NERVE IMPULSE

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June 15, 1955

The purpose of this paper is to suggest as a hypothesis a new theory of the transmittal of intelligence in man through the nerve impulse. Special emphasis will be given to a possible means of explanation of the distortion of such intelligence signals in diseases such as the epilepsies.

The above will be incorporated in Section I of the paper. Section II will deal with a new hypothesis of nerve impulse propagation. Section III will consider some proposed prosthetic and therapeutic devices which are broadly part of the basic thinking with which this paper contends. The ideas expressed have been justified as much as possible by existing work and publications which, while seemingly unrelated to each other, helped underline the unity of the theme.

I.

Impulse and Its Meaning

The writer would like to propose that cerebral activity in the form of electrical signals triggers off a muscular action not only by a known pathway between the brain and muscle, but by the fact that this pathway is in reality a coded system where pulsations of certain frequencies seek to travel in a diffused manner, and at random find "correct" pathways. The particular neuron synaptic arrangements which allow the impulse through act in the same manner as a coded relay would in an electronic system; the impulses search through the nerve pathways rejecting those which do not have the proper threshold and traveling only down the randomly found pathway which does have the correct threshold and will take their value of frequency in order to energize a particular action. In other words, the neuron or relay responds selectively to pulse patterns of set electrical values. (There seems to be no doubt that these values are influenced and to some extent shaped by the blood's chemistry.)

A possible explanation of the diffusedness of electrical signals and their ability to find correct paths is that the originating volley may fire indiscriminately and seeks to travel at random through the nerve pathways; however, the muscle nerve thresholds of most organs are above the particular energizing value of the signal and are therefore ineffective. The volley that was fired seeks the path of least resistance and finds the low threshold paths where response is obtained.

There are certain clues which suggest that this may be correct. Weiss (10) made some interesting experiments on frogs where removing an organ from the frog or adding an organ did not stop the nervous system from accommodating itself to the change so that natural movement could still take place. If it were a specific nerve or fiber which did a particular thing, then this would be seemingly impossible; but if there were neuron pathways that could have the same value of voltage current and pulsation frequency, then one could understand how the nervous system can maintain use of an organ even after some nerves have been destroyed. This work could be accomplished by the original signals seeking many pathways and finding the correct ones that would respond to them. These assumptions would explain the lack of any physically known pathway to new organs described by Weiss.

To sum up the above, we may say that as part of the information integrating process, a volley is fired which seeks all paths indiscriminately but only discharges across those which are responsive to the particular voltage and current pulse conditions which allow them to be triggered by the initial volley.

We can relate the above to the epilepsies which, in the writer's opinion, are nothing more nor less than the predisposition of certain pathways of low threshold values together with certain muscles which react, re-energizing the low threshold pathways to start a self-induced oscillation. The pathways affected need not be tied to a useful function. Epilepsy is energization in a needless manner of functions which by happenstance can be energized. The fact is that various muscles can be energized which are at cross purposes to each other.

Any type of energization whether loud clap, blinding lights in front of the eyes, or touch, could fire the same reaction of epileptic seizure patterns. It is not necessary to say the diffusion of the signal precludes any known specific triggering device, rather, the signal seeks to find the pathway randomly that will allow it through to the muscles which then refire back to set off seizure. This, of course, does not mean that there are not certain pathways established in the human body for certain muscles at certain threshold settings. What it does say is that these settings can be so modified that unwanted movement can be elicited from the muscles.

Threshold conditions of the pathways are probably modified in varied ways by disease, heredity, or merely by chance. One should recall the millions of neurons in the human body in order to keep in mind the possibilities that chance changes of the threshold, other than that which nature originally dictated, considered in the light of statistics, could have some real effect on the pathways.

Support of the theory that neurons fire proprioceptive fibers in muscles which in turn fire back to the same cerebral source and set off a continuous self-induced discharge can be found in the article "Cerebral Responses to Nerve Stimulation in Man" by G. D. Dawson (1).

It has also been stated (1) that the triggering which takes place in the low threshold afferent fibers induces volleys in these fibers which produce the greater part of the cerebral responses. In some forms of epilepsies involving sensory means as a triggering agent, such as touch, our explanation seemingly could hold true. It has been pointed out in the literature (11) that response to touch fires off seizures and that some patients can take corrective measures by putting counteracting forces on themselves to inhibit such action. What has been accomplished is a dampening action of the frequency which removes it from the critical point of self-induced refiring. Therefore, there must be some disagreement with one of the earliest and greatest investigators in the field, Mr. Hughlings Jackson's assertion that "The first question in my mind is not, 'Is it a case of epilepsy?' but 'Where is the lesion permitting occasional excessive discharge'"(4, p. 142) While certainly a lesion is an attributable factor for discharge, another causative factor could be the general and genetical factor of certain low threshold pathways. Of interest on this point is the work of Eccles (2).

Of special interest are the findings of G. D. Dawson (1) where the responses to electrical stimulation of healthy people were only one-fifth to one-tenth as large as the response to the same type of stimulation in a patient with myoclonus. He further states, "It seemed that the fibres concerned had a lower mean threshold to this form of stimulation than had the motor fibres, and that therefore they probably conducted more rapidly and were of larger diameter than the motor fibres. The group of nerve fibres which conduct most rapidly and have the lowest threshold to electrical stimulation contains fibres carrying impulses from stretched muscle and also, as has been shown by Kugelberg (1944), fibres mediating the sensation of touch." And, "Since stimulation of the skin in healthy people produces a cerebral response it seems likely that the response to stimulation of a mixed nerve is also in part due to a volley in cutaneous afferent nerve fibres." (1, p. 327) It would be apropos to quote the entire conclusion of his article on cerebral responses in man:

"The experiments described suggest that the cerebral responses which may be detected in healthy man, after electrical stimulation of nerve, are probably produced by excitation of at least two kinds of nerve fibre. One type of fibre is that which carries afferent impulses from cutaneous receptors and the other is probably that carrying impulses from proprioceptors in muscle. The records made through skin show that 70 per cent of the nerve action potential which can be detected is due to activity in fibres with a lower threshold than motor fibres; it is the volley in these low-threshold afferent fibres which produces the greater part of the cerebral response. The relative contributions of the cutaneous afferent fibres and of the afferent fibres from muscle to this group of low threshold fibres is not clear from these experiments. The records of nerve action potentials also indicate that variation in the size of the afferent volley was not the cause of the variations in size of the cerebral responses to successive stimuli of the same kind; no cause for this variation has yet been found but it seems that, even with a sub-maximal stimuli, it is not peripheral. On the other hand, the same methods show that, with different types of stimuli, the peripheral differences in the resulting afferent volleys may alone be enough to account for the considerable differences in the cerebral responses produced." (1, p. 329)

Eccles also says, "The responses to receptive synaptic bombardment is of great interest because it would normally be produced by receptor organ discharges and if intense enough, it would give rise to rhythmic discharges of motoneurones." (2, p. 309)

Inasmuch as synapse means resistance and resistance is the measure of whether certain signals are of a level as to allow their further passage, we might consider that one could pick a particular current frequency level at certain points of the memory section of the brain (we will discuss this more fully as we go on) and the nerve response which is modulated by the resistance at that pathway's synapse allows a path to be formed.

The concept of the frequency as a cause of the seizure is based upon the well known experiments of rhythmatic flashings of light in the eyes, the instances of music inducing seizure, and the manipulation of certain parts of the body. All this would suggest that rather than having a level of excitation alone as the trigger, certain signals pictured as a frequency phenomenon are the triggering means. We must then consider the action as a pulsation "beat" or resonance of a certain frequency which synchronized with muscle response can cause further self-induced reaction.

Of possible value then, as part of the hypothesis, is the idea that the muscle's electrical activity is sequenced and synchronized with the nerve's activity at some frequency level which could seem to perpetuate an oscillation or seizure once it has begun.

Of outstanding importance is Penfield's finding (7) that memories can be called forth from an individual by electrical stimulation, irrespective of the will to recall. This would indicate that there is a real basis for considering memory in the same manner as the memory of a type of computer where bits of information are stored in individual units, then called forth as needed in response to signals which are coded directly to them. In other words, assuming that neurons have received memory information at certain current and frequency levels, a signal which can duplicate the original can evoke similar type responses. Probably a great number of neurons are scanned and at random the neurons are selected with the proper value which can respond. Mr. W. Grey Walter (9) has suggested that the brain does operate on some form of scanning principle. The fact that one can "search the memory" in actuality would indicate that a deliberate effort can be made to energize the memory mechanism so that scanning can take place and if one has the clue in his mind, this clue can evoke like responses. An example is the recollection of a person's name by hearing similar sounds. These could act as a localizing means to search a particular level for a particular response. Possibly this is an answer which Gestalt psychology would find valid. We know a square irrespective of its size, since the square has a characteristic pattern of response in which size itself has no more than a passing relationship, so we may recall a memory because of its characteristic frequency pattern. What we are suggesting here is, of course, a memory with a certain pulse pattern of frequency acting on neurons so that when the signal coincides with a particular neuron's need, energy is released in the form of a nerve impulse.

Our theories of memory and epilepsy have significant bearing on one another when we consider deja vu. The writer's explanation of deja vu is that a triggering action does take place. It need not be a similar circumstance so long as it is one which in itself could evoke sensorially a pattern reflected in the cerebral functions which would fire off a like memory pattern. Even if the event had not existed before, the mind does not know the difference. All it knows is that it has received a similar pattern. So as not to consider this fantastic, let us again go back to the important Penfield discovery. The brain did not know the difference between an artificial pattern invoked and one in which its own internal process was called forth. Another corroboration is that epileptic seizure can be called forth in anyone, normal and afflicted persons alike, and it can be brought out in various ways. Who is to say that a seizure brought on by flashings of light in front of the eyes is not the same in its result as one through manipulation of a certain portion of the body. The firing effect takes place in either way but in both manners the firing of the neurons must find a pathway which will allow them to start a self-induced reaction.

We must have an explanation for the means of firing a response. We suggest that the level of excitation is continuously being raised through pulsations of energy at certain frequencies which can set off muscular responses that are in synchronization with the irritating or exciting agent so that a resonance is developed between the incoming and outgoing signals. In order to more fully substantiate this conception of frequency resonance as a cause of seizure, we need not only consider various rhythmatic phenomena as a means of inducing seizure; rather, we should also consider specifically the method of how the firing action develops. This leads us to a statement which, while controversial, is, in a sense, supported by the findings of experimental clinicians. The nerve impulse is not, in our opinion, a simple on-off action as usually described but rather an action which is inherently modified by activities both preceding and following it.

There is evidence that the nervous system can be regarded in the same manner as a biased electrical circuit. The bias concept is based upon the fact that a system which is to be energized to perform a function will react more quickly and without surges, if to begin with, there is slight energization. This is analogous to what the physiologists call the sub-threshold action. This concept should affect our thinking of the nerve impulse as a strictly on-and-off event. The problem is not as simple as it sounds. For example, the brain receives all sorts of signals at random and probably the bias level is a part of and influenced by these signals so that when attention is focused on a particular event, the triggering or the raising to the higher level of the energizing impulse takes place as a result of all these considerations. Actually, if one compares electrical readings of brain waves at rest and at a higher peak level, it is evident that such a bias action is taking place.

In the epilepsies, there is certainly evidence that would point to the fact that the "spikes" can be considered as actually the triggering of the seizures. Comment has been made that the "spikes" are the result and not the cause of such seizure. Such debate would seem to be academic inasmuch as reproduction of a seizure can be induced artificially ("Epileptic discharge and electrical stimulation produce parallel effects.") (8, p. 207) and as Hill (5) pointed out very adequately, irrespective of whether nerve impulses are natural or artificial, they seem to have the same characteristics. To explain this further, we can say that electrical energy may only be the result of certain actions which make for the nerve impulse. However, despite this, it is classic to use electrical action as a means to achieving this very same nerve impulse. We must, therefore, judge only by the results and the results suggest that, much like a thyratron tube, the nerve will not respond except when some actual "spike" occurs to trigger an electrical circuit. It would seem that the energization of a seizure by the frequency of a "spike" can do the same in a human nervous system. The probable manner of triggering is through the repetition of impulses, none singly able to fire by its own energy level. However, each helps to raise the bias or threshold so that the level of action is reached by this means.

We must take in account several factors to make this a valid theory. In doing so we should look upon the nervous system as an electrical differential acting as a servo mechanism.

We should consider as an important point the "accommodation of a tissue (5) to a slowly increasing current which does not excite even though it attains a value far greater than if applied suddenly. An explanation would be that frequency response (frequency taking in account the time element of an applied current) does not allow for ready self-adjustment to the triggering means. The absorption of energy from the pulse is of much greater degree depending on frequency. The pulses do not allow accommodation to take place, and thus the level can be raised, but raising of a current slowly permits easier accommodation, by virtue of the fact that the servo adjustment in point of time (therefore, frequency) allows adaptation to take place. However, a pulse of energy--and it has been mentioned in the literature that the initial pulse is much stronger than needed to fire a response--makes it much more difficult in time for the adjustment to take place and the action of accommodation lags behind the initial impulse. Therefore, if it were just the point of value of current alone, the neurons should fire, but what is signified is the necessity of energization of the neuron by making sure that the servo action of the accommodation always lags behind the amount of energy received. This would again point out that there is a high amplification factor or leverage inherent in any situation where a neuro-pathway has a low threshold. We can assume that self-induction can be established between the muscles with low thresholds and the cerebral frequencies which excite at a particular point. Since the synapse can respond differently under different situations and since the synapse is considered resistance, a proportionate increase of current acts much in the same way as a null finding system in a servo mechanism, where one can balance a bridge at different current levels.

Second, it has been accepted that a sub-threshold current leaves behind it, in spite of its failure to excite, a condition of enhanced and later diminished excitability (5) showing again that what we are thinking about is a variable system and not a simple on-and-off mechanism. While a more complex thought than the on-off principle, it is certainly better suited to our knowledge of higher form servo mechanisms which are of the modulated rather than the on-and-off type. It has been pointed out in the literature (5) that sub-threshold excitation can mean a faster response.

Adrian's proof that the nerve's method of signaling when a stimulus is increased in size is to fire more rapidly, should indicate support of the bias theory.

The argument can be made that irrespective the nerve will only fire or not fire. This seems to be specious reasoning. It would be preferable to say that under certain prerequisite conditions of modulation, which means adjustment of resistance at the synapse in conjunction with bias, a nerve impulse can be set off. To put this on a facetious level--An attractive young woman is asked whether she will go to a certain fashionable restaurant with a young man. The name of the restaurant does not fire a "yes" or "no" response on her part (at least it should not). Her decision is modified and, in fact, limited by the particular individual who is asking. She might answer "maybe" and if her interest is stimulated enough, she might accept the invitation the second time. There are also, of course, many electro mechanical analogies.

To carry the modulated concept further, we may consider that bias provides some flux leakage across the air gap (which is all the synapse may be). We can consider the refractory period as a time lag due to adjustment of the synapse and nerve cell, as the time necessary for building up of the potential through chemical action. We will consider the "short circuit" effect as a variable, modified by sub-threshold excitation; in other words, chemical interaction with a modified electrical field. It is known that temperature can affect the short circuit effect. It should also be considered, therefore, that the heat level is being raised by a bias method. As proof of this, we may consider Hill's claim (5) that the difference between a system at rest and a system fully energized is surprisingly small--something on the order of 50%. Therefore, the system at rest must be generating heat. The point is, we should not consider the system at rest as an absolute or static system but interpret it in the light of a dynamic system with heat fluctuations going on at all times depending on the amount of bias in the system as a whole and preparing it for instantaneous action. By having an air gap with "flux" leaking through we can see where the synapse could vary by the amount of leakage and certainly by building up the bias across the synapse the triggering action to the connecting neurons could vary.

The synapse's function would seem to be very vital. Here again it appears that the "accommodation" factor means that not enough current can be accumulated at one point at one time to bridge the synapse, but that it must be a function of current in time. It would also seem that the theory of the synapse must be further resolved for an understanding of the epilepsies. If the bias (or nominal electrical activity) is "large" enough, the spikes could be self-induced. It is worth repeating Eccles' statement that "The response to repetitive synaptic bombardment is of great interest because it would normally be produced by receptor organ discharges, and, if intense enough, it gives rise to rhythmic discharges of motoneurones." (2, p. 309)

II.

Hypothesis of Neuron Expansion

The writer would like to suggest another theory. An interesting experiment based on the following idea is possible:

Would not the theory of nerve impulse propagation be just as correct if one were to assume that the nerve expands* in the direction of energization and that this in effect is all that the synapse is? In other words, expansion of the neuron would mean the touching physically (or at least closing the air gap considerably) of a neighboring neuron and impinging action could take place. Such a hypothesis could help explain self-induced oscillation, refraction, and in fact, would have some meaning for the theory of memory. The question of nerve expansion by energization should be ascertainable in a controlled laboratory test. It would be interesting to note if expansion (or contraction) taking place would vary with frequency. It is also worthy of note that in the field of electromechanics magnetostrictors use the theory of expansion with current level.

* Since suggesting this hypothesis I have come across the work of Eccles where he states that "The pre-synaptic impulse becomes a more effective synaptic exciter because repetitive stimulation temporarily alters the spatial relationship of the synaptic knobs to the post synaptic membrane, e.g., the knobs may become larger and/or in closer apposition thereto. It is to be noted that this facilitation process is approximately thirty thousand times longer in duration than the process due to the facilitation potential (F.P.) and thus is more likely to provide a basis for an explanation of those prolonged functional changes in the nervous system that occur in conditioned reflexes, and which presumably depend on some change in the form or structure of the synapse (Konorski, 1948)." (2, p. 311) It would seem from this statement that there is every likelihood that the writer's suggestion may have some real meaning.

III.

Prosthetic and Therapeutic Suggestions

A. In a paper titled "The Use of Electro Mechanical Motion to Replace the Loss of Human Movement," dated June 5, 1950, the writer suggested the following:

"The idea of using the above thought, i. e., in the prosthetic sense, has gained new interest with Weiner's popularization of cybernetics. There comes to mind the following example: Say the human body suffers paralysis in the leg. Usually it is the nerve which has the damage, and for this example, we will take that for granted. The muscle while remaining intact will, after disuse atrophy and, in some cases disintegrate so in this example we must keep in mind the immediate use of the device which we are about to describe.

"Since a nerve reaction is an electro-chemical combination with the chemistry, for the most part, aiding in setting up the 'electrical current,' and since a nerve action works on the all or nothing principle, it would seem to me possible that an outside electrical charge could be hooked up in such a way as to replace the dead nerve structure in its function of energizing the muscle and at least a limited use could be had therefrom.

"To carry the thought further, there have been recent studies, namely in Chicago and in England, which would have a tendency, despite the diffused nature of the electrical reaction, to pin down and actually calibrate the amount and type of electricity which certain muscles receive.

"It seem possible to find the exact wave form and pattern and perhaps we might even use an oscilloscope and by duplicating closely the original lengths and pattern to receive a given reaction with similar results. While it is true that any electrical current above a certain point will make muscles react (this is a classical electrical medical experiment), there is a field open of duplicating the brain or spinal column reaction. In other words, to record and duplicate a set of electrical chemical conditions to react perhaps automatically at a given time."

The above action could be accomplished through "broad" response in a general area or through actual surgical means of providing microscopic electrodes for the needed result. It would seem that printed circuitry and a battery much like in a hearing aid could have some real promise in this field.

B. Concerning the epilepsies, the writer feels that what we are seeking is a specific means of controlling the disease through the understanding of the causation involved. Means of raising the threshold of epileptic action through decreasing the electrical responsiveness of the blood stream should be considered rather than the use of general nerve depressants which are inherently of a diffused nature in their application.

C. We should aim for the "draining off" of excessive electrical activity so that the threshold is never reached. This would mean that a triggering agent would have to be in the system which, when certain electrochemical phases of activity are reached, could cause change in the system, the effect of which would be the dissipation of electrical energy so that the discharge could not continue to be self-induced.

D. We might also consider how heat affects the blood stream and electrical potential of the nervous system. It would seem a necessity to have clinical verification of the electrical action which takes place in a human while the body temperature increases. Many modifications of this technique should be attempted in order to find all the ramifications. It seems probable that there are also chemical changes in the system from heat. Viewed from the reference point of physics, molecular movement in response to heat and its effect on the ionization process would seem to offer a fruitful basis for the solution of this problem. It would appear that thermal devices could also be considered in the prosthetic sense.

There are many clues (some contradictory) to the problem, which are yet unresolved and seemingly need more investigation. For example, High fever has been considered a cause of epilepsy. On the other hand, Wilson (11) states that older writers on the subject thought fevers were beneficial and he himself has observed improvement of epilepsy in cases of measles and chickenpox. It is reasoned that lesions or scar tissues result from high fevers and there is evidence that scar tissue can cause epilepsy. But the point of body temperature having effect on the individual's threshold is important. Considering a cause, we note that in the use of tubes in electronics, the thin surface film or coating on a cathode may be destroyed by heat, which then impairs or destroys the function of the cathode for the efficient emission of electrons. As a matter of interest, this is accomplished by bombardment of the cathode by positive ions.

A point to be considered is: Could not high temperature similarly affect the "thin surface film or coating" of the nerve or covering surrounding the nerve, so as to set up the conditions for epileptic seizure?

If the reverse is true, as has been suggested, then would it not mean that higher temperatures would offset the servo feature mentioned previously balancing the bias against the resistance of the synapse? In fact, what is suggested is that saturation (term used "electrically") takes place.

It is well to consider that in an electrical circuit, it is not just a relay which burns up, but that the wire leading to the relay shows the effect of over-heating and in fact, this in itself, can lead to the destruction of the relay. It is also well known that electrical resistance increases with heat which would be an added means of inducing increased heat. Therefore, we must consider in some detail the probability not only of scars on the brain as being analogous to relays, but the conducting wire must also be considered as having similarity to the nerve conductor.

E. Another point of interest is to use electrical stimulation as a means of anesthetic where pain is blocked out by the null effect of nerve impulses meeting.

F. Salts have been mentioned continuously as epileptic therapeutic means. Is not a measure of the saline content of the blood indicative as a new means of therapeutic value? Actually, do not bromides react in such a manner? When acid is consumed, is it not the store of fuel needed for intense propagation?

G. If a subject can have seizure induced by feel, a mechanical clamp worn properly at all times might be useful; if by sound, a hearing aid which filters out certain frequencies; if by sight, eye glasses which provide a filtering service.