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the NATURE OF INHIBITION, *and the* ACTION OF DRUGS UPON IT.

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BY inhibition we mean the arrest of the functions of a structure or organ, by the action upon it of another, while its power to execute those functions is still retained, and can be manifested as soon as the restraining power is removed.

It is thus distinguished from paralysis, in which the function is abolished, and not merely restrained.

Inhibition is one of the most perplexing problems in physiology, and we have at present no satisfactory hypothesis regarding it. It plays, however, such a very important part in pharmacology, that we cannot pass it over; and as it is through the action of drugs upon the various functions of the body that we have already arrived at a knowledge of inhibitory actions, which would otherwise have been impossible—as, in fact, pharmacology has here quite outstripped physiology—we are obliged to enter into some hypothetical considerations, in order to be able to form some kind of idea regarding the mode of action of many drugs.

Hypotheses serve as "pegs on which to hang facts," and by their aid the isolated facts which few memories could carry may be arranged, and their relation to each more readily perceived. A hypothesis serves also as a guide for further experiments, by which it may be either disproved or supported. Should facts be against it, so much the worse for the hypothesis; it must be discarded, and another tried in its place; but if facts agree with it we obtain a means of predicting phenomena, and make another step in knowledge. Like other useful things, hypotheses are not without danger, and sometimes do harm by satisfying people and stopping further inquiry. Thus Sultzer noticed the peculiar taste produced by the contact of two dissimilar metals with each other and with the tongue forty years before Galvani; but at that time the doctrine of vibrations was employed to explain all natural phenomena, and he concluded that some peculiar vibration occurred from the contact of the metals, which produced the peculiar sensation on the tongue. All the world were satisfied with the explanation, and thus a prominent fact slept in obscurity from the time of Sultzer to that of Galvani, no further attempts being made to determine the nature of the vibrations or the laws which governed them.[1] Yet in their proper place hypotheses are most useful, and but for the hypothesis that light, heat, and sound are due to waves, our knowledge of their phenomena would be much less than it is.

The cases of inhibition, as we may term them, which we meet with in the study of physics, are the production of complete silence by the interference of two sounds, and of darkness by the interference of two rays of light.

When two sounds or two rays of light are combined,

[1] Rees' Cyclopedia. Article "Galvanism."

so that the crests of the waves of which they consist coincide, the sound becomes louder and the light brighter. If they are thrown together, so that the crests of the waves in the one sound or ray coincide with the sinuses or hollows of the other, they completely counteract each other, and silence or darkness is produced.

When the waves are of different rhythms, the crests and hollows of the two sounds or rays, which at one time coincide, will gradually interfere, and again gradually coincide, so that rhythmical alternations of loud sound and silence, of bright light and darkness, are produced.

A good example of interference or physical inhibition, and one that affords an illustration well suited to our purpose,

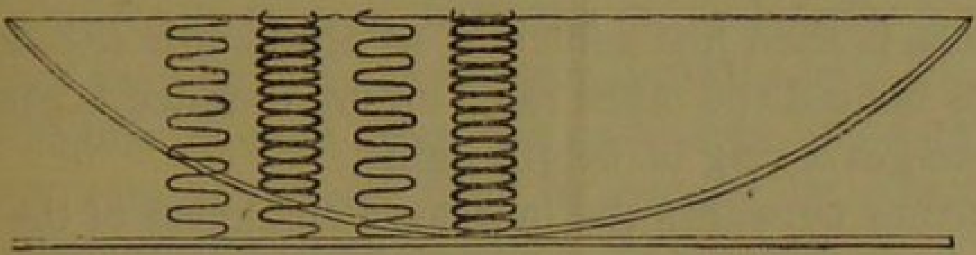


FIG. 1.—A very diagrammatic representation of interference in Newton's rings.

is that of Newton's rings. When a lens of small curvature is placed on a plane surface of glass, a series of rings is observed, starting from the centre of the lens and passing concentrically outwards. If monochromatic light is used, such as pure yellow light, pure red light, &c., these rings are alternately bright and dark; but if white light is used, they appear as a number of circular bands of different rainbow colours. The cause of these rings is, that though the surface of the lens appears to the eye to be in contact with the plate of glass over a considerable area, it is not really so; a very fine film of air of varying thickness being interposed between them.

When a ray of light passes through the lens on to the glass, part of it is reflected back from the lower surface of the lens, and part of it from the upper surface of the glass plate. Between those two points there is a very minute film of air: *one ray has therefore to travel somewhat further than the other.* The distance which it has to travel is only through the extremely thin layer of air lying between the surface of the lens and the glass and back again ; but this distance at some places is just sufficient to throw the waves in the one beam *half a wave-length* behind those in the other, and to produce darkness by their interference.

As we recede from the point of most complete contact between the lens and the glass, the thickness of air increases, the ray has somewhat further to travel, and the distance is then just sufficient to throw it *a whole wave-length* behind the other ray ; no interference is produced, and we get a ring of bright light.

Further outwards the increased thickness of the film of air is again sufficient to throw one ray *a wave-length and a half* behind its fellow ; interference is again produced, and darkness is the result.

With rays, then, of one colour, or of one wave-length, we get alternately light and darkness by interference.

But it is evident that the extra distance which the waves have to travel in order to produce interference will not be the same for long and short waves ; and thus it is found that when white light, which contains rays of different wave-lengths, is used, the rings, instead of being alternately light and dark, are coloured.

The very distance which was sufficient to throw the red rays half a wave-length behind the other, and to produce interference, will throw, let us say, the violet rays a whole wave-length behind, and thus there will be no interference, and *vice versâ;* the distance which causes interference of the violet rays does not cause interference of the red, and so on with other colours.

Thus the spaces which would have been perfectly dark when rays of pure red or pure violet, or more correctly ultra-violet, were used, would be filled up by the other if used together, and when white light is used, the various waves interfere at different places, and so we get a series of rainbow colours.

The extra distance which one beam has to travel in order to produce interference with another is *not absolute*, but relative to the wave-length. This relation differs for different wave-lengths, and therefore if the relative distances remain constant, the effect of the beams on each other will vary if their wave-lengths be changed.

It is obvious that if both the wave-lengths and the distances they have to travel remain the same, the effect of the beams on each other will be altered by any change in their rate of travel such as would be effected by altering the media through which they pass.

This is a most important point in regard to the hypothesis of the causation of inhibition by interference of vibrations in the nervous system. It may therefore be useful to illustrate this further, and probably it could not be done better than by using, with a little modification, the example given by Sir J. Herschel in his article on Light in the Encyclopædia Metropolitana. "Let R be a reservoir of water, from which the channels A and B proceed, to join each other at P; they are supposed to be equal in every respect except that B is longer than A. If a wave from the reservoir enters the openings of A and B at the same time and travels at the same rate along them, the wave which passes through A will reach P sooner than the one which passes through B, so that the water at that point will be agitated by two waves in succession. But let the original cause of undulation be continually repeated so as to produce an indefinite series of equal and similar waves. Then if the difference of lengths of the two canals A and B be just equal to half the interval between the summits of two consecutive waves, it is evident that when the summit of any wave propagated along A has reached the point of intersection P, the depression between two consecutive summits (viz., that corresponding to the wave propagated along A and that of the wave immediately preceding it) will arrive at the intersection P by the course B. Thus in virtue of the wave

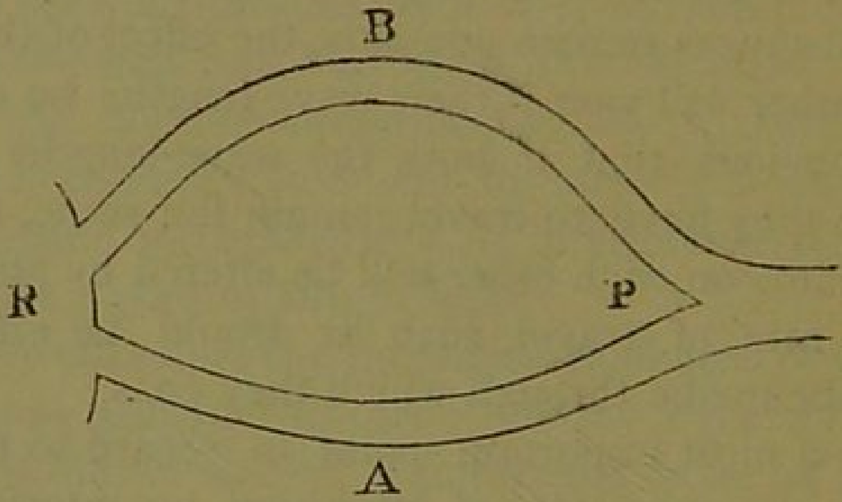


FIG. 2.—Diagram to illustrate Sir J. Herschel's observations on interference. Adapted from his article on "Absorption of Light," Phil. Mag. 1883, p. 405.

along A the water will be raised as much above its natural level as it will be depressed below it by that along B. Its level will therefore be unchanged. Now as the wave propagated along A passes the intersection P, it subsides from its maximum by precisely the same gradations as that along B, passing it with equal velocity, rises from its minimum, so that the level will be preserved at the point of intersection P undisturbed so long as the original cause of undulation continues to act regularly.[1] So soon

[1] This actually happens in the harbour of Batsha, into which the waves pass from the open sea through two channels of unequal length.

as it ceases, however, the last half-wave which runs along B will have no corresponding portion of a wave along A to interfere with, and will therefore create a single fluctuation at the point of concourse P."

It is obvious that if everything else remains the same, the effect which the waves have upon each other at P will be altered if the rate at which they travel is increased or diminished.

The more the speed is increased the less effect comparatively will the greater length of B have in retarding the wave which flows along it, so that its crest will no longer coincide with the trough or sinus of the waves in A, but will, on the contrary, coincide more nearly with the crest of one of the waves in A.

The more the speed is diminished, the more will the wave in B lag behind that in A, so that its crest, instead of coinciding with the trough between two crests of the waves from A, will gradually come to coincide with the crest succeeding the trough, and thus double its magnitude instead of destroying it.

We see, then, that under the conditions we have supposed either increase or diminution in the rapidity of their transmission may convert the interference of waves into more or less complete coincidence, and the effect of the two waves may thus be doubled instead of neutralised by their superposition.

The alteration which is produced in the mutual effect of two waves by increase or diminution of their rate of transmission along channels of constant length supplies us, I think, with a test by which we may ascertain the truth of the hypothesis that inhibitory phenomena in the animal body are due to interference. For if it be true we ought to find that a nerve which produces inhibitory phenomena when excited under normal conditions will gradually lose this power when the rate of transmission along it is increased or diminished, as, for example, by the influence of heat or cold, and will gradually acquire an exactly contrary or stimulating action. This, I think is shown to be the case by our experimental data so far as they go.

Several authors have pointed out the analogy between inhibitory phenomena in the animal body and the effects of interference of waves of light or sound. This has been done with special precision by Bernard[1] and Romanes.[2] The tendency to do away with the idea of distinct inhibitory centres is gradually spreading, but hitherto no attempt has been made to bring all the phenomena of inhibition under one general rule or to explain the mode in which they are affected by the action of drugs. The object of the present paper is to gather together some instances of inhibition which we find in the body, and to see whether by the theory of interference it is not possible to explain both the curiously perplexing exceptions which we meet with in physiological experiments, and the still more perplexing action of drugs on inhibitory phenomena.

One of the most striking examples of reflex action and of inhibition is the effect of a slight touch or touches, and of firm pressure upon the palms of the hands, the soles of the feet, or the axillæ, and in some persons also the knees. In many persons a very slight touch or succession of touches upon these parts is sufficient to throw first the respiratory muscles, and then the whole body, into violent convulsions. Indeed, it is stated that during the persecution of the Albigenses by Simon de Montfort several people were tortured to death by tickling the soles of their feet with a feather. The stimulus here

[1] Bernard, La Chaleur Animale, Paris, 1876, p. 371.
[2] Romanes, Phil. Trans. 1877, p. 730.

applied, and the consequences it produces, appear to be out of all proportion to one another; the stimulus being almost infinitesimal, and the consequences enormous.

In the case of Newton's rings it might be possible with much trouble to throw a different beam into such a condition that it would interfere with one of the beams in the rings, and produce darkness, but in the rings a similar effect is produced in a very much simpler way by alteration of part of the same beam. A similar occurrence is to be observed in the inhibition of the reflex action on tickling.

By a very powerful effort of the will we may completely arrest the reflex movement which would otherwise occur, and allow the limb to remain perfectly passive. But the same effect is produced in a much simpler way by applying a firm pressure instead of a slight touch. The firm pressure neutralises the effect of the touch in regard to motion, and not only are no reflex convulsive actions produced, but no tendency whatever to them is felt.

But while the pressure has neutralised the tendency to motion, and has altered the character of the sensation, it has not neutralised sensation. On the contrary, it has rendered it more definite, so that one can distinguish with much greater certainty the particular point of the surface which has been touched. Increased pressure has thus inhibited motion but increased sensation.

In a paper on "Inhibition, peripheral and central," which I wrote in the West Riding Asylum Reports in 1874, I tried to explain these phenomena in the following manner: "It appears to me to be in all probability due to there being two sets of ganglia in the cord itself, one motor and one inhibitory. The motor is more readily excited than the inhibitory, and causes violent movements, which the inhibitory centres of the brain cannot restrain without the greatest difficulty, though they are readily controlled by the inhibitory ganglia in the spinal cord. A slight titillation excites the motor, but not the inhibitory spinal ganglia ; a stronger pressure stimulates the inhibitory centres also, and thus arrests the movements without any action being required on the part of the inhibitory centres in the brain. We may try to explain this, by supposing that there are two distinct sets of nerves proceeding from the skin to the cord, one of them having the power to excite inhibitory, and the other to excite motor centres. Further, we must suppose that these sets of fibres are endued with different degrees of excitability, the motorial ones being stimulated by a slight touch, but the inhibitory ones only by a stronger impression.

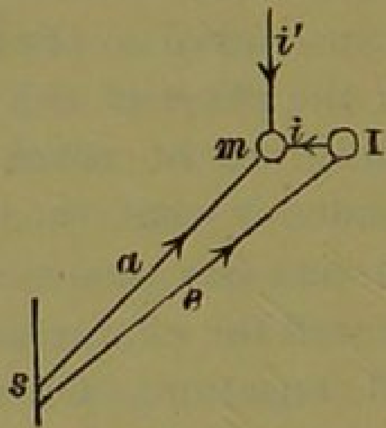


FIG. 3.

"This is represented in Fig. 3, where *s* is the skin ; *a*, the fibres proceeding from it to the motor ganglion, *m* and *e*, those going to the inhibitory ganglion, I ; *i* is the fibre by which I arrests the action of *m*, and *i* that by which the brain exerts a similar action. The different fibres by which *m* acts on the muscles have not been introduced into the diagram.

"This hypothesis, however, is a very clumsy one, and we explain the facts quite as well by supposing that there is only one set of afferent nerves (*a*, Fig. 4) from the

kin to the cord, which transmit a slight impression only
the motor ganglia, *m*, but convey a stronger one along
' to the inhibitory ganglia I, also, which then react
rough *i* upon the motor ones. This latter supposition
enders intelligible the fact that it is only when some-
ing is drawn quickly and lightly across the skin, so as
make a slight and transient impression on the ends of
any sensory nerves, that tickling is felt. If the pressure

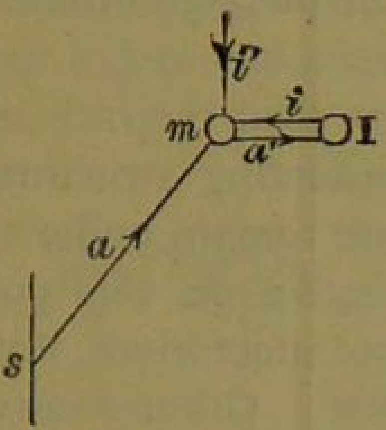


FIG. 4.

the skin is heavier, or if the motion over it is slow, the
fect is quite different, and this is just what we might
xpect if a short and slight impression travels only to the
otor ganglia, and a stronger or more lasting one goes to
e inhibitory beyond them.''

These diagrams themselves are suggestive of interfer-
nce; but I did not in that paper say anything regarding
, contenting myself only with the term inhibition. One
eason that prevented me from considering inhibition in
nimals as corresponding closely to the interference of
ght, was that the rapidity of transmission of nervous
npulses was differently given by different observers, and
ideed, according to Munk, it varies along the course of
ne same nerve.[1]

Unless the rate of transmission of impulses is constant,
ne cannot expect interference to produce inhibition. But

[1] Archiv. f. Anat. u. Physiol. 1860, p. 798.

in his observations on Medusæ, Mr. Romanes found that when the circumference of the bell in a medusa was cut into a long spiral strip, leaving only the centre of the bell uninjured, stimuli applied to the extreme end of the strip passed along it, and were delivered to the centre of the bell, just as if they had been applied to the central part itself—all passing at the same rate they did not interfere with one another. But when the strip was pressed upon or stretched, the passage of impulses was interfered with.

This seems to show that the rate of transmission of a stimulus along a conducting structure is a definite one, provided the structure remain under the same conditions. But still more instructive on this point are the experiments with the Ton-inductorium, invented by my friend Prof. Hugo Kronecker. Other observers have found that when a muscle is irritated by an interrupted current applied to its nerve, the tetanic contraction into which it would be thrown by twenty interruptions per second ceased when the interruptions became as frequent as 250 per second. By using an interrupted current induced by the vibrations of a magnetic rod, which gave out a definite tone, Kronecker and Stirling were able to throw the muscle into tetanus with no less than 22,000 interruptions per second. This success is probably to be attributed to the regularity and equality of the stimuli applied by Kronecker's method, while the fact that their predecessors got no tetanus with more than 250 interruptions per second is probably due to interference of the stimuli they applied.[1] Kronecker's observations show, I

[1] It must be borne in mind, however, that the overtones of such a vibrating rod are in the ratio of n, $3n$, $5n$, &c., and not in that of n, $2n$, $4n$, like those of a vibrating string or pipe. Quincke (Poggendorff's Annalen, 1866, vol. viii. p. 182) failed to silence the sounds of such a rod by means of an interference apparatus.

think, how definite must be the rate of transmission of stimuli along a nerve so long as it remains under the same conditions, and give us a basis for extending the theory of interference from waves of light and sound to vibrations in nervous and muscular tissues.[3]

We are justified, I think, by these experiments in considering that interference may occur in the nervous system, and that one part may exercise an interfering or inhibitory effect upon the other, which is constant under normal conditions, but will be modified when these conditions are altered.

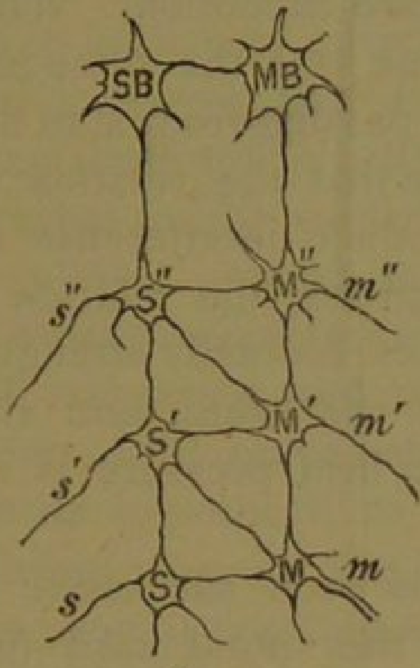


FIG. 5.

Let us now try to apply this hypothesis to the reflex action which we have just been discussing.

Let S, S′ and S″ be three sensory cells in the spinal cord, M, M′ and M″ motor cells, *s* and *s′* sensory nerves, and *m m′* motor nerves. S B is a sensory and M B a motor cell in the brain. When *s* is stimulated by a slight touch, the stimulus is transmitted up to S, thence to M, and down *m* to muscles, thus causing reflex

[1] *Vide* Hermann's Handbuch d. Physiol. Bd. i. Th. i. p. 44, and Bd. i. Th. i. p. 39.

contraction. This is increased when a number of slight touches are made over a limited surface, as in tickling, because then S and S′ are both stimulated, and more motor impulses are produced. But when harder pressure is made on *s* the stimulus, instead of being confined to S, is transmitted to S′ and thence to M, as well as direct from *s* to M. Thus two impulses are sent to M, which, starting at the same time from *s*, have had a different length to travel round. This different length, we suppose, is just sufficient to allow the impulses to interfere with one another in M and thus destroy each other's action in regard to motion. When *s*′ is also irritated at the same time as *s*, the same interference is produced by a stimulus passing from S′ to S″, and then to M′. But at the same time that the relation of S′ S″ to M and M′ is such as to produce interference and inhibition in regard to motor impulses, the relation to each other is such that the impulses mutually strengthen one another on their way up to the brain, and thus the sensation which we perceive on firm pressure is more definite and better localised.

On this hypothesis each successive layer of sensory and motor cells in the spinal cord may have several different functions: (1) Each cell may exercise its own sensory or motor functions in relation to the sensory or motor nerves connected with it; (2) it may exercise an inhibitory function on the sensory and motor cells above or below it, and also on other sensory or motor cells on the same plane with itself; (3) it may have a stimulating function on other cells above, below, or on the same plane as itself, increasing instead of abolishing their action.

The effect that any sensory or motor cell produces when stimulated is not determined then simply by the *roperties* of the cell itself, but by its *relations* to other ells or fibres.

Motion, sensation, inhibition, or stimulation are not ositivé, but simply relative terms, and stimulating or nhibitory functions may be exercised by the same cell ccording to the relation which subsists between the vave-lengths of the impulses travelling to or from it, the istance over which they travel, and the rapidity with vhich they are propagated.

M. Vulpian has observed that the excitability of the ower parts of the spinal cord increases as the upper part s gradually shaved away, so that each layer of the cord ppears to exercise an inhibitory action on the one below it. I. Brown-Séquard supposes that in each layer of the erebro-spinal system there are both dynamogenic elements nd inhibitory elements for the subjacent segments.

We are, in fact, almost obliged to assume that each erve-cell has two others connected with it, one of which as the function of increasing, and the other that of re-training the function of the nerve-cell itself.

Applying this same hypothesis to Newton's rings, we vould say that certain parts of the lens or of the glass late possessed the property of interfering with the rays f light, or were inhibitory centres for them. Others gain had the property of increasing the brightness, or vere stimulating centres for them; and, moreover, that ifferent parts of the lens or of the glass plate contained ach its stimulating and inhibitory centres for different oloured rays.

The multiplication of centres in the lens and glass late soon becomes more than the imagination can well take n; and we are at present almost precisely in the same ondition regarding inhibitory and stimulating centres in he nervous system.

As soon as we get rid of the idea that the darkness caused by the interference of the rays of light at certain points is due to some peculiar property inherent in the glass, and attribute the interference simply to the relationship between the waves of light and the distance they have to travel, the whole thing becomes perfectly simple and the same is, I think, the case in regard to inhibition in the nervous system.

Let us now take a few more examples of inhibition.

We find in experiments with the frog's foot exactly the same as on our own hand. Thus, when a little turpentine is placed upon the toes it excites a violent reflex, but if a little turpentine be injected under the skin of the same foot, the reflex is abolished.[1] We find also that irritation applied to a limited region of the skin usually causes marked reflex, but if the same stimulus be applied to the sensory nerve supplying that region, the reflex is very much less.[2] In the cases just mentioned the irritation is applied to sensory nerves of the same part of the body, and close together, and the explanation of its different results is the same as that already given for the different effects of tickling and pressure. Different sensory nerves on the same side of the body, but at some distance from each other, will also cause inhibition of motor reflexes: thus it has been shown by Schlosser[3] that simultaneous irritation of the skin over flexor and extensor surfaces will lessen reflex action.

Some years ago I observed that frogs suspended by the fore-arms with cords, or tied with their bodies against a board, reacted less perfectly to stimulation of the foot by acid than a frog suspended by a single point, as i

[1] Richet, Muscles et Nerfs, Paris, 1882, p 710.
[2] Marshall Hall, Memoirs on the Nervous System, London, 1837, p. 48.
[3] Arch. of Physiol. 1880, p. 303, quoted by Richet, *op. cit.* 709.

Türck's method. Tarchanoff[1] has also observed that frogs held in the hand respond less perfectly than when hung up; the gentle stimulation of the sensory nerves in the skin of the body appearing to exercise an inhibitory action over the reflex from the foot.

The injection of acids or irritating solutions into the mouth[2] or dorsal lymph sac[3] also exercises an inhibitory action on reflexes from the foot.

A similar effect is produced by irritating the sciatic nerve on one side by a Faradaic current, and applying a stimulus to the other foot. So long as the irritating current is passed through the sciatic nerve, no reflex movement can be elicited by stimulation of the other foot; but so soon as the Faradaic current stops, the reflex excitability again appears in the other foot.[4] As this phenomenon occurs when the influence of the brain and upper part of the spinal cord has been destroyed by a section through the cord itself, the inhibition which occurs must be due to an action which takes place in the lower portion of the spinal cord.

Stimulation of the nerves of special sense has also an inhibitory action on reflex movements. This we can readily see in ourselves, by observing our actions in the dark. If we touch something cold or wet, or if something suddenly comes against our face, we give an involuntary start, sometimes almost a convulsive one. If, however, we were able to see, we should not give a start in the least when we touched a piece of wet soap, or when the end of a curtain suddenly came against our cheek.

[1] Quoted by Richet, *op. cit.* p. 709.

[2] Setschenow, Physiologische Studien über die Hemmungsmechanismen für die Reflexthätigkeit des Rückenmarks im Gehirn des Frosches, Berlin, 1863, p. 33.

[3] Brunton and Pardington, St. Bartholomew's Hospital Reports, 1876. p. 155.

[4] Nothnagel, Centralblatt d. med. Wiss. 1869, p. 211.

Without entering into the nervous mechanism through which sight effects this change in our actions, but only reducing it to its simplest form of expression, as we would in talking of animals, we say that the stimulus to the sensory nerves of the hand or cheek, by contact with the wet soap or with the curtain, caused in us a reflex spasm, which was inhibited by the stimulus applied to our optic nerves. A similar occurrence is observed in frogs, and the reflex actions produced by stimuli applied to the feet are much stronger when the inhibitory effect of the optic nerves upon them is removed by covering up or destroying the eyes, or by removal of the optic lobes.[1]

Regarding the optic lobes, we will have a good deal more to say presently, for they have been considered to be special inhibitory centres, and are often known by the name of Setschenow's centres.

If we try to explain all those instances of inhibition by the assumption of special inhibitory centres for each action, we must suppose that centres exist in connexion with every sensory nerve, which lessen or abolish the ordinary reflexes produced by stronger or weaker stimulation applied to the nerve. Besides this, we must suppose other centres which inhibit motor actions in other parts of the body: as for example, when irritation of the extensor lessens reflex excited by irritation of the flexor surfaces, or *vice versâ*, or when the irritation of one sciatic stops reflex action from mechanical irritation of the other foot. A special inhibitory centre must be placed also in the optic lobes in connection with the optic nerves. This complication reminds us of the multitude of inhibitory centres which one must imagine in glass, in order to explain the occurrence of Newton's rings by

[1] Langendorff, Arch. f. Anat. u. Physiol. 1877; Von Boetticher, Ueber Reflexhemmung, Inaug. Diss., Jena, 1878, p. 12.

them, but it seems to me that all these cases are readily explained on the hypothesis that the motor and sensory cells concerned in them are so placed with relation to each other that the stimuli passing from them produce interference *under normal or nearly normal conditions of the organism.*

A spot of light may be caused to disappear by throwing another ray upon it, so as to interfere with it, but it may be also made to disappear from the place where it was, by simply reflecting it somewhere else.

A similar occurrence to this takes place in the body, and although two stimuli may interfere with and destroy each other, we not unfrequently find that the apparent abolition of the effect of a stimulus is simply due to its diversion into some other than the usual channel. In very many cases, where we have inhibition we have also diversion; and it is not at all improbable that when the stimulus is very strong complete inhibition may be impossible by interference alone, and can only be effected by diversion of part of the stimulus. We have already said that two waves of sound will neutralise each other and produce silence, but this only occurs when the waves are not too powerful. When they reach a certain intensity they produce secondary waves which give resultant tones, and several facts seem to point to an analogous condition in animal organisms.

We have hitherto considered cases in which the inhibition was probably brought about by interference of two stimuli, so that the one counteracts the other in much the same way as two rays of light interfered with one another in Newton's rings. In one case which we have mentioned, the movement of the hand when it is tickled is entirely arrested by a strong effort of the will, and the hand is allowed to remain perfectly passive and limp.

Here we suppose the impulse sent down from the motor centres in the brain to interfere with that which has originated in the cord by irritation of the sensory nerves, and to counteract it so that no muscle whatever is put in action. But very frequently we find that a result apparently similar is produced by a different mechanism, viz. by diversion of the stimulus into other channels. In the former case the arm is felt to be quite limp, but in the latter, though it is quite quiet, it is perfectly rigid—all the muscles being intensely on the stretch. Here the stimulus which would usually have excited convulsive movements of the arm, and probably of the body, resulting in a convulsive start, have been diverted from the body into other muscles of the same limb.

A similar power of diverting a stimulus is seen in the instinctive muscular efforts which any one makes when in pain. One of the most common of these is clenching the teeth, and it used to be a common practice in the army and navy for men to put a bullet between the teeth when they were being flogged, and at the end of the punishment this was usually completely flattened. A patient seated in a dentist's chair usually grasps convulsively the arms of the chair, or anything which may be put into his hand ; and there can be little doubt that pain is better borne, and appears to be less felt, when the sensory stimulus occasioning it can thus be diverted into motor channels. In children the motor channels into which diversion usually takes place are those connected with the respiratory system, and the sensory stimulus works itself off in loud yells. At a later age the stimulus is often diverted into those motor channels through which reaction occurs between the individual and his surroundings. Thus most people probably remember how a kick on the shin at football often served simply to accelerate their speed; and during the heat of battle the pain of a wound is often but little felt, the stimulus having been diverted into motor channels.

Many more instances might be given of the effects of diversion of stimuli, but having discussed this subject at length in a former paper,[1] I shall not pursue it further here.

Sensory stimuli are also capable of inhibition by interference. Hippocrates[2] noticed, and it is a matter of general observation, that pain in one part of the body may be lessened or removed by the occurrence of pain in another. In many instances, the removal of the pain from one part may be indirect, through the action exerted on the vessels by the pain in the other part. But in some instances it may be, and probably is, due to the direct interference of sensory impressions.

This question of the removal of pain by the interference of waves in the sensory nerves or nerve-centres has been very fully and clearly discussed by Dr. Mortimer Granville.[3] Starting from the hypothesis of interference, he has also devised a plan of treatment which appears to give satisfactory results. By means of a small hammer moved by clockwork or electricity, he percusses over the painful nerve in order to induce in it vibrations of a different rhythm to those which are already present and which give rise to the pain. Thus he percusses rapidly over a nerve when the pain is dull or grinding, and percusses slowly when the pain is acute, in order to produce interference if possible. In many instances the

[1] Brunton, "Inhibition, Peripheral and Central," West Riding Asylum Reports, 1874.
[2] Hippocrates, Aphorisms, sec. i 46; Sydenham Soc Ed. vol. ii. p. 713.
[3] Mortimer Granville, Nerve Vibration and Excitation. (London: Churchill, 1883.)

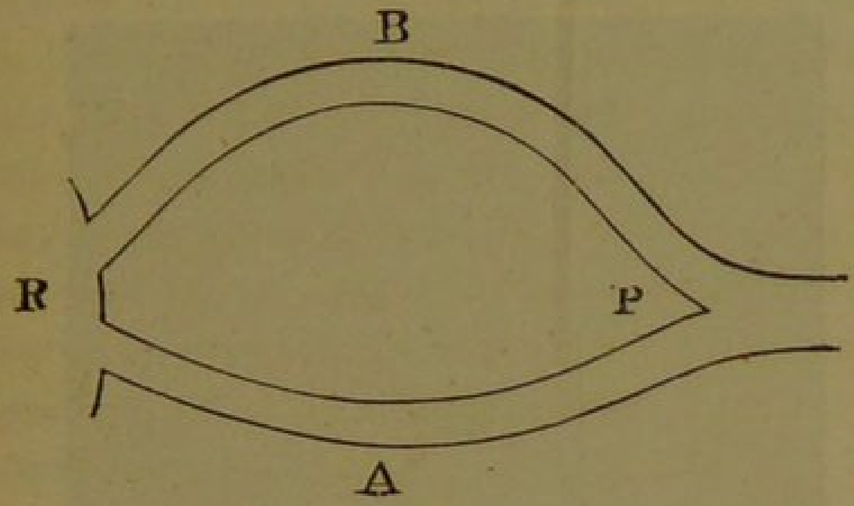
treatment is successful, and its success affords additional support to the hypothesis on which it is based.

We have hitherto spoken of reflex inhibition in the cerebro-spinal axis alone, but we find also reflex inhibition of motor actions produced by irritation of sympathetic nerves; and, *vice versâ*, we find inhibition of the movements of internal viscera produced by irritation of cerebro-spinal nerves. Thus strong irritation of the sensory nerves of the liver, intestine, uterus, kidney, or bladder, occasionally abolishes the power of walking or standing. Irritation of a sensory nerve will frequently arrest the movements of the heart.

The phenomena which occur in swallowing afford an excellent example, not only of inhibition occurring in parts innervated by the sympathetic system, but also of partial diversion of stimuli. Kronecker has found that when we swallow, the food or water is sent down at once into the stomach by the contraction of the muscles of the pharynx, and that afterwards a peristaltic contraction of the œsophagus occurs. When several attempts to swallow are made one after the other, however, the œsophagus remains quiet until they are ended, and then it occurs at the same interval of time after the last, that it would have done after a single act of swallowing.

If we now refer again to our diagram (Fig. 2, which for convenience we repeat here) we will see that it answers just as well for the contractions of the œsophagus as for the tides at Batsha by simply giving a different meaning to the letters. Let R now instead of representing a reservoir or the open sea represent the ganglia of the pharynx, A and B the nerve fibres which conduct nervous impulses from these ganglia to P, and let P be the ganglia of the œsophagus which stimulate its muscular fibres to peristaltic action. A single wave passing from causes two waves at P, one succeeding the other, but a umber of waves from R under the conditions supposed lso cause only two waves: one at the beginning and one t the end, for during all the intermediate period they eutralise each other.

It might perhaps seem that the two stimuli should cause wo contractions of the muscular fibres of the œsophagus. But it frequently happens that a single stimulus is unable) produce muscular contraction. It only increases the xcitability of the contractile tissue to a second stimulus, nd when this is applied contraction ensues. The effect



IG. 2.—Diagram to illustrate Sir J. Herschel's observations on interference, Adapted from his article on "Absorption of Light," Phil. Mag. 1883. p. 405.

f the first wave then would be to increase excitability, nat of the second wave to cause contraction (Mosso). This well shown in the accompanying tracing from the contractile tissue of Medusæ, which I owe to the kindness f my friend, Mr. Romanes. He has found that when ery slight stimuli, such as weak Faradaic shocks, are pplied, the first has no apparent action, but the effect of ach successive stimulus is added to that of the preceding nes, until contraction is produced. Two shocks were pplied before the first small contraction shown in the racing occurred, and the shocks are all of the same strength, although the last ones produce the maximal contraction of which the tissue is capable, and the first had apparently no effect at all. This relation of the contractile tissue to stimuli is usually expressed by saying that the tissue has the power of summation.

At the same time that a stimulus is sent down from the pharynx to the œsophageal ganglia, which has an inhib'tory action, there appears to be another sent to the medulla oblongata, which acts on the roots of the vagus nerve. This latter stimulus has a very curious effect, viz. inhibition of inhibition. The vagus usually exercises an

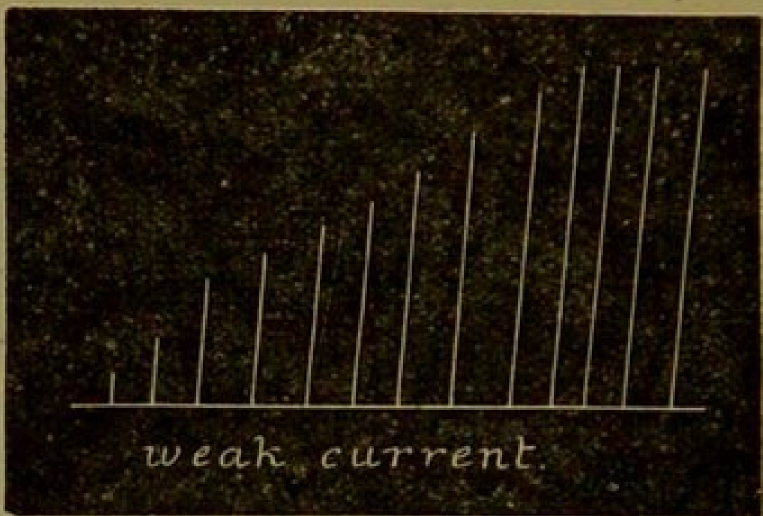


FIG. 6.—Showing the increasing contractions of the tissue of medusa when stimulated by repeated weak induction shocks of the same intensity.

inhibitory action on the heart, rendering its beats less rapid than they would otherwise be, but during swallowing this inhibitory action is removed and the heart pulsates at nearly double its normal rate.[1] Here we seem to have a stimulus one part of which passes along one path, while another part is diverted and passes along another. Each part interferes with the nervous actions which would occur in its absence, but one part interferes so as to prevent, and the other so as to increase muscular activity in the œsophagus and heart respectively.

[1] In my own case the proportion is 120 to 76.

The same diversion of a stimulus which we find in the case of the œsophagus seems to occur frequently throughout the body. Thus we find it almost invariably in relation to the vascular changes which occur on stimulation of a sensory nerve. When a sensory nerve going to any part of the body is irritated, the vessels of the district which it supplies usually dilate, while those of the other parts of the body contract.[1] The stimulus in this case passes to the vasomotor centre, and thence is reflected as an inhibitory stimulus in one direction and as a motor stimulus in another.

Some results of the greatest interest have recently been obtained by Dastre and Morat, in some experiments which they have made on the subject of vascular dilatation or inhibition.

In many cases the stimulation and inhibition of vascular nerves take place in the medulla oblongata, or in the spinal cord, and the inhibitory and motor centres are close to each other; but in other cases, such as those experimented on by Dastre and Morat,[2] we find the inhibitory and motor centres separated from one another, some of the motor centres being in the cord and some of the inhibitory in a ganglion situated nearer the periphery.

It was previously known that in some cases, as in the dilatation of the vessels of the submaxillary gland on irritation of the chorda tympani, small ganglionic structures were situated at the terminal branches of the nerve, and it was supposed that these ganglia, by their interposition between the nerve and the structure on which it was to act, converted its motor power into an inhibitory one. The experiments of Dastre and Morat are more definite on this point. Excitation of the cervical sympathetic

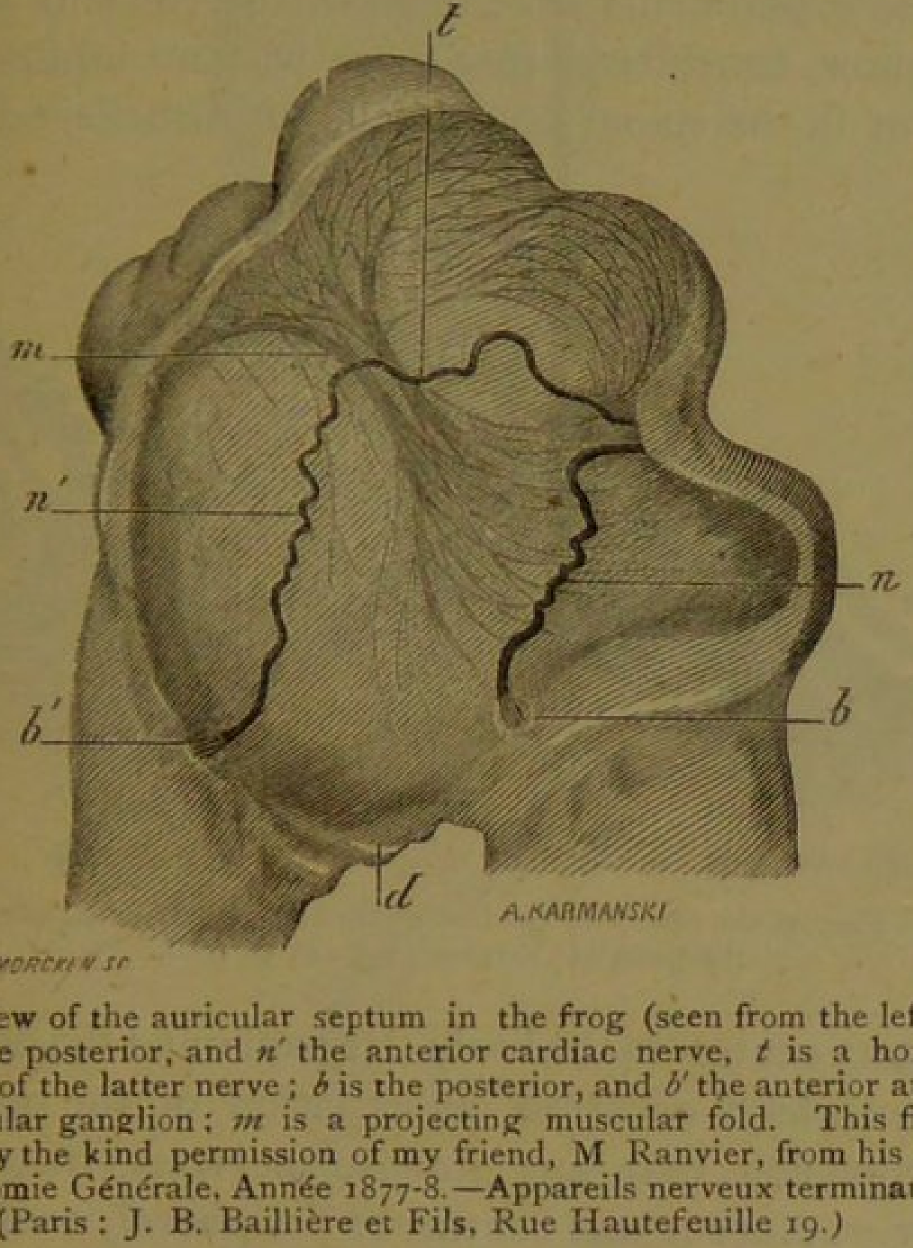
[1] Ludwig and Loven, Ludwig's Arbeiten, 1866, p. 7.
[2] Archives de Physiologie, 1882, tom. x, p. 326.

nerve has the effect of causing the vessels of the ear to contract very greatly in the rabbit, but irritation of the same nerve causes in the dog enormous dilatation of the vessels of the mouth. Moreover, in the rabbit this constricting action on the vessels of the ear is exerted only when the nerve is irritated between the first cervical ganglion and the ear. When the nerve is irritated beyond the cervical ganglion, instead of causing constriction, it produces dilatation.

In order to explain this action, the authors suppose that the fibres of the sympathetic, in passing through the ganglion, end in the ganglionic cells, and thus suspend the tonic action which they exert on the constricting fibres which issue from the ganglion and pass to the ear. It seems to me, however, that a more satisfactory explanation of this fact also is afforded by the hypothesis of interference.

In the cerebro-spinal system, cells being ranged above, below, and around one another with free communication between them, we have ample provision for the passage of two stimuli along paths of such different length, as to enable them to interfere with and inhibit each other.

But in peripheral nervous mechanisms, such as those in the heart of the frog, where we have no such provision, and the cells are not only few in number but not arranged in strata, we find a special form of ganglion cell which seems constructed for this very purpose. This is the spiral cell described by Beale, in which we find one nerve-fibre twisted round and round in a way which reminds us of a resistance coil in a galvanic circuit. The object of this peculiar arrangement has, so far as I know, not been discovered; but it seems to afford the exact mechanism which is wanted in order to alter the distance two stimuli have to travel nd thus allow them to interfere with and inhibit each ther. The occurrence of these ganglia in the heart and ther viscera seems to afford in itself some support to the ypothesis here advanced; but we will defer the consideration of the mode in which inhibition occurs in the eart and other internal viscera, and pass on at present



G. 7.—View of the auricular septum in the frog (seen from the left side). *n* is the posterior, and *n′* the anterior cardiac nerve, *t* is a horizontal portion of the latter nerve; *b* is the posterior, and *b′* the anterior auriculo-ventricular ganglion; *m* is a projecting muscular fold. This figure is taken by the kind permission of my friend, M Ranvier, from his Leçons d'Anatomie Générale, Année 1877-8.—Appareils nerveux terminaux, t. 6, p. 79. (Paris: J. B. Baillière et Fils, Rue Hautefeuille 19.)

the effect of various parts of the central cerebro-spinal stem upon each other.

The first important contribution to our knowledge of hibitory centres in the brain and spinal cord was that Setchenow. He found that when the cerebral lobes a frog were removed, voluntary motion was abolished, but reflex action became somewhat more marked. On removal of the optic lobes, the reflex action became very greatly increased, and if, instead of removing them they were stimulated either chemically by a grain of salt laid upon them, or electrically, reflex action in the limbs was greatly retarded or completely abolished.

These experiments were repeated by Herzen, who, like Setchenow, considered that there was no inhibitory mechanism in the spinal cord itself, but disbelieved also in

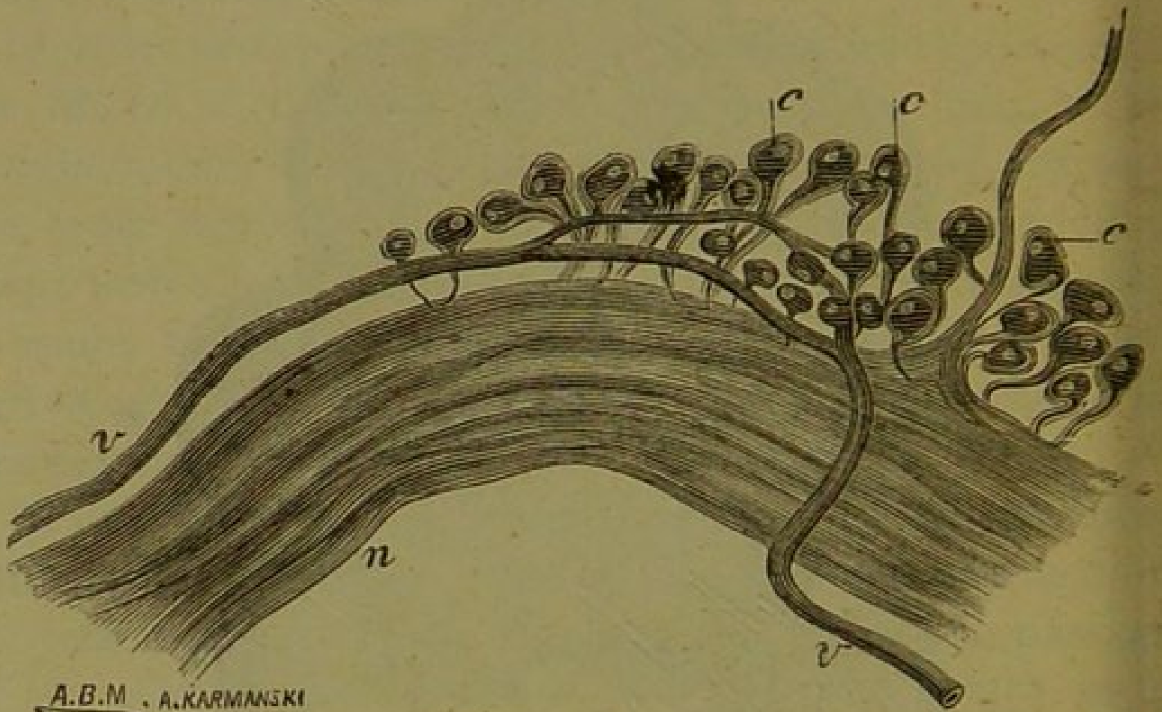
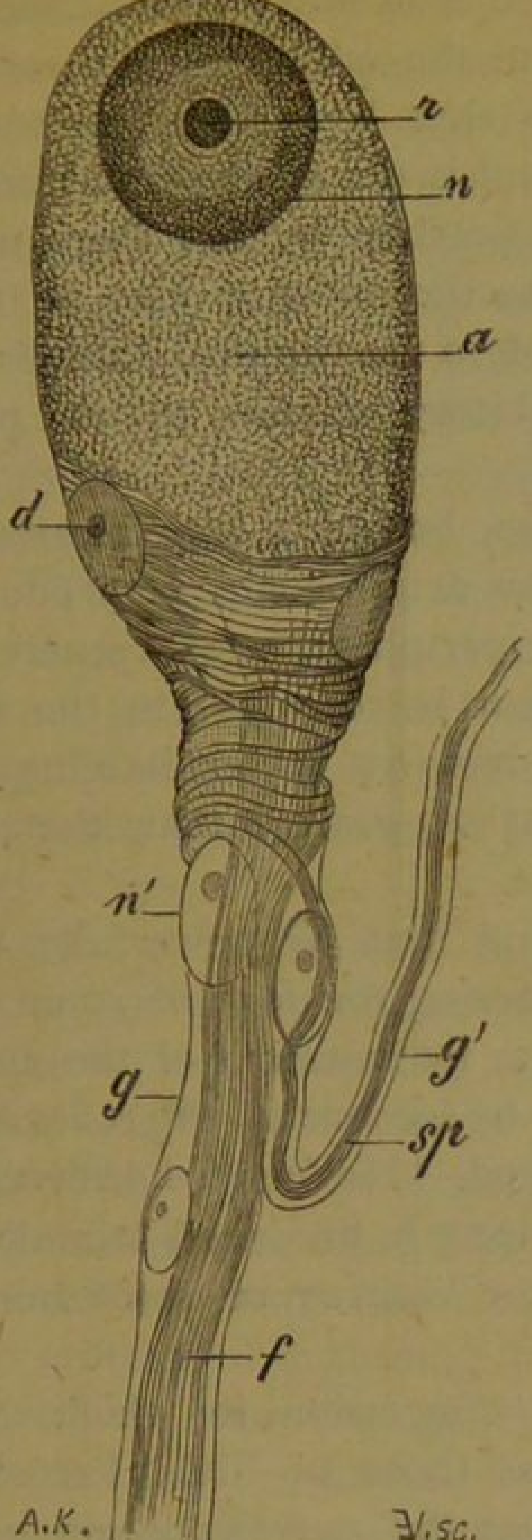


FIG. 8.—Part of the posterior cardiac nerve more highly magnified, showing the ganglia (Ranvier, *op. cit.* p. 106).

inhibitory centres in the brain. He explained the depression of reflex which occurred on irritation of the optic lobes by supposing that any intense nervous irritation, no matter whether it was central or peripheral, caused great depression of reflex action both when the brain was intact and when it was divided, as in Setchenow's experiment. Setchenow again repeated his experiments, and came to the conclusion that it was uncertain whether the inhibitory mechanism could be excited reflexly from the periphery. He made, also, a sharp distinction between ctile and painful impressions upon the skin. For



G. 9.—Spiral ganglion cell from the pneumogastric of the frog. This figure is not taken from the cells in the cardiac nerves, as in them the connection between the spiral and straight fibres has not been clearly made out, but it is probable that these cells have a structure similar to the one figured (Ranvier, *op. cit.* pp. 114-20). *a* is the cell body, *n* the nucleus, *r* the nucleolus. *d* nucleus of the capsule, *f* the straight fibre, *g* Henle's sheath, *sf* spiral fibre, *g'* its gaine, *n* nucleus of Henle's sheath (Ranvier, *op. cit.* p. 114).

ctile impressions he considered that there was no inhibitory mechanism in the brain. Further investigations still, showed that both chemical and electrical irritation would excite the inhibitory apparatus, and he therefore considered that both excito-motor and depressor fibres were present in the same nerve-trunk.[1] Goltz found, in opposition to Setchenow, that there was an inhibitory apparatus for tactile reflexes also in the frog's brain, but this he found in the cerebral lobes,[2] while Setchenow denied any inhibitory function to that part of the brain altogether.

He found also, however, like Herzen, that complete abolition of reflex action could be produced by powerful irritation of any peripheral sensory nerve, and considers that the irritation is conveyed to the reflex centre, and diminishes or destroys its excitability for the original stimulus, without supposing that there is any special inhibitory centre.

Lewisson found that by powerfully compressing the neck, or by squeezing the feet, or some other part of the body of a frog, or by irritation of the cutaneous or muscular nerves, or by electricity, the reflex excitability could be much depressed. He found, however, that unless the irritation was strong it produced stimulation both of the reflex and motor centres of the brain instead of depression.[3]

The general conclusion to which all these experiments, as well as those of Fick,[4] Freusberg, and others lead is, either that the nerves contain both excito-motor and reflex depressing fibres, or that excitement and

[1] Uber die elektr. und chem. Reizung der sensiblen Ruckenmarksnerve des Frosches, 1868. Quoted by v. Boetticher, *op. cit.* p. 6.

[2] Goltz. *op. cit.* p. 42.

[3] Lewisson, "Ueber Hemmung der Thätigkeit der motor. Nervencentre durch Reizung sensibler Nerven," Archiv. f. Anatomie u. Physiol. 1869.

[4] Fick, Verhandlungen der physikalisch medicinischen Gesellschaft z Wurzburg, April 23, 1870.

epression can be produced by the same nerves under ifferent conditions.

Freusberg,[1] who discusses the question of inhibition in n able and thorough manner, comes to the conclusion nat all instances of inhibition including the different ffects of weak and powerful stimuli applied to the same erve, and also the inhibitory effects of stimulation of ifferent nerves on each other, are not due to specific hibitory centres, but to a remarkable property of the ntral nervous system, which does not allow of its fferent parts being simultaneously set in action by fferent causes. This conclusion, although it may be arer the truth than the hypothesis of separate inhi-tory centres, is not satisfactory, for it still leaves us in e dark regarding the way in which the central nervous stem comes to possess the remarkable properties which attributes to it.

Setchenow explains the increased rapidity of reflex tion after section of the cord below the medulla longata, by supposing that there are two paths along ich the stimulus usually passes from the sensory to motor tracts. The one goes directly across, and s is the path taken after section. The other goes up the medulla, and then down the cord. This is the th taken under ordinary conditions; but besides the parent unlikelihood that the stimulus should take this ger path under normal conditions, an objection has en raised to it by Cyon which seems fatal.

Cyon finds that when the so-called inhibitory centres stimulated, although reflex contraction of the leg is parently delayed for a long time, this delay is to a great ent only apparent and not real.[2]

[1] Freusberg, "Ueber die Erregung u. Hemmung d. Thätigkeit d. vösen Centralorgane," Pflüger's Archiv. x. 174.
[2] Cyon, Ludwig's Festgabe, p. clxviii.

It is true that the vigorous contraction of the muscles which suffices to raise the limb is much delayed, but a contraction of these muscles commences at very nearly the same time that it would do if the inhibitory apparatus were not stimulated. This shortening of the muscle goes on very gradually for a considerable time, and then culminates in a sudden vigorous contraction, the total height of which is greater than that of the contraction which would have occurred without irritation of the inhibitory centres. It is very difficult to explain this result on the ordinary hypothesis, but easy enough on that of interference. According to it we suppose that a stimulus applied to the foot has been transmitted as usual from the sensory to the motor cells of the cord, and thence to the muscles, so as to initiate contraction in them. This stimulus would correspond to the first half wave in the diagram (Fig. 2). The subsequent waves of stimulation which would have proceeded from the motor ganglia have been interfered with by the stimuli passing down from the so-called inhibitory centre, but their times being not arranged so that each wave from the brain should fall half a wave length behind that in the cord, the stimuli at length cease to interfere, and the contraction, which has gone on gradually increasing as the interference diminishes, at last finishes abruptly.

The part of the brain which ought to correspond in higher animals to the optic lobes in frogs is the corpora quadrigemina, but irritation of these parts has not been found to have any marked inhibitory action upon reflexes in the limbs.[1]

Irritation of the frontal lobes in puppies has, however

[1] Setschenow Physiologische Studien über die Hemmungs-mechanismen für die Reflexthätigkeit des Rückenmarkes im Gehirn des Frosches, p. (Berlin: Hirschwald, 1863).

been found by Simonoff[1] to exercise an inhibitory action; but, according to Ferrier, abolition of the frontal lobes in monkeys does not produce any very obvious effect upon the animal.[2] We know that by an effort of the will, we are able either to increase or diminish reflex action, and it might appear probable that irritation of the motor tracts in the cerebrum might have an inhibitory action on reflexes. Irritation of the cerebral motor areas has not been found to exercise any definite inhibitory action upon reflexes, but on the other hand Exner[3] has found, if a stimulus be applied simultaneously to a motor area in the brain and to an extremity, the two stimuli aid one another, and produce a greater effect than they would separately. As irritation of the cerebral motor areas, therefore, does not exercise a definite inhibitory action upon reflexes, but does under certain conditions markedly increase them, one might expect that their removal would diminish reflex action. Such a diminution actually occurs when they are destroyed in disease, but when the brain is removed layer by layer in operations upon animals, it is usually found that the reflex increases in proportion to the quantity removed. When the whole brain is removed, the reflex action is greater than when it is present, and as the cord is cut away layer by layer, the excitability of the segment below appears to be increased; each layer, as has already been mentioned, appearing to have an inhibitory influence on the one below it. But this is not always the case, because we sometimes find on removal of the various parts of the brain or of the spinal cord that the section completely abolishes reflex action for the time.

We are accustomed frequently to cloak our ignorance of the true cause of this abolition by saying it is due to

[1] Simonoff, Arch. f. Anat. u. Phys p. 545, 1866.
[2] Ferrier, Functions of the Brain, p. 230 (London, 1876).
[3] Exner, Pflüger's Archiv. xxviii. 487.

the shock of operation or something of that sort; but looking the facts fairly in the face, we find that sometimes removal of the upper part of the brain or spinal cord causes increase and sometimes diminution of reflex-action in the parts below. At present we have no satisfactory explanation of this phenomenon, but if we suppose in the one case the nervous matter to have been removed in such a way as to cause an interference of the stimuli passing along from cell to cell, and in the other to cause a coincidence, we can readily understand the occurrence of the two different conditions. Moreover, we have said several times, that inhibition or stimulation are only relative conditions depending on the length of path along which the stimulus has to travel, and the rapidity with which it travels. The length of path remaining the same, the occurrence of stimulation or inhibition depends upon the rapidity of passage of the stimulus. The same length of path which is just sufficient to throw successive impulses of a slowly travelling stimulation half a wave-length behind the other, and produce inhibition, may be just sufficient to throw the vibrations of another more rapidly transmitted stimulus a whole wave-length behind, and produce increased instead of diminished action.

If the hypothesis that inhibition is produced by interference be true, we shall be able to test it by seeing whether stimulation of certain nerves which, under the ordinary conditions produce inhibition, do so when the rate of transmission of nervous impulses is altered. The length of path being the same, if we alter the rapidity of transmission it is probable that as the rapidity diminishes, the inhibition will be converted into stimulation, again possibly passing into inhibition, according as the stimuli, which we normally suppose to be half a wave-length behind each other, are thrown a whole wave-length, or a wave-length and a half behind each other. At a certain period, also, the waves of stimulation will be neither a whole nor a half wave-length behind each other, but the fraction of a wave-length. In such cases we shall neither have constant coincidence, nor constant interference, but we shall have rhythmical coincidence and rhythmical interference, the result of which will be that we shall neither get constant motion, nor constant arrest of motion, but alternate motion and rest. In other words, we shall neither have complete rest nor tonic contractions, but intermittent or clonic contractions. Now this condition is exactly what we do find when one sciatic of a frog is irritated twenty-four hours after it has been exposed. We have already mentioned that when irritated immediately after exposure it had the effect simply of abolishing reflex action in the other leg; but the same irritation applied in the same manner after many hours, instead of causing arrest in the other leg, causes clonic convulsions.[1]

This occurrence is very hard to explain on the ordinary hypothesis of separate and distinct inhibitory centres, but it agrees perfectly with the hypothesis that inhibition and stimulation are merely relative conditions.

I have repeated Nothnagel's experiments, but I have not got the same results. Irritation of the sciatic nerve indeed caused a certain diminution in reflex at first, but irritation after twenty-four hours caused no clonic convulsions, it merely appeared somewhat to stimulate reflex action in the other leg. The reason of this discrepancy in our results is probably that the temperature was different in the two cases. Nothnagel's results were published in March, and his experiments were probably

[1] Nothnagel, Centralblatt f. d. med. Wiss. March 28, 1869, p. 211.

performed during cold weather, while mine were done during very mild weather. If the effects which he noticed were due to definite inhibitory centres in the spinal cord, similar experiments should have had similar results in his hands and mine. If on the other hand the effects simply depend on the rate of the transmission of nervous impulses, it is easy to understand why the results were different in the two cases.

There are also certain phenomena connected with the action of drugs on the spinal cord which are almost inexplicable on the ordinary hypothesis, but which are readily explained on that of interference. Thus belladonna when given to frogs causes gradually increasing weakness of respiration and movement, until at length voluntary and respiratory movements are entirely abolished, and the afferent and efferent nerves are greatly weakened. Later still, both afferent and efferent nerves are completely paralysed, and the only sign of vitality is an occasional and hardly perceptible beat of the heart and retention of irritability in the striated muscles. The animal appears to be dead, and was believed to be dead, until Fraser made the observation that if allowed to remain in this condition for four or five days, the apparent death passed away and was succeeded by a state of spinal excitement. The fore-arms passed from a state of complete flaccidity to one of rigid tonic contraction. The respiratory movements reappeared; the cardiac action became stronger, and the posterior extremities extended. In this condition a touch upon the skin caused violent tetanus, usually opisthotonic, lasting from two to ten seconds, and succeeded by a series of clonic spasms. A little later still the convulsions change their character and become emprosthotonic. These symptoms are due to the action of the poison upon the spinal cord itself, for they ontinue independently in the parts connected with each egment of the cord when it has been divided.

This action may be imitated by a combination of a aralysing and exciting agent such as strychnia and aethyl-strychnia. Fraser concludes that the effects of rge doses of atropia just described are due to a com-ined stimulant and paralysing action of the substance on e cord, and that the difference in the relations of these ffects to each other, which are seen in different species f animals, may be explained by this combination acting n special varieties of organisation.

A condition very nearly similar to that caused by tropia is produced by morphia. When this substance given to a frog, its effects are exactly similar to ose produced by the successive removal of the different arts of the nervous system from above downwards. Goltz as shown that when the cerebral lobes are removed from e frog it loses the power of voluntary motion and sits till; when the optic lobes are removed it will spring when imulated, but loses the power of directing its move-ments. When the cerebellum is removed it loses the ower of springing at all; and when the spinal cord is estroyed reflex action is abolished.

Now these are exactly the effects produced by morphia, e frog poisoned by it first losing voluntary motion, next e power of directing its movements, next the power of pringing at all, and lastly reflex action. But after reflex ction is destroyed by morphia and the frog is apparently ead, a very remarkable condition appears, the general accidity passes away and is succeeded by a stage of xcitement, a slight touch causing violent convulsions ist as if the animal had been poisoned by strychnia.[1]

[1] Marshall Hall, Memoirs on the Nervous System, p. vii. (London, 837). Witkowski, Archiv für exper. Path. und Pharm., Band vii. p. 247.

The action of morphia here appears to be clearly that of destroying the function of the nerve centres from above downwards, causing paralysis first of the cerebral lobes, next of the optic lobes, next of the cerebellum, and next of the cord. But it seems probable that the paralysis of the cord first observed is only apparent and not real, and in order to explain it on the ordinary hypothesis we must assume that during it the inhibitory centres in the cord are intensely excited so as to prevent any motor action, that afterwards they become completely paralysed, and thus we get convulsions occurring from slight stimuli.

On the hypothesis of interference, the phenomena produced both by atropia and by morphia can be more simply explained. These drugs, acting on the nervous structures, gradually lessen the functional activity both of cells and of fibres; the impulses are retarded, and thus the length of nervous connection between the cells of the spinal cord, which is calculated to keep them in proper relation in the normal animal, just suffices at a certain stage to throw the impulses half a wave-length behind the other, and thus to cause complete inhibition and apparent paralysis.

As the action of the drug goes on, the retardation becomes still greater, and then the impulses are thrown very nearly, but not quite, a whole wave-length behind the other, and thus they coincide for a short time, but gradually again interfere, and therefore we get on the application of a stimulus, a tonic convulsion followed by several clonic ones, and then by a period of rest. This explanation is further borne out by the fact observed by Fraser, that the convulsions caused by atropia occurred more readily during winter, when the temperature of the laboratory is low and the cold would tend to aid the action of the drug in retarding the transmission of impulses.[1]

[1] Transactions of the Royal Society of Edinburgh, vol. xxv. p. 467

The effect of strychnia in causing tetanus is very re-arkable; a very small dose of it administered to a frog st renders the animal most sensitive to reflex impulses, that slight impressions which would normally have no fect, produce reflex action. As the poisoning proceeds, slight stimulus no longer produces a reflex action limited a few muscles, but causes a general convulsion through-it all the body, all muscles being apparently put equally the stretch. In man the form assumed by the body is at of a bow, the head and the heels being bent back-ards, the hands clenched, and the arms tightly drawn the body.

My friend Dr. Ferrier has shown that this position is ie to the different strengths of the various muscles in e body. All being contracted to their utmost, the stronger erpower the weaker, and thus the powerful extensors the back and muscles of the thighs keep the body arched ckwards and the legs rigid, while the adductors and xors of the arms and fingers clench the fist and bend e arms, and draw them close to the body.[1] The con-lsions are not continuous, but are clonic; a violent con-lsion coming on and lasting for a while, and then being cceeded by an interval of rest, to which after a little ile another convulsion succeeds. The animal gene-lly dies either of asphyxia during a convulsion, or of pppage of the heart during the interval.

When the animal is left to itself the convulsions—at ast in frogs—appear to me to follow a certain rhythm, e intervals remaining for some little time of nearly the me extent.

A slight external stimulus, however, applied during the terval—or at least during a certain part of it—will bring the convulsion. But this is not the case during the

[1] Brain, vol. iv. p. 313.

whole interval. Immediately after each convulsion has ceased I have observed a period in which stimulation applied to the surface appears to have no effect whatever.

It is rather extraordinary also, that although touching the surface produces convulsions, irritation of the skin by acid does not do so.[1]

The cause of those convulsions was located in the spinal cord by Magendie in an elaborate series of experiments.

Other observers have tried to discover whether any change in the peripheral nerves also took part in causing convulsion; but from further experiments it appears that the irritability of the sensory nerves is not increased.[2]

According to Rosenthal, strychnia does not affect the rate at which impulses are transmitted in peripheral nerves; according to him, however, it lessens the time required for reflex actions. Wundt came to the conclusion that the reflex time was on the contrary increased.

In trying to explain the phenomenon of strychnia tetanus on the hypothesis of interference, one would have been inclined by Rosenthal's experiments to say that strychnia quickened the transmission of impulses along those fibres in the spinal cord which connect the different cells together.

The impulses which normally by travelling further round fell behind the simple motor ones by half a wave-length, and thus inhibited them, would now fall only a small fraction of a wave-length behind, and we should have stimulation instead of inhibition.

Wundt's results, on the other hand, would lead to the same result by supposing that the inhibitory wave was retarded so as to fall a whole wave-length behind the

[1] Eckhard, Hermann's Handb. d. Physiol. Band ii. Th. 2. p. 43.

[2] Bernstein quoted by Eckhard, *op. cit.* p. 40. Walton, Ludwig's Arbeiten, 1882.

otor one. On the assumption, however, that the fibres hich pass transversely across from sensory to motor lls, and those that pass upwards and downwards in the rd connecting the cells of successive strata in it, are ually affected, we do not get a satisfactory explanation the rhythmical nature of the convulsions. By supsing, however, that these are not equally affected, but at the resistance in one—let us say, that in the longidinal fibres—is more increased than in the transverse ores we shall get the impulses at one time thrown cometely upon each other, causing intense convulsion, at other half a wave-length behind, causing complete laxation, which is exactly what we find.

This view is to some extent borne out by the different ect produced by a constant current upon these convulons, according as it is passed transversely or longidinally through the spinal cord. Ranke found that en passed transversely, it has no effect, but when ssed longitudinally in either direction, it completely ests the strychnia convulsions, and also the normal lexes which are produced by tactile stimuli.

Ranke's observations have been repeated by others th varying result, and this variation may, I think, be plained by the effect of temperature.

Near the beginning of this paper I mentioned that the uchstone of the truth or falsehood of the hypothesis of hibition by interference was to be found in the results quickening or slowing the rate of transmission of muli.

Heat and cold are the two agents regarding whose tion in this respect we have the most trustworthy perimental data. In peripheral nerves, heat up to a rtain point quickens the transmission of stimuli, and ld retards it. In the spinal cord warmth increases the excitability, and at a temperature of 29 to 30 may of itself cause tetanus.[1] Cold also beyond a certain temperature increases the reflex excitability.

The effect of warmth and cold upon strychnia tetanus is what we would expect on the hypothesis of interference. With small doses of strychnia warmth abolishes the convulsions, while cold increases them. When large doses are given, on the contrary, warmth increases the convulsions, and cold abolishes them.[2]

We may explain this result on the hypothesis of interference in the following manner:—

If a small dose of strychnia retard the transmission of nervous impulses so that the inhibitory wave is allowed to fall rather more than half a wave-length, but not a whole wave-length, behind the stimulant wave, we should have a certain amount of stimulation instead of inhibition. Slight warmth, by quickening the transmission of impulses, should counteract this effect, and should remove the effect of the strychnia. Cold, on the other hand, by causing still further retardation, should increase the effect. With a large dose of strychnia, the transmission of the inhibitory wave being still further retarded, the warmth would be sufficient to make the two waves coincide, while the cold would throw back the inhibitory wave a whole wave-length, and thus again abolish the convulsions.

The effect of temperature on the poisonous action of guanidine is also very extraordinary, and is very hard to explain by the ordinary hypotheses, although the phenomena seem quite natural when we look at them as cases of interference due to alterations in the rapidity with

[1] Cayrade, Recherches critiques et exper. sur les Mouvements Reflexes p. 48.

[2] Kunde and Virchow quoted by Eckhard, *op. cit.* p. 44; Foster, Journal of Anatomy and Physiology, November 1873, p. 45.

ich the stimuli are transmitted along nervous struc-
es. Guanidine produces, in frogs poisoned by it, rillary twitchings of the muscles, which are well rked at medium temperatures, but are abolished by remes of heat and cold. Thus Luchsinger has found that, en four frogs are poisoned by this substance, and one placed in ice-water, another in water at 18° C., a third water at 25° C., and a fourth in water at 32° C., the illary twitchings soon disappear from the frog at 0° C., l only return when its temperature is raised to about C. In the frog at 18° C. convulsions occur, which are l greater in the one at 25° C. In the frog at 32° C., on other hand, no trace of convulsions is to be seen; the mal appears perfectly well, and five times the dose of poison, which at ordinary temperatures would con-se it, may be given to it without doing it any harm, so g as it remains in the warmth,[1] although when it is led down the effect of the poison at once appears.

Another cause of tetanus that is difficult to understand the ordinary hypothesis of inhibibitory centres is the ilar effect of absence of oxygen and excess of oxygen. en an animal is confined in a closed chamber, without gen it dies of convulsions; when oxygen is gradually oduced before the convulsions become too marked, it overs. But when the pressure of oxygen is gradually sed above the normal, the animal again dies of convul-ns. This is evidently not the effect of mere increase tmospheric pressure, but the effect of the oxygen on animal, inasmuch as 25 atmospheres of common air required to produce the oxygen convulsions, while mospheres of pure oxygen are sufficient. This effect readily explained on the hypothesis of interference supposing that the absence of oxygen retards the

[1] Luchsinger, Physiologische Studien, Leipzig, 1882, p. 44.

transmission of impulses in the nerve-centres; so tha we get those which ought ordinarily to inhibit one anothe coinciding and causing convulsions. Increased suppl of oxygen gradually quickens the transmission of impulse until the waves first reach the normal relation, and then, th normal rate being exceeded, the impulses once more near coincide, and convulsions are produced a second time.

In discussing the action of the nervous system we hav hitherto taken into account only that of the nerve fibril and left out of the question the nerve cells. We ha assumed that the waves arrived in the reservoir (in o diagram) from a distance, and were simply transmitt along channels, but in the nervous system we have take into account the origination of the waves in th nerve cells themselves, as well as their propagation alo the nerve channels.

There is a great difference between the function of t nerve cell and of the nerve fibre analogous to that whi exists between the cell and the wire in a galvanic batte The particular form of energy which we met with in bo cases originates in the cell and is transmitted along th fibre or the wire. In both cases also the energy appea to originate from chemical changes going on in the ce Material waste of some sort goes on in both, and in bo the products of this waste if allowed to accumulate w by and by arrest the action.

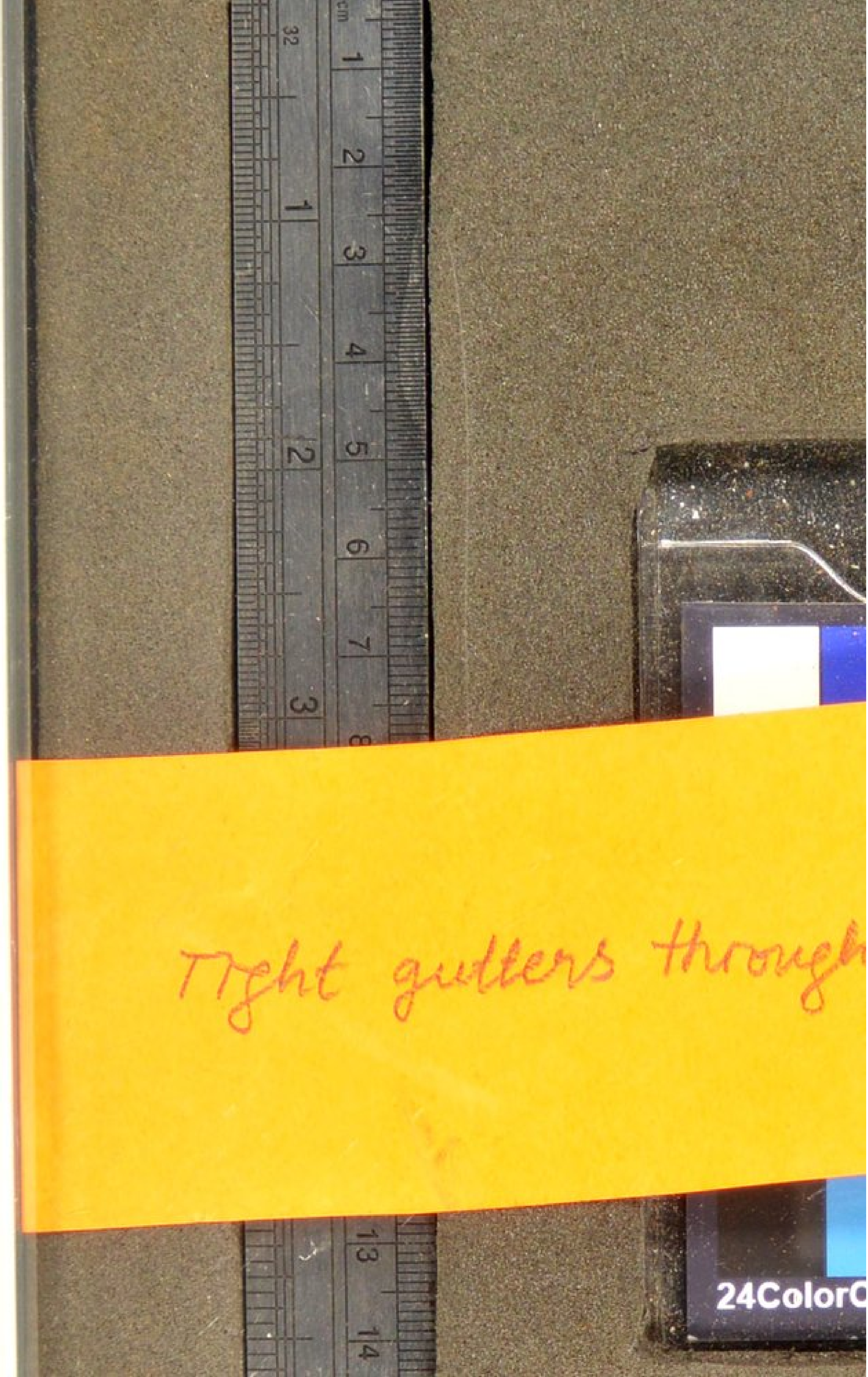
We find an indication of the difference between t amount of chemical change which goes on in the ner cell and in the nerve fibre in the amount of blood su plied to each respectively. The nerve cells are abu dantly supplied with blood, and the nerve fibres v sparingly so. The free supply of blood secures to t nerve cells both the supply of fresh material and rea removal of waste products.

Perhaps the best illustration that we can find in physics the processes which take place in the nervous and ıscular systems is however afforded by singing flames which the sounds and movements are produced by ry numerous small explosions: for both in the nervous d muscular systems the tissue change appears to go on a series of small explosions. The material which lds nervous and muscular energy undergoes oxidation; t the oxygen concerned in the process is not derived ectly from the external air. Substances which yield ygen are contained within the tissues themselves just nitre is contained along with oxidisable substances in harge of gunpowder.

In this paper also we have spoken of waves of nervous erference as if they were simple, but it is much more bbable that they are very complex, resembling much re the beats of sound produced by two singing flames ich are not in unison, than simple waves of water.

The number of nervous discharges which issue from motor cells of the spinal cord during tetanus and set muscles in action is, according to Dr. Burdon Sandern, about 16 per second, but in all probability each of se impulses consists of a large number of small vibrans. In rhythmical actions, such as that of the respiran, we have probably at the very least three rhythms, , exceedingly rapid vibrations in the nervous cells; d, slower vibrations or beats from 16 or 18 per second, ich issue from them and excite the muscles to action; d 3rd, a still slower rhythm, of 16 per minute, probably to interference between groups of cells, which leads inspiratory movements alternating with rest or with ive exspiration. The consideration of these comcated phenomena would, however, at present lead too far, and they as well as the subject of nervous interference in the heart and rhythmic contraction of muscles, must be reserved for another time.

In this paper I must be content with the attempt to show that inhibition and stimulation in the nervous system are not dependent on special inhibitory or stimulating centres, but are merely relative conditions depending on the length of path along which the stimulus has to travel and the rate of its transmission. The test of the truth or falsehood of this hypothesis is to be found in the effect of alteration in the rapidity of nervous transmission upon inhibitory phenomena. The application of this test appears, so far as our present data go, to support this hypothesis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