plot experimental result in terms of interval between successive stimuli rather than frequency. Fig. 8 presents such a plot and describes, presumably, the time course of the enduring depression.

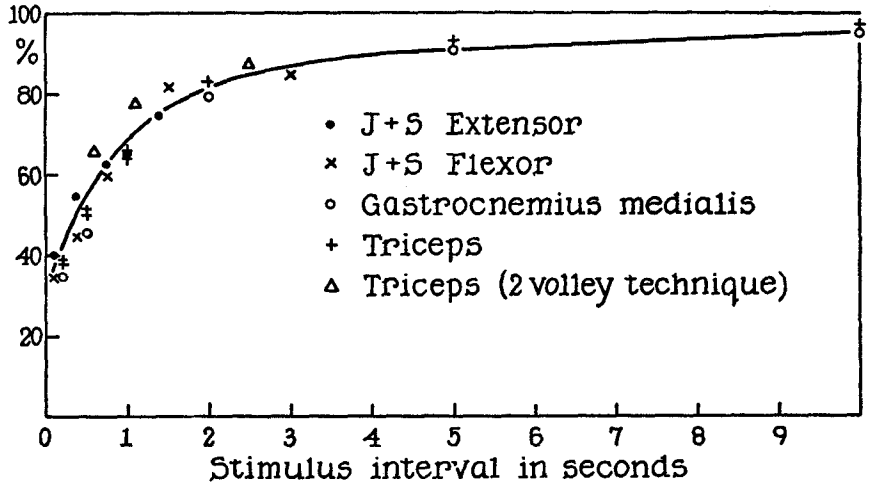

FIG. 9. Comparison of low frequency depression in flexor and extensor nuclei and also of depression as revealed by the two volley technique and by frequency-amplitude series. Method of plotting as in Fig. 8 but note the expanded scale of stimulus interval.

Before discussing further the agency for low frequency depression one may dispose of the question of congruence between the results of two shock exploration and frequency-amplitude series. Again plotted as functions of stimulus intervals rather than frequency in Fig. 9 are the results of three experiments from the present series selected for displaying essentially similar degrees of depression of response. To these have been added the data of Jefferson and Schlapp concerning depression in an extensor nucleus and a flexor nucleus respectively (reference 9, Figs. 1 and 2). Finally there is included the result of an experiment employing the two volley technique, the points representing, on the ordinate, mean amplitude of the second of two maximal reflex volleys for a large number of observations, taken at a repetition rate of 3 per minute to avoid added frequency effects. This is expressed in percentage of the mean response amplitude of regularly interspersed control reflex volleys.

Because the two volley technique reveals a depression identical in time course

with that evidenced in frequency-amplitude series it seems a valid conclusion that the two techniques do, in fact, yield similar information concerning one and the same fundamental process. Thus one supposes that the low frequency depression described by Jefferson and Schlapp (9) and the so called "subsynaptic depression" of Brooks, Downman, and Eccles (4) represent a single phenomenon, the time course of which is presented in Fig. 8.

That group II and group III afferent fibers in action do not participate as causal agents for the low frequency depression, nor, for that matter, significantly modify the course of depression is sufficiently indicated for the low frequency range by the results of Jefferson and Schlapp (9), which have been confirmed in the present study. By exclusion, then, low frequency depression, just as high frequency depression, can be considered a consequence of action on the part of group I fibers.

Relation between Group I Afferent Input and Degree of Depression.—Granting the role of group I fibers in production of low frequency depression one might hope to eliminate the group IB afferent fibers as significant contributors to that depression. One approach to the problem is to compare the relation between afferent volley size and degree of depression with that between afferent volley size and intensity of some known group IA action upon motoneurons. Suitable bases for comparison are provided in Hunt's (8) study of facilitation and inhibition of monosynaptic reflex discharge in which it was shown that these functions, in approximation, are related in degree linearly with group I afferent volley size.

The results of experiments designed to reveal the relation between afferent input and depression are presented in Fig. 10. Of necessity one must resort to the two shock technique so the validity of the results as concerns low frequency depression necessarily depends upon the comparability of result derived from the use of the two methods. In each experiment the oscilloscope sweep was set at a repetition rate of 6 per minute and all sweeps photographed. The stimulators were arranged so that two successive shocks could be applied to the selected muscle nerve at a fixed interval, that being approximately 500 msec. On alternate sweeps the first, or conditioning, shock was omitted. One beam of the oscilloscope was employed to monitor the conditioning afferent volley, this being recorded at the cord-root junction after conduction centrally from the peripherally located stimulating electrodes. The second beam displayed the monosynaptic reflex responses to the first and second afferent volleys. By this arrangement magnitude of the first afferent volley, which was varied from zero to maximum for the group I band of fibers, gave a measure of input. Magnitude of the monosynaptic reflex response to the measured conditioning afferent volleys gave a measure of output. Finally, comparison between the magnitude of monosynaptic reflex response to the second, fixed, maximal afferent volleys when anteceded by the conditioning volleys, and when not so

anteceded, gave a measure of the degree of late depression imposed by any given magnitude of conditioning volley. The relations between degree of depression and input, obtained in four experiments, are displayed on the left of Fig. 10, the simultaneously obtained relations between monosynaptic reflex output and input on the right.

In the course of experiment it very soon became evident that the relation between group I afferent input and degree of depression was, over a considerable range, linear, but that some secondary effect was influencing the relation

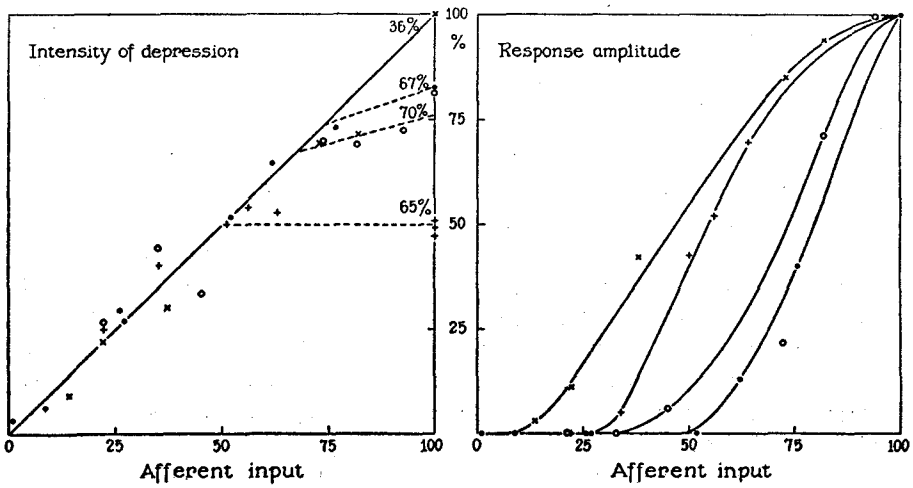

FIG. 10. To the left are plots representing degree of depression of test monosynaptic reflex volleys as a function of measured amplitude of graded afferent group I conditioning volleys timed to antecede the test volleys by a fixed interval. To the right are plots of the monosynaptic reflex output in response to those same measured, graded, group I afferent conditioning volleys. In this way transmission and depression can be compared directly. In all four experiments are represented.

as input approached maximum if the degree of attainable depression was large. In order to present this result graphically straight lines were drawn through the approximately linear portion of the plotted results for each individual experiment and extrapolated to maximal input to give, for each experiment, the greatest degree of depression hypothetically obtainable at that maximal input. The experimental values for degree of depression then were recalculated employing in each case the hypothetical maximum as 100 per cent on the scale of ordinates. This served to scale the linear portions of the input-depression relations from the individual experiments to a common plot, which is given by the solid line on the left of Fig. 10. Such deviations from linearity as occurred in the individual experiments are expressed by the broken line

continuations from the linear function. At the top of each plot is given in percentage the absolute magnitude of depression realized in each of the several experiments.

It is evident that the smallest afferent volleys exert an enduring depressant action and that this grows *pari passu* with increment in afferent volley size until such volleys are between 60 and 80 per cent maximal. With further increment the degree of depression developed may fall far short of expectation. Some upward convexity of the curve is to be expected, on the basis of Hunt's observations, in the range of group I input above 85 per cent, but the defect in growth of depression with input is, in three of the four experiments, more severe.

In his study of the monosynaptic reflex input-response relation Rall (18) came to the conclusion that the monosynaptic reflex afferent fibers were concentrated in the lower 60 per cent with respect to threshold segment of group I afferent input. Were this so it would provide a convenient explanation for the input-depression curves of Fig. 10 from which one would conclude that depression was strictly limited to origin in action by group IA fibers. Unfortunately for this explanation the simultaneously recorded input-output curves shown to the right of Fig. 10 have the form described by Hunt (8) rather than that described by Rall (18) which is to say that output increases throughout the entire range of input. This implies that the departure from approximate linearity in the input-depression relation cannot be for want of group IA afferent input. It is for this reason that one is led to suppose that some secondary factor in effect places a ceiling upon the realizable degree of depression.

The most likely explanation for the ceiling effect emerges from the fact reported elsewhere (15) that individual motoneurons can be classified, with respect to the influence of low frequency depression, and in the first approximation, into two principal types: those that fall out of the response zone at fairly low frequencies by reason of the low frequency depression and those that are highly resistant to low frequency depression. To account for the occurrence of a ceiling one has only to suppose that the monosynaptic reflexes whose behavior is represented in Fig. 10 pertained to motoneurons some 60 to 70 per cent of which were of the former type, the remainder of the latter type. Thus, as the growing conditioning volleys reached the point of depressing subsequent test response by some 60 to 70 per cent the remaining test response, pertaining to resistant motoneurons, would give little expression to further growth of the conditioning volleys, and the depressive action accountable to them.

The experiments described in connection with Fig. 10 are consistent with the notion that group IA monosynaptic reflex afferent fibers are the agents responsible for low frequency depression, for the relation between input and depression, except for the ceiling imposed, is that to be expected of known group IA action. To the extent that one would expect contribution by group IB fibers,

if anything, to introduce an upward concavity to the curves it may be supposed that group IB fibers are non-contributory in the circumstances of experiment. While this does not constitute rigid proof, significant participation of group IB is unlikely.

One fact concerning low frequency, or enduring, depression is abundantly documented by the experiments of Fig. 10. A comparison of the simultaneously recorded input-depression and input-output relations shows that the depressive action does not involve discharge of motoneurons (*cf.* references 4, 7).

On the Mechanism of Enduring Depression.—An impressive degree of agreement exists concerning location in the presynaptic elements of the agency for low frequency (or enduring) depression in the monosynaptic reflex pathway. The important question then is whether the presynaptic elements act upon themselves so to speak to reduce efficacy, or whether they act upon motoneurons to raise threshold. By use of the designation "subsynaptic depression" Eccles would appear to favor action upon the motoneuron but in attributing it to exhaustion of a chemical mediator (reference 9, discussion) appears to favor reduced efficacy. Evanson (7) suggests as mechanism reduction of the transmitter potentiality of the presynaptic endings, which is to say reduced efficacy.

When in a pathway consisting only of presynaptic and postsynaptic elements one finds a number of phenomena displaying apparently identical intensity-time courses, it is economy of hypothesis to suppose that they may have common origin. In study of the spinal monosynaptic reflex pathway a number of phenomena have emerged that do in fact display apparently identical courses. These are: (1) that member of dorsal root potential sequence designated as D.R.IV.R. (13, 16); (2) the early post-tetanic potentiation that is seen after brief high frequency tetani (6, 13); (3) the recovery of presynaptic structures from anodal type block which characterizes the period prior to onset of late potentiation after more enduring tetani (13); (4) depression in a homonymous pathway after one or several shocks (4, 5, 9, 3, 7); and (5) the low frequency depression of repetitive stimulation. All five of these phenomena on adequate evidence have been assigned to the presynaptic structures. Fig. 11 serves to illustrate the similarity between certain of these phenomena: (1) D.R.IV.R. potential, which is represented by the solid line plotted by tracing on graph paper the original records from two experiments projected at suitable magnification; (2) the depression following a single shock, represented by filled circles; and (3) the low frequency depression observed in two experiments, represented by open circles and crosses.

By its nature D.R.IV.R. represents hyperpolarization of the terminal regions of the presynaptic fibers relative to the polarization level of their more proximal regions. As such it is an appropriate agency for the production of early potentiation following brief tetani, and for anodal type block following more severe tetanization. In giving rise to these phenomena the process underlying

D.R.IV.R. must be acting in such a way as to alter synaptic efficacy. Thus the intrinsically generated hyperpolarization, in the manner of anodal polarization generally, would augment impulses if not too severe and would when intensified lead to block. Such a reversal of action by intensity change is acceptable according to first principles. It is something else to suppose that when less intense the same process acting in the same way would reverse its action from increasing efficacy, as in early potentiation, to decreasing efficacy, as in enduring depression. This in essence is the observation of Beswick and Evanson (3)

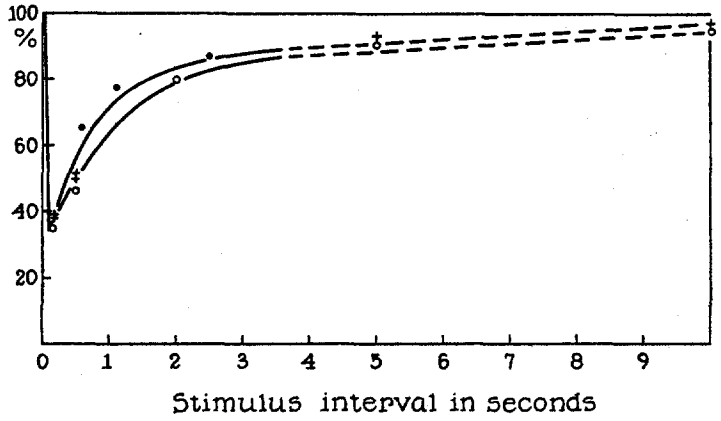

FIG. 11. The D.R.IV.R. potential as recorded from a dorsal root that has carried a short high frequency burst of afferent volleys (*cf.* reference 13, Fig. 10) is represented by the solid lines traced from the recordings in two experiments. Filled circles represent the course of enduring depression according to the two shock technique. Crosses and open circles represent the course of low frequency depression. The broken lines are extrapolations from the recorded course of D.R.IV.R.

who have noted that one volley produces enduring depression of a subsequent test reflex, that two or more volleys intensify the depression, and that further change results in a transition from intensification of depression to its replacement by early potentiation. The alternative then, since influence on the presynaptic fibers themselves leads to potentiation and finally block, is to suppose that the enduring depression results from action of presynaptic fibers not upon themselves but upon the motoneurons.

Such action by the presynaptic fibers upon the motoneurons could be considered as occurring in parallel with the action those fibers exert upon themselves. Following one or a few stimuli action upon the motoneurons would predominate, with hyperpolarization in the terminal regions of the presynaptic fibers becoming more and more significant, as further increase in stimulation takes place, eventually to predominate causing potentiation and finally block.

Such a distinction between two phases of action provides a thinkable basis for the reversal from depression to early potentiation as described by Beswick and Evanson.

If enduring depression is the result of presynaptic action upon the motoneurons one might reasonably expect to find some sign of depression by the use of heterosynaptic reflex testing. Evanson (7) has failed in his search for heterosynaptic depression utilizing the synergic pathways of triceps surae. Similar experiments, forming part of the present series, employing synergic pathways stimulated both at the periphery in muscle nerves and at the dorsal root level have produced equivocal results, for the most part negative.

It may be noted at this juncture that Larrabee and Bronk (11) and also Lorente de Nó and Laporte (17) have encountered in mammalian and turtle sympathetic ganglia prolonged depressions bearing a general resemblance to that here discussed and which are detectable by heterosynaptic test. It is of additional interest that Larrabee and Bronk found in some experiments that the depression was undetected by heterosynaptic test.

Bernhard (2), Brooks, Downman, and Eccles (4), and Eccles and Rall (5) have all reported occurrence of heterosynaptic depression in monosynaptic reflex paths, in some cases inconsistently, but the conditioning test stimulus intervals were not such as to reassure one as to enduring quality. Because of the inconsistent nature of experimental evidence, for which the reasons are obscure, one is not prepared to state that a synergic pathway does exhibit enduring depression. On the other hand, failure to find convincing evidences of enduring depression by means of heterosynaptic test (this being the important reason for proposing, as Evanson has, that depression results from reduced presynaptic efficacy) does not uniquely dispose of the alternative concept that depression results from a depressive action upon the motoneurons. As the matter rests the logical difficulties of the reduced efficacy hypotheses would seem to outweigh the single dubious advantage. This unsatisfactory situation exists, incidentally, whether or not any credence is to be accorded the notion that depression may be linked in some way with other processes that exhibit similar characteristics, notably that underlying the D.R.IV reversal.

SUMMARY

A study has been made of the depression that occurs when a monosynaptic reflex pathway is subjected to repetitive stimulation.

Reflex depression has a dual origin. High frequency or early depression is postsynaptic in origin and results from subnormality in the motoneurons. Low frequency, late, or enduring depression is presynaptic in origin.

The conditioning volley–test volley technique and the frequency-mean monosynaptic reflex amplitude relation yield similar information concerning reflex depression. Each method has its advantages and for some purposes one or the other of the methods necessarily must be employed.

The results of a variety of experiments are consistent with the proposition that reflex depression in the monosynaptic reflex pathway originates by action in the group IA afferent fibers of muscle origin that are responsible for monosynaptic reflex transmission.

Depression is present at a frequency of 0.1 per second (6 per minute) and absent at a frequency of 0.05 per second (3 per minute). Thus it is impractical for most purposes to employ repetition rates that satisfy the requirement for designation as "single shock" stimulations.

The temporal course of enduring depression has been determined. It is identical with that for a number of other phenomena observable in monosynaptic reflex pathways, which suggests a common origin. The mechanism of low frequency or enduring depression is discussed in the light of this suggestion.

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