THE SOURCE OF EXCITATION IN LATE RIGIDITY, THE MANIC-DEPRESSIVE SYNDROME AND THE EPILEPSIES, AND THE MECHANISM OF RECURRENCY.

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The Source of Excitation in "Late" Rigidity.

The writers of text-books do not give us much aid in gaining a true idea of the cause of "late" rigidity—rather the reverse, for they seem to think it necessary, always, to drag in "decerebrate" rigidity as an essential preliminary towards understanding the factors in the case.

Now "decerebrate" rigidity is a clear-cut example of a "release" phenomenon. It is the instant result of loss of inhibitory control. Its manifestation, like that of all "release" phenomena, is immediate.

"Late" rigidity is, as its name says, late. Its manifestation may be weeks, and in some instances even months after the incidence of the lesion causing it. You must surely agree with me that such a quality precludes the possibility of its inclusion in any ordinary category of "release" phenomena. That understood, we will get down to our subject.

Most of us are interested in the source of the excitation manifested the epilepsies and in the manic-depressive syndrome. The fact that these syndromes are often manifested secondarily to lesion in the brain has suggested a study of lesion in the cord, where nerve-fibre and cell-body are perhaps better known.

Pure lesion of the pyramidal tract in cord or brain is followed by at least three kinds of rigidity—"initial" (7), "early" (7), and "late" (7) rigidity. The first, the "initial," is due to the irritation of the presence of the lesion itself. The second, the "early," is due to the irritation of inflammation around the lesion. Each of these irritations or excitations descends in the lesioned fibres on the

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efferent side of the lesion, and the rigidity caused by each has come and gone long before "late" rigidity begins to be manifested.

"Late" rigidity, the third mentioned, is not caused by excitations descending in the lesioned fibres efferent to the lesion, for the simple reason that by this time they are non-irritable, dead, and gone. The excitations that cause "late" rigidity must, therefore, travel to the muscles by another route; for we know that the excitations are not myogenic, but neurogenic. Now, as they are neurogenic, all that we need do to find the source of the excitation is to follow the course of the neurons from the affected muscles, back along the arcs, until we find it.

The "late" rigidity has followed upon, let us say, a pure pyramidal lesion in the cord. All the muscles below the level of the lesion have become hypertonic, and as this hypertonicity is neurogenic, it must have descended to each muscle as a state of excitation in its effector neuron. This neuron, the effector neuron, has its cell-body in the anterior horn. It is the common final path, amongst others, of the arc of the proprioceptive spinal reflex and of all the descending extra-pyramidal tracts. Now we know that it does not derive its state of hyper-excitation from the proprioceptive, or myotatic, spinal reflex because the rigidity is neurogenic, not myogenic. Nowhere can I find any reason to suggest that the state of hyper-excitation is derived from any of the descending extra-pyramidal tracts. Nor can it be that a state of hyper-excitation has descended by irradiation in the anterior column of grey matter to which the effector neuron belongs, for then there would be rigidity of the muscles above the level of the lesion—a thing that never does take place. Among the contributors to the common final path there remains only the neuron of the posterior horn. This neuron is stationed as an intermediate neuron between the receptor-neuron of the cutaneous-sensory spinal reflex and the effector-neuron and between the pyramidal tract and the effector neuron. We must take it, then, that this intermediate neuron is the pathway by which the state of excitation is conveyed to the effector-neuron. Not, however, from the receptor neuron of the cutaneous-sensory spinal reflex does this state of excitation come, for it is "under our eyes," as it were, and no cause for excitation is to be seen. Nor can the intermediate neuron receive its state of excitation by irradiation from above down the column of grey matter of the posterior horn to which it belongs, for that would, again, necessitate a state of rigidity in the muscles above the level of the lesion—a thing unheard of. It remains, therefore, that the state of

excitation must come to the intermediate neuron (posterior horn-cell) from the pyramidal tract. It cannot come from the pyramidal tract below the level of the lesion, for that part is inactive, and functionless, if not dead. Nor can it come from the pyramidal tract above the level of the lesion, for such a state of excitation there would cause a state of rigidity of the muscles above the level of the lesion—a thing unknown. We seem, now, to have come to a " dead-end " ;

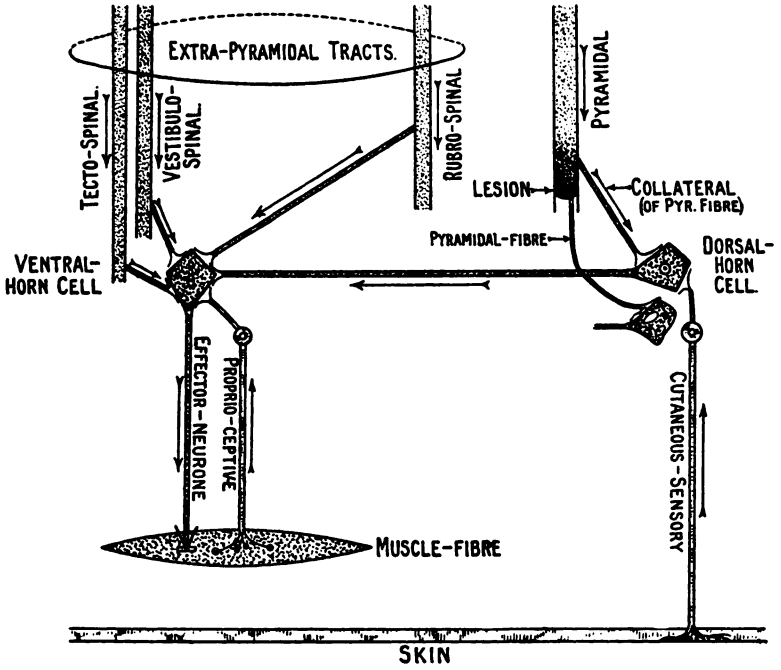

FIG. 1.

but " dead-end " there cannot be, for we know that " late " rigidity is neurogenic. *If* there were a pathway that came from the pyramidal tract close above the lesion, and, by circumventing the lesion, gained a posterior-horn cell below the level of the lesion, a state of excitation could, in this way, be conveyed from the pyramidal tract above the level of the lesion to the muscles below the level of the lesion. Now such a pathway is afforded by the pyramidal collaterals, but only by those collaterals that, branching off, pass down outwith the area of the lesion to gain posterior-horn cells below the level of the lesion. Now the supreme point is this:

Have we any reasonable data on which to base a belief in the probability of a state of excitation existing within the limited area that is bounded by the central face of the lesion and the nearest collateral above?

I think we have; but to get at it, it is best now to look at the lesion from the physiological angle and consider it in the light of a state of complete nervous-conduction block. And here the laboratory comes to our aid, for an experiment with complete nervous-conduction block has been made in the muscle-nerve preparation, wherein the central end of the nerve is kept under continuous stimulation during and beyond the gradually-induced resolution of a non-irritating, imposed state of complete nervous-conduction block. At the moment of renewal of nervous conduction, when resolution of the block is complete, it is found that the initial strokes of the muscle tracing record a state of hyper-excitation—which quickly regains normality. I read these initial strokes of hyper-excitation as the outward expression of a state of hyper-excitation that has been created in a small area of the axonal tissue right at the central face of the imposed block.

If you agree that the facts in this experiment permit of such an inference, we can return to the case of complete nervous-conduction block due to lesion of the pyramidal tract in the cord in a living subject. Here—where the central face of the block is subjected to a battery of nervous impulse excitations, minimal and subminimal—I make the suggestion that a state of hyper-excitation is created in an area of axonal tissue at the central face of the block, and that throughout the weeks this area will tend to extend. The only possible direction for such extension is up-stream, and the up-stream limitation of the extension will be the presence of a by-path through which the state of hyper-excitation can escape or drain away. The pyramidal tract in the cord throws out collateral branches from its fibres; and the collateral that is utilized as a by-path can only be that one which is nearest to the complete nervous-conduction block in its pyramidal fibre, and which, evading the site of the lesion, can reach the posterior-horn cells below the level of the lesion. It would seem to take about three weeks for the hyper-excitation from the face of the block to reach this collateral (1).

And now, as far as I have been able to uncover them, source, process and pathway lie open to the examination and critical consideration that I would ask you to be so kind as to bring to bear upon them. The sympathetic system has not been brought under

consideration, as it has not yet been generally conceded that it has any effect on muscle tonus, though it is known to delay the onset of fatigue (6).

The process we have defined above is readily referred to as a process of "block-reaction through by-path." As a process, let me repeat, it should be severely criticized before acceptance, for if proved unassailable it will have to be reckoned with throughout the whole nervous system right up to the highest levels, wherever a state of complete nervous-conduction block happens to have a by-path from the afferent side of the arc in which it is situated.

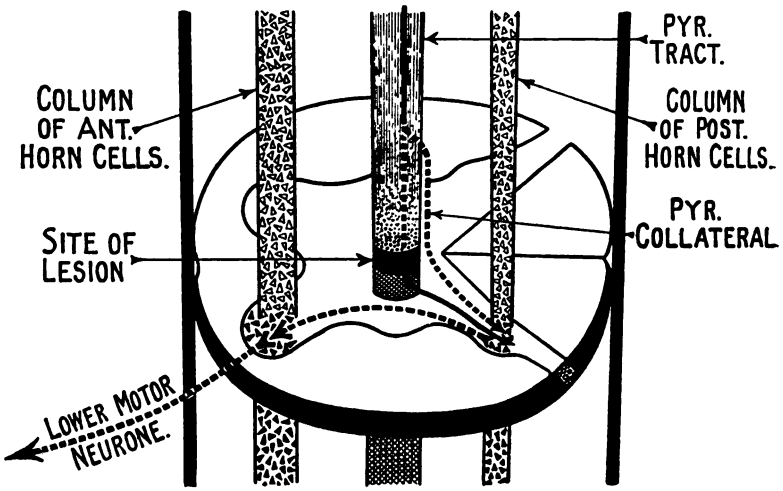

FIG. 2.

The process, of course, must not be expected to transgress the law of uni-directional conduction in the synapses.

The process we have put forward is not without a fair amount of indirect support. For instance, "late" rigidity does not follow a pure lesion of any, or all, of the extra-pyramidal tracts in the cord; *they* have no collaterals. Complete transverse section of the cord is never followed by "late" rigidity; but when all the descending tracts (in one side of the cord) alone suffer lesion (collaterals and grey columns remaining intact), "late" rigidity always supervenes. A case is mentioned in Sir J. Purves Stewart's book (1) in which just a small shred of nervous tissue was all that prevented the condition of "isolated cord"—and yet that shred was sufficient to allow of the subsequent development of "late"

rigidity. I take it that there must have been non-traumatized collaterals in that shred, and that they constituted the essential and sufficient vehicle for the manifestation of the " late " rigidity.

Bazett and Penfield's (2) findings (quoted by Brain and Strauss) in hemi-decerebration also lend support to the process we are advocating. They " were able, by means of a special technique, to keep the decerebrate preparations alive for several weeks (2) ; but they found that the primary homolateral hemi-rigidity passed off after a certain period and gave way to a contra-lateral hemi-rigidity (2). They say that " the primary homolateral rigidity must be regarded as an irritative phenomenon and is merely transitory " (2). The primary homolateral rigidity is, therefore, an " initial " and " early " rigidity. Irritative excitations pass down the lesioned fibres on the efferent side of the lesion—such fibres as those that go from above to control the vestibular nuclei on the same side. In regard to the " late " contralateral hemi-rigidity, the only possible explanation, in my opinion, is that of the backward extension of hyper-excitation, by block-reaction process, in vestibulo-petal fibres whose bilateral nuclei inter-communicate across the median line, and thus give a by-path to the opposite vestibular nuclei.

Again, take that notable case of a soldier wounded in the Great War. The cortical sensory reception area of one hemisphere was removed by the fragment of a shell, and this was followed eventually by severe and persistent pain. This pain could only be " thalamic pain." The orthodox interpretation of this " thalamic pain " is that it is due to loss of the cortical control over the thalamus as a result of the ablation of the cell-bodies of the neurons of the cortico-thalamic fibres. It can be argued, however, that since there can be no sensation without stimulation, and since, at the late date in this case with which we are dealing, there are no pain stimulations to arouse thalamic sensations of " mass pain," there can be no thalamic " mass pain " ; and yet there is thalamic pain, only too real and persistent. To my mind the only possible solution of this paradoxical state of affairs is that a state of hyper-excitation extends back to the pain-cell bodies of the lesioned thalamo-cortical neurons, through the process of " block-reaction."

Further indirect proof is conveyed by the close correspondence between the length of time from the incidence of the lesion until the manifestation of the late rigidity and the length of nerve-fibre from lesion to by-path. The distance between lesion and by-path in a pyramidal lesion in the cord is probably much shorter than

that between the lesion of the same tract in the brain (say from hæmorrhage into the internal capsule) and the by-path which starts out from the cortex. In the former "late" rigidity becomes manifest in about two to three weeks, in the latter in about twelve weeks (1). In a lesion of the short nerve-fibres of the extra-pyramidal system in the locality of the basal ganglia, "late" rigidity may make its appearance as early as one week after the primary acute attack of epidemic encephalitis. Of course, in "late" rigidity we all feel that something must be maturing in time-space on account of the very fact of its lateness in manifestation.

And now, a word about the "late" rigidity that follows lesion of the pyramidal tract in the brain—say from hæmorrhage

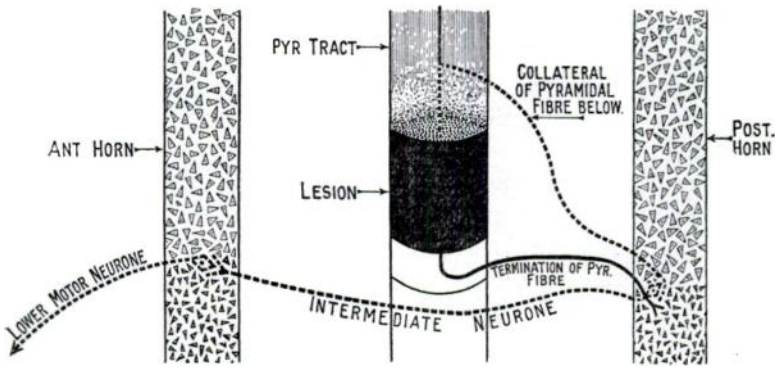

FIG. 3.

into the internal capsule. No collaterals are given off by this portion of the tract. The state of hyper-excitation has free way to extend right up into the cortex. Within the cell-bodies of the higher neurons, as a state of hyper-excitation, it can extend or irradiate to associated neurons on the same level. These may present themselves as by-paths, but they can only be so if they can descend outwith, and past, the lesion in the internal capsule, unharmed. The fronto-pontine tract does this by descending through the far anterior end of the internal capsule. Apoplexy in the internal capsule, when consistent with viability, is found restricted to a relatively small area within the capsule. The fronto-pontine fibres terminate in the tonus-reflex centres within the pons. The route taken is, therefore, quite extra-pyramidal. Jacob would have us regard the extra-pyramidal system as a part of the voluntary (pyramidal) tract through which cortical impulses are directed

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to the anterior horns. Dr. S. A. Kinnier Wilson (3) impresses on us the fact that "a large part of every voluntary movement is both involuntary and outside of consciousness." This by-path, therefore, besides being "the only way," gets high physiological commendation. Note that the resultant "late" rigidity has that "selective accession of tone" (3) characteristic of pyramidal rigidity. And that is why I have suggested that the by-path descends through the particular reflex-tonus centres in the pons instead of through the greater centres for general reflex-tonus higher up.

Extra-pyramidal rigidity.—In her *Observations on the Parkinsonian Syndrome in Lethargic Encephalitis*, Dr. Ivy Mackenzie (4), referring to vestibular lesion and its extensor rigidity, says there is reason to believe that the vestibular nuclei become foci of irritation through the receipt of stimuli from sources of central origin, and that we are dealing with a delayed and remote reaction of structures whose function in the harmony of nervous integration has been impaired.

He seems puzzled about this hyper-excitation which comes from a distance; he cannot place its hidden source. But, thanks to the block-reaction process, the solution of the difficulty is now simple. The situation and its interpretation may be put in this way: Nerve-fibres from Deiter's nucleus (lateral vestibular nucleus) run forward in an encephalad direction to the oculo-motor nuclei and the colliculi; in doing so they traverse the mesencephalon (which is the commonest site of epidemic encephalitis) and sustain a lesion; the mechanism of "block-reaction process" thus becomes operative and a state of hyper-excitation invades the lateral vestibular nucleus; this nucleus is a reflex-extensor-tonus centre; the vestibulo-spinal tract conveys the state of hyper-excitation to the anterior-horn cells of the extensor muscles and extensor rigidity is manifested.

Dr. S. A. Kinnier Wilson (3) frowns at a statement of the Vogts in which the suggestion is put forward that the source of the corpus striatum syndrome is without the corpus striatum. But something must be forcing their minds in that direction. They are sensing the operation of something that does take place—at least elsewhere—and of the nature of which they are not yet aware.

In regard to the more common type of encephalitic rigidity (extra-pyramidal), which is a mixed flexor and extensor rigidity with flexor predominance in hypertonicity, I ask you to envisage a lesion and states of complete nervous conduction block in many of the fibres from the globus pallidus composing the ansa lenticularis;

states of hyper-excitation from " block-reaction " extend back to the globus pallidus; irradiation to unaffected associated neurons takes place and descends in their efferent by-paths to the red nucleus and vestibular nuclei (which are controlled by the globus pallidus), to be expressed as flexor and extensor rigidity. As this is a pallido-genic rigidity, it affects all the muscles generally, in contra-distinction to the selectivity seen in pyramidal rigidity.

Lesion of a proportion of efferent fibres from red nucleus to substantia nigra would also tend to accentuate flexor rigidity.

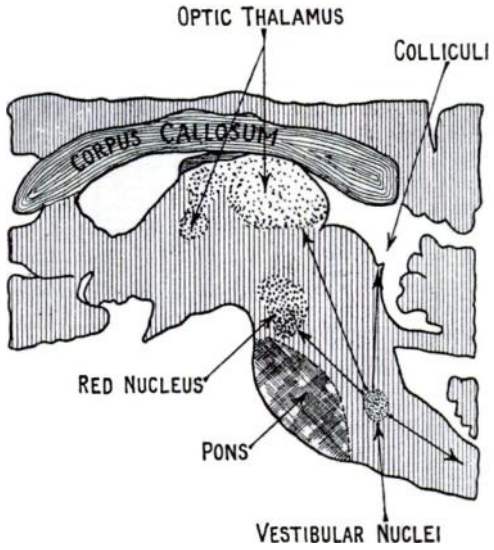

FIG. 4.—(Modified, after Foix and Nicolesco.)

In leaving the subject of " late " rigidity there is one pertinent fact I would ask you not to forget, *viz.*, that lesion of a descending tract in the cord is followed by " late " rigidity only when the tract has collaterals. No collaterals, no " late " rigidity! No by-paths, no " late " rigidity!

The Source of Excitation in the Manic-depressive Syndrome, and the Mechanism of Recurrency.

(a) *The manic phase.*—Away back in 1911 Dr. R. M. Marshall (5) drew our attention to the " periodic attacks of excitement and depression in the chronic insane," and from a study of them argued

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a state of molecular disorder in the nervous system of the primary or adolescent manic-depressive psychosis.

Gross organic disease of the brain means lesion, and lesion means complete nervous-conduction block. Molecular disease or disorder of the nervous system may also mean complete nervous-conduction block.

This state of block will be present during the " interval " between attacks, as well as during the attack, and some deficiency or lack should then be discernible. " The interval " patient is lacking in emotivity, initiative, spontaneous sociability and enterprise. He seems " tame " and " colourless," suggestible and fairly easily guided. The *élan*, urge and *joie de vivre* are but shadows of themselves and the rivers of the mental life run low. The outstanding defect seems to be in the supply of affect, with its power to incite—which is greatly diminished.

It seems as if a majority of the organic excitations, which are psychically interpreted as cœnæsthesis, or affect, must have somewhere, in part, sustained a state of complete nervous-conduction block.

The hyper-excitation of the " block-reaction " can here be taken as a summation of affective energy.

This force, by irradiation to the neurons of the unblocked pathways, would soon escape and rush into consciousness and peripheral expression, were it not held up by another force, the force of inhibition—cerebral inhibition.

But this inhibition can suffer fatigue, and be overcome, as its opponent goes on increasing in strength.

Then follows the precipitation of the manic attack by the out-rush of affective energy, which incites ideation and races to relief in wild motor expression.

Sometimes " the attack " is not so precipitate. Then little tricklings of overflow appear, seen as fleeting flushings of the skin, vagrant myalgias, odd little motor excursions, impulsive purposeless little apprehensions and alarms—all in their small way flagging warning of the coming outburst. Any sudden increase in affectivity may precipitate an overflow.

Half an hour before a dance, during " the interval " between her manic-depressive attacks, a patient was presented suddenly with a rather nice lace collar to wear at the dance. Her delight was great. The affect was great. A manical attack was precipitated and she could not grace the dance with her presence that night.

The major function of the brain is said to be inhibition. Its

employment not only spares us from irrelevant extraneous disturbances, but retains for us some reserve of neuronic and muscular energy for emergency calls; for it is said that we never do call upon all the neurons and fibres of the muscle groups employed at any one time, no matter how great the muscular effort may have to be.

In hypnosis the unconscious discretionary use of inhibition, as regards retention of reserve, seems to be abrogated when a supreme muscular effort is suggested, so that every motor neuron and muscular fibre of the requisite groups are called into play without reserve.

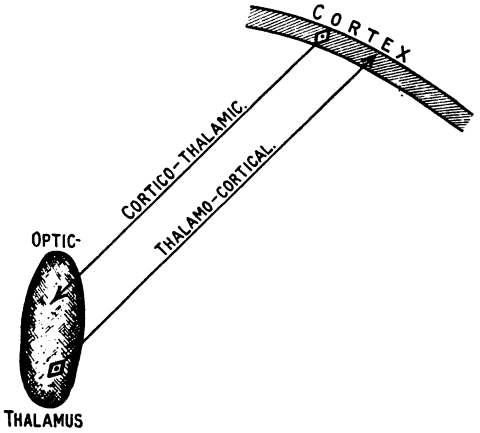

FIG. 5.

Some of us may have seen a girl in her 'teens under hypnosis, with head on one chair-back and heels on another, sustain the weight of two or three people without quiver or give from a rigid maintenance of the horizontal position.

Again, everyone of us must have witnessed the sight of a slightly built maniacal woman requiring the services of three or four nurses of much greater weight and musculature to prevent her going in a certain direction where possibly she might come to harm.

In such cases the motor neurons and muscle-fibres in each particular group used are all functioning without reserve—inhibition has been abrogated. There is a drug that has a similar effect on inhibition—caffeine. Caffeine, according to Prof. C. Lovatt Evans (6), " diminishes every inhibitory process."

The writer has given caffeine in the " interval " between manic

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phases, and has found that it precipitates slight manic attacks which last for a day or so, and " the interval " is prolonged to two or three times its ordinary duration except for these occasional little manic episodes; and further, that when the true recurrent attack takes place it is not so exuberant, language, behaviour and excitement are definitely modified for the better, and the mentality is not so confused; impulse is more controllable, and there are fewer records requiring entry in the minor accidents book. The inhibitory clutch seems to begin to grip as the manic " attack " passes off, and summation may be said to begin to wax as the manic " attack " wanes.

Administered during " the interval " caffeine lifts the clutch and a minor manical "attack" is precipitated. It is this effect of caffeine occurring several times during " the interval " that prolongs the duration of " the interval "; and although I have not given caffeine during " the attack " when it subsequently developed, yet " the attack " is potently modified as compared with an " attack " following an " interval " in which caffeine has not been administered. Strychnine is said to have the same effect on inhibition as caffeine. During " the interval " in recurrent mania " block-reaction " causes an up-stream summation, irradiation to associated neurons follows, inhibition prevents the expression of this hyper-excitation (efferently) from these associated by-paths, summation proceeds until it is too much for the powers of inhibition and " the attack " is then precipitated. The two leading factors in the case are " block-reaction " and " inhibition of expression through by-path "; these cause increasing summation until the inhibition is overcome. The mechanism of recurrency runs smoothly before our eyes.

I would localize the situation of the states of complete nervous conduction-block nearer to the afferent than the efferent side of the great galaxy of cerebral associational neurons, and in these arcs which serve for organic and cœnæsthetic presentations rather than in the arcs of the sensori-motor system.

With atropine, by the way, I have been successful in holding up the threatened precipitation of the manic attacks for a day or two, but those patients who had this treatment seemed to sit very taut and quiet, in apparent misery. Independently of each other, they besought me to refrain from asking them to take this medicine. Their request was granted, and in a short time they were wholeheartedly enjoying the exaltation and freedom of expression so characteristic of the " manic attack." The sympathetic serves

for the expression of unconscious emotion. Atropine blocks conduction in the myo-neural junctions of the autonomic part of the sympathetic system. *Atropine administered during the full-going manic attack modifies its expression considerably—the expression of reverberation in the sympathetic is damped down.*

After $\frac{1}{100}$ gr. of pilocarpine I have observed a maniacal patient, who had been ceaselessly perambulating the floor of the ward, suddenly sit down, and in a calm assured voice state that she was

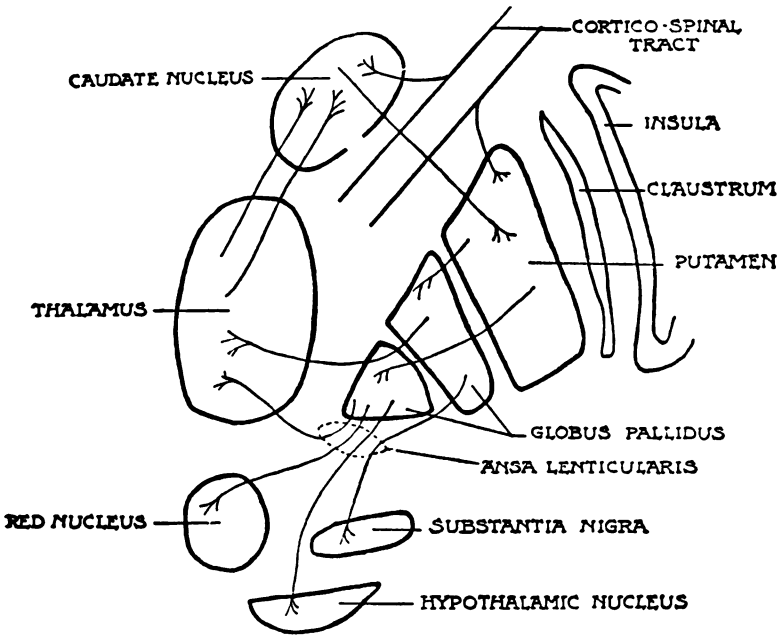

FIG. 6.—Fibre connections of the corpus striatum. (After Ranson.)

now quite cured and well. She was; and soon she was discharged recovered. This was many years ago, and the patient has not had any recurrence since.

(b) *The depressive phase.*—In health, physiological functioning gives a feeling of well-being.

When an excess of excitation floods this physiological state, as in mania, functioning is put into high gear, the feeling of well-being rises to exaltation, and ideas come speedily to the surface, to dart about with the Brownian-like movements of a restless irresponsibility.

Toxæmic conditions of the body, on the other hand, interfere with physiological functioning, and a feeling of ill-being is experienced.

Naturally a state of facilitation becomes created in the high arcs that subserve the conduction of these organic impulses which make up the cœnæsthetic record of the feeling of ill-being.

All other arcs, especially in their synapses, instead of becoming subject to facilitation, have their thresholds for conduction raised by the state of toxæmia.

Now, on top of these feelings of ill-being comes the precipitation of a flood of excitation from "block-reaction"; naturally it will flow into the channels of facilitation, and the high thresholds will be left "high and dry."

Thus the feeling of ill-being becomes so strongly accentuated that the whole attention is drawn towards this point of suffering, and so engrossingly held that only the depressive ideation relative to this-thing-that-is-being-attended-to is permitted to enter into the field of consciousness.

The mechanism is the same as in the manic attack, only it is operating under modified conditions.

The Source of Excitation in the Epilepsies, and the Mechanism of Recurrency.

The late Sir Frederick Mott maintained that there was a real kinship between mania and epilepsy. In epilepsy I would again put forward the two factors of "block-reaction" and "inhibition of the extension of hyper-excitation along the by-paths" as operative in the summation of the excitation and in the precipitation of the epileptic attack—when the inhibition is overcome by the major force of the summation.

Be the lesion that causes the block reaction gross or molecular, its situation must be among a different system of nervous arcs from those involved in the initiation of the manic-depressive syndrome, since the energy summated and precipitated in the epileptic is so much more speedily acquired and dissipated than in the manic or depressive patient.

Let us nominate the sensori-motor system as the one involved. Its reactions are always notably speedy. The epileptic attack is notable, apart from the loss of consciousness, decidedly as a motor manifestation.

The manic attack, however, might be said to be primarily an emotional (psychical) manifestation, with motor concomitants.

In the manic-depressive "interval" the patient exhibits a subdued mood, a paucity of affect, and a slight lack of initiative. In the epileptic "interval," apart from a slight retardation in speech suggestive of states of conduction-block, there seems to be a definite and remarkable condition of persistent motor urge. In some cases this motor urge becomes obsessive—as if an echo of the tension of the undischarged summation were ceaselessly reverberating among associational neurons stationed just slightly prior, in the arcs, to the higher motor neurons.

Bromide retards the onset of the epileptic attack; and Prof. C. Lovatt Evans (6) tells us how it is able to do so: "Bromide has no depressant action on the central nervous system," he says, "but rather a specific reinforcing effect upon all its inhibitory activities." It reinforces inhibition. It retards the onset of the epileptic attack. Nothing further is wanted; and I now place the two factors—"block-reaction through by-path" and the "conquest of inhibition"—in your hands to link together as a working mechanism explanatory, not only of the manic-depressive syndromes and the epilepsies, but also of their recurrent manifestation.

In the psychical realm the apposition of conditions of block and hyper-excitation is not unfamiliar. In delusion there is the "blind spot" in judgment. Some component or other is suffering from a condition of persistent or temporary block, and the defective conclusion has a hyper-intensity that causes it to take precedence among the ordinary cursory ideas in the mind. In mental dissociation it is the dissociate ideation which has the mandate in mentation.

In hallucination the presentation of reality suffers block, and the pathological representation that is substituted has a vividness whose very intensity convinces the subject that its reality is undisputable. Then, again, there is the well-known Freudian mechanism of the repressed, or buried, complex of conflict, and the uprising, through by-paths, of affect so powerful as to thoroughly dominate ideation. It is all very intriguing; but, for the moment, the writer is content if he can establish the neuro-pathological principle of a purely physical process of block-reaction through by-path.

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