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BRAIN MECHANISM[1]

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I CAN think of no better way of beginning than by recalling another function due to the Pilgrim Trust at which I was present six months ago. I recall it in gratitude to a foundation which has preserved so much that is worth preserving in Great Britain, and because this particular occasion concerned a scientist who might be claimed from both sides of the Atlantic, since he belongs to the period of our common ancestry. The occasion was the presentation by the Trust to Trinity College, Cambridge, of some of the private library of Sir Isaac Newton, scholar and fellow of the college and afterwards president of the Royal Society. The presentation was made in the great library built by Christopher Wren at the request of Isaac Barrow, the master of Trinity who recognized the genius of Newton and did all he could to foster it, and the books are now in the shelves at the south end of the library near the Newtonian telescope and the statue of Lord Byron.

The war has prevented an international celebration of three famous men who were born or died 400, 300 and 200 years ago, Copernicus, Newton and Lavoisier, and the Royal Society has been forced to honor its greatest president without the ample banquet which would normally have shown our devotion to science. But the meetings in his honor have made us more aware of those aspects of Newton's work which are overshadowed by the "Principia" and the "Optics." As far as mathematical physics was concerned Newton had only to be and all was light. But there is also the less triumphant figure, Newton the student of the occult, the interpreter of the book of Daniel, the half-believer in Hermetic secrets, who could scarcely bear to be distracted from these things by the mathematical problems which he could not resist solving, who spent the best years of his life in chemical experiments which have had no result. His

[1] The second Pilgrim Trust Lecture to be given in the United States. This address was delivered at the United States National Museum, Washington, D. C., under the auspices of the National Academy of Sciences, on April 24, 1944.

nephew, Humphrey Newton, has left us a picture of him working day and night in his rooms by the great gate of Trinity, with the furnace burning continually and the old, mouldy book on the transmutation of metals by his side. As a rule he seems to have enjoyed himself thoroughly, but it was here that ultimately the clouds gathered over his mind until his friends took him to London and gave him new and less exacting interests. It always gives me a thrill of pride to recall that I lived for four years in Newton's rooms in Trinity, but I have been glad that his great intellect had left no traces of its struggles to harass later tenants.

Stukeley in his memoir says, "As to chemistry we may presume Sir Isaac from his long application to that pyrotechnical amusement had made important discoveries in this branch of philosophy," and he repeats the story that Newton had written a treatise on chemistry which was unluckily burnt in a fire, though it seems that the little dog, Diamond, who is blamed for upsetting the candle is as apocryphal as Newton's cat and kitten. But fire or no fire Newton could scarcely have reached any general laws of chemical affinity, for so many of the relevant facts were not yet discovered. The whole mass of quantitative relations had still to be worked out, as the earlier astronomers had worked out the data of planetary motion. So Newton's natural philosophy deals only with matter in general and takes no account of chemical change.

It takes no account of life either, for Newton was not interested in living things. But I have not brought in the contrast between Newton the physicist and Newton the alchemist without a reason. It is that I proposed to talk of a subject which inherits some of the glamor of seventeenth century chemistry or alchemy. The physiology of the brain has not the economic attractions of the philosopher's stone but it has the same kind of appeal to our curiosity, to our desire to know more perhaps than is good for us. For other kinds of physiology may tell us about living matter, but the physiology of the brain might give the answer to some vital questions about our own minds and might even help to decide what sort of universe we are really in, whether it is the mechanical universe of the seventeenth century or something much more modern and uncertain.

Detailed knowledge of the brain is all of very recent date. In Newton's time it was known that the brain was in touch with the nerves from the sense organs, but up to 1860–1870 there was really nothing to show what sort of events took place in it. Then came the discovery of the speech centers by Broca and of the motor area by Hitzig and Fritsch and with that the search for mechanism in the brain could really begin. There were definite pathways and cell groups for particular operations, for the comprehension of words, for skilled movements and so on. The brain came to be thought of as a great mass of nerve cells and interlacing fibers, and the tracing of pathways through it became the main task of the neurologist. And this happened not so very long ago, for David Ferrier, one of the most successful pioneers in cerebral localization, used to visit the National Hospital at Queen Square when I was a resident there.

Between that time and the present, one of the major developments came from Sherrington's work on the spinal reflexes. This has a special claim to be mentioned here, for it was Sherrington's visit to Yale in 1905 to give the Silliman lectures which led to the publication of his book—"The Integrative Action of the Nervous System." This was an immediate classic. Sherrington's aim was to make the reactions of the spinal cord intelligible by analyzing them into their simplest components. To achieve simplicity the spinal cord had to be isolated from the brain which normally directs it. The spinal reflexes are therefore the reactions of a mutilated fragment of the nervous system and they are produced in a thoroughly artificial setting. But Sherrington's study of them showed first that in these simplified conditions they could be produced with mechanical regularity, and second that these simple reactions could be combined together so as to build up much more elaborate patterns of activity. After this work it seemed much more reasonable to speak of the mechanism of the spinal reflexes and to suppose that more complex behavior might come of their integration. It is true that nowadays the fashion is to decry this kind of analysis and to maintain that the organism can only be considered as a whole. We may have reached that stage, but we have learned a great deal from the analysis none the less. Sherrington himself was content with the activities which do not involve the cerebrum and would always be classed as reflex in spite of their complication, adjustments of posture and locomotion for instance. The cerebrum seemed to him to introduce quite a different order of complexity; and it was Pavlov who developed the idea of a truly mechanical brain—with the warning that we can not expect to understand the mechanism which underlies behavior if we speak or think of it in terms which imply the mind.

Pavlov's teaching, like Freud's, has been publicized too much and has suffered from it. It has left an enduring mark on neurology but much more as the basis of a particular technique of research than as the basis of a philosophy. For in the present period new information about the working of the brain has been accumulating at such a rate that the theories are scarcely worth making. As usual in physiology the new information has come as the result of technical improvements in other fields, in brain surgery, in experimental psychology and particularly in the detection of small electric currents. I can only deal with a few lines of work which will show how things are developing. They may well make a familiar story to you since it is in the United States that much of the development has taken place, but it is this continued, rapid advance which is my main theme.

First of all we have had far more detailed studies of the mechanism of reflexes. Sherrington stimulated nerves and recorded the reflex contractions of individual muscles. In this way he could tell how faithfully the signals coming out of the cord to the muscles copied those which he had sent into it—whether the reflex pathway had inertia or was dead beat and what sort of changes occurred in it. But nowadays the signals which enter and leave the cord can be split up into the individual nerve impulses of which they are composed. These are recorded electrically and their appearance can be timed with an immensely greater accuracy. Recording the electric changes which accompany nervous activity is an old story: it was used by Gotch and Victor Horsley 50 years ago to trace the pathways of conduction from the brain to the cord, but the modern development, started by the work of Gasser and Erlanger at St. Louis, has now reached such precision that we can make a time table accurate to a ten thousandth of a second for each pulse of activity. And with micro-electrodes the search can be carried deep into the cell masses of the gray matter. But the outcome is still the same. When the conditions are standardized we find an exact precision of response within the central nervous system, a mechanical regularity extending to the units as well as to the summed effect of the whole mass of nerve cells and fibers. There is much more to be done, but so far there has been no hint of any processes outside the range of a mathematical universe.

But very naturally the reactions which are submitted to this kind of minute analysis are not a random sample. They are selected just because there is some chance that the analysis can be made, and nearly all of them have been reactions of the local executive parts of the nervous system, the spinal cord and the brain stem. If these parts are not directed by the brain the animal does act—or react—as if it were an automaton, with a mechanical regularity which allows us to predict exactly what it will do in the circumstances. In the intact animal there is the same local mechanism of nerve cells and fibers in the cord but it is made use of by the brain to bring about an entirely different sort of behavior—one which seems far less automatic. A brainless cat will lift its foot each time the skin is pinched, but a normal cat may do almost anything and will probably do something different each time. Evidently when the brain is in control the connection between incoming and outgoing signals is far more obscure.

Here we are still on the outskirts. A great deal is known about the nervous pathways in the brain and about the sort of activity which takes place in the nerve cells, but it does not get us very far. We are dealing with what seems to be no more than a great sheet of nerve cells linked by nerve fibers to some central cell masses and to the rest of the nervous system. We can be fairly certain, too, that its working must depend on the spatial distribution of activity in it. This is determined by the particular pathways which must be taken by the incoming and outgoing messages, for the messages are all in the same form wherever they come from and it is because they arrive in different regions that we interpret one as sight and another as sound. Thus if we look at a bright cross the initial event in the brain will be the development of cellular activity (which we can record electrically) in a more or less cross-shaped area at the back of the occipital lobe, and if we listen to a voice the same kind of activity will appear in the temporal lobe with a pattern, in space and time, corresponding to the areas of vibration in the cochlea. Probably each smell will influence the olfactory area in a similar way—we do not yet know enough to say what sort of shapes will correspond to—say—the smell of a violet or of an onion, but we can be fairly certain that all these different pictures—of visual, auditory, olfactory and tactile stimuli—are made up of the same elements, rapid sequences of nerve impulses distributed more or less thickly over the receiving areas and calling up more or less activity in the nerve cells there.

The detailed mapping of the patterns formed in the brain by the sense organs—the patterns which mirror the external world—is an achievement of the last few years and much of it has been done not 100 miles from where we are now. But it tells us only about the way in which information is sent into the brain and not about the way in which the brain reacts to it. In fact, the mapping has to be done in a brain which is anesthetized so that the sensory picture can stand out against a quiet background. Otherwise there would be a constantly changing activity to confuse the map. It is this activity, in all parts of the brain, which should tell us how the sensory pictures are recognized and used to guide our behavior, but to analyze it we need to know what is going on in the brain of a conscious subject. The arrival of a sensory message in the anesthetized brain is like the ringing of a telephone bell in a house where all the inmates are asleep. Naturally we should like to go on with the story, to find out what happens when the nerve-cells are awake and can attend to the message, how they recognize the author of it and decide on the answer they shall give. In fact, we want to know what happens in the normal unanesthetized brain when a familiar sensory picture appears and calls up associations and movements.

Here there are only some odd scraps of information. The difficulties seem to be mainly technical. As far as we can tell any change in nerve cell activity should produce a corresponding change in the electric currents in the surrounding medium, and if we could record at will from any group of nerve cells in the brain we should be in a fair way to knowing what happens when a new sensory picture is thrown on the cortical surface. But in a man with an intact skull we can not place electrodes in immediate contact with the brain and so we can only record the average of all the electric changes over a fairly large area—the average activity of several million nerve cells and not the exact events in each. It is remarkable that such an average should give anything that can be recorded, but that it does so was shown 15 years ago by Hans Berger. Berger found that in a subject at rest and with eyes closed a regular series of potential waves could be detected by electrodes on the head. These come from the cerebral cortex and indicate an activity in the nerve cells over a fairly large area. But unfortunately Berger's α rhythm seems to be some sort of basic activity of the undisturbed brain. It has a fixed frequency (8–10 a second) and disappears as soon as visual attention is aroused. Thus the α waves can not tell us much about the specific activities by which the brain patterns are analyzed. One thing they can do, however, is to show something of the nervous processes which underlie a shift of attention from one field to another. In man, for instance, where vision is the predominant sense, the rhythm comes and goes whenever the attention is transferred from the visual field to the auditory and *vice versa*. From the size and distribution of the waves, therefore, we can form some idea of the extent of the brain surface which may be normally involved in vision and hearing.

The α waves show us no more than the basic rhythm of those parts of the brain which are awake but have little to do. But there is a further development which tells us something about the specific activities of the visual regions. It depends on forcing the nerve cells to work in unison by illuminating the field with a flickering light. When this is done the potential changes over the occipital region have a frequency corresponding to that of the flicker and are large enough to record through the skull. We have therefore what amounts to a method of tracing the visual signals in the brain, for we can make them fairly easy to recognize as long as the time sequence is preserved.

I will not trouble you with all the details of these flicker rhythms except to say that they seem to reveal an interesting borderland between the primary visual area and the rest of the brain. In this borderland (which extends well beyond the boundaries of the occipital lobe) the spatial as well as the temporal pattern of the excitation is preserved to some extent, but the spread of the visual signals into it is governed partly by the degree of attention given to the visual field, for the diversion of attention to another task will often disorganize the rhythm. And there are all sorts of interactions between the flicker rhythm and the α rhythm, which tends to reassert itself when attention weakens, and may combine with the flicker rhythm, if the two frequencies are suitably related, or may supplant it altogether.

Another point about the activity in this borderland area is that it is far from being an exact copy of the patterns of light and shade which fall on the retina. There is evidence of a good deal of interaction, not only between different points on the same side of the brain but between the two sides. For instance, if we look at a field of which only the right or the left half is flickering, the flicker potentials will appear on the opposite side of the head—this is where the signals of the flicker would arrive. But if the two halves of the field are made to flicker at different rates, my own brain, at any rate, gives up the unequal struggle and produces a confused medley of frequencies much the same on both sides.

In interpreting results of this sort it is very easy to be misled, for it is a long way from a flickering screen to the occipital lobes and a still longer way from there to the mind. The flicker waves do seem to be somewhere on the direct route, however, for when they change in rate or regularity there is usually a change in the sensation which has the same direction, faster or slower, though we may not be able to analyze it more precisely. Unfortunately with present techniques the method can only be applied to visual events. A repeated noise like that of a machine gun does not give a corresponding series of potential waves large enough to detect through the skull—either because they are not developed over a large enough area or because the area is unfavorably placed. I am afraid, therefore, that the present technique of recording brain events, by oscillographs connected with electrodes on the head, is not likely to lead very far. But such a technique may soon be superseded; judged by the standards of modern physics it is already obsolete, and I think we should look forward to the possibility of being able to record all the electrical events—the changing potentials and ionic movements—within the brain in far greater detail and without hindrance from the skull.

What can we expect if such a development occurs, as I think it is bound to do sooner or later?—when we can study the whole changing pattern of activity in the cerebral hemispheres from moment to moment?

It will not necessarily tell us much about a most important and characteristic property of the brain, its power of learning, of forming associations or conditioned reflexes, for this must depend on changes which are persistent and may not give rise to electrical effects. In fact, it may need a biochemical and histological survey to show us why the dog comes to salivate whenever the dinner bell is rung. But an electrical survey could scarcely avoid giving some entirely novel information about what is happening in the brain when we think or solve problems or decide what to do. The progress of neurology has been full of surprises and it will not do to predict: but sooner or later we are likely to reach a position where some very fundamental problems ought to arise. For example, in the brain of a conscious man will there be the same mechanical precision in the response of nerve cells and cell masses to the signals which reach them? Isaac Newton in one of his few excursions into neurology remarks that "the soul may determine the passage of animal spirits into this or that nerve and so may cause all the motions we see in animals." Is there any chance that we shall reach a position where such a possibility might be put to experimental test?

I have the feeling that we shall always find a catch somewhere, as I suppose the alchemists always did when it came to the final moment of projection. The problem may become more and more meaningless as we seem to come nearer to it, or perhaps it will become obvious that it is not one which could ever be solved by beings like ourselves. However, this really does not matter, for we can be quite certain of one thing: whatever the final outcome of inquiries about the mechanism of the brain there is an immense amount waiting to be found out on the way. It is almost within our grasp even now. Before the war the younger generation of neurophysiologists were advancing at a pace which accelerated every year, and those of us who dated back to the string galvanometer were already out of breath. When they come back again we may confidently expect to be left so far behind that these philosophic speculations will be our only consolation. The alchemists may have wasted their time in futile attempts to reach a goal which was not there, but they turned into chemists soon enough. In the same way the search for the mechanisms of the brain, though its goal, as we see it now, is perhaps unattainable, may lead us to a new understanding of human behavior—a synthesis of physiology and psychology. And with that in mind we can end with another quotation from Newton—which sums up what I have tried to say:

> As in mathematics so in natural philosophy the investigation of difficult things by the method of analysis ought ever to proceed the method of composition; and if natural philosophy in all its parts by pursuing this method shall at length be perfected, the bonds of moral philosophy will also be enlarged.

OBITUARY

FRANCIS PERRY DUNNINGTON
1851–1944

FRANCIS PERRY DUNNINGTON was born in Baltimore on March 3, 1851. At the age of sixteen he entered the University of Virgina, where he remained until called by death on February 3, 1944, just one month before his 93rd birthday. He graduated with the B.S. degree in 1871 and the following year received the degrees of C.E. and M.E. In the same year he was made adjunct professor of analytical chemistry and was promoted to a full professorship in 1884. From 1908 to 1919 he was professor of analytical and industrial chemistry, after which he retired from active teaching. He was a fellow of the American Association for the Advancement of Science and held membership in the American Chemical Society, the British Association for the Advancement of Science, the Chemical Society (London), American Electrochemical Society, the Franklin Institute and Phi Beta Kappa. When the first edition of "American Men of Science" appeared in 1906, a star was prefixed to the word *Chemistry* following Professor Dunnington's name, which means that he was ranked among the leading thousand scientists in the United States and one of the 175 American chemists whose work at that time was considered to be the most important.

Professor Dunnington's early training in chemistry was under that most able teacher and great chemist, John W. Mallet. He was associated with Dr. Mallet until the latter's retirement in 1908.

When Professor Dunnington graduated in the early seventies, the demand for chemists in industry was small and so he embarked on a career of teaching and investigation. He became recognized as one of the outstanding analytical chemists of his time. His publications number 68, many of them being joint reports on work with his students. Perhaps his greatest contribution to science was the discovery of the extensive