*The Factors in Rhythmic Activity of the Nervous System.**

By T. Graham Brown (Carnegie Fellow).

(Communicated by Prof. C. S. Sherrington, F.R.S. Received April 11,—
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(From the Physiology Laboratory of the University of Liverpool.)

I. *Introduction.*

In a communication upon the intrinsic factors in progression presented to the Society in July of last year† the author drew the conclusion that the rhythm of progression is of central origin. In then enquiring into the nature of that central origin he suggested that the movements are determined by a balance between equal and opposite states of excitation—flexion producing and extension producing.‡

An obvious line of research is thus presented by the possibility that reflex stimuli which normally evoke opposite reactions (flexion and extension), that is, opposite states (of excitation and inhibition) in one and the same centre, when applied at the same time and with appropriate strengths of stimulus may give a rhythmic response.

When that communication was made such experiments had actually been performed and had yielded positive results. The facts were not recorded because it was intended to give them in greater detail at a later date. They have been embodied in a thesis presented to the University of Edinburgh; but as some time must pass before they can be published in full it is desired to give a brief account of them here.

II. *Methods.*

The muscles selected for examination were *tibialis anticus* and *gastrocnemius* —a flexor and an extensor of the ankle. These were prepared in a manner already described,‡ and their movements in response to stimulation of the ipsilateral and contralateral long saphenous nerves examined. The muscles wrote, by means of levers attached by threads to their tendons, upon the blackened surface carried by a kymograph.

* The expenses of this research have been defrayed by a grant from the Carnegie Trust.

† 'Roy. Soc. Proc.,' 1911, B, vol. 84, p. 308.

‡ 'Quart. Journ. of Exp. Physiol.,' 1911, vol. 4, p. 331.

III. *Rhythmic Responses to Simple Stimuli.*

The simple stimulus usually evokes a muscular response characterised by contraction of one muscle and relaxation of its antagonist.

Occasionally in the ipsilateral flexion-reflex the flexor contraction dies down during the process of the stimulus and at the same time an extensor contraction appears. At the cessation of stimulation there may be a flexor rebound. In a similar manner the contralateral extension-reflex occasionally exhibits contraction of both the antagonists. Tracings demonstrating these points have already been published.*

A third type of reaction is seen in the rhythmic responses which are occasionally evoked.

In the low spinal preparation these are rare but may be evoked after a mechanical stimulation of the upper part of the lumbar portion of the divided spinal cord. This often evokes a state of maintained extension, and a flexion-reflex then super-added may produce a rhythmic reaction. This resembles the "balanced" phase of the progression reaction obtained on rapid division of the spinal cord.†

So too may a reflex stimulus applied shortly after such a rapid division—when the phenomenon is in the third phase of maintained extension.

In the decerebrate preparation there is a much greater tendency to the appearance of rhythmic reactions in response to simple stimuli. Tracings in which this is evident have already been published.* These may appear when, as was described above in the case of the low spinal preparation, there is no such artificial background of maintained extension. But it must be remembered that in the decerebrate preparation there is always the background of decerebrate rigidity—that is, a maintained extension, and there is usually evident contraction of both antagonists. These rhythmic reactions resemble the movements of progression and are reciprocal in the two muscles. It happens very rarely that they resemble the movements of the scratch-reflex. Both muscles contract together, and the "beats" seem to occur as relaxations of these contractions. They occur alternately in the two muscles, the point of maximum relaxation in one corresponding to the point of maximum contraction in the other.

Another rhythmic response in the simple reflex is the "rhythmic rebound" already described by the author.* This occurs especially in the decerebrate preparation and after cessation of a stimulus. The movements undoubtedly resemble those of progression.

* 'Quart. Journ. of Exp. Physiol.,' 1911, vol. 4, p. 331.

† 'Roy. Soc. Proc.,' 1911, B, vol. 84, p. 308.

IV. *Rhythmic Responses to Compounded Stimuli.*

Sherrington* has pointed out that weak inhibition is often accompanied by tremor. In this paper he refers to the reflex inhibition of the state of decerebrate tonus by a stimulus which produces a flexion-reflex. Dr. Forbes has informed me that he observed, some time since, a similar tremor on pitting two opposite reflex stimuli one against the other. Sherrington has also shown that the tremor is reciprocal.†

In the present experiments two opposite reflex stimuli were also pitted against one another, but the rhythmic response which was evoked cannot be described as "tremor." It is far more akin to the rhythmic movements of the act of progression.

The results were obtained in the low spinal and in the decerebrate preparations. In both kinds of preparation it was found in some cases that although a simple contralateral stimulus when applied alone gave a response of steadily maintained extensor contraction, and although a simple ipsilateral stimulus similarly applied gave pure maintained flexor contraction, yet when these were applied together the response became a rhythmic alternation of flexion and extension.

Thus if the contralateral stimulus was first applied it evoked a maintained contraction of the extensor. If then an ipsilateral stimulus was applied the extensor response ceased to be steady and became rhythmic. On then taking the ipsilateral stimulus off again the extensor response again became steady (figs. 1 and 2).

In a similar manner the steady maintained flexion evoked by the ipsilateral stimulus might become rhythmic on the application of the contralateral. In some cases there was a contraction of both muscles and each of these was rhythmic. The rhythmic movements were reciprocal—that is to say that one rhythmic "beat" was in process of relaxation while the synchronous "beat" in the other muscle was in process of contraction (fig. 3).

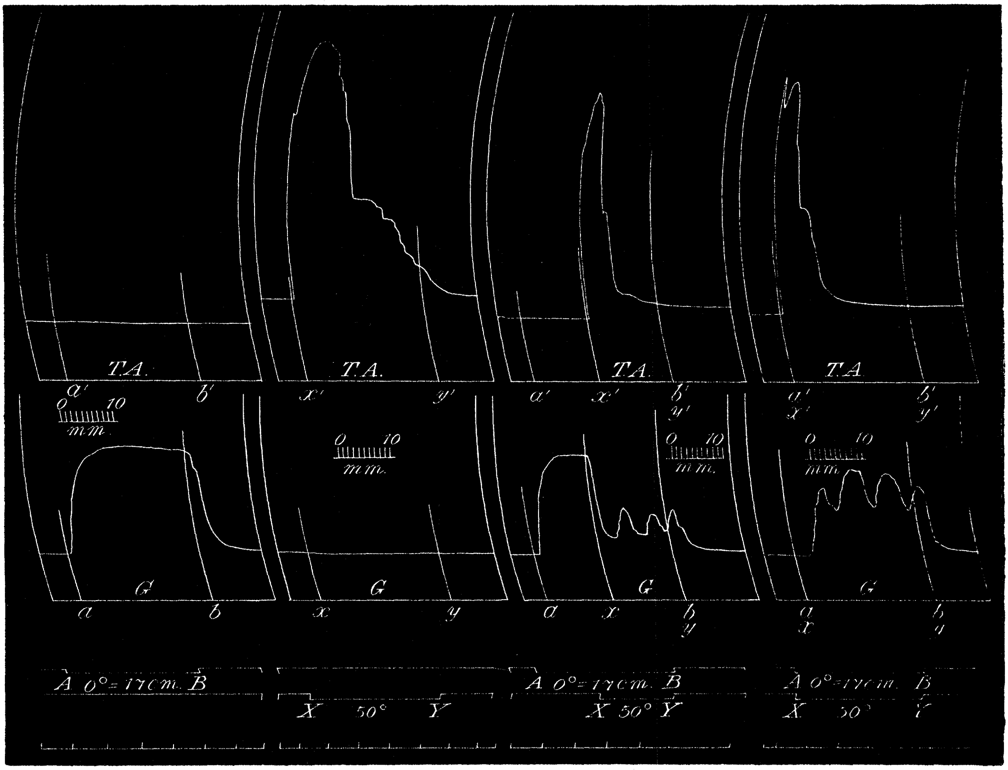
These phenomena were also seen in muscles after the division of their proprioceptive afferent nerves.

In all these cases the rhythmic phenomenon occurs only when the strengths of stimuli bear a certain fixed relationship to one another. If one stimulus is progressively increased and compounded with the fixed opposite stimulus a rhythm present gradually decreases in distinctness, and finally disappears.

The rate of the rhythmic movements usually lies between one and two beats per second.

* 'Quart. Journ. of Exp. Physiol.,' 1908, vol. 1, p. 67.

† 'Roy. Soc. Proc.,' 1909, B, vol. 81, p. 249.



a *b* *c* *d*

Fig. 1.

Experiment 30, 31.3.11.—Ordinary decerebrate preparation, a series of four reactions.

In the first of these (*a*) a simple contralateral stimulus is applied between the marks A, B, of the signal line (ordinates *a*, *a′*; *b*, *b′*). This evokes a simple reaction of maintained extensor contraction—the crossed extension-reflex.

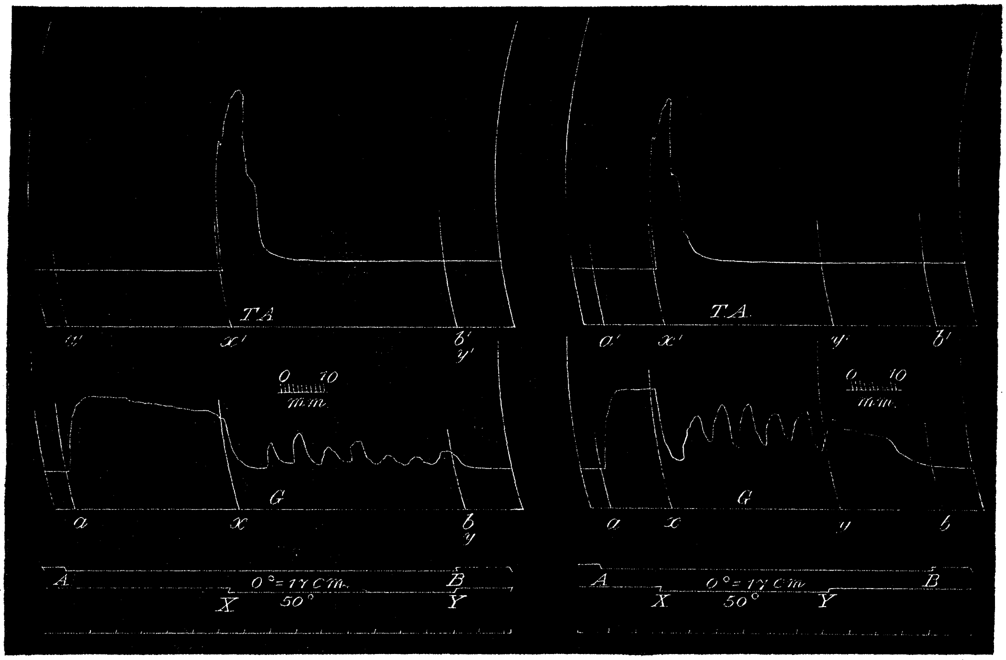
In the second of these (*b*) a simple ipsilateral stimulus (signal X, Y—ordinates *x*, *x′*; *y*, *y′*) evokes a simple reaction of maintained flexor contraction—the ipsilateral flexion-reflex.

In the third of these (*c*) the contralateral stimulus is first applied (A—B) and then evokes maintained extensor contraction. During this stimulus an ipsilateral one is added (X—Y). This gives a smaller flexor contraction than in "*b*," and at the same time there is a rhythmic movement in the extensor tracing.

In the fourth record (*d*) both stimuli are applied at once, and the extensor movement—the latency of which is increased—is rhythmic from the first.

The strengths of the ipsilateral and of the contralateral stimuli remain the same throughout this series.

In all the figures the upper tracing is that of the flexor—*tibialis anticus*, and the lower that of the extensor—*gastrocnemius*. The upper signal line is that of contralateral stimuli, the lower that of ipsilateral. The lowest line marks seconds and millimetre scales are reduced in proportion with the tracings. Corresponding ordinates on the tracings mark the beginnings and terminations of the stimuli, and the rise of the levers denotes contraction of a muscle—the fall relaxation.



e *f*

Fig. 2.

Experiment 30, 31.3.11.—A continuation of the last figure. Two reactions.

In the first of these (*e*) the contralateral stimulus is applied for some time (about six seconds) before the ipsilateral stimulus is added. They then run together for about eight or nine seconds. During this time the extensor movements—which before were maintained—are rhythmic.

In the second reaction (*f*) the ipsilateral stimulus is applied earlier, but is taken off again before the termination of the contralateral. Here the extensor contraction is maintained before the commencement and after the termination of the ipsilateral stimulus, but when both stimuli run together it is rhythmic.

V. *Other Forms of Rhythmic Movements.*

The author has previously described movements of progression which occur under narcosis in the rabbit.* Similar movements have been seen in the guinea-pig under suitable circumstances. These in their rhythm seem to bear the simple relationship of 1 : 4 to the rhythm of the "beats" of the scratching movements which occur under narcosis in the guinea-pig. In the rabbit the relationship seems to be commonly 1 : 2.

Similar movements also occur in the cat. These are of additional interest, in that they may be observed in the same individuals from which records of the other movements of progression, provoked in other ways—*e.g.*, reflex, central on cutting spinal cord, etc.—were subsequently obtained.

* 'Quart. Journ. of Exp. Physiol.,' 1911, vol. 4, p. 151.

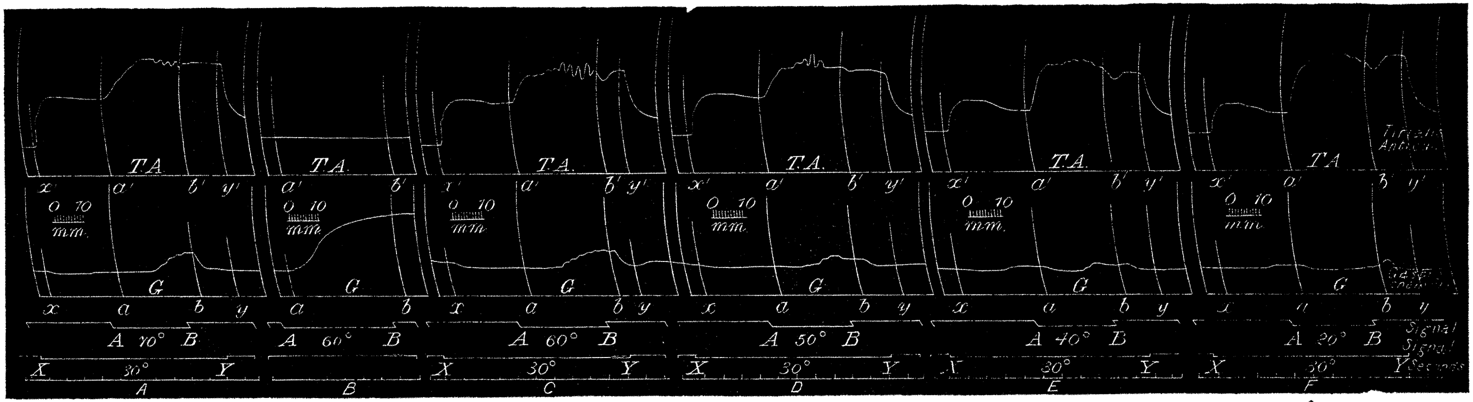


FIG. 3.

Experiment 25, 15.3.11.—Ordinary decerebrate preparation, a series of six reactions.

In this series the second (*b*) is a reaction of pure maintained extensor contraction in response to a simple contralateral stimulus. The other reactions are all in response to compounded ipsilateral and contralateral stimuli. The strength of the ipsilateral stimulus remains constant, but that of the contralateral is progressively increased. It will be noticed, for instance, in the first reaction, that before the application of the contralateral stimulus the ipsilateral gives a reaction of pure maintained flexion.

In the first reaction (*a*)—as well as in the succeeding ones—the application of the contralateral stimulus gives an *augmentation of the flexor contraction*. This is remarkable, as that stimulus alone (*b*) gives extensor contraction. This is soon followed (in "*a*") by a contraction of the extensor, the latency of which is great. At this point both muscles are contracting together, and a rhythmic movement is seen here in the flexor tracing. A slighter rhythmic movement is present in the extensor tracing.

In the third reaction (*c*) the strength of the contralateral stimulus has been increased. The rhythmic phenomenon in both muscles is more marked and a minute examination shows that it is reciprocal—so that the contraction phase in one is accompanied by a relaxation phase in the other.

In the fourth reaction (*d*) a still stronger contralateral stimulus gives an increased flexor augmentation. The rhythmic phenomenon is less marked, and so too is the extensor contraction.

In the fifth reaction (*e*) a yet stronger contralateral stimulus gives a greater augmentation of the flexor contraction. This is still less rhythmic. In the extensor tracing there is first a marked relaxation and then a slight contraction.

In the final reaction (*f*) a stronger contralateral stimulus gives a greater augmentation of the flexor contraction. This is now arrhythmic, and there is almost no evidence of extensor contraction—only of relaxation.

(At the end of this series a pure contralateral stimulus gave a reaction of pure maintained extensor contraction as before.)

The rate of the rhythm of these movements is about one to two beats per second. Under normal circumstances it has been observed to be as slow as 0·6 beat per second, and as fast as 2·5 beats per second. In asphyxia the beats become markedly faster (besides changing in other ways), and their rate may then rise to one of 3·3 beats per second, or even more.

The movements have been registered as they occurred in the isolated muscles as well as in the intact hind limbs. They have then an appearance exactly similar to that of the rhythmic movements seen in some of the other types of progression examined.

Another form of progression is that obtained on electric stimulation of the cut surface of the spinal cord. This also closely resembles the other forms in appearance and in rate of rhythm. If the strength of the exciting stimulus be progressively increased the rhythmic reaction becomes less well marked and finally disappears, the reaction becoming one of pure maintained contraction.

VI. *Comparison of the Different Forms.*

When one or more of these different forms of progression—in narcosis; on electrical stimulation of the spinal cord; on rapid section of the lower thoracic spinal cord; in response to simple peripheral stimulation, either as a direct response or as a "rebound"; and in response to compounded peripheral stimuli—occur in the same individual, the general appearances of the different reactions are seen strikingly to resemble one another. Even peculiarities present in one variety may be present in the other. Thus, in one instance, the rhythmic rebounds ensuing on cessation of a reflex stimulus presented the peculiarity that the "beats" were arranged in groups of two, the second of which was smaller than the first. The "beats" of the progression movements which were evoked subsequently on section of the spinal cord also presented this peculiarity.

VII. *The Conditioning of Rhythmic Movements.*

These experiments seem to shew that rhythmic movements similar to those of progression may be evoked on compounding two antagonistic excitabilities, that is, two antagonistic states of excitement and inhibition in each centre. They therefore seem to confirm the suggestion previously put forward that this is the method of the determination of progression.

In the first place the direct compounding of antagonistic excitations—seen in the compounding of stimuli which evoke antagonistic reflexes—may in certain cases produce the phenomenon.

Secondly, the application of a simple stimulus may also do so. But in

these cases there is really a compounding of two antagonistic excitations—for there must be a background of maintained extension, as in the decerebrate condition, or as in the experiments in the low spinal preparation in which the mechanical stimulation of the spinal cord produced the maintained extensor contraction.

Even in the case of the simple reflex there may be a compounding of two antagonistic excitations apart from any background present. This may be the case if the afferent nerve can activate (excite) both centres (extensor and flexor), although not with equal effect. Such a condition may occur if the nerve split in the spinal cord and one part goes to each centre to excite it. Or it may occur if the afferent nerve stimulated in these experiments contains fibres some of which pass to one of the antagonistic centres and some to the other.

That such a double reciprocal innervation may occur even with a simple stimulus—that is, a stimulus applied to a single afferent nerve—seems to be shewn by the fact that sometimes contraction of both muscles may occur during the process of the stimulus.

Another point which seems to lend support to this view is the occurrence of flexor and of extensor "rebound contraction after excitation." If rebound be a phenomenon associated with a state of inhibition it must seem that even in the efferent centre of the contracting muscle there is a certain factor of inhibition produced by the peripheral stimulus.

It may be stated here that the corresponding phenomenon "flexor (or extensor) rebound relaxation after inhibition," which had not been observed when the above phenomenon was described,* has since been seen by the author in the case of the extensor muscle. An ipsilateral stimulus which evoked flexor contraction, and along with that a well-marked extensor relaxation, at the cessation of its stimulation was followed by an additional extensor relaxation.

VIII. *Theories of Rhythmic Activity.*

It is not intended here to discuss these in detail. It may be remarked, however, that certain evidence given in this paper seems to be directly opposed to three well-known theories.

In the first place the occurrence of relaxation in a rhythmic phenomenon may markedly precede the occurrence of the synchronous contraction of the antagonistic muscle.*† This phenomenon would not be possible if the state of inhibition was conditioned by a phenomenon of "drainage" as suggested

* 'Quart. Journ. of Exp. Physiol.,' 1911, vol. 4, p. 331.

† 'Roy. Soc. Proc.,' 1911, B, vol. 84, p. 308.

by McDougall,* and a theory of rhythmic movement founded upon this conception can hardly be a correct one.

In the second place the intrinsic factor in the production can hardly be a metabolic one. That is to say, that it cannot be intrinsically conditioned by the metabolic activity in the moto-neurones. Were this the case, a rhythmic response would follow each expression of activity of the centres. But this is not the case. The application of a continuous stimulus to a single peripheral afferent nerve usually evokes a response in which the one muscle contracts continuously—that is (as regards such coarse rhythms as those of the scratch-reflex or of progression), arrhythmically. But two such stimuli, which evoke antagonistic activities when compounded together, may give a rhythmic response. The intrinsic condition of the rhythmic phenomenon lies not in the efferent centres themselves, but in some property of their inter-dependence and inter-relationship.

The third theory to account for rhythmic activity is that which assumes a peripheral self-generated antagonistic stimulus. That this is not a correct one is shown by the occurrence of the phenomenon after the de-afferentation of the muscles.†

The theory suggested to account for rhythmic activity is the following: The cell-bodies and their processes of the efferent neurones of the antagonistic muscles form centres which mutually inhibit each other. A stimulus which falls upon one will therefore through it inhibit the other. But if this inhibition reduce the activity of the second centre, that will inhibit the first less, and so the process will proceed until there is a limit set to this "progressive augmentation of excitation."

But if a stimulus fall more or less equally upon the two antagonistic centres—or if two equal stimuli fall upon them—that which is most activated will have its excitability increased by "progressive augmentation" up to a certain point. The limit may be set by a process of inhibitory fatigue. If this proceeds the balance will turn in the opposite direction, and there will be a progressive augmentation of excitation in the other centre until it too reaches its limit, when the process will set in in the other direction again. In such a scheme there is, however, no explanation of the occurrence of inhibition before excitation in time. It is not difficult to overcome the difficulty by postulating a pair of "interposed centres" between the afferent neurone and the efferent centres, and by supposing that these too mutually inhibit, and that, in addition, they inhibit the

* 'Brain,' vol. 26, p. 153.

† 'Roy. Soc. Proc.,' 1911, B, vol. 84, p. 308; 'Quart. Journ. of Exp. Physiol.,' 1911, vol. 4, p. 331.

crossed primary centres. It will be observed that in this scheme no explanation of the nature of the inhibitory process is given.

Summary.

1. In the case of simple peripheral stimulation the reflex response is sometimes of a rhythmic character. It then resembles the rhythmic movements of progression which sometimes occur in the cat during the state of narcosis.

2. The rhythmic reaction occurs sometimes during the application of the stimulus and sometimes at its cessation as a rhythmic rebound.

3. In the low spinal preparation the rhythmic reaction during stimulation is rare. It is seen almost alone after the production of an artificial state of maintained extension by mechanical stimulation of the spinal cord, and in response to flexion-producing stimuli. Here it looks as if the reaction was conditioned by the pitting against one another of two opposite activities.

4. In the decerebrate preparation of the cat, rhythmic responses may appear in reaction to flexion-producing stimuli. Here there is already, in the decerebrate rigidity, a state of maintained extension.

5. Both in the normal and in the de-afferented conditions of the low spinal and decerebrate preparations the compounding of reflex stimuli, which, taken singly, produce opposite reactions (flexion and extension), sometimes results in a rhythmic reaction. The rhythmic movements may occur in both muscles, and they are then reciprocally alternate.

6. These rhythmic responses occur, as a rule, only within a restricted range of strength of stimulation. If either stimulus be increased in strength, the response during the compounding of the two stimuli ceases to be rhythmic.

7. As already published, a rhythmic response is obtainable on rapid division of the spinal cord. The movements of this are exactly similar to the movements of progression. There is first a phase of maintained flexion, and at the end a phase of maintained extension. These, on the whole, are arrhythmic, and between them is a phase of " balance " in which the rhythmic movements are most perfect.

8. This previously led to the suggestion that the rhythmic phenomenon is conditioned by a balance of two equal and opposite activities, that is to say, by activities which produce in the same centre equal and opposite effects (excitation and inhibition). In the experiments here given there seems to be evidence that this suggestion is correct.

9. The various rhythmic movements—during stimulation, rhythmic rebound, on compounding equal and opposite stimuli, on rapid division of the spinal cord, on unipolar electric stimulation of the cut surface of the

spinal cord, and the rhythmic movements which occur in narcosis—are closely similar, and seem to be instances of the rhythmic phenomenon of progression.

10. It occasionally happens that a rhythmic response which more resembles the scratch-reflex is obtained on simple peripheral stimulation. There both antagonistic muscles contract at the same time, and there occur reciprocally alternate "beats" as depressions from the plateaus of maintained contraction.

11. The explanation of the occurrence of rhythmic action seems best to be given on the assumption that the two antagonistic centres mutually inhibit each other, and that they are very nearly equally activated by the evoking stimuli. In such a case there will be balanced against each other in each centre antagonistic forces of excitation and inhibition. And in this balance and a phenomenon of fatigue and recuperation of the mutual inhibition is probably to be found the explanation of rhythmic activity.

12. The occurrence in the simple reflex of "rebound contraction after excitation," described previously, and of the allied "rebound relaxation after inhibition," here described for the first time, seems to shew that even there there may be a double excitation of the two antagonistic centres.

13. Evidence given here and in other cases seems to cast doubt upon certain hypotheses of the nature of rhythmic activity :—

(*a*) As the phenomenon of relaxation not infrequently occurs in time before the accompanying phenomenon of contraction in the antagonist it seems hardly possible that the "drainage" theory of inhibition is an adequate one, or that it can serve as a basis for a theory of rhythmic activity.

(*b*) That the phenomenon is not conditioned intrinsically by the conditions of metabolic activity in the moto-neurones is shewn by the experiments here given, in which two stimuli, when given separately, condition arrhythmic responses, but when compounded in appropriate strengths condition rhythmic responses. This can only mean that the centres normally discharge arrhythmically—as regards such coarse rhythms as that of progression—and therefore that the rhythm is conditioned by some property of their interdependence and inter-relationship.

(*c*) On the other hand, the present experiments demonstrate—as the author has done previously—that the rhythm is conditioned centrally and not by an "automatic" peripheral proprioceptive interference. In addition to this the present experiments show that the rhythm on compounding of opposite stimuli may be obtained in the low spinal preparation. This shows that the rhythm is conditioned at the lowest levels, and is not produced, for instance, by the evocation of the activity of a rhythmically discharging centre in the higher parts of the nervous system—a possi-

bility that could not be overlooked if the phenomenon occurred alone in the decerebrate preparation.

14. A possible explanation of the conditioning of rhythmic activity is given in the present paper in a contracted form. It has already been presented, along with a more detailed account of these experiments, to the University of Edinburgh.

Reflex Rhythm Induced by Concurrent Excitation and Inhibition.

By ALEXANDER FORBES, M.A., M.D., Harvard.

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(From the Laboratories of Physiology in the Harvard Medical School and in the University of Liverpool.)

CONTENTS.

I. *Introduction.*

In a paper on "Antagonism between Reflex Inhibition and Reflex Excitation,"* Sherrington has shown that the combined effects of excitatory and inhibitory stimuli produce a response intermediate between those of the two stimuli acting singly. Prof. Cannon, of Harvard, called my attention to certain minute oscillations which occur in Sherrington's myograph line where it represents the response of muscle to the combined effects of the opposed stimuli,† and suggested that these might have an important significance. They might mean that the nerve impulses in breaking through the opposition imposed by inhibition were subjected to a condition analogous to a stream of air passing out from a tube under water.‡ It seemed possible that just as the air bubbles will be larger and more infrequent if the opening of the tube

* 'Roy. Soc. Proc.,' B, vol. 80, p. 565.

† *Cf.* also 'Roy. Soc. Proc.,' B, vol. 81, p. 258.

‡ *Cf.* Rosenthal, 'Die Atembewegungen und ihre Beziehungen zum Nervus Vagus,' Berlin, 1862.