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THE CHRONAXIC SWITCHING IN THE NERVOUS SYSTEM[1]

By Professor LOUIS LAPICQUE

PHYSIOLOGY has until now paid but very slight attention to the important part which time, in the sense of duration of the stimulus, plays as a condition of excitation, and has given no thought whatever to the correlations of such time characteristics among functionally related cells. I shall not here inquire into the historical reasons for such an oversight or show in detail how Du Bois Reymond, the omnipotent master of electro-physiology for half a century, was to blame for this. But I must mention the pioneers, Fick, Brücke, Engelmann, who had begun to open the way seventy years ago, but whose valuable work on the time factor in excitation has long been buried in undeserved oblivion. Engelmann went so far as to use the phrase "physiological time" to indicate the difference between quick muscles and slow ones, noting that excitability was correlated with contractility in this respect. But he drew no further inferences from this relationship, and his remark awakened no echo.

In order to indicate the possible physiological significance of the time factor of excitation let me review some of the classical notions as to the mechanism involved in the central nervous system.

A spinal reflex is generally accepted as the elementary unit in terms of which the more complicated functions are to be explained. But, as Sherrington has emphasized, the ordinary flexion reflex of the decapitated frog, as it pulls up its leg when pinched, is by no means a simple phenomenon. Any reflex motion, as well as any voluntary motion, implies coordination. Every joint is provided with antagonistic muscles, which tend to move it in opposite directions when they contract, and if all should contract at the same moment motion would not result, but

[1] Introduction to the Dunham Lectures at the Harvard Medical School, 1928–29.

merely rigid posture. Such a phenomenon can be seen in true tetantus or in strychnine spasms. In the reflex which we took as an example the flexor muscles contract, the extensor muscles do not. Following a very gentle pinch the response may be so limited as to raise up only the pinched toe; a little stronger stimulation will cause a raising of the whole foot; with a still stronger one the foot flexes upon the leg, the leg upon the thigh, and even the thigh upon the hip. That is to say, when the reflex spreads it does not involve muscles at random, not even the neighboring muscles in topographical order; but instead we see something that we must call selection. In his well-known book, "The Integrative Action of the Nervous System," Sherrington says: "Increase in intensity of stimulation of the plantar skin does not, in my experience, make the spinal reflex action flow over, so to speak, from the flexor muscles to the extensors."

Is there any anatomical arrangement that could explain this matter? Investigations attempted by Sherrington for this very purpose give no explanation. He states, "The afferent fibers from each even small area of the skin of the foot do not enter together as a tiny group into the spinal cord in any single filament of a single afferent root, but scatter, and make their entrance into the cord *via* a number of rootlets, belonging not merely to one, but to two or even three adjacent afferent spinal roots . . . their collaterals and terminals must, as it were, seek out the motor cells of the above-cited flexor muscles, and . . . leave the motor cells of other muscles, for instance, of the extensors, alone."

I have quoted Sherrington's own words, not to suggest that Sherrington was satisfied with such an explanation, but in order to show, by an example textually borrowed from one of the keenest investigators neurology has ever known, how narrow was the point of view in this direction. Every explanation of nervous conduction turned on geometrical arrangements.

About the time that Sherrington's book was published, I was first proposing the introduction of a *temporal* point of view. The time factor was not yet as sharply defined as "chronaxie" now is, but nevertheless I had already recognized its importance in the function of the neuromuscular relay.

In outline the conception is this: every anatomical element, every kind of cell, reckons time according to a particular standard, say thousandths or perhaps hundredths of a second. In a given neurone, nervous impulses on the one hand, and excitability, on the other, are governed by this particular time standard. The impulse coming from one neurone to another can only stimulate the second one if the temporal characteristics of both are equal, or nearly so. In other words, excitation will pass easily if neurones in anatomical connections are "isochron," but will not pass at all if the neurones are "heterochron." As a matter of fact, the motor impulse of a peripheral nerve will no longer activate the striated muscle it controls if either the nerve or the muscle has been poisoned so as definitely to change its natural time factor.

Now that radio has become so popular the following comparison will make clear this change of point of view. For ordinary telegraph and telephone, as well as for electric bells, the only thing which counts is connection—conducting wires, keys, switches, and so on—in short, a system of channels opening to the current a pathway materially defined. The classical conception of the nervous system is implicitly identical, referring the problems of its behavior to the presence of continuous pathways. These pathways were formerly thought to be constituted of fibers and cells, more recently of chains of neurones, or sometimes of transneuronic fibrils, but in any case physiologists wanted primarily to be able to indicate pathways on a sheet of paper.

In wireless, different waves cross each other simultaneously in the field of the receptor, but the only waves which count are the ones having a period, reciprocally a length, tuned to the time constant of the apparatus. Several sets of apparatus placed side by side and bathed by the same waves but differently tuned will function independently of each other. One may be talking while the others are silent. The chronaxic theory of nervous function has not been deduced by transposition of the principles of the wireless telephone. It is quite different, and furthermore it was formulated ten years before the invention of the radio; but for the particular case which we have considered such a transposition is sufficient to show the possibility of a non-anatomical explanation.

It is not necessary to suppose that the afferent fibers have been clever enough to get in touch with the flexor motor neurones while carefully avoiding the extensors. If the chronaxie of the flexor neurones differs sufficiently from that of the extensors, the sensory impulse, reaching both at the same time, but tuned to one of these chronaxies, will not be able to stimulate the neurones with a different chronaxie.

These differences of chronaxie really exist.

We know, from accurate measurements, that in the nerve-muscle preparation excitation fails to pass when the chronaxies of nerve and muscle differ in the ratio of 1 to 2 or more.

Bourguignon, who is a physician well acquainted with the chronaxic method, has studied for years the excitability of the voluntary muscles in man. Reviewing his figures he recognized, without having foreseen such a result, that for every limb the chronaxies of the extensors on one side and the flexors on the other side always differ in the same ratio: 1 to 2.

Soon after an independent research gave the counter-proof. Strychnine intoxication makes flexors and extensors contract simultaneously, causing the well-known tetanus. Now Bremer and Rylant in 1924 and 1925 have observed that under the influence of this poison the chronaxies of all nerves tend to become alike and even equal.

These facts afford a solution of the question of reflex coordination as already proposed. No matter if afferent fibers touch extensor as well as flexor motor neurones; the spread of impulses may follow the temporal laws of wireless, not the geometrical laws of electrical bells.

We have not yet considered the whole problem of nervous function. We have discussed the reflex of a decapitated animal pulling back its extended limb when stimulated. But this limb, if previously flexed, will often respond to a similar stimulation by extension. In general it is well known that a spinal reflex may be reversed by modification of posture. Moreover, if we examine the behavior of a normal animal with its nervous system intact, we see that stimulation of any point on the periphery may elicit a response at any point of the body, either remote or neighboring, and initiate any kind of motion. And when we say motion, we must always think of coordination, that is, selection between antagonists, at every joint. But, as in the reversal of the reflex we considered, this selection must vary under different conditions.

If we had to deal with a railway system, we should obviously think of switching, a piece of rail being moved off or on, and the same could be said of any system of electric circuits. If we understand that in the case of the nervous system all material structures are motionless, and that the selection among the various pathways depends on the relation of the time constants of adjacent neurones, we can speak of "switching" in this case also, with a newly assigned meaning. Every neurone ramifies in order to meet several other neurones and each of these ramifies in turn, and so on. An infinite number of neurone pathways start from each point on the body and we can trace one of these paths from neurone to neurone to any effector organ. Among such numberless anatomical pathways a given scale of chronaxies facilitates conduction in certain paths and hampers or even blocks the others. If some of these chronaxies happen to change, obviously some of the open pathways will be blocked, and, conversely, some of the others will be changed from impassable to passable. The possibility of such chronaxic switching would give at least the necessary starting-point for an explanation of nervous function. The question is whether such switching really occurs.

It is generally believed that the chronaxie of a neurone depends on its substance and structure. We must now add the idea that this constitutional chronaxie can be modified by the action of other neurones. The need of such an influence was noted in the first sketch of the theory twenty years ago, but it was verified experimentally for the first time in 1923 by Mme. Lapicque. She noticed that the motor nerve of the gastrocnemius, studied in an injured or even a decerebrate frog, shows a variable chronaxie, as a rule smaller than the value characteristic for the leg severed from the body. Severing the nerve from the spinal cord, or transection of the bulb, that is, removing the control of the encephalon, reestablished the usual chronaxie at a constant value. This proved that the mesencephalon has the power of modifying the chronaxies of peripheral motor nerves. In contradistinction to the constitutional chronaxie we will call this modified value the "subordinate chronaxie."

Thus we see how the variety of reactions in an animal with its nervous system intact can be explained. The brain is able to switch the impulse from one effector organ to another because it can functionally connect or disconnect any given neurone path by tuning its elements. Moreover, the brain itself is composed of neurones presumably subject to the same laws, that is to say, these neurones have each a constitutional chronaxie which can be modified by the action of any neurone in contact with it. In fact a series of recent researches have shown that the chronaxie of the cortical motor centers is essentially variable. This topic was first investigated by my assiduous collaborators, M. and Mme. Chauchard. They were originally led into error by the action of anesthetics, which considerably increases the cortical chronaxie in doses practically insufficient to modify the chronaxie of peripheral nerve. (By the way, I am inclined to believe that anesthesia may depend in large measure on the chronaxic disjunction so produced.) But even apart from this action we have to deal with a continually changing chronaxie. Two years ago, a young American psychologist, Rizzolo, of Columbia, worked on this question while in my laboratory. He succeeded in modifying systematically the chronaxie of the cortex by application of heat or cold or previous electrical excitation to the part of the body connected with the motor area under investigation. At nearly the same time, another of my disciples, Henry Cardot, now professor of general physiology at Lyons University, with several collaborators, found very different values for one and the same center, changes in this case being induced particularly by activity of the vagus nerve or of the thyroid gland.

Thus we see that this power which we attribute to the brain, of switching by tuning of chronaxies, is not an anthropomorphic fancy, hidden behind a supposed mechanism. This power will appear as an obvious consequence of the nature of the mechanism itself when research along this line has been sufficiently advanced. In the meantime, the analysis of spinal reflexes, either simple or complicated, should be first worked out, for this is the best way to reach little by little a knowledge of the entire nervous system. Perhaps I may cite very recent researches, or rather the first result of a series just initiated. We have found that the chronaxie of the motor neurones of each muscle, in a decerebrate animal, undergoes large variations according to the posture of the limb. This indicates that reversal of a reflex depends on chronaxic switching.

Our theory easily solves the problem of inhibition. This phenomenon, until now so mysterious, does not raise any difficulty for the theory of chronaxic switching. Let us consider the question in terms of the same classical example of an elementary nervous function that we chose for excitation itself. In the so-called "simple reflex" we have seen that extensors must not contract at the same time as flexors. There is something more than this. These extensors, in the state we call rest, are really in a condition of slight tension, designated long ago as "tonus." This tonus depends on a slight continued nervous activity. Sherrington, as is well known, has shown that in the flexion reflex at the very moment when their antagonists contract, the extensor muscles relax; that is to say, their tone is inhibited. We explain this in terms of our theory, by assuming that in the chain of neurones carrying the tonic impulses there is one whose chronaxie may undergo such a change as to produce disjunction. This is obviously only one particular aspect of the switching mechanism. We have pointed out that as between two or more pathways anatomically established, homochronism and heterochronism serve to open one of these pathways and close the other. Inhibition may be regarded as simply the closing of certain pathways. If alteration in the chronaxie of nervous elements explains the opening of nervous pathways it likewise explains their closing.

THE AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

THE SECOND BERKELEY MEETING OF THE PACIFIC DIVISION. II

By Dr. ARTHUR G. VESTAL, Secretary

AMERICAN ASSOCIATION OF ECONOMIC ENTOMOLOGISTS—PACIFIC SLOPE BRANCH

(Report by R. E. Campbell, Secretary)

Three sessions were held separately and one with the termite investigations committee. Chairman O. H. Swezey opened the first session with a discussion of the evolution of certain insect species in Hawaii. E. O. Essig reported that beans taken from Indian graves in Peru of periods A. D. 1 to 500 and 1000 to 1500 showed the work of the bean weevil, and one nearly perfect specimen was obtained. Ralph H. Smith showed how various practices affected the mixing and application of oil sprays. G. P. Gray and A. F. Kirkpatrick showed that a heavy dose of HCN gas followed by a light dose is more destructive to scale insects than light followed by heavy dose. They gave added proof that in certain districts the black scale is more resistant to HCN than in other districts. F. B. Herbert discussed codling-moth control in the northwest. A paper by S. L. Allman gave details of the control of the codling-moth in Australia. A. M. Boyce told of progress in study of the walnut husk fly, a new injurious insect in southern California. W. B. Herms announced that all stages of the Hippolates fly have now been found and the breeding-places located. E. A. McGregor reported promising results in the control of citrus thrips and citricola scale by the use of very finely divided sulphur. Perez Simmons described certain advantages of ethylene gas for fumigating dried fruit to kill insects. H. J. Quayle gave observations on the Mediterranean fruit-fly in Florida. Don C. Mote gave an account of the habits of the strawberry crown borer. The crawling of newly hatched larvae down the outside of the crown may prove to be its vulnerable point. F. H. Wymore showed that hydrated lime and gypsum applied with or without an arsenical will control cucumber beetles. There was little injury from the lime. R. L. Webster reported on serious damage to potatoes in western Washington from larvae of flea-beetles. H. R. Hagan gave a paper on the principal fig insects of Smyrna, and methods employed to meet the new requirements in figs shipped to this country. G. H. Vansell reported that the German requirement of diastase in honey is unjust, as many types of honey are naturally very low in diastase. Efforts by G. H. Vansell and