Importance of Stimulus in Repair and Decay of the Nervous System. By F. W. MOTT, F.R.S., M.D.

THE title of my paper is almost a platitude, for we all know from experience that stimulus is essential for the generation and regeneration of nerve structures and function; and that the importance of stress (excess of stimulus) incidental to modern civilisation and town life in the production of nervous diseases and insanity is beyond dispute; yet when we are asked to give precise data to prove these premises, the matter is not so easy.

The nature of stimulus.—Nerve stimulus is a molecular vibration travelling at a definite rate (30—33 metres a second) along a nerve; the amount of energy liberated by the stimulus is not necessarily proportional to the exciting stimulus; in fact, it is usually disproportional. The passage of a stimulus along a nerve does not cause fatigue; if a neuron ceases to function from excessive stimulation, it is due to the effects of fatigue products upon its terminal arborisations at the periphery or in the central grey matter. The whole nervous system may be considered to be composed of physiologically correlated nervous units, each of which has a nutritional independence, a *vita propria*. The vulnerable parts of the neuron are the terminal expansions of the essential fibrillary conductile substance which is continuous through the body of the cell on the one side with the axon and its terminal arborisation or end organ; on the other with the branching processes of the dendrons in the central grey matter. Delay to the passage of stimulus takes place at the neuronic threshold, that is at the point of junction of the terminal arborisation of the fibrils of one neuron with the next in the series; it is here in the delicate gossamer of the grey matter that ingoing stimulus is reflected to outgoing channels; it is here that it may spread and cause the liberation of stored energy, or redistribution of active energy; it is here that the blood-supply is most abundant and oxygen is continually used up, and carbon dioxide and heat produced.

Currents which represent nervous energy are continually flowing in all directions in the central nervous system. They

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flow with the greatest readiness along systems of neurons which have by habit and use been most functionally correlated; and then less *potential* is used and less fatigue experienced than when new paths have to be opened up by attention.

A stimulus has been defined by Sir William Gowers ("Dynamics of Life") as a process which causes another process greater in degree, *e. g.* tickling the sole of the foot with a feather; but, as he points out, unless there is *conscious attention* you do not get the successive series of violent muscular discharges. But what is this attention? a concentration of consciousness upon the stimulus from without; the seat of consciousness is in the cerebral cortex, the arrival and departure platforms of all afferent and efferent stimuli. The muscular discharge is partly spinal reflex, but also cortical reflex. Bubnoff and Heidenhain showed experimentally that stimulation of the skin by stroking increased the excitability of the cortex to faradic excitation, and probably each successive excitation of the skin, in addition to the stimulus provided by excitation of the peripheral afferent nerve-endings, increases the excitability and diminishes the resistance to the passage of stimulus in the spinal and cortical circles of neurons (*vide* figure, p. 671). But we believe that inhibitory impulses are continually flowing from the cerebral cortex to the spinal centres, which inhibitory impulses antagonise both cortical and spinal reflex discharges. Experiments of Sherrington and Hering support the view that these impulses are conducted by the pyramidal systems. We could then explain the successive series of violent muscular discharges in tickling by arrest of this inhibitory controlling function of the cortex. Now, if we suppose that there is normally a correlative localised and specialised antagonism between augmentor and inhibitory impulses flowing from the cerebral cortex, when once the balance between the two is turned and effectual control lost, the outgoing flow of nervous energy is along the lines of least resistance, and becomes semi-automatic, and incapable of control by attention, although consciousness obtains. Does attention, then, mean concentration of potential and liberation of nervous energy? If so, in this case the distribution would be along particular efferent systems of neurons; and can we thus explain the phenomenon of conscious attention being

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necessary in order that tickling may produce the successive series of violent muscular discharges, and thus support Sir William Gowers' proposition that the stimulus in this case causes another process enormously greater in degree? Or should we adopt the view that stimulus in semi-automatic and subconscious movements may flow in and flow out without using up comparatively any potential? In fact, there may be even a storage of energy by a bio-chemical transforming process, especially in those structures which have been latest developed, and which form the great bulk of the central nervous system, viz. the association neurons. Resistance to the passage of impulses occurs where delay is greatest, viz. at the junctions of the dendrons of one neuron with the terminal arborisations of the axon of another; but, as Von Monakow points out, no sensory neurons are in direct relation with motor neurons, and the delay therefore occurs especially where intercalary association neurons (which even in the grey matter of the spinal cord are much more numerous than the motor neurons) intervene. The great bulk of the brain is made up of association neurons, and their numbers in the cerebral cortex are infinite. Yet we must suppose that every *conscious* sensation, however simple, affects the whole cerebral cortex, leaving traces of its passage in the form of molecular changes, which facilitate more and more up to a certain point the passage of the same excitation the oftener it is repeated. These molecular changes may be bio-chemical or bio-physical in the substance of the neurons or their synapses. I should incline to the opinion of Sir William Gowers that the changes occur at the synapses, which are the innumerable anatomical or physiological junctions of the neurons. It is even possible to conceive a hypothetical substance representing latent nervous energy in these synapses.

Is nervous energy derived directly from the transformation of chemical energy incidental to the life of the neurons? or are we to accept the entirely opposite view of Professor Gotch, who maintained in a recent paper read before the Psychological Society at Oxford that all nervous energy comes from without, there is no storage or accumulation of energy, *only* redistribution; there is a greater amount of ingoing than outgoing stimulus, the balance being converted into chemical and thermal equivalents? This hypothesis was mainly supported

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by various experimental observations by him on the lower animals.

I would agree with Gotch that there is no spontaneous discharge from the spinal motor neurons, directly or indirectly; a present stimulus is necessary. Again, I would agree with him that there is possibly a greater total amount of ingoing than outgoing energy, but I disagree with him entirely in not allowing the possibility of storage or accumulation of energy by a process of transformation of bio-physical into bio-chemical energy.

Every thought, feeling, and emotion has its particular muscular concomitant; it may not be sufficiently intense to rise into consciousness—indeed, we can only be made aware of its existence by the concentration of consciousness upon ingoing impressions from the muscles, especially those depending upon the minute alterations in the tensions of the eye muscles and the muscles of expression. Darwin showed the intimate relation of the emotions to their muscular concomitants. Even the patient suffering with auditory hallucinations probably is affected simultaneously with a particular motor attitude of attention with its corresponding ingoing stimuli, both kinæsthetic and auditory sensations being fused in consciousness. There is, however, no proportional relationship between the mental effort involved in attention and the muscular mass moved—and therefore the consequent incoming kinæsthetic impressions; just as there is no proportional relationship between the area of cortex representing specific movements and the mass of muscles moved. Eye, face, and hand movements represent the great bulk of the excitable area of the cortex.

Attention, we may suppose, represents a liberation of nervous energy in the cortex cerebri, either due to a direct bio-chemical generation in the neurons, or to accumulated energy transformed. The sense of nervous fatigue is distinct from muscular fatigue; it is the result of the lowering of nervous potential which especially is used up in processes involving attention of a constantly varied nature; for continuous attention to one thing, no matter how complex, leads to the nervous process becoming more or less subconscious and semi-automatic; the discharge of nervous energy becomes diminished, and less fatigue is experienced in connection there-

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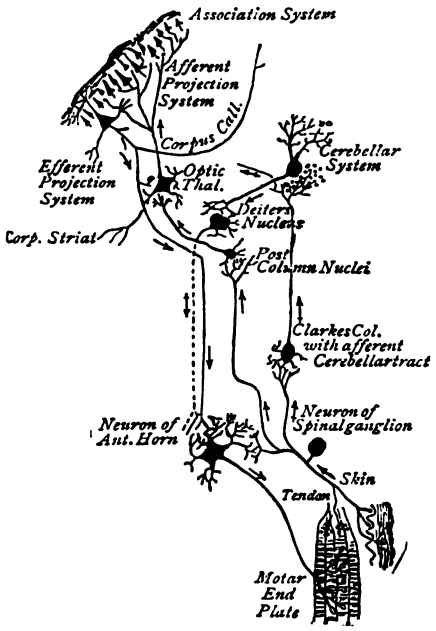
with. Professor James remarks that in action grown habitual, what instigates each new muscular contraction to take place is not a thought or a perception, but the sensation occasioned by the muscular contraction just finished. A glance at the diagram representing the three nervous circles which are in



continuous molecular vibration will indicate how, when once habitual movement has been started by a signal from the brain, stimulus will flow in and flow out. The volitional signal as a result of experience and associative memory has arranged a correlation of subcortical afferent, efferent, and association neurons in such a way that stimuli flow in from sentient structures, and flow out to synergic groups of agonist and antagonist muscles in co-ordinate and orderly sequence, so that the most perfect precision of movement is accomplished with the least expenditure of nervous and muscular energy. In locomotor ataxy the ingoing sensory channels are abolished, and co-ordination has to be effected by new paths (visual and vestibular) involving attention. Practice makes perfect, and habit diminishes the constant attention with which our daily

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acts of life are performed; but habit, or this tendency of stimulus to flow along lines of established least resistance (Bahnung), not only allows us to do the right thing at the right time, but often compels us to do the wrong thing at the wrong time. The oftener a wrong thing is done, just as a right thing, the more likely is the establishment of loss of control and establishment of lessened resistance along the wrong neurons to become permanently installed; and it seems probable that many neuroses and psychoses keep themselves going simply because they happen once to have begun, *e.g.* epilepsy, hysterical contracture, catalepsy. Again, the commonest subjective symptoms of insanity, delusions, illusions, and hallucinations may be explained thus. Auditory hallucinations, so frequent a symptom in the insane, often commence as *simple* noises; these are followed by "voices," which eventually become so distinct and real that the greater part of the patient's psychical existence is determined by and concentrated upon this abnormal stimulus from within, indicating progressive strengthening and fixation of the perverted functions of the mind, and progressive weakening and dissolution of the normal functions. If we suppose that the total nervous potential (stored nervous energy) is at the disposal of the whole nervous system, then in the insane we must suppose that it is constantly being used up in a wrong way. Although there is undoubtedly a trophic independence of the neurons it is doubtful whether there is an anatomical, and there is certainly not a physiological independence. Seeing that the sign of life and the fundamental property of living matter is the capability of transforming energy, it is conceivable not only that incoming energy may be stored, but redistributed.

The effect of stimulus depends not only upon the intensity of the excitation, but also upon the excitability of the neurons stimulated. Thus stimuli which are insufficient to rise into consciousness may do so by attention, and this constitutes what might be termed the subjective attitude of the individual, and is therefore a personal equation. But the personal factor itself may vary according to the health of the individual and the quality and quantity of the blood supplied to the nervous system, especially to the cerebral cortex.

Every day experience shows that alterations in the blood, whether caused by subminimal defects, by poisons engendered

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within the body, or poisons derived from without, will change the *subjective attitude* of the individual to the stimuli which are continually flowing into the central nervous system by all the external and internal sensory channels maintaining the normal reflex muscular tonus upon which, in great measure, the sense of well-being depends. The sensations coming from internal structures which we cannot explore by sight or touch are normally of such low intensity as not to rise into consciousness, although with phasic or periodic regularity stimuli continually flow from the viscera into the central nervous system. If they exceed a certain intensity they give rise to ill-defined uneasy sensations, and when intense they may assume the forms of pain which may be referred in consciousness (that is by the cortex cerebri) to morphologically correlated skin areas. But by morbid introspective concentration of consciousness (associated often by the knowledge of the possession of an organ which they believe with reason or not to be delicate or diseased) these normally absent or ill-defined visceral sensations may be intensified into severe pains. The psychopath and neurasthenic hypochondriac may be thus liable to suffer; when his nervous potential is beginning to run down, his higher controlling centres of the cortex are the first affected, and no longer exercise a restraining influence upon incoming stimuli; consequently every peripheral excitation, even those of low intensity, may produce a maximum effect upon consciousness. Many poisons produce similar effects. The question arises, how do the higher centres control consciousness in attention? For attention is both a positive and negative process as regards stimulus. We cannot concentrate consciousness upon stimulus from some external object without shutting out of consciousness all other stimuli. Is this a process of switching off as well as switching on of active potential, or is the negative effect the result of opposition of nervous currents (as in the correlative antagonism of muscles) resulting in the production of thermal and chemical equivalents (heat and CO_2) removed by the blood? The latter hypothesis would explain the fatigue occasioned by concentrated attention, especially upon continuously varied objects. Every stimulus revives the past, and behind the association wave which rises into immediate consciousness is an unseen ocean, which under normal circumstances is kept out of consciousness. In insomnia and delirium of fever, and certain poisons, such as haschisch,

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where the higher controlling centres are fatigued or paralysed, the negative process no longer takes place, but mainly the positive in the perceptive and ideation centres. Often because these lower centres are also partially affected, the ideation is grotesque, confused, and abnormal. These mental states are mainly related to visual stimuli, because vision and its associations play by far the most important part in our psychical existence.

But I will now pass from these speculations to the more solid ground of physiological and anatomical facts.

Experiments have shown that nerves are incapable of fatigue, or at least that they continue to conduct impulses without any apparent loss of excitability to electrical stimulation for a long time.

The experiments of Halliburton and Brodie upon the nerves of the spleen show that a non-medullated nerve is just as difficult to fatigue as medullated nerve; and these observers conclude that while fatigue is demonstrable in nerve-cells, it has never yet been shown to occur in nerve-fibres of either the medullated or non-medullated variety. This does not, however, imply that nerve-fibres undergo *no* metabolic changes during the transmission of a nerve impulse. It probably means that the change is slight, and the possibility of repair in the healthy nerve great; and that fatigue in the usual acceptation of the term cannot be demonstrated.

Certainly Dr. Waller's experiments tend to show that during the passage of a current along a nerve some transformation of energy occurs, as evidenced by the electrical variation and the formation of carbon dioxide; (1) and Waller puts forward an ingenious explanation when he says, "I wonder does this carbon dioxide become altogether dissipated? may it not perhaps be re-involved in some storage combination, as the nerve-fat, perhaps, that is so prominent a constituent of fully evolved nerve? Such nerve consists of proteid axis and fatty sheath; the axis, which is the offshoot of a nerve-cell, is the specially conductile part; the sheath is a developmental appendix, not directly connected with any nerve-cell; yet cut nerve and sheath as well as axis undergo Wallerian degeneration, which is evident proof of a functional commerce between sheath and axis. You have seen, further, that such nerve is inexhaustible; yet that it exhibits very clear symptoms of chemical change

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after action. All these things, to my mind, reconcile themselves with the notion that the active grey axis both lays down and uses up its own fatty sheath, and that it is inexhaustible, not because there is little or no expenditure, but because there is an ample re-supply."

Although Waller's explanation is not supported by the experiments of Eve, Brodie, and Halliburton on non-medullated nerves, yet to my mind there is much to be said in its favour, which I will show by certain observations.

If we can look upon a nerve impulse as a molecular wave of increasing irritability propagated along its fibres, the electrical variation and the production of carbon dioxide marking its passage are evidences of a discharge of energy in another form, both the added energy of the impulse and the electrical energy must be transformed latent chemical energy of the fibre. The added energy may come from chemical changes in the myelin. If this is inconsiderable in the fibre with its neurilemmal sheath, it may be considerable in the delicate myelin sheath covering the terminal brushwork of fibrils which enter the grey matter, for it is here that the oxygen supply is most abundant; and the relation of the oxygen to the molecular vibration along the fibril is most intimate, for they are only separated by the extremely delicate sheath of myelin, whereas in the peripheral nerve-fibre these intimate relations between the nerve current and the oxygen of the blood do not exist.

That the myelin serves another purpose than an insulator is highly probable for the following reasons:

(1) Impulses transmitted by the non-medullated fibres of visceral and vascular structures are of low intensity as compared with the medullated fibres of somatic structures. It would serve no useful purpose for these impulses to be of high intensity and to rise into consciousness. They only do so when the nerves are in an abnormally irritable state from inflammation or disease; on the other hand, it is essential that we should be aware of the slightest touch of the skin, and it is conceivable that we are aware of these very slight impressions by *added energy*, derived from metabolic changes in the myelin, as the stimulus traverses the neuron. Each internodal segment may act, as Sherrington suggested a little while ago, as an electrolyte.

(2) The metabolic activity of the nervous tissues may be

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shown by the examination of the cerebro-spinal fluid and of saline extracts of nervous tissue. The observations of Gumprecht and Gulewitz show that minute traces of choline can be detected in normal cerebro-spinal fluid ; likewise traces can be proved to exist in the saline extract of perfectly fresh nervous tissue, especially in the grey matter, sufficient, indeed, to yield both chemical and physiological tests indicating its presence. Halliburton and I have shown that choline is a product of degeneration of the complex phosphoretted fat of myelin called protagon. It may be supposed that anabolic and katabolic processes continually lead to the recomposition and decomposition of this chemical basis of myelin. Whatever view may be taken as to myelin being a source of nerve energy, there can be no doubt that—

(3) The development of the myelin sheath is related to the passage of stimulus along the axial fibre, for we find the ingoing tracts of the central nervous system are myelinated before the outgoing, and in the cortex cerebri of the new-born child we have each myelinated sensory sphere representing a centre of elemental consciousness unconnected by any myelinated efferent projection or association systems, except some fibres of the corpus callosum which unite the two halves of the brain, and unify these elemental spheres of tactile consciousness of the two halves of the body. As a result of ingoing impressions reflected down the cortical efferent tract to the cord, myelination of this projection system occurs, and with it the development of conscious response to stimulus (or elemental volition) ; later the dawn of intelligence is coincident with the development of function of the association systems as shown by the myelination of the fibres of other parts of the brain, and then a simple sensation limited to a sphere of elemental consciousness is presumably impossible ; for even the simplest sensory stimulus perceived must be accompanied by a spread to association systems, resulting in associative memory.

(4) Again, it is known that the myelin sheath of the optic nerves of an infant born at full term is not so well developed as the myelin sheath of an infant born at eight months, and who has lived a month with its eyes exposed to the light. The experiments of Ambron and Held and Berger upon animals born blind have shown that if the eyelid on one side be stitched up, so that the stimulus of light does not act upon

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the retina to the same degree as on the other side, the myelination is more advanced in the optic nerve of the eye exposed to light. We have in this experiment a direct proof of the influence of stimulus in the production of myelin.

(5) The converse is also true; the absence of the inflow of stimulus leads to slow regressive atrophy—first of the protagon in the myelin sheath, next of the axis-cylinder process. This is strikingly shown in the nerves, posterior roots, and their projections in the spinal cord, following the amputation of a limb. In the case of the sensory neurons the posterior spinal ganglion cells are the last to show changes. There is, in fact, an atrophy in inverse order of structural development. The last to come, the first to go. The efferent fibres which supplied the muscles that were removed in the amputated limb also undergo atrophy from lack of stimulus. In intra-uterine amputations, and those in early infancy, atrophy arrests developmeut not only of the spinal afferent and efferent neurons, but of the cortical centre of the limb, as was first shown by Edinger and our president, Dr. Wiglesworth. Again, the atrophy of correlated groups, systems, and communities of neurons which are in physiological, but not necessarily in direct anatomical association, is due to failure of stimulus and disuse. Thus a lesion destroying the thalamus in one half of the brain produces atrophy of the whole cerebral cortex of the same side, of the opposite half of the cerebellum, and of associated structures in the spinal cord. This was shown in a striking manner in a paper published in *Brain* by Dr. Tredgold and myself.

(6) The failure of the formation of myelin, or, at any rate, the normal formation in regenerating nerves when stimulus is diminished or absent. Lately I have been engaged with Professor Halliburton in endeavouring to ascertain if, in the absence of stimulus, nerves regenerate as readily as when stimulus exists. It has long been known that sensation returns before movement, and in some experiments which we made concerning the chemistry of regeneration we were of opinion that the sensory nerves regenerated before the motor, at least small cutaneous branches had a better developed myelinated sheath than the motor nerves obtained from the same limb. Of course this is not a strictly conclusive experiment, for other conditions may have favoured the earlier myelination of the one than the other.

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The observations we have lately been engaged in were made with a view of ascertaining the part stimulus plays in regeneration; it is well known that electricity, massage, and passive movements facilitate the return of function. And while not denying that this may be due in great measure to improved lymph and blood supply, it may also be due to stimulus of the nerve structures undergoing regeneration. One would expect that if the limb of an animal were rendered motionless, stimulus produced by every change in position would be wanting; but such a condition must be brought about without interfering with the nutrition of the limb or the connection of the nerves with their trophogenetic centres. Professor Sherrington and I showed that the fore-limb of a monkey can be deprived of voluntary movement by section of the posterior roots of the sensory neurons of the limb. We showed that this loss of movement was not due in any way to affection of the efferent path, for stimulation of the cortex cerebri produced movements equally well on both sides. The immediate effect of the operation, if a sufficient number of roots had been cut, was a very great loss of reflex tonus, and the animal in the majority of cases was unable to perform any voluntary movements. Dr. Warrington has shown that chromolytic changes occur in the posterior and lateral groups of the anterior horn cells as a result of this section of posterior roots; it may be presumed that the withdrawal of the normal stimulus incidental to reflex muscular tonus may be associated with this change. The observations which Halliburton and I have been making are as follows:—A sensory paralysis of the fore-limb of monkeys was produced by section of the posterior roots, then both ulnar nerves were cut at the elbow and sutured; the nerves were examined after different periods of time had elapsed, first by stimulation of the nerves under an anæsthetic; second, by histological investigations. Various difficulties have arisen owing to anastomosis of the ulnar and median nerves, so that our results are as yet inconclusive, although they strongly support the view that stimulus does play an important part in regeneration and myelination of the motor fibres; for in a few successful observations we found that stimulation with the strongest faradic current of the ulnar nerve below the suture on the side in which the posterior roots had been cut was attended

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by movement, whereas on the other side a moderate current gave a contraction.

Likewise histological observations, as far as they go, show that the nerves are in a more advanced state of regeneration on the side in which the roots have not been divided than the other. I may say that section of the roots has no effect upon the nerve above the lesion. It therefore looks as if the passage of stimulus incidental to muscular movements plays an important part in the generation of ingoing currents and myelin formation.

The effects of excessive stimulus.—The passage of currents through neurons is attended by katabolic changes, and if the neurons are in a low state of nutritional equilibrium the processes of disintegration are in excess of those of integration. The nutritional state of the neurons depends upon several circumstances: first, the inherent durability or *vis propria*; and secondly, the supply of nutrition, both as regards quantity and quality of the blood and lymph.

The vulnerable part of the neuron is that most remote from the cell body and its nucleus—the terminal arborisations, where the discharge of energy, and presumably the katabolic processes reach their maximum. Thus it is in the primary degenerations we find a number of factors conspiring together to produce degenerative changes, which commence in the fine collaterals and terminals and proceed back towards the cell of origin.

The reason why stress or excessive stimulus can be an important factor in the production of degeneration when the neurons are subjected to the influence of poisons is probably that the nutritional equilibrium cannot be maintained, disintegration processes attended by the discharge of energy being in excess of integration.

The action of poisons in the blood may be selective, affecting certain systems, groups, or communities of neurons; or taken as stimulants to excite to further action the neurons in a low state of nutrition, they blunt the natural safeguards of pain and weariness, which serve as signals for repose and recuperation; for pain, as Sherrington defines it, is a psychical adjunct of a protective reflex. It is the neuropath, psychopath, and neurasthenic who take to alcohol in order to give them fresh nerve energy, who are liable especially to suffer from the effects of the poison.

In my practice at the hospital and in the asylums I have been

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struck with the importance of excessive stimulation in determining degenerative lesions in those parts of the nervous system most subject to the stress. This view of the importance of stress in the production of degeneration was emphasised by Edinger and supported by experiments; he found that poisons such as pyridin injected into animals produced a severe anæmia, but degeneration does not result therefrom. If, however, these animals (rats) are put into a wheel cage and made to do excessive work, degeneration of the posterior columns in some respects resembling tabes occurs; also chromolytic changes in the anterior horn cells were found.

These facts, moreover, show that degeneration occurs in the terminals of the posterior spinal neurons, presumably from the fact that the degeneration is shown by the Marchi reaction in the fine myelinated collaterals and the myelinated fibres of the posterior columns, which are without a neurilemmal sheath.

Under the influence of the poison there is a nutritional deficiency of the whole of the nervous system, but the rats placed in a wheeled cage, and made to go on working continuously although fatigued, are unable to get rid of the fatigue products, and the sensory fibres of the reflex arc are continually stimulated and discharging energy under unfavourable nutritional conditions, the result being that the disintegration processes are in excess of integration, and progressive degeneration ensues.

Edinger claims that this experimentally produced degeneration stands in close relationship both as to cause and localisation to the tabetic degeneration of the posterior columns in man.

Observations which I have made on a very large number of tabes cases support Edinger's statement; the syphilitic poison produces a loss of durability, or, as Sir William Gowers terms it, an "abiotrophy," and therefore a nutritional deficiency which interferes with the balance of repair to waste. The great majority of my patients suffering from tabes had led an active life, or followed an occupation involving stress of the legs. In some the disease commenced in the arms; and this is of interest, because one was a mounted policeman, and the pains were first felt in the arm with which he held the reins; two were packing-case makers, and one was a parcels post sorter. As a rule, Charcot's knee-joints are, according to my experience, much commoner in women, and I attribute this in a great

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measure to the kneeling which they do; whereas the most marked case of tabo-arthropathy of both knees in a man which I have seen was in a carpet planner. A great many other instances of tabes I could bring forward did time permit, but I will content myself with enumerating some other nervous diseases illustrating the effect of stress in determining the seat of degeneration. A man who suffered with alcoholic dementia, paralysis, and wasting of the muscles of the upper extremities—the lower being unaffected, which is unusual—was shown to me as a case of progressive muscular atrophy, and I found that he was a Covent Garden porter, employed in carrying heavy boxes on his shoulders all day. Two cases of amyotrophic lateral sclerosis have come under my notice, in one of which the disease began in the right hand and arm; the man was a cooper, and wielded all day long a 4-lb. hammer; the other was a waiter who carried his tray on his left hand, and the disease correspondingly began in the left hand and arm. Experience, therefore, shows that in nervous diseases stress plays an important part in determining the seat of degeneration in a system which is subject to poison or inherited or acquired loss of durability.

In seven cases of conjugal tabo-paralysis which have of late come under my observation the history was usually this,—that the wife developed the disease after the husband, probably because she was infected by him with the syphilitic poison, the mental disease arising as a result of this, and of the worry occasioned by her husband's illness. However, it would be absurd for me to point out to an audience of alienists the fact so self-evident that mental stress is an exciting factor in the production of insanity. But I have often thought how little is done in our asylums in the way of applying stimulus or diminishing it by hydrotherapy, massage, and electricity in carefully selected cases.

(1) There is no direct chemical proof that CO_2 is evolved. Waller infers that it takes place because the effect of long-continued activity or the galvanometric response of nerve is the same as that produced by exposing a nerve to a small dose of that gas.

Discussion

At the Annual Meeting of the Medico-Psychological Association, Liverpool, 1902.

The President.—We owe Dr. Mott a very special debt of gratitude for coming among us to-day and giving us an account of these exceedingly interesting

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researches, which it is impossible to value too highly. Our asylums we know are full of patients who have come there as the result of over-stimulation of the nervous system. Anything which will put this inquiry on a scientific basis, and show us the physical causes underlying these conditions, is of the utmost value. The other point which Dr. Mott touched upon rather briefly—the repair of the nervous system—is of almost equal importance. We have many cases which we find lapse into stupor. In those stimulus is very important from the point of view of cure. Many are purely cases of over-stimulation and require rest. We have to be careful not to begin our stimulating process too soon. The whole subject is one of extreme interest and value. I will ask Professor Sherrington to address us.

Professor SHERRINGTON.—I must thank you, sir, for the privilege, being a visitor here, of being allowed to listen to the admirable and valuable address by Dr. Mott. I have often heard him before with great advantage to myself, but I doubt if on any occasion I have listened to him with greater profit. Dr. Mott has touched on so many points, and so many are of practical value, that I am incapable of dealing with any beyond some aspects of the questions which appeal to the laboratory man. As physiologists we are particularly grateful for such work on account of the help it gives in a problem which physiologists consider most urgent—the answer, namely, to the question Dr. Mott so frequently referred to, and which he insisted was proved—the intercommunication which must and does occur between the independent units constituting the vast network of the nervous system. To what he has to say on that subject the physiologist listens with confident and attentive expectation of help. The nature of this intercommunication —the view that whatever the functional mode of conjunction, the nervous system is and must be one—is the answer to the question which Dr. Mott told us. I wish Professor Gotch were here. One would like to hear him defend his view, which Dr. Mott mentioned with great reserve, that the nervous system only liberates the same amount of energy as a stimulus communicates to it. I would like to have it examined, and if found unsound rejected as early as possible, because one of the most helpful of the assumptions we can use in dealing with the problems of the nervous system and of diseases of the nervous system is that which regards the nervous system as more or less a reservoir of energy to be discharged, the discharge depending very much on the condition of the reservoir itself; but it is very far from being a rigid system, which simply conveys in various directions within itself the amount of energy conveyed to it by some peripheral stimulation. What Dr. Mott has told us with regard to the nutritional character of the disturbance which use or stress causes seems to me largely bound up with the periodicity, the proportion between exercise and rest. That results very distinctly from what he said, that a certain amount of exercise is extremely favourable. The beautiful and ingeniously devised experiment which he brought before us shows in a conclusive manner the influence which a certain amount, not an abnormal amount, of functional exercise has on the repair of these units of the system. There is evidence of a similar kind which can be ranged alongside of his, that the closure of one eye for some weeks in a newly born animal, complete closure, retards the development of the myelin sheath of the fibres of the optic nerve on that side. Well, this instance shows in the most striking and undeniable way the influence of nerve stimulus upon nutrition. At the same time we have well-known examples of the harmful effect of too great excitation. If, therefore, there are these two results at the extremes of the range, then there must be between them a position, a zero position, of normal nutrition, a position in which nutrition is most beneficial. I presume that the same question underlies the arrangement of hours of work and rest in the schoolroom, which is at present largely occupying the attention of many experimental observers; in other words, there must be a particular apportionment between length of lesson and playground interval which will secure the largest amount of general nutritional welfare to the nervous system of the child. To return to the view which Dr. Mott commented upon in Professor Gotch's argument, there are very strong points to urge against it. I would like to mention one or two of them. That a nerve cell, or still more a chain of nerve cells, gives out the same amount of energy, or rather less energy, than is conveyed to it in the stimulus of the system is hardly borne out by the somewhat analogous case of the nerve cells of the muscles. Regarding the whole

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of the organism as made up of units which have the same fundamental qualities, we have the fact that a nerve cell of the muscles multiplies the energy conveyed to it perhaps half a million times. Let us take a laboratory instance which occurred to me while listening to Dr. Mott. We have a number of dogs in which the spinal cord has been completely transected. After a certain time the spinal reflexes beyond the point of transection have been very brisk. We have one of those æsthesiometers, Frey pattern, which can be pressed on the section and used as a stimulator. Adjusting this so that it just suffices to excite sensation when applied to the tip of the forefinger, the amount of mechanical energy used in the application of the bristle at the end of a penholder is not more than enough when measured on a delicate chemical balance to shift the scale; it represents the tenth of a milligramme or less. In these dogs by that means we have elicited reflex action shaking the whole posterior half of the animal, and conveying movement to the anterior half as well. There we have a case in which the multiplication of energy must be many millionfold. I saw in the laboratory of Professor Gould many years ago a dog which by large lesions in the cerebral hemispheres had been reduced practically to the condition of a reflex animal. It was simple enough as the animal walked along to flash a bright light in one eye. That caused it to swerve to the opposite side. The amount of energy conveyed to the nerve in the vibrations of ether as compared with the amount necessary to deflect the course of a heavy animal is an instance of multiplication manifold.

Although the result is more or less an intricate one, controlled and regulated by the condition of the reservoir in which the explosions of energy occur, it is useful to have before us the relation of stimulus to the exertion of nerve force, and it is more and more useful in view of such doctrines as Dr. Mott has exemplified and illustrated. In the light of these doctrines the whole series of phenomena—the processes of disease and of what is akin to disease, exaggerated fatigue—become much more easily explicable. It has been a privilege as well as a pleasure to listen to what Dr. Mott has had to say.

Dr. WARRINGTON.—I should like to associate myself with the concluding remarks of Professor Sherrington. The paper we have heard this morning is extremely suggestive and at the same time very practical, because observations like these we have just heard tend to prevent the routine observation and routine reflection which is so harmful. It is a gratifying feature of research in neurology that it is assuming a practical aspect. I have no new facts to bring forward, but I may say a few words on what the study of the histology of the nerve cell shows. One goes back to the original observation of Mann and Hodge on fatigue, where they have shown that actual morphological alteration takes place. The protoplasm of the nerve cell has been aptly described as consisting of a working material and of a fundamental basis. We know that, for instance, in the salivary glands marked changes of structure occur during hours of fatigue. One thing which strikes me in studying the histology of the nervous system is that there must be an extremely rapid restoration of equilibrium in all kinds of animals. As far as histology goes I do not think we find evidence of chromatolysis in the normal condition. Whatever changes take place in life must be very rapidly repaired. I regard the appearance of cells showing chromatolytic change as distinctly unusual unless there is some morbid process attached to it. The effect of excess of stimulation has been alluded to by Dr. Mott. To his remarks I have little to add. As he has pointed out, the vulnerability of the nervous system in those diseases in which excess of stimulus plays an important part must depend on inherent or acquired want of stability. That, I think, is important, and it appears obvious in many cases. Dr. Mott has brought forward a number of actual clinical examples where excess of stimulus has been connected with degenerative changes in the neuron. I mention the case of a young man of twenty, an expert pianist, who developed what I took to be the symptoms of chronic anterior horn disease. It was limited to the right hand, the hand which he used a good deal in playing. It struck me as a good example. I advised him to drop excessive pianoforte playing. I have watched him now for three years and he has got no worse.

We have Edinger's well-known experiment in which fatigue *plus* a poison produced degeneration of the posterior columns. Similar changes occur where the

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stimulus is deficient. Dr. Mott has mentioned the changes which take place when the afferent impulses are cut off. These and like observations, when the axon is divided and chromatolysis results in the cells of the region, show how excess or deficiency of stimulation is connected with nutritional change. Lugaro maintained that after section of the peripheral axon of the posterior spinal ganglion cell that cell did not as a general rule recover. There the resulting alteration of the stimulus must have been, and is, very much larger than occurs when the axon on the cord side of the root-cell is severed. The anterior horn cell may be regarded as part of the arc receiving impulses in a downward direction and in an upward direction, and again as giving them off; and it will be seen that interference with this periodical stimulus is very readily attended by changes in the nerve cell. As a rule, if the efferent axon is cut, the cell after a time repairs and equilibrium is restored; nutrition also becomes normal. But it is an interesting fact that sometimes nutrition is not restored; the cell dies. For some reason, I do not know why, but we do know, that after section of the efferent axon the disturbance may be so great that the nucleus becomes extruded and the cell perishes. I was much struck by the remark Dr. Mott made in emphasising the *vis propria* of individual cells. That is always to be borne in mind in working at these histological changes, and I think it accounts for some of the difference of observations made in regarding the localisation of nuclei of origin.

Dr. CLOUSTON.—As practical men we are much indebted to Dr. Mott for enabling us to breathe the air of science in so pure a form. The first part of the paper we shall probably not feel ourselves qualified to discuss. One point mentioned by Dr. Warrington is the curious independence of neurons in close proximity to each other. Ford Robertson mentioned to me the other day a curious case of general paralysis which had certain mental and motor features, but the lesions were extremely circumscribed. You had certain small groups of neurons completely destroyed, and immediately, in the same field of the microscope, neurons in the most extraordinary state of perfection; it was the most marked localisation I have ever seen. These are things we do not explain, whatever theory of general paralysis we adopt. A burning question with us is whether we should treat some of our patients by bed or by exercise. Dr. Mott's remarks bear on that subject. "If we could devise a drug by which the patients could be put to sleep, if we could suspend the higher neurons for, say, a week, suspend consciousness, and at the same time allow nutrition to go on," one has always been saying. The absurdity of the position is shown at once by Dr. Mott's observations. You suspend the oncoming stimulus, and the patient, instead of getting up better, might get up very much worse. Then as to the use of massage, many people went massage mad. It was used for every kind of disease, and especially in incipient cases of melancholia. A great many of these incipient melancholiacs were greatly aggravated by the course of massage to which they were subjected. Taking the ordinary case of melancholia, you have to establish a nutritional equilibrium. But when you get a case of excited variability have you not rather to establish a kinetic equilibrium? You have to prevent the waste of outgoing energy both in those cases and in cases of mania, but the kinetic equilibrium may not be the same as nutritional equilibrium. That they must have a close relationship to each other I admit, but what we have to prevent is the burning up, the explosion, the waste of the higher energy of the cortex in a useless way. That is a question we have to face every day. In regard to the manner in which we deal with many of the maniacal patients, there is the process of putting the patient in dark seclusion. You remove many of the stimuli; you employ a degree of restraint which prevents a great explosion of muscular energy. A great many cases are much the worse for this treatment. It is one of the most important of clinical questions how much we should allow muscular energy to be expended. Now we see how physiologically important it is that the patient should take a walk in the sunshine. You have the stimuli from the brain and the outward stimulus from the sunlight. Speaking of stimuli, I think Dr. Mott said too much about stimuli of the mechanical kind and too little about stimuli from proper nutrition. If you stimulate without the proper supply of blood there must be loss of energy. It is absurd to say the central nervous system does not bottle up energy; the fact is unbelievable by any practical man. The central nervous

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system does bottle up energy as much as if you put wine into a bottle and drink it yourself; the experiments show this strongly. As to warm baths, they exercise a soothing influence. We have not got, however, into the trick of using them rightly. Some of us have cured patients in twenty-four hours with warm baths, others have killed them. Then, again, there is a clinical fact of the utmost interest, that an insane patient is always worse in the morning. By every principle he ought to be better, but he is not. When he is getting better, and has been subjected to stimuli in the sunshine, the first thing we notice is that he has an hour of sanity nearly always in the evening. He has been maniacal in the morning, but turn on the electric light in the evening, and he becomes sane and conscious. This saneness later on disappears. That is a clinical fact in our daily experience, and it is a fact of the greatest importance. I said to the head nurse in the hospital the other day, referring to a woman who had just begun to have an hour's sanity in the evening, "Are you not clever enough to make that two, three, or four hours instead of one?" "If you and I," she replied, "were clever enough to discover that, we should cure 20 per cent. more."

Dr. HYSLOP.—I would like to ask Dr. Mott whether he considers the work done by Flechsig regarding the development of the brain in childhood, which has been described as a development underlying the mental functions of man generally, as sufficient proof that you have development of mind coincidently with these physical developments. I believe Flechsig's work in this direction has been in part misleading. He has described the development of sensorial functions and motor functions, but we want something deeper. In some idiots and imbeciles we have found that there may be these developments physically without coincident development mentally. That Flechsig did not take into account. Dr. Mott showed us a diagram of sensory nerves appearing to come from the muscular substance. I have not been able to trace the evidence which proves that these are in reality sensory nerves. I am inclined to think from the experiments of Goldscheider and others that we have no such thing as pure muscular sensation. We have sensations of pain, but I believe we get our sensation altogether from the cartilages and the skin. As to other organic sensation, I do not believe we get any sensation whatever except from pain. It may be open to argument from a psychological point of view that we can remember a pleasurable sensation such as the appeasement of hunger, but then that is merely the removal of a sense of pain. The sensations we derive from muscles and from viscera are really those sensations of actual pain which it is assumed have a totally different anatomical basis. The point on which one can agree with Dr. Mott and appreciate to the full is that relating to the nerve-cell. We are coming to accept the unit theory of cells in the brain, by which we assume that each cell is discrete, and that function is by contact and not by structural continuity. If we can establish that theory we shall have taken a great step towards the elucidation of various problems of consciousness; many problems of physiology will become more clear, and we shall have a much more definite basis to work upon as explanations of mental phenomena. One point we have got to remember is, that by cutting off sensory stimulation you may cause the death of the cell. Berkeley of Baltimore, who experimented with alcohol on rabbits and other animals, has described the process of cellular degeneration—first the decay of the myelin sheath, and then degeneration of the nucleus constituting the cytoclasis of the cell. To-day we have to thank Dr. Mott for carrying us still further, and for enabling us to recognise that, so long as a current can pass, the nucleus will remain in full life and regeneration is possible.

Dr. MOTT in reply said: First I must thank the members of the Association for kindly giving me their attention, as I fear that I have taken up more time than was intended, and some parts of my paper which were of a speculative nature had to be omitted. I also wish to take the opportunity of thanking the President for his kind allusions to my remarks, and especially I wish to congratulate the Association on having present one of the most distinguished physiologists in Europe, one who has added so much to our knowledge of neurology and experimental psychology, Prof. Sherrington, whom I wish to thank most warmly for his appreciative remarks upon my paper, also for his suggestive criticisms upon certain points therein, which I put forward with the express purpose of raising discussion as to their validity. At this late hour of the

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morning, when other important papers are awaiting delivery, I will not trespass long upon your time and patience.

There are a great many points which I should like to touch upon. One in particular is the very remarkable experiment alluded to by Prof. Sherrington, and which is distinctly in favour of the storage of energy and even the formation of nerve energy, which appears to be quite independent of the amount of incoming stimulus. He wishes that Prof. Gotch were here; at the meeting of the Psychological Society at Oxford we were all wishing Prof. Sherrington was there. He seemed in some doubt as to whether I had accepted Gotch's new views. I admit the possibility of all stimulus coming from without, but disagree entirely with the doctrine that there is no storage. It is a remarkable fact that the nervous system does not undergo wasting, and the metabolism, although extremely complex, is not massive in healthy conditions. May it not be that the neurons have the property of converting the molecular vibrations of incoming stimuli into stored nervous energy, which we regard as "potential," and which can be redistributed as from a reservoir? At some future period I hope to bring forward some facts in support of this. Of course this is a mere theory, and I have only advanced it with a view of promoting discussion and, as Dr. Warrington suggests, of avoiding the routine reflections. I was much interested in what he said with regard to the independent *vis propria* of individual nerve-cells, and particularly struck with this in the observations I made on the effects of poisons and experimental anæmia, which are fully related and illustrated in my Croonian Lectures, 1901. I think this will explain the observations of Ford Robertson referred to by Dr. Clouston.

We are all very glad to hear the practical remarks of Dr. Clouston; there is one point, however, to which I should like to call attention. He relates what is well known, that an insane patient is always worse in the morning. We cannot wonder at this, for besides the fact that a patient who is the subject of hallucinations is more troubled in the evening and at night, his whole attention, which I maintain to be a loss of energy, is concentrated upon these abnormal stimuli. It is well known that one form of hallucination will call up another; thus visual hallucinations will occasion auditory hallucinations, and *vice versâ;* and if thus the natural periodic recuperation—and by this I mean physiological and not artificially produced sleep—is interfered with, there is necessarily a lowering of nervous potential. Again, in the early morning, when the temperature is lowest, the nutritional exchange and the vitality of the organism is at its lowest ebb. At such a time death frequently takes place.

Dr. Clouston also alluded to the influence of light. I had a striking example the other day of the effect of shutting out the light in the production of symptoms of insanity. When testing an insane tabetic I covered up his eyes in order to test the skin sensibility of the chest; he immediately began to hear voices, and he told me that he invariably heard the voices at night. An interesting fact which is very difficult to explain is the abeyance in the symptoms of ataxy and progress of the disease in patients who are afflicted with optic atrophy. Is it because the stimuli which enter the nervous system by the visual sense are cut off, and with them a great part of the excitation which leads to the using up of nerve potential, thereby conserving tissues which have a lowered durability, but are able under these conditions to maintain nutritional equilibrium?

Dr. Hyslop's remarks touch upon many points in anatomy, physiology, and psychology; it is always well to have criticism, for that purpose my paper was written, and I am much obliged to him for taking an opposite view, but I am sorry that time does not permit me to enter the arena with Dr. Hyslop, except to touch upon the following. He denies the existence of the muscular sense, and considers that I have no right to make the diagram which shows fibres proceeding from muscle to the central nervous system. I always thought Prof. Sherrington had, by the most conclusive and beautiful experiments, shown that from one third to half of the fibres entering muscle came from the posterior spinal ganglia and were sensory in function. The kinæsthetic sense is in my opinion a fundamental principle in psychology, and depends upon a complex of sensations in which the alteration in the tension of the muscles is the principal factor by virtue of stimulus of the sensory fibres proceeding from muscle and tendon. I would request Dr. Hyslop to argue this point with Prof. Sherrington.

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(Prof. SHERRINGTON.—I think I can do that better at luncheon.)

Dr. Hyslop has taken exception to Flechsig's work. I admit that much of it has been disputed and some of it refuted, but on the main points I touched upon he has undoubtedly shown the correlation between the development of the elemental functions of mind and the formation of the myelin. With regard to the myelination of imbeciles and idiots I cannot see any reason to throw doubt there on Flechsig's work, for in proportion to the grade of amentia there is a failure of development of the later developed and more superficial myelinated fibres of the cortex. With regard to Berkeley's work, I believe it mainly rested upon observations made by the Golgi method; I do not like to dispute the labours of such an eminent man, but I am convinced from experience that this method is not reliable for pathological changes, especially if they be acute.

This reply was curtailed owing to pressure of time, but has by the courtesy of the Editors now been slightly extended.

Some Remarks on the Surgical Treatment of Insanity.

By DAMER HARRISON, F.R.C.S.Edin.[1]

MR. PRESIDENT AND GENTLEMEN,—While recognising the undoubted fact that what may be called ordinary insanity has no demonstrable lesion, the disorder being in the "subtle chemistry of the nerve-cells, and that no surgical procedure can correct aberration in tissue chemistry," I still think there are a small number of cases, not only of traumatic but also of non-traumatic origin, in which surgical treatment may have beneficial results.

There is reason for believing that mental impairment much more frequently follows head injuries than is generally admitted. Within a comparatively recent experience I have met with four such cases following fractures of the base, one following bullet wound of the brain, and four cases of decided insanity following fracture or blows upon the vault. The number of cases of insanity due to head injury appears to be about 2 per cent. of all cases, and it is only a limited proportion of these which are open to relief by operation; for it is essential that some localising indication of a lesion should exist which can readily be reached, to justify surgical interference.

The actual lesions found at operations are very variable: Depressed bone, with or without osteophytes or splinters from the inner table; thickened bone arising from a circumscribed inflammation of the vault; cysts of hæmorrhagic origin, either upon or beneath the dura or cortex; diseased bone; foreign body within the cranium (bullet); adhesions of the cortex

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