On

The Return of Coordinated Movements after Nerve Section and after Nerve Crossing.

By

Robert Kennedy, M.A., B.Sc., M.D., Glasgow.

In accordance with the Regulations I hereby declare that the investigations herein recorded, and the composition of this Thesis are my own work.

Robert Kennedy.

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originating ~~in a cell situated~~ at the periphery, and received by a cell in the central nervous system, or vice versa. It has long since been shown that nerve fibres are capable of conducting impulses in either direction, but functionally from their anatomical connections, the individual nerve fibres are conductors for impulses only in the one or in the other direction. Thus on severance of the posterior spinal root distal to the ganglion only certain fibres degenerate, and the conductivity of the nerve only for afferent impulses is lost, while severance of the anterior root is followed by the degeneration of the remainder, with loss of functions depending on efferent impulses.

But the conception of nerve fibre and its terminals carries us further, and leads to the view that a particular nerve fibre is concerned only with the conduction of impulses from a particular point, e.g. from a particular sensory area in the skin, or on the other hand that it is concerned with the passage of impulses from a particular central cell to particular end organs. The individual nerve fibres are thus viewed not as common conductors for impulses originating from different points, but each as a specific conductor for impulses starting in a particular cell and received at the other end in a particular cell. Thus a transverse section of a mixed nerve with its innumerable nerve fibres might, if knowledge were sufficiently exact, have each of the latter named according to its origin or distribution.

It is true that the passage of the nerve fibres between the peripheral organ and the brain is not necessarily continuous, but may be interrupted by the intervention of cells; but in the modern conception of the neuron, the cell body situated in the cornua of the cord connects directly with the peripheral organ by means of its neuraxon, while the cell body ~~in the cornua~~ receives ~~or passes on~~ its stimulus from another definite cell, situated it may be in the cortex by means of the neuraxon of the latter. The individual nerve fibres in a nerve must, however, be regarded as paths for the conduction of impulses each from a definite point to a definite point.

A nerve is thus both from the point of view of its morphology and of its physiology a highly specialised structure, and it is not surprising, therefore, that the study of its repair after division should lead to problems of great difficulty.

Two modes of repair after division have been described, namely, that by first intention, and that by regeneration of the peripheral segment. In the former case, it is supposed that after the division of the fibre, the two ends speedily become connected again, so as to restore the fibre as before the division. After such a process of reunion, the peripheral segment is still the same structure which, before the division, conducted the impulses. This view then carries with it the supposition that when the nerve fibres heal by this process, the Wallerian degeneration does not take place; that after the section the peripheral end becomes again connected with its trophic centres before the advent of degeneration, so that by the early restoration of the influence of the centres, the degeneration is avoided. The evidence which is advanced by those who regard this as a possibility is the early return of function, but before such a process can be accepted as possible, it would be necessary to have anatomical proof from microscopic preparations of the peripheral segment of a recently divided and reunited nerve, that the peripheral segments of the fibres present the normal characters of adult medullated fibres, and that degeneration remains are absent. This is what I have been unable to find satisfactorily in the papers of those authors who claim that healing by first intention is possible, the evidence relied on being chiefly that of early return of function.

In the other process of repair of a nerve, after destruction of the peripheral segment by Wallerian degeneration, the peripheral segment is regenerated, and the continuity of the nerve to its end organs thus restored. On the process by which this is effected there has been much difference of opinion. That described by Ranvier (17) of outgrowth, from the central segment, of processes from the old axis-cylinders, which continue their growth till they reach the end-organs is the view which has been most widely accepted, while the other view is that simultaneously with the degeneration new fibres are formed in the peripheral segment, independently of the central segment, and that these become connected with the old fibres of the central segment. The process described in the former view necessarily requires for its accomplishment a considerable period of time, a period of time which is longer the further the section is made from the peripheral terminations of the nerve. It is the acceptance of this view which gave origin and support to the view of healing by first intention, as something had to be supposed to explain cases of early return of function after section. On this view, and on the view of development of the nerve fibres advanced by Kölliker (13) and His (8-10) is founded the modern conception of the "neuron". According to the second view, it is not necessary to suppose a lengthened period of time, or a different period of time according as the section is made near or far removed from the terminals, until the nerve becomes again a functional structure.

Both from clinical and from experimental experience, it is established that early return of function can take place; but there are certain fallacies which should be guarded against in judging of the value of early return or of late return of function after section. Thus where early return of function takes place after nerve section, it is necessary to remember the possibility of a vicarious nerve supply, and where late recovery takes place, this is not conclusive evidence in favour of the view of Ranvier, as the reunion of the nerve at first may be inadequate to permit of function being carried on through the segment of reunion. Thus failure of the wound to heal without suppuration will lead to delay or even to failure of reunion. Early return of function may, therefore, mean vicarious nerve supply, and late return may mean only inadequate reunion of the nerve.

But there are certain cases in which very early return of function occurs after suture, which preclude the possibility of vicarious nerve supply, and which cannot be explained as cases of healing by first intention without degeneration of the peripheral segment. I refer to cases in which reunion has failed after the section, and in which after a period more or less prolonged, an operation is undertaken for the secondary reunion of the central and peripheral ends. In such cases no vicarious return of function has taken place, and yet after reunion at the secondary operation, the function which for a long period has been in abeyance speedily returns. Such return of function can only be explained as due to the secondary operation restoring the conductivity of the nerve, and the speed with which function returns implies the view that the peripheral segment, though separated from its centres, has in the interval formed new fibres in a condition, when united to the central segments, to conduct impulses. But what is remarkable about such cases is that not only does sensation return in the parts which were formerly insensitive, but, though at first indefinite, within a remarkably short period of time, localisation becomes perfect. Thus in cases which I have published (12) in which the nerves had been completely divided, and had not reunited, and in which a secondary operation was followed by return of sensation in a few days, localisation was found by repeated examinations to be well established by at least a month. It is easy to understand, on the supposition of independent regeneration of the peripheral segment, how function might return in a very short time after reunion, but the speedy or even remote perfection of localisation is not what we should expect from our conception of the functional differentiation of the nerve fibres. How is it possible that immediately after division of a nerve or more so, in a secondary operation for repair of a non-united nerve, in bringing the ends together by suture, that the central ends of the individual nerve fibres can be brought to lie opposite their proper peripheral ends? We should certainly expect that considerable confusion of localisation of sensation, and of coordination of movements should result from unavoidable imperfect coaptation. This difficulty is common to all the views of repair of divided nerves. In healing by first intention, if it exists, and in healing by regeneration of nerve fibres by independent formation in the peripheral segment, it is scarcely possible that the nerve ends will be so accurately coapted that all the corresponding nerve fibre segments will be brought into apposition. With the view of Ranvier the position is no better, for there the sheaths of Schwann of the old fibres, which are to act as the guide for the growth of the new fibres to the terminal organs can scarcely be supposed to be brought by the suture into line with their proper central segments. Also if we take the view held by Vanlair (24-25) and others that the new sprouting fibres simply run in the endoneurial spaces, how can the new fibres be guided to their appropriate terminal organs?

From these considerations I have been led to inquire if a difference in the resulting return of function will obtain between reunion with the most accurate coaptation, and reunion with the most extreme displacement of the

one segment with reference to the other. In two dogs I divided the sciatic nerve at the level of the trochanter, and after rotating the peripheral segment to the extent of a semicircle reunited it to the central end.#
To insure that this displacement was accurately carried out, the suture was placed before the division of the nerve. The nerve having been raised from its bed on the point of the finger, it was transfixed by the needle threaded with chromicised catgut. The needle was then carried through below the nerve, and the nerve again transfixed at a lower level in the same direction as before. Next

I am indebted to Professor McKendrick for suggesting this form of experiment. Experiment I was performed in the Physiological Laboratory, University of Glasgow, and the other experiments in the Glasgow Veterinary College, thanks to the kindness of Principal McCall, while the remainder of the work was carried out in the Zoological Laboratory, University of Glasgow.

the nerve was divided between the two points of transfixion, the result being that on tying the suture the peripheral segment was rotated with reference to the central segment through a semicircle. Thus the two segments were coapted so that the fibres of one side in the central segment were brought into line with those of the opposite side in the peripheral segment. Only the fibres in the centre of the nerve were approximately correctly coapted. In a third experiment, to serve as a control to the first two, the same nerve was divided at the same point, and accurately coapted, the suture being placed before the division so as to insure accuracy of coaptation in the normal position.

Experiment I.

On January 19th, 1898, a collie bitch, aged 15 months, having been anaesthetised by means of a subcutaneous injection of 0.5 gram. sulphate of morphia, followed by inhalation of ether, the hair was shaved from a considerable area around the trochanter and tuber ischii of the left side. The skin was then thoroughly scrubbed with soap and warm water, next with turpentine, then with alcohol, and finally with 5% carbolic lotion. The precaution taken to prevent contamination of the wound during the operation was to fix round the body a jaconette sheet with an oval aperture in its centre sufficiently large to expose only the field of operation. The instruments, dressings, ligatures &c to be used had all been previously sterilised. After sterilisation of the hands, the sciatic nerve was exposed as it passes between the trochanter and the tuber ischii. The nerve held up on the point of the finger, was transfixed by a flat needle threaded with chromicised catgut. The needle having been drawn through was passed underneath the nerve, and the nerve again transfixed parallel to the first transfixion, and in the same direction but about a quarter of an inch lower down, and drawn through leaving the catgut suture in place. The nerve was then transverse ly divided between the two points of transfixion, and the suture tied. The result of the two ends having been transfixed by the catgut in the same direction was, of course, that on tying the knot the two ends of the nerve could only be brought into apposition after rotation on their long axes with reference to each other through a semicircle. Thus the fibres running down the external side of the central segment were brought into appositon with the fibres on the internal side of the peripheral segment, and vice versa, the displacement of the ends of the fibres being thus made as extreme as compatible with coaptaton of the two ends of the nerve. The subcutaneous tissue and the skin were then separately united by sutures, dressings applied, and the entire limb fixed by plaster of Paris bandages, commencing above the toes, passing up the limb, and round the body, a thick double copper wire moulded to the parts being incorporated in the bandage.

The effect of the morphia was to keep the dog in narcosis sufficiently long to allow of complete drying of the plaster of Paris without breakage.

At the end of the second day, the animal was able to stand on the splint. There was no sensation on pricking the foot with a needle, except over a small area on the inner side of the innermost toe from twigs of the saphenous nerve.

By the end of the third day the dog was walking freely about, using the splint as a support, but dragging the foot along the ground with the dorsal surface down. The foot was therefore bandaged so as to keep the plantar surface down, in order to prevent further excoriation of the dorsal surface.

At the end of the seventh day, on removing the supporting bandage from the foot, the dog was able to walk across the room, placing its foot with the plantar surface down. On passing a projecting board on the floor, the foot was turned back and the animal rested on the dorsal surface, but next step the foot was restored to the normal position with the plantar surface down. On pricking the skin with a needle the animal gave no sign of pain, although it turned round and commenced to lick the paw vigorously.

At the tenth day the first definite sign of returning sensation was got, as the animal now withdrew the limb when the paw was pricked.

At the end of the 14th day the splint was removed and the wound was found healed, and the stitches were removed. The animal then walked well on the unsupported leg, always placing the plantar surface of the paw correctly, although it threw the leg a little outwards in a movement of circumduction at each step; but it was not markedly lame. Occasionally it missed a step carrying the leg forward with a hop.

On the following day the sound leg

was held up without supporting the weight of the body, and it was found that the dog was able to walk supporting the hind part of its body entirely on the affected leg. Occasionally the foot was placed with the dorsal surface down, and to give it support a figure of eight bandage was again applied to the paw to hold it in the extended position.

At the end of the 19th day, the dog was running about without any trace of limping, and while running about only once or twice the paw was observed to be turned over on the dorsal surface by the toes scraping the ground, but on these few occasions the normal position was regained at the next step. The position of the leg in standing, walking, and running was the same for the affected as for the other leg, and the degree of voluntary extension and flexion at the tibio-tarsal articulation was the same in the two legs. Only slight atrophy was noted in the mus-cles, no hair had fallen out, the nails were normal, and two small erosions on the dorsum of the paw, caused by scraping along the floor during the first day that the animal was walking about, were now healed.

The animal distinctly now felt the prick of a needle in the paw, as when this was done it always looked sharply round, and attempted to withdraw the limb, at times attempted to bite, and always turned and licked the paw. In testing the sensation of the paw, sensation on the inner side was not taken as evidence of returning function, as this part was sensitive from the earliest examination, being innervated by twigs of the saphenous nerve. The difficulty of ascertaining the return of sensation is illustrated by the fact that when pricked on the sound leg or paw the dog sometimes gave no sign.

On the 21st day sensation was considerably improved, as during the examination of the paw, the animal's head had to be held as it frequently snapped when the foot was pricked. An attempt was made to ascertain the localisation of sensation by blindfolding the animal and attaching a bulldog forceps to the limb; but it was futile, as the animal's first endeavours were always to remove the bandage from its eyes.

On the 31st day the animal was photographed in the standing posture assumed by itself. (Plate I.)

On the 54th day the animal having been again anaesthetised by chloroform and ether, after having a subcutaneous injection of sulphate of morphia, the skull was trephined over the region of the crucial sulcus on both sides, and this region of the brain exposed. Stimulation of the centre for the hind leg on the post-crucial gyrus by a faradic current just to be felt on the tip of the tongue gave no reaction, but when the current was slightly increased, the normal reaction was induced, being the same movement as obtained on the right leg by stimulation of the centre on the left hemisphere. The movement consisted in advancement of the leg as in walking, and no other movement could be induced, until the current was greatly increased, when general convulsions of the body ensued.

The seat of suture of the nerve was next exposed, and the nerve was found united, there being a neuroma at the seat of reunion. The torsion of the nerve produced at the operation was clearly maintained. The peripheral segment showed this torsion commencing about one and a quarter inches from the seat of reunion. Stimulation with a very weak interrupted current induced contractions when the electrodes were placed above the seat of reunion, on the neuroma, and below the neuroma. The animal was then killed, while still under the influence of the anaesthetic, and various portions of the reunited nerve removed for microscopic examination.

On excising the segment of reunion, the upper and lower transverse sections exposed, showed that the nerve at this level consisted mainly of two fasciculi; one large and the other small. On comparing the proximal and distal ends of the segment, it was ascertained that the position of the large fasciculus exposed at the one end corresponded with the position of the small bundle exposed at the other end, and vice versâ, thus proving that the nerve had reunited in the position, which was given it at the operation.

Experiment II.

On 13th April, 1898 a collie bitch, aged one year, having been anaesthetised by means of a hypodermic injection of 0.5 gram. morphia sulphate, followed by inhalation of ether and chloroform, and the same anti-septic precautions having been taken as before, the same oper-ative procedure was carried out as in the case of Experiment I, i.e. the left sciatic nerve was divided at the level of the trochanter, and the ends sutured together with carbolised catgut, wit:

the central and peripheral segments rotated on their long axes in opposite directions, with reference to each other to the extent of a semicircle. The fascia and skin were separately sutured, and the hip, knee, and ankle joints immobilised by means of plaster of Paris bandages.

On the following day, the animal was making no attempt to walk on the splint. There was no sign given of sensation on pricking the paw with a needle, except over the small area on the inner aspect of the paw which is supplied by the saphenous nerve. The paw was fixed by a figure of eight bandage, to keep the foot from being turned over with the dorsal surface down, and thus becoming abraded in the event of the dog making attempts to walk.

At the end of the second day

the dog was sitting up, resting on the splint. When pulled along by its collar, it walked on the splint, but dragged the paw along the ground dorsal surface down.

On the following day the animal was walking freely about, but when the foot was unsupported by the bandage, it always was dragged dorsal surface down.

This state lasted till the end of the 7th day, when it was found that, while no evidence of returning sensation could be obtained, the animal had now regained some control over the paw, as it walked well, and with the paw left unsupported placed it correctly on the ground plantar surface down. Occasionally the toes catching on the ground the paw was turned over, and rested on the dorsal surface, but after having been scraped along the ground in this position for two or three steps was again voluntarily replaced in the correct position.

At the end of the 8th day the plaster of Paris splint was removed, and the wound was found healed by first intention, and the stitches were removed. The leg was somewhat atrophied, but there was no other trophic change. The animal used the leg in walking, not however resting its whole weight on the limb, but as a rule it placed the paw correctly plantar surface down, readjusting it, when it turned over, as it occasionally did by the toes scraping the ground.

Improvement in walking advanced day by day, the foot turning over on the dorsal surface less and less, until, when examined at the end of the 21st day, the animal constantly walked on the leg, always placing the plantar surface down, and supporting the entire weight of the hind part of the body on the affected leg in the normal position, while the sound hind leg was held up. Sensation was now evidenced as when the part of the paw formerly anaesthetic was pricked with a needle, the animal withdrew the limb.

At the 30th day the complete recovery of the use of the leg was maintained, and the muscles were much increased in bulk. The dog was therefore killed, and the seat of suture exposed. The nerve was found reunited, the seat of reunion presenting a slight swelling on the central and peripheral ends united by a short segment having the diameter of the normal nerve. The torsion given at the operation was clearly visible. Stimulation above and below the seat of reunion evoked contractions in the muscles of the leg.

Experiment III.

On 13th April, 1898, a collie bitch, aged about six months, was anaesthetised by a hypodermic injection of 0·4 gram. morphia sulphate, followed by inhalation of chloroform. The same antiseptic precautions as before having been taken, the left sciatic nerve was exposed at the level of the trochanter, divided, and accurately reunited in the normal position with carbolised catgut. The accuracy of adjustment was secured by placing the suture before the division of the nerve, the suture having been carried through at two points a quarter of an inch apart, passing through the nerve in opposite directions. After section the tying of the catgut suture therefore brought the two ends together as nearly as possible in the normal relationship to each other. The limb was then immobilised in the same manner as in the other experiments.

On the following day sensation tested in the paw was found to be absent except over the inner side.

On the 3rd day the animal was walking on the splint, but dragging the paw along dorsal surface down. This condition lasted till the 7th day, when the animal was found to walk with the plantar surface of the paw on the ground. The paw, however, frequently turned over with the dorsal surface down, and was then dragged, and was so till the foot was passively again placed in the normal position, apparently there being no voluntary power of re-adjustment.

On the 8th day the plaster of Paris splint was removed, and the animal was found to be able to use the leg for walking, not however resting the full weight on it. It walked with the plantar surface down, but frequently the paw turned back with the dorsal surface down, but now it had regained sufficient power to enable it to voluntarily readjust the position. The wound was found healed and the stitches were removed. There was no return of sensation as far as could be ascertained.

Improvement in the muscular power and control advanced, and on the 11th day the animal was able to run about freely on the leg, only occasionally getting on to the dorsal surface of the paw, and then voluntarily re-adjusting it after one or two steps. There was distinct evidence of returning sensation, as when pricked over the formerly insensitive region of the paw and leg, the animal whined and withdrew the limb. When pricked on the paw while standing it at once withdrew the leg with flexion at the tibio-tarsal joint.

The dog by the 14th day was running about apparently quite recovered, and never treading on the dorsal surface of the paw. The only differences to be found in the two legs were the less keen sensation, and the slight atrophy of the muscles.

On the 49th day the animal was killed, and the seat of section having been exposed the nerve was found united, a neuroma having been developed at the seat of section.

Stimulation with a weak current above and below and on the seat of reunion caused muscular contractions. The muscles were apparently normal, although somewhat less bulky than those of the opposite side.

Comparison of Experiments I, II, and III.

The conditions of these three experiments coincided so closely, that a comparison between the three is justifiable. All the dogs were of the same kind, and all were young. The same nerve in all was divided at the same point, and the healing of the wound in all was satisfactory, in no case becoming septic.

In Experiments I and II, however, the peripheral was sutured to the central segment after having been rotated on its long axis to the extent of a semicircle, while in Experiment III the reunion was made in the normal position. Experiment III was, thus, a control experiment to ascertain if any important differences could be detected in the course of recovery of function in the two cases, namely, in the case where the corresponding central and peripheral segments of each of the nerve fibres were brought to lie as closely as possible opposite each other, and, on the other hand, in the case in which these two segments were displaced from each other as far as compatible with suture of the nerve stem, non-corresponding segments of the nerve fibres being thus brought into apposition.

During the first six days the course was the same in all three. Thus after a day or two the dogs were up, and walking about on their splints, but with no return of function, the paw being simply dragged along the ground dorsal surface down.

In all three the 7th day brought the first improvement; for on this day all were able to walk with the plantar surface of the paw on the ground.

In all the foot frequently was turned over while walking, bringing the dorsal surface into contact with the ground, and in Experiments I and II the animal had the power voluntarily to readjust the abnormal position of the paw and again place it plantar surface down, while in Experiment III no voluntary power in this respect was shown, and the foot had to be passively replaced in the normal position. No sign of returning sensation could as yet be got on pricking the affected parts with a needle.

On the 8th day the plaster of Paris splint was removed in the case of Experiments II and III, and in both the animal was able to use the leg for walking without any support, flexing and extending the leg at the tibio-tarsal joint, and placing the plantar surface of the paw correctly, and now voluntary power to replace the paw when it turned over had been regained in Experiment III.

The first sign of returning sensation, namely, withdrawal of the limb on pricking the paw with a needle, was shown in Experiment I at the 10th day, and in Experiment III on the 11th day, while Experiment II showed no sign, till the 21st day; but the evidence as to the date of return of sensation was very unsatisfactory as the animals were of such a docile nature that they often allowed the sound leg to be pricked without making any sign. There is, therefore, no doubt that during the early days of returning function the animals would not be likely to show signs of sensation, if this was less keen than normally.

At the 14th day the splint was removed in the case of Experiment I, and the animal used the leg perfectly in walking and running, always placing the plantar surface down, and in Experiment II, the foot very seldom turned over on the dorsal surface, and in Experiment III, the same progress was made.

By the 21st day all had recovered not only the use, but also the power of the leg so perfectly that the animals appeared to be perfectly normal, only close inspection showing that the affected limb was somewhat less bulky than the opposite limb.

Microscopic Examination.

Methods. Immediately after the death of the animals, portions of the nerves were removed for histological investigation. The portions removed were — a portion including the segment of reunion, portions from the central segment, various portions from the peripheral segment and its branches muscular and cutaneous, and a portion from the opposite sciatic at the level of the section.

A number of glass rods with the two ends bent over in the form of rings were at hand, and the portions removed were each stretched between the two rings of one of the glass rods. The glass rod is, I think, preferable to wood or cork for stretching, as by its use there is no possibility of contamination of the fixing reagent.

The portions of the nerve fixed to the glass rods were then placed in Müller's fluid, in which with frequent renewals of the fluid they remained for eight or ten weeks. They were then prepared for paraffin, imbedded, and longitudinal sections of the seat of reunion, and longitudinal and transverse sections of the remaining portions prepared with the Cambridge rocking microtome, and fixed in series on albuminised slides.

The chief method of staining employed was that recommended by Stroebe (23), but as I had formerly some difficulty in getting adequate staining of the axis-cylinder by this method, although closely following the directions given in Stroebe's paper, I give here the steps of the process which I have followed, and by which fairly good differentiation of the axis-cylinder has been obtained. The deviations from the method are principally those of time allowed for each step.

1. After removal of the paraffin the slide bearing the series of sections is washed for a few minutes in running water, so as to displace the alcohol, and then placed in a tube containing freshly prepared saturated aqueous solution of Anilin blue (Grübler's for Stroebe's stain) in which it remains for 24 hours.

2. The slide is then washed in running water for some minutes.

3. 15 drops of a 1% solution of caustic potash in absolute alcohol are added to 12 c.c. absolute alcohol, and the slide after having the superfluous water removed is placed in the dish containing this liquid. The dish is rocked from side to side, and the blue stain is extracted from the sections, and this process is continued until the sections have a blanched blue appearance

usually about one minute or less. Formerly I allowed the sections to remain in this destaining liquid too long, waiting for the clear brown red colour described by Stroebe to appear. But this tint never appeared, and the sections when examined were found to be over-destained, and the axis-cylinder therefore badly differentiated. I found afterwards that with thicker sections cut in celloidin the sections did assume a brownish red tint in the destaining liquid, while the stain was removed in brownish red clouds; but with the extremely thin sections cut by the rocking microtome it is only at the moment at which the sections are placed in the liquid that a slight brownish red cloud is extracted, after which the blue of the section simply continues to fade. The obvious explanation of the difference is that with the thicker sections the brownish red altered stain is not so easily washed out by the alcohol, and remaining entangled in the tissue gives the section the brownish red tint, while with thinner sections the altered stain is at once washed out by the alcohol leaving the bluish tint unaffected.

4. The slide is next washed in running water for some minutes, when the intensity of the blue is somewhat restored.

5. The slide is then placed in a tube containing anilin water safranin solution, in which it remains for half an hour.

6. It is then rinsed in water, dehydrated rapidly in absolute alcohol, and treated with oil of cloves. This is allowed to remain on till the red colour begins to fade, but before the bluish colour reappears, when the oil is drained off.

7. The clove oil is then washed off with xylol, and the sections mounted in balsam.

Much depends on stopping the extraction of the safranin by the oil of cloves at the right moment, as if not allowed to act long enough the axis-cylinders appear red, and if, on the other hand, allowed to act too long, the colour is extracted from the myelin and nuclei.

An addition to the method which gives very beautiful results in some cases is rinsing the slide after removal from the safranin solution, for a few moments in a very dilute aqueous solution of eosin. With this addition, all parts of the section are stained red, except the axis-cylinder which stands out in blue, and the clear differentiation thus obtained between the young axis-cylinder and the connective tissue fibres is of much advantage; but the objection to the method is that the eosin is apt to stain also the axis-cylinders so intensely as to be incapable of being removed by the oil of cloves, unless the immersion in eosin is very short, and possibly in all cases some of the finer axis-cylinders are thus stained.

Histological Characters.

The central segments of all three down to about 5 mm. of the seat of reunion present the characters of a normal nerve. (Plate V) Comparison with sections made from the opposite sciatic brings out only one difference, namely, that the nerve is thicker than the normal sciatic, and that this increase in bulk is due not to any numerical increase in the nerve fibres, not to any hypertrophy of the fibres themselves, nor to overgrowth of connective tissue, but to the fact that the nerve fibres are separated from each other by wider spaces than in the normal nerve. The increase in thickness is, then, due to distension of the lymphatic spaces surrounding the nerve fibres. At a distance of about 5 mm. from the termination of the central segment, the alteration in character of the nerve commences, for here many of the medullated nerve fibres are seen to cease abruptly, often in bulbous ends and their place to be occupied by a bundle of young nerve fibres. As the termination of the segment is further approached this replacement of old fibres by new becomes more and more complete, until finally about 2 mm. from the termination no adult medullated fibres are present, and the entire fasciculus is composed of new-formed nerve fibres. The only difference between the three central segments is that of stage of development, for while in Experiment I no distinct traces of degenerative products remain, in Experiment II there are distinct remains of the old myelin between the young nerve fibres, and also, but to a much less extent, in Experiment III.

The peripheral segments (Plate VI) of all three agree in presenting full regeneration by young nerve fibres, and this is the case throughout the whole extent of the nerve and its branches muscular and cutaneous. All were examined both close to the seat of reunion and far removed from it without showing any adult nerve fibres.

In Experiment I the nerve close to the seat of reunion presents many young fibres which are well developed, each presenting a clearly defined axis-cylinder, traceable for considerable distances in the section, a thin but well marked medullated sheath, and a delicate sheath of Schwann, having at intervals spindle shaped nuclei encroaching on the medullary sheath. Such fibres are however very much smaller than the medullated nerve fibres of the central segment. Many other fibres are present which show less distinct characters and are finer, but in which the axis-cylinder is equally distinct, but with less prominent medullated sheath; while in other cases the axis-cylinder is so indistinct as to be recognisable with difficulty and only in parts of the fibre, the parts in which it is not recognisable looking very like connective tissue fibres. In this section of the segment there are a few bulky leucocytes present but no distinct remains of degenerated old fibres.

In portions of the branches of this nerve from the middle of the leg the most striking difference is that there are present remains of the degenerated old fibres — balls of myelin arranged one behind the other forming short spindle shaped groups, together with many leucocytes loaded with degeneration products. But between these degeneration remains are present abundant young nerve fibres either singly or in bundles.

In Experiment II the peripheral segment presents also an abundant supply of young nerve fibres, but being at the 30th day of development the stage is not the same as in Experiment I, which is at the 54th day of development. The essential differences are that the young nerve fibres do not show the medullated sheath so distinctly as do the furthest advanced fibres in the case of Experiment I, and that degeneration remains are still present close to the seat of reunion lying between the young nerve fibres, while in the sections prepared from the terminal divisions of the nerve the degeneration remains are still more abundantly present, with the young fibres still finer and less distinct.

In Experiment III at the 49th day of development, the young nerve fibres are not quite so far advanced as in Experiment I, and some distinct remains of old degenerated fibres are still present not only in the terminal divisions of the nerve, but also close to the seat of reunion.

In the nerve cicatrices, (Plates (II, III, IV)) the appearances presented in each of the three experiments show no important differences. The fasciculi of the central and of the peripheral segments pass into the cicatrix, the individual nerve fibres diverging to some extent, the fibres of the central segment at this point being as in the peripheral segment in every case new-formed fibres. The continuity of these fibres across the cicatrix is not traceable, although in some parts, especially in the case of Experiment I, it is clear that the fibres do in reality pass right across, but they are not traceable simply from the fact that they pass out of the plane of the section. This in Experiment I is shown in the middle line of the section, in which fibres may be traced for a considerable distance until they suddenly terminate, their further course being contained in other sections of the series. But fibres which for some distance have run parallel, but which drop out of the section when traced centralwards, continue their course into the peripheral segment. In the greater part of the cicatrix the fibres evidently run a very tortuous course, as they are seen in the sections cut in all directions, some showing for short distances in longitudinal section, while others appear as small clusters of transversely cut fibres. The whole cicatrix has a fairly dense appearance being made up of an interlacing tangle of fibres. Much of this tangle is composed of undoubted young nerve fibres, the stain bringing out the axis-cylinders, but in addition there are present undoubted connective tissue fibres, and fibres of which it is doubtful whether they belong to the one or to the other category. The appearances presented are, in short, those of a neuroma, and this description may be applied to the cicatrices from all three experiments.

Deductions from Experiments I, II & III.

The results of these experiments show that in the dog there is in the case of section of the sciatic nerve no important difference in the return of function, whether the two ends of the nerve are sutured so as to bring as nearly as possible the corresponding segments of the fibres into accurate apposition, or whether by rotation of the peripheral segment the ends of nerve fibres which do not correspond are brought into apposition. Provided that the two ends of the divided nerve are brought together whether in the old relationship or in a new, reunion of the nerve follows, and the normal function returns. This return of function also not only is qualitatively the same in the two cases, but the time taken for the first evidence of restoration to be exhibited is also the same, namely, seven days, and the further improvement which rapidly follows runs in both cases essentially the same course. The volitional coordinated movements of the hind leg were regained as soon in Experiments I and II as in Experiment III. This is the more striking in a nerve like the sciatic which not only is distributed to so many different structures, but which is composed of nerve fibres which supply antergic muscles, or muscles with antagonistic functions. Thus, when the animals commenced to walk on their splints, the paw was always dragged along the ground with the dorsal surface down and the toes directed backwards; but on the seventh day, being placed in walking with the plantar surface down, indicated a return of function in the extensor muscles; and it is noteworthy that in Experiments I and II there was more control over the extensor muscles than in Experiment III at the seventh day, as in the former cases, the animals had the power voluntarily to readjust the position of the foot when it turned back a power not shown in the latter case till the day following.

Such early return of function suggests the likelihood of the nerve having united by first intention, but as stated above such a view implies that Wallerian degeneration had not taken place, being prevented by the early reunion of the peripheral segment to its trophic centres, and that the nerve fibres of the peripheral segment in the reunited nerve are the identical fibres which existed before the section. That this was not the case is proved by the microscopic examination; for not only are no adult nerve fibres found in the peripheral segment, but in all cases evidence of degeneration of the old fibres is abundantly present.

Vicarious nerve supply has often been suggested as an explanation of early return of function but in the experiments this possibility is quite excluded, from the extensive distribution of the sciatic. Thus the section of the sciatic at the level of the trochanter certainly paralysed all the muscles below the knee joint, and thus the recovery of flexion and extension of the paw and at the tibio-tarsal articulation implies regained conductivity of the sciatic, as there is no other nerve entering the leg which could possibly have taken up the functions of the sciatic. The prompt muscular responses elicited by stimulation of the nerve above, below, and on the cicatrix at the final examination also proved that the muscles were still innervated through this nerve.

The early return of function is adequately explained by the view of regeneration of nerves which I have already elsewhere advocated (12), namely, that the young nerve fibres are formed in the peripheral segment simultaneously with the degeneration process, and that they become connected with those of the central segment by young fibres formed in the cicatrix from cellular elements which have migrated into the cicatrix from both ends of the nerve, the cellular elements in question being derived by proliferation from those of the sheath of Schwann.

The uniform time at which function commenced to return, and the uniform rate with which improvement advanced are, I think, explained by the fact that in all cases the wounds healed without becoming septic, a result due not only to the strictest antiseptic precautions, but also to the complete immobilisation of the entire limb while the process of healing was in progress. A nerve may certainly unite and conductivity ultimately be restored even although the wound becomes septic, a fact of which I have recently obtained clinical proof, but the return of conductivity is in such cases uncertain: it may never return, but if it does so it is much delayed. But if the wound runs an aseptic course, the experiments would seem to show that return of function takes place uniformly, and no matter whether the two ends of the nerve are united in their old relationship or not.

The uniform manner in which return of coordinated function was established in the experiments might be hypothetically explained in different ways. Thus it might be supposed that in the cicatrix, in Experiments I and II, which formed between the two divided ends of the nerve crossings of the young nerve fibres were effected so as to place the corresponding nerve fibre segments in connection. Such a view need not imply such an improbable property as inherent faculty or instinct in the nerve fibres to grow towards their appropriate peripheral segments, but might possibly be brought about by a process more in accord with natural law. Thus at the earliest stage of development of nerve fibres in the cicatrix, when the spindle cells derived from the immigrated neuroblasts were making connections one with the other, it is conceivable that the nervous impulses would at first pass into the network of spindles in the cicatrix, and be communicated to the fibres of the peripheral segment diffusely, the impulse passing along a single central fibre being diffused through many or all of the nerve fibres in the peripheral segment. On such a supposition, it is possible that the old path in the peripheral segment would be the easiest for the passage of the impulse, and that the connections in the cicatrix which established the passage between the corresponding ends of the fibres would, therefore, from being the most selected route, become more rapidly developed, structural development thus following on functional activity. Thus, in the cicatrix paths of connection between corresponding nerve fibre segments would be established.

On such a supposition it would be expected that the microscopic appearances would be different according as the two nerve segments were accurately coapted or not, as in the former case the connecting nerve fibres might be expected to follow an approximately direct course in the cicatrix, and in the latter to follow a crossed course, to show in other words a decussation. But the microscopic appearances in the three cicatrices as stated above presented no very marked differences, in each case showing throughout much convolution of the young nerve fibres. The microscopic appearances, however, although they do not prove that corresponding nerve fibre segments become connected, do not disprove it, as in Experiment III the convoluted course exhibited by the nerve fibres does not necessarily preclude the possibility of the corresponding fibres connecting, although by a tortuous path. It is, therefore, impossible to state from the above experiments whether or not the return of coordinated movements was the result of the reestablishment of the old paths for nervous impulses, although the histological appearances render the possibility extremely doubtful.

The return of function might be explained in a different way. Thus it is possible owing to the intimate admixture of the nerve fibres in the nerve stem, that despite the altered relationship of the two segments, yet fibres were brought into juxtaposition which innervated muscular fibres in close proximity, i.e., muscular fibres belonging to the same muscle or group of muscles, and that therefore the resulting incoordination was so slight as to be without functional importance. Such a supposition would of necessity leave much to the operation of chance, and would mean in a nerve like the sciatic with its extensive distribution to antergic muscles, that the functional result would be the balance between the number of fibres distributed to flexor muscles, and the number to extensor muscles which happened to be brought into apposition. It can scarcely be supposed that the admixture of nerve fibres in the nerve stem or the relation in which the two segments are placed in different cases of suture, is so uniform that this balance would be identical in different cases, and consequently on such a view a difference in development of returning function would be expected, not only in different cases of experiments such as I and II, but a marked difference in development of function would be expected between cases of accurate and of inaccurate coaptation. The supposition is therefore an unlikely one, as not only did Experiments I and II agree in the date of returning coordination and in following a practically identical course, but the same also occurred as between Experiments I and II and Experiment III.

The third hypothesis which may be brought forward to explain the results, is that although non-corresponding segments of the nerve fibres were made to connect by the mode of suturing the nerve, yet the nerve centres brought by the altered paths into connection with new peripheral endings were capable speedily of altering their characters, and of supplying the required nervous impulses in perfect coordination. This hypothesis implies a capacity of the organism to undergo a profound change in the functions of the central nervous system. It implies that the centres controlling different groups of muscles can interchange their functions and carry on coordinated movements as before. Before considering how such a change might take place, it is necessary to ascertain if it is possible to obtain proof of the possibility. This question has frequently been tested by means of nerve crossing, or the division of two neighbouring nerves and cross union of the ends by suture, to ascertain if under the new conditions the animal would regain its lost functions.

The first experiment of this kind was conducted by Flourens (3.) as early as 1824. In a cock he cut "the two chief nerves which go from the brachial plexus, the one to the superior aspect, and the other to the inferior aspect of the wing." On section of these nerves the wing drooped completely, and its extremity could not be moved at all. He then crossed the nerves "joining the superior end of the one nerve with the inferior end of the other and vice versâ" and maintained them in this position by means of sutures. "At the end of some months the animal had perfectly regained the use of the extremity of its wing which no longer drooped, and made use of it for flying quite as well as before the experiment." On exposing the nerves which had been crossed, he found that the position in which he had placed them had been maintained. He irritated the exposed nerves above, below, and on the seat of reunion and found that irritability and conductivity were present, but he does not make it clear whether the point of reunion (point grossi de la reunion) was one which embraced all four ends, or if there was a separate enlargement at the two seats of reunion.

The objections which have been urged against this experiment are that no sufficient precautions were taken to prevent confluent reunion of all four ends, and that the nerves might have reunited in their normal continuity in the common cicatrix, that no sufficient description is given of the return of voluntary coordinated movements to enable the reader to judge if this had been restored (Schiff), and that the recovery of function might have been due to the tensors of the patagium, whose supply remained intact (Cunningham). We have, however, although the description is brief, the statement of Flourens that the wing was used for flying as well as before the experiment. That the conductivity of the nerves had been restored, and the crossing effective would appear from his statement "when I pinched the superior nerve above the point of reunion, it was the muscles of the inferior aspect which contracted; and it was, on the contrary, the muscles of the superior aspect of the wing which contracted when I pinched the inferior nerve likewise above the point of reunion".

Some years later the idea occurred to Schwann (21.) of the improbability, after division and reunion of a nerve, of the nerve fibres uniting as before the division, and he thought that probably many of the sensory fibres might be brought to lie opposite motor fibres and unite with them, and with the perfect restoration of function which ensued after reunion of the nerve Schwann thought that possibly some of the sensory fibres became paths for the transmission of impulses to muscles. To test this he divided in a frog both sciatic nerves, and after reunion and perfect restoration of function he exposed the roots of the sciatic nerves, and irritated the posterior roots after severing them from the spinal cord, to ascertain if thereby mus-cular contractions could be evoked. But the experiment was negative, as as no muscular contractions resulted, and on irritating the anterior roots the normal results followed. This experiment was also performed by Steinrück. This method of testing the question is futile, as even although muscular responses had been obtained on irritating the posterior spinal roots, these might have been due to the irritation of recurrent fibres from the anterior roots.

Following these workers came Bidder (1) Gluge and Thiernesse (6-7) and Philipeaux and Vulpian (16) who experimented on the crossing of functionally different nerves, to see if union could be effected between such. Bidder (1842) united the central segment of the divided hypoglossal to the peripheral segment of the divided lingual and vice versâ. In those cases in which he found a partial restitution of function — contraction of the muscles on irritating the central segment of the hypoglossal — he found that there had been a certain amount of reunion of the two segments of the hypoglossal, and concluded that a functional union between sensory and motor nerves was unlikely. Gluge and Thiernesse (1859) performed the same experiment, and found no physiological union of the two nerves, and concluded that such was not possible.

Philipeaux and Vulpian (1859) crossed the central segment of the vagus with the peripheral segment of the hypoglossal nerve, and obtained contractions in the mus-cles of the tongue on irritating the vagus. All these experimenters aimed at testing the possibility of nerves of different functions uniting and changing their function, their point being to find if the nerve current in the two was different or the same. They did not evidently require the return of voluntary function, but would have been content to have found acquired conductivity to electrical stimuli.

Rawa (18.) in 1885 published in extenso the results of his experiments, which had appeared two years previously in abstract. There are two parts to his research, 1st, cross union of nerves of the same function but of different distribution, and, 2nd, cross union of nerves of different functions. In the former part, the nerves which he chose to cross were the posterior tibial and the peroneal, aiming thus at a crossing of the nerve which supplies in the hind limb the extensors of the foot with that which supplies the flexors. Experiencing the difficulty of getting the two nerves crossed to heal separately, and not in a common cicatrix, the method by which he chose to eliminate this source of error was to make one cross only, and to freely excise the uncrossed central and peripheral end.

This method, however, can give with the two nerves in question, only defective results, or results difficult to interpret, as the animal under such circumstances cannot be expected to make a perfect recovery; and with the restoration of function of the two united ends of the nerves, the formation of a contracture could only be expected, a contracture which would mask any voluntary efforts at motion.

He, however, describes in several instances return of voluntary flexion, where the central end of the peroneal nerve was united to the peripheral end of the posterior tibial, and of extension, where the central end of the posterior tibial was united to the peripheral end of the peroneal. On the crossed nerve being exposed, irritation of the central segment resulted in contraction of the muscles supplied by the peripheral segment of the crossed nerve.

He points out that when an extensor nerve was crossed with a flexor nerve, the change of flexion and extension did not ensue at once but slowly; and in several instances he determined that the return of voluntary movements did not coincide with the date of reunion, but were effected at a much later date.

He concludes, 1st, That in reunion of the peripheral end of a motor nerve with the central end of another, the function of those muscles which the former supplies becomes restored, and, 2nd, That the direction of the voluntary motor impulses which emanate from the centre, can be at will altered, and that they will always accomodate themselves to their peripheral end organs.

In the second part of his research, he crossed the vagus with the hypoglossal, usually only one central end being united to one peripheral end, the remaining two ends being excised to the extent of 1 to 2½ cm. In those cases in which he united the central end of the hypoglossal to the peripheral end of the vagus, after some months he divided the vagus of the opposite side in order to ascertain if the function of the crossed vagus was carried on through the hypo-glossal, and in the cases in which he had crossed the central segment of the vagus with the peripheral of the hypoglossal, after some months the opposite hypoglossal was cut. In a large number of experiments in which the former operation was carried out, the great majority of the animals succumbed very soon after the division of the vagus of the opposite side, so as to make it clear that no adequate vagus function was supplied through the hypoglossal, but in a few cases the animals lived long enough and the effects of the division of the second vagus were so slight as to lead Rawa to conclude that the crossed hypoglosso-vagus was transmitting effective impulses. Similarly in the cases of union of the central end of the vagus to the peripheral of the hypoglossal, he concludes that impulses transmitted through this crossed nerve can call forth normal movements of the tongue.

He concludes that by a successful union of nerves of different functions the peripheral organs retain as before all their requirements. The explanation which he gives of his results is that the central nervous system can innervate organs which do not belong to them, as soon as it is united to them by nerve conductors, and on the contrary that peripheral organs can receive impulses from nerve centres to whose innervation they do not belong.

The publication of these results induced Schiff (1885) (20.) to commence a series of experiments to test the matter. He expresses surprise at Rawa's results, and indicates that the movements observed in the affected foot may have been erroneously regarded as voluntary, when they were really merely passive movements, produced by movements at the knee joint. This as I have shown is a possibility, considering that in Rawa's experiments only one cross was made, the healing therefore resulting in contracture of the flexor or of the extensor groups. Schiff, therefore, thought to settle the matter by crossing two efferent nerves which control movements of a different type, e.g., one voluntary movements, and the other rhythmic movements. He, therefore, crossed the peripheral segment of the hypoglossal with the central segment of the vagus, making only one cross, and excising widely the other two ends. If the peripheral organs determined the kind of movements which returned, then Schiff expected to find some return of normal motion in the paralysed moiety of the tongue, but if, on the contrary, it was the central apparatus which determined the character of the movement in the peripheral organs, then he expected to find movements of a rhythmic type develop in the tongue. As a matter of fact he found, after four months, on the surface and border of the tongue that movements were developed, which could not be taken for rudimentary or returning voluntary movements. Reichert (19.) who examined the animals at six months for Schiff, reports that in the affected moiety of the tongue there was no return of voluntary movements, but that in their place were developed circumscribed areas of rhythmic movements between which and the movements of respiration there was an unmistakable relation. He also described a series of vermicular movements occurring in the posterior and middle thirds of the tongue during deglutition, and the same during vomiting. Schiff and Reichert both conclude their papers by combating Rawa's conclusions, the former holding on the other hand that it is the nerve centres which determine the movements which are produced at the periphery in a crossed nerve, and that the peripheral segment only determines the locality in which these specific movements are manifested, and that "ni l'instinct, ni le besoin, ni la volonté, ni la prétendue loi de l'harmonie, ne peuvent changer directement les mouvements prédéterminés par le mécanisme de l'organe nerveux central." (p. 732.)

The next contribution to the subject was made by Stefani (22), (1886) whose experiments point to the same conclusions as those of Rawa, but as they are much more convincing and as they resemble closely my own experiments, I shall quote them more in detail.

He gives two sets of experiments in dogs, viz:- one, an example of four similar, in which he crossed the median with the musculo-spiral, and three, in one of which he crossed the median with the musculo-spiral, in one the median and ulnar with the musculo-spiral, and one in which he crossed the central end of the median with the peripheral end of the musculo-spiral, the peripheral end of the former and the central end of the latter being freely excised to prevent reunion. In all the latter three experiments he examined the state of the cerebral cortical centres after return of function.

In the first series of experiments, of which one is published, viz:- cross union of the median to the musculo-spiral, it was not till the 108th day that the dog was commencing to show return of voluntary extension. By the 202nd day it could support itself on the points of its toes, and at the 271st day it could place the palmar surface of the paw on the ground, give the paw when asked, and hold a bone against the sound paw, but flexion was so pronounced that it was difficult to judge of the amount of return of extension. At the 311th day the dog was killed and irritation of the central segment of the median gave no contractions in the muscles, but of the central segment of the musculo-spiral, flexion. He concludes that the dog is able to carry out with the paw voluntary coordinated movements, to hold a bone, and give the paw, although the nerves of flexion serve for extension, and vice versa.

His second series of three experiments were of the same kind, but had added to them the examination of the condition of the cerebral cortical centres on recovery of function. In Exp. I the median was crossed with the musculo-spiral, and extension commenced to return on the 30th day. At the 45th day the dog placed the palmar surface of paw on the ground correctly in walking and running, gave the paw when asked, and used the paw in holding a bone. Later on a flexor contracture developed, and at the 121st day the examination of the cortical centres showed that the cortical area for the fore limb had lost its irritability. He concludes that after crossing, complete voluntary movements are regained, but that there is loss of irritability of the cerebral cortical centres.

In his second experiment of this series, in which he crossed the median and ulnar with the musculo-spiral, the examination after complete recovery of function showed that the crossing had failed, that the ulnar had reunited, that part of the central segment of the median had reunited with its own peripheral segment, and that the great bulk of the musculo-spiral had reunited. But on cortical stimulation he found movements of the arm, underarm, and foot, and this he correlates with the failure of the crossing.

In his third experiment he united the central end of the median with the peripheral end of the musculo-spiral, and excised long portions from the unsutured central and peripheral ends. At the 33rd day he found extension commencing in the foot, and at the 47th day the animal supported itself on the palmar surface of the paw in walking and running. At the 102nd day the cerebral cortical centres were stimulated and no irritability could be found. The stimulation of the nerves at the seat of re-union showed that the central end of the musculo-spiral had not reunited, while stimulation of the central segment of the median gave usually extension but sometimes flexion, showing that some of its fibres had formed connections with the peripheral segment of the median.

He concludes from his experiments that the execution of coordinated and voluntary movements is possible, although the relationship of the nerves to their centres is altered, and that the altering of the relationship of the nerves to the centres entails the abolition of the irritability of these cerebral centres.

In relation to the subject of cerebral localisation of function, he takes the view that the cerebral cortical centres do not represent areas in which and in which alone are to be found the only conditions necessary for the innervation of a particular movement, a conclusion which coincides with that expressed by Rawa, who holds that the topography of the cortical centres is not of necessity fixed, but that it can be altered by altered external influences.

Howell and Huber (1892) (11.) also conducted some experiments in crossing the median and ulnar of dogs. Like others who have worked at the subject, Howell and Huber also experienced the difficulty of getting the nerves which they crossed to unite without fusing in a common mass, and therefore in there remaining experiment contented themselves with one crossing, excising widely the remaining two ends. The dogs operated on appear to have been very little affected by the division and crossing of their nerves of flexion; for these authors state that on the second day after the operation with both median and ulnar cut on the left side high in the arm, and with the ulnar cut on the right side at the level of the elbow, there was very little evidence of any paralysis or even of awkwardness. Before the end of the first week the closest scruting could detect no awkwardness of movement, except possibly when the animal was running rapidly up stairs. They allude to the fact that the median and ulnar supply synergic muscles, and have a close origin, and that a more interesting experiment would be the crossing of the musculo-spiral and ulnar, and think that such would be successful.

Experiments of the same kind were carried out by Cunningham (2.). (1898) He invariably made a double crossing, and the precaution taken to prevent confluent reunion of all the nerve ends was to wrap round each union a layer of fascia. In his first set of experiments he crossed the median with the ulnar, and found as did Howell and Huber, that this operation inconvenienced the animals very little; but in all his dogs ~~there~~ was persistent overextension. In one of the animals voluntary flexion could be detected. In all of these experiments the cerebral cortical centre for flexion of the limb was stimulated, and in all flexion of the paw was the result.

In his second set of experiments he crossed the musculo-spiral nerve with the ulnar and median. This was done on nine dogs, but only four were successful. One of these always came down on the dorsal surface of the paw in attempting to walk, and it was difficult to determine whether it had the power to extend at all, but a subsequent examination by electrical stimuli showed that the nerves had united, and recovered irritability and conductivity. In the other three dogs he found the same progress. Thus one of the animals continually held the forearm flexed, and the paw was not allowed to touch the ground, till the 264th day, when the animal attempted to use the foot in walking, always putting down the dorsal surface on the ground. At one year and five months, while the forearms scarcely differed in size, there was incoordination exhibited. He gives a list of these incoordinated movements of which may be quoted, that when the animal was ordered to give the paw it lifted up the forearm but flexed the paw, and that when it walked the leg was advanced and at the same time the paw quickly flexed. On cortical stimulation the results which he obtained were very different from those quoted above from Stefani's paper, as stimulation of the area for flexion of the paw gave extension; and of that for extension, flexion of the paw.

In his third set of experiments he united the central end of the divided hypoglossal to the peripheral end of the divided recurrens, and found that the nucleus of the hypoglossal did not take on the character of a rhythmic discharging centre when united to the recurrens.

He therefore holds that after crossing two motor nerves the cortical representation of the groups of muscles supplied by the crossed and united peripheral segment is "the same as the cortical representation of the group of muscles that were previously innervated by the central portion before its section.", but that this cortical representation differs from that existing before the nerves are crossed in so far that the cortical impulses produce incoordinate movements of the muscles supplied by the united crossed nerve. He holds also that if the two groups of muscles are synergic, the resulting incoordination, as in his first series of experiments, is very slight, but that if the crossed nerves are those which supply widely different functions, eg., antagonists, as in his second series, the adult dog does not regain the power of performing intentional co-ordinated movements, and that there is, as in his third series, abolition of rhythmic action, when a non-rhythmic centre is made to connect with the peripheral segment of a nerve, which formerly conveyed impulses from a rhythmically discharging centre.

Important evidence was recently brought forward by Langley (14-15) in a series of experiments to determine if efferent cranial "autonomic" nerves could connect with the sympathetic nerve cells of the superior cervical ganglion. He united the central segment of the vagus to the peripheral segment of the cervical sympathetic, taking precautions which seem to have been effective, to prevent reunion of the divided nerves. From the results of stimulation of the nerves he concludes that "when the central end of the vagus is joined to the peripheral end of the cervical sympathetic, the vagus is capable of acquiring an influence upon all the structures which are normally influenced by the cervical sympathetic." He assumes that it is not the afferent fibres nor the efferent fibres to striated muscles, which make this connection, but the visceral ("autonomic") efferent fibres, eg., motor fibres to the oesophagus and stomach, to the lungs, and inhibitory fibres to the heart. But he points out that there being no pilo-motor fibres in the vagus, this function must be assumed by one class changing to another class.

He next discusses the possibility of the acquired functions of the vagus being called into activity by normal stimuli. In proof of this, in one experiment, he got the effects of stimulation of the cervical sympathetic by stimulation of the centres of the vagus reflexly. Also by noting the rate of diminution or disappearance of the paralytic symptoms after the vagus had been joined to the cervical sympathetic, eg., contraction of the pupil, dilation of the vessels of the ear, &c, he concludes "that the vagus was exercising a greater or less tonic action upon those structures upon which the cervical sympathetic normally exercises a tonic action."

He also united the central end of the lingual to the peripheral end of the cervical sympathetic, and noted the recovery of most of the functions of the sympathetic, which he takes to be the result of the connection of the sympathetic formed with the vaso-dilator and secretory fibres present in the lingual from the chorda tympani, and concludes that "the evidence strongly favours the view that the vaso-dilator fibres of the lingual (chorda tympani) after becoming connected with the nerve cells of the superior cervical ganglion, become motor fibres for unstriated muscle, and in especial vaso-constrictor fibres for the arteries of the ear." (p. 268)

There are two vastly different results which may be looked for in experiments on nerve crossing, viz:— the return of conductivity through the composite nerve, with the possibility of muscular contractions even voluntary being evoked by impulses passing along the nerve, and in the second place not only the return of conductivity, but the complete reestablishment of coordinated movements. All who have tested the matter since the publication of Rawa's experiments have admitted the former possibility, but as shown above a division of opinion obtains in respect of the latter possibility. Rawa (18.)

Stefani (22), Howell and Huber (11) and Langley (15) affirm the possibility, while Schiff (20) Reichert (19) and Cunningham (2) deny it.

Two important differences in the details of the experiments which have been published by these authors, may account in a measure for the division of opinion. The experiments differ in the nerves chosen for crossing, and in the methods of establishing the crossing. Thus Rawa, Stefani, Howell and Huber and Cunningham have conducted experiments on nerves of the extremities supplying muscles which are under the control of the will, while the experiments of Schiff and Reichert, of Langley, and some of those of Rawa and Cunningham refer to nerves innervating muscles with which the will has little to do. There is a difference again between experiments conducted on nerves which innervate voluntary muscles, according as the nerves crossed each supply groups of muscles of the same action (synergic) or groups of muscles of antagonistic action (antergic); for if the crossing cannot be compensated for, it is in the latter case that the incoordination of movements is likely to be more pronounced. Thus Howell and Huber and Cunningham found little incoordination as the result of crossing the median and ulnar, but Cunningham found no return of coordinated movements on crossing the musculo-spiral with the ulnar and median: but against him stand Rawa and Stefani who, with the same form of experiment, both conclude that return of coordinated movements is possible. Schiff's and Reichert's conclusions agree with those of Cunningham, but the experiments of the former were on nerves which for the most part innervate involuntary functions, and therefore the non-appearance of alteration of function in the crossed nerves cannot be taken as excluding the possibility of this occurring in nerves which transmit voluntary impulses, and which, therefore, have this advantage in any process of education in the stage of alteration of function. Schiff now recognises this. To his paper which is reprinted in his collected memoires, there appears an addendum in which he criticises the views of Rawa and Stefani. He seems to have performed similar experiments on the nerves of the extremities and like Stefani to have found restoration of coordinated movements. This result he explains as due to the volitional correction by the animal of movements which sensation informs it no longer result from the same impulses as before the experiment. He still however maintains the impossibility of an alteration of function after crossing nerves like the vagus and hypoglossal. This difference between nerves of voluntary and those of involuntary function, however, according to Rawá does not obtain, that the latter may have their coordinated functions restored through the former, and vice versā, and this view is confirmed by Langley who finds that normal sympathetic functions can be innervated by impulses starting in the vagus centres, and conducted through the vagus nerve.

The mode of carrying out the experiments has also influenced the results. Thus, in order to prevent confluent reunion Rawa, Schiff, and Langley crossed only one peripheral and one central end widely excising the other two ends. In Schiff's and in Langley's and in certain of Rawa's experiments this method did not vitiate the results, as the two nerves were distributed to entirely different structures. But in Rawa's experiments on the nerves of the extremities this method as stated above is not compatible with perfect recovery of the limb, as thereby either the flexor or the extensor groups of muscles only were innervated, the opposing group being left unsupplied, a condition necessarily resulting in contracture, which must have made the interpretation of the results extremely dubious. Cunningham, however, made a double crossing, and prevented confluent reunion by stitching round each seat of union a layer of fascia, while Stefani made double crossings in all his experiments except one, but except in the latter seems not to have taken precautions to prevent confluent reunion, except the distance which separated the two points of union. That this was not a safe procedure is shown from the fact that one of his experiments had to be rejected on account of confluent reunion.

Stefani's results although very convincing were not followed by a perfect use of the limb by the animal, permanent over-flexion developing in all in which the crossing had been effective. This is to be explained from the fact that he crossed in these the musculo-spiral with the median only, leaving the ulnar nerve intact. A method of this kind leaves one nerve to supply the flexors as before, while the entire supply of the extensors has to be carried on through the crossed nerve. The balance of opposing action of the two groups is thus disturbed, and the flexors are more than likely in the course of the experiment to exhibit a preponderance of action. The conditions were rightly arranged in Cunningham's experiments in which both median and ulnar were crossed with the musculo-spiral, but he of course did not find return of coordinated movements.

I therefore decided to conduct an experiment of the same kind as those of Cunningham following certain principles which appear to me to be essential in any experiment intended to elucidate the question if restoration of voluntary co-ordinated movements will result after crossing two nerves which supply voluntary muscles. These principles are:—

1st The nerves crossed must supply groups of muscles of antagonistic action, eg., flexion and extension.

2nd The crossings must involve all the nerves of the limb which conduct efferent impulses so as to exclude the possibility of a vicarious supply.

3rd The entire supply of the flexors must be crossed with the entire supply of the extensors, in order to maintain the balance of opposing action and to obviate the development of contractures.

4th There must be some precaution taken to prevent confluent union of all the nerve ends in a common cicatrix, involving the possibility of failure of the crossings.

I therefore united the central segments of the median ulnar, and musculo-cutaneous nerves to the peripheral segment of the musculo-spiral nerve, and vice versâ, dividing the four nerves on each side of the anconeus internus muscle (inner head of the triceps), the result being that when crossed and united by suture, the two points of union were separated by the muscle, which formed an effective bar against occurrence of confluent reunion.

Experiment IV.

On May 4th, 1898, a young collie bitch was narcotised by a hypodermic injection of 0.5 gram. morphia sulphate followed by inhalation of ether, and the inner side of the right fore limb having been shaved, an incision, using all antiseptic precautions, was made from the reflexion of the skin at the axilla downwards to the elbow. The musculo-cutaneous, median, and ulnar nerves were thus exposed lying on the inner face of the anconeus internus muscle. The posterior border of the anconeus internus was then defined and this muscle pulled forward and inward

This allowed the musculo-spiral nerve to be exposed as it runs close to the outer side of the anconeus internus to reach the outside of the limb. The four exposed nerves were then divided at levels which, when the crossing was effected, allowed the two seats of suture to lie one on either side of the anconeus internus, separated by the whole bulk of that muscle. The central segments of the musculo-cutaneous, median, and ulnar were then sutured to the peripheral segment of the musculo-spiral and vice versâ, the cutaneous wound stitched, and the entire limb fixed with plaster of Paris, the bandages passing also round the body to immobilise the shoulder joint.

In fourteen days it

was found on removal of the splint that the wound had become septic, and was discharging pus copiously, and that there was no evidence of returning function.

At the end of four weeks no return of function had occurred, and in walking the limb hung helpless from the side, and the wound was still discharging pus. It was therefore thought advisable to kill the animal, as the septic condition would not be favourable for satisfactory healing of the nerve.

The examination of the field of operation showed that the central segment of the musculo-spiral was badly united in a large cicatricial mass with the peripheral segments of the median ulnar and musculo-cutaneous, while the central segment of the latter three nerves were well united in a spindle shaped swelling with the peripheral segment of the musculo-spiral, and that the anconeus internus muscle had formed an efficient bar against confluent reunion.

Stimulation of the central segments of the median, ulnar and musculo-cutaneous, and of the peripheral segment of the musculo-spiral evoked strong contractions of the extensor muscles of the fore-arm, and no contractions in the flexor muscles, while no contractions in any muscle followed stimulation of the central segment of the musculo-spiral.

Efficient union had thus

been effected between the central segments of the nerves supplying the flexors with the peripheral segment of the nerve supplying the extensor muscles.

Experiment V.

On 15th June, 1898, a collie dog, aged 10 months, was anaesthetised by inhalation of ether after having had a subcutaneous injection of 0.5 gram. sulphate of morphia, and the inner side of the right fore-limb together with the adjacent pectoral region having been shaved and disinfected, an incision was made from the axilla downwards and backwards to the olecranon. The same procedure was then carried out as in Experiment IV.

i.e. the musculo-cutaneous, median and ulnar were defined on the inner surface of the anconeus internus muscle, that muscle then drawn inwards and forwards, and the musculo-spiral nerve pulled into the field of operation. The latter nerve was divided well behind the anconeus internus, all its branches to the extensor muscles of the elbow joint coming off from its central segment. The median, ulnar, and musculo-cutaneous having been divided at a level corresponding to that at which division of the musculo-spiral had been effected, the central segment of the former three nerves were united to the peripheral segment of the latter nerve and vice versâ, in both cases by a single suture of chromicised catgut. On completion of the crossing, it was seen that the two points of union were well separated by the anconeus internus muscle, and that there was no tension. The fascia and skin were then separately sutured, and a plaster of Paris casing applied from the toes up the limb, and round the body.

The wound in this case did not run a perfectly aseptic course, as on removing the splint on the 10th day, there was some pus on the dressings, and the lower two stitches had given way, but no pus exuded from the wound on pressure. The wound was cleansed and the lower part resutured and a new plaster of Paris casing applied, and on removing this on the 19th day, the wound was found soundly healed.

The following is the course which was run as far as return of function is concerned.

From the 1st till the 18th day there was absolutely no evidence of recovery of function. Although the limb was supported by the plaster casing, it was not allowed to touch the ground while the animal walked, but was held projecting downwards and backwards. No test could elicit any evidence of return of sensation in the paw.

On the 19th day the plaster splint was removed and the animal in walking and in running occasionally momentarily placed the palmar surface of the paw on the ground, at once withdrawing it, and keeping it held up.

On the 21st day it was

found that the dog frequently put its weight in walking on the affected leg, but the paw always turned over dorsal surface down, and finding no support in this position the limb suddenly flexed at the radio-carpal articulation, and the animal landed on the end of the radius. This occurred occasionally, but as a rule it kept the leg drawn up while walking or running. To keep the limb in the normal position and prevent the development of contracture, and also to prevent further abrasion of the skin over the radio-carpal joint, a plaster of Paris bandage was applied from the toes up to the middle of the arm. With this support the animal commenced to use the leg in walking and was soon doing so constantly; but this, of course may have been as far as concerned the muscles of the forearm, in large measure if not entirely a passive movement.

On the 29th day the plaster splint was removed and then the animal as a rule walked on the end of the radius with the paw doubled back, this being the result of placing the dorsal surface of its paw down instead of its palmar surface. On a few occasions, however, it placed its palmar surface correctly, but this was so infrequent that it might have been accidental. The splint, however, was not re-applied but a calico bandage was fixed round the radio-carpal joint to protect the skin from injury.

On the 30th day the foot was more frequently placed correctly on the palmar surface, and on the following day still more frequently, and at the 32nd day the animal walked and ran full speed always placing the paw with the palmar surface down. On this day there was, therefore, a complete return of coordinated movements, as exhibited in walking and running, but the muscles of the forearm were evidently very weak. The animal however did not spare the leg, with the result that in a few days the muscles became so weak that the dog was unable to support the weight of its body on the limb. A short plaster splint was therefore again applied to immobilise only the radio-carpal articulation, and to keep it extended. With this support the animal used the leg perfectly in walking and running always placing the palmar surface down.

On the 90th day the short splint which had been removed and reapplied for a few days two or three times since the last note, was again removed and the animal was then using the leg perfectly in walking and running and from this date continued to do so. It gave the paw correctly on request, the paw being held extended when the limb was raised.

After this the recovery of power was retarded by a synovitis and slight overextension commencing in the radio-carpal articulation, but this yielded to treatment by immobilisation of the joint.

At the 115th day while the dog was walking about the room it accidentally without seeing placed the affected paw in a dish of water. Sensation must have been well developed, as it started back, quickly withdrawing the paw.

At the 177th day the condition was again examined, and it was found that the muscles of the right forelimb were greatly increased in bulk, and that the difference between the two forearms was not very marked. The coordination of movements of the right limb was perfect in walking, running, and jumping, and in running rapidly up and down stairs, the dog never making a false step. While standing the animal was observed to make voluntary flexion of the paw raising the foot from the ground, extend and again replace the paw on the ground correctly. It gave the paw at once on request, the paw being held out fixed in extension. When gnawing a bone it was observed to fix it between the palmar surfaces of the two paws as under normal conditions. There were no trophic disturbances in the skin of the paw, the nails and hair being normal.

The only abnormal conditions which could be ascertained were as follows. When the animal planted its two fore limbs forward, and rested its whole weight on them, an attitude which is frequently assumed by dogs, the affected limb showed rather more overextension at the radio-carpal articulation than the sound one. Also as the result of the synovitis from which it had suffered, there was slight swelling at the radio-carpal joint, and when the paw was flexed, it became fixed when it formed an angle of about 80° with the fore-arm. The muscles of the forearm were still not so bulky as those of the normal limb.

The animal was photographed on the 93rd and on the 161st days from the date of the operation. (Plates VII, VIII, and IX)

Physiological Examination. On 10th December, 1898, the dog having been anaesthetised with chloroform, the roof of the skull was removed so as to expose the portion of the cortex around the crucial sulcus of both hemispheres. The electrodes from a secondary coil with a strength of current only sufficient to be felt on the tip of the tongue were applied on the post-crucial gyrus of the right hemisphere at a point corresponding to that indicated by Fritsch & Hitzig as the centre for the hind limb. No reaction followed, but on slightly increasing the strength of the current the normal reaction, namely, advancement of the left hind limb was induced. The electrodes were then applied further out on the post-crucial gyrus, and an area was found here which gave strong flexion of the left fore paw. Stimulation was then applied at a point still further out and further forwards, this point being situated on the sigmoid gyrus in line with the crucial sulcus, and strong extension of the left fore paw was the result. Stimulation of these three points on the right hemisphere gave thus the reactions described by Fritsch and Hitzig.(3)

The left hemisphere was then examined. The centre for the hind limb was first determined, and it was found to correspond closely in position with that of the right hemisphere, and to give the same movement of the hind limb. The electrodes were then applied to the point on the post-crucial gyrus corresponding in position with the centre for flexion in the right hemisphere. Vigorous extension of the right forepaw was the result. The electrodes were then applied at the point corresponding to the extension centre of the right hemisphere, and here also extension of the right forepaw was the result. The cortex was stimulated around this area at several points but no flexion movement at this examination could be obtained.

The seat of crossing of the nerves was then exposed, and it was seen that the two points of union were widely separated, one lying on the internal face and one on the external face of the anconeus internus muscle. The central segments of the ulnar, median, and musculo-cutaneous traced from above, bent outwards to pass to the outer side of this muscle, where their junction with the peripheral segment of the musculo-spiral could be seen. The central segment of the musculo-spiral passed under the central segments of the median, ulnar, and musculo-cutaneous about 2 cm. above their point of union with the peripheral segment of the musculo-spiral. It passed downwards on the internal face of the anconeus internus to make connection with the peripheral segments of the median, ulnar and mus-culo-cutaneous about 2.5 cm. lower down. No communication between the two points of union could be seen.

The nerves were then stimulated, each being insulated on a plate of ivory. Stimulation of the central segments of the median, ulnar, and musculo-cutaneous held up together gave vigorous extension of the paw. Held up separately, stimulation of the ulnar gave strong extension at the radio-carpal articulation and also feeble extension of the digits, while stimulation of the median and of the mus-culo-cutaneous gave powerful extension of the digits and less marked extension at the radio-carpal articulation, the movements being stronger in the case of the median.

On the other hand stimulation of the central segment of the musculo-spiral gave strong flexion of the paw.

The skin and fascia were then removed from the muscles of the forearm in order to see if stimulation of each of the nerves evoked contractions only in the flexor or only in the extensor muscles. Stimulation of the central segment of the musculo-spiral was then seen to give contractions of the flexors and no movement in the extensors, while stimulation of the central segments of the median, ulnar, and musculo-cutaneous gave contractions in the extensors, and no movement in the flexors.

The cerebral cortex was again examined to observe the effects of stimulation on the exposed muscles. It had during the examination of the nerves been protected by the soft parts which had been fixed over it. Stimulated on the centre for flexion on the post-crucial gyrus the effect was to give on the right hemisphere flexion of the left paw, and on the left hemisphere extension of the right paw and strong visible contractions in the extensor muscles and no movement in the flexor muscles. Stimulated on the centre for extension on the right hemisphere the result was extension of the left paw, but now on the left hemisphere the exposed flexor muscles of the right forearm gave strong contractions. These however were usually accompanied by stronger contractions of the extensor group the result being as a rule to give feeble extension of the paw. A point could not be found to give on stimulation contractions of the flexor group quite unaccompanied by contractions of the flexors. During the examination of the cortex a point which was noted was that the excitability of the centres in the left hemisphere seemed to be greater than that of those in the right hemisphere as the movements caused by stimulation with the same strength of current were more vigorous in the right than in the left limb. The points at which stimulation gave these results were marked immediately on completion of the examination and are shown in Plate XII.

The dog was then killed without having been allowed to regain consciousness.

The dissection of the parts (Plates X, XI) after death showed that the nerves had united in the position in which they had been placed at the operation, and without any communication either between the two points of union or by means of any anastomosing branches. In order to establish this latter point a careful dissection of the whole nervous supply of the limb was made. The musculo-spiral traced from the brachial plexus gave off from its central segment all its branches to the group of mus-cles which extends at the elbow joint. These branches were all traced into their muscles to ascertain that no abnormal communication was made with the peripheral segment of the musculo-spiral. The central segment then instead of continuing its course round the humerus passed to the internal face of the anconeus internus mus-cle. In this course it passed under the central segments of the median, ulnar, and musculo-cutaneous, crossing them about 2 cm. above their point of junction to the peripheral segment of the musculo-spiral, and attached to them merely by loose connective tissue. About 2½ cm. lower down it passed into the apex of a pyriform swelling to the base of which were attached the peripheral segments of the median ulnar and musculo cutaneous, there being also a small subdivision of the ulnar. These peripheral segments followed a normal distribution, with one exception, that being that at the flexure of the elbow joint the musculo-cutaneous gave off a considerable branch which joined the median.

The central segments of the median, ulnar, and musculo-cutaneous after following their normal course to about the level of the middle of the humerus, turned backwards and outwards to reach the posterior border of the anconeus internus crossing over in their course the central segment of the musculo-spiral. They passed together, the ulnar accompanied by a small subdivision, over the posterior border of that muscle to reach its external face on which about 0.5 cm. from the posterior border was situated the junction with the peripheral segment of the musculo-spiral, which followed a normal distribution.

Deductions from Experiment V.

In the above experiment, therefore, there was complete return of voluntary coordinated movements of the affected limb. These were not decidedly shown till about the 30th day, although attempts in this direction were exhibited earlier. After they were decidedly shown the animal, probably from overuse of weakened muscles, again ceased using the limb properly, but by the 45th day the normal use of the limb again was restored with a decided increase of power. This advance was again retarded, apparently from the same cause, i.e., overuse of weakened muscles, but by the 90th day the normal function of the limb became permanently restored, a restoration which was not materially affected by a passing synovitis of the radio-carpal joint, and when killed on the 178th day, as the report of the experiment shows, the limb presented only trivial abnormalities not sufficient to interfere with functional usefulness.

Important factors in obtaining return of function are prevention of suppuration in the wound, immobilisation of the entire limb during healing, and maintanance of the limb in the extended position, until voluntary function returns. If the latter precaution is not observed, the position of flexion which the limb assumes while still paralysed, is apt to pass over into a condition of contracture, which will hinder functional restitution.

The complete return of voluntary function in this experiment might have been due to failure of effective crossing, as the central segments might have succeeded in making connections with their proper peripheral segments, a result which may happen unless proper precautions are taken to prevent its occurrence. The physiological examination, however, showed that the crossing had been effective, that irritation of the central segments evoked contractions only in the muscles supplied by the crossed peripheral segments, and this was also established by subsequent dissection, which showed that the two points of junction were widely separated with a muscle between them, and that there was no communication between them. The dissection also showed that there were no communicating branches between the nerves crossed or between the central and peripheral segments of the divided nerves, and, the nerves throughout the entire limb having been dissected, the possibility of the existence of abnormal anastomotic or supplementary nerves was excluded.

The nerves crossed involved the entire supply to the muscles below the elbow joint, and of these the entire supply of the flexors was crossed with the entire supply of the extensors. With the ulnar and median was included the musculo-cutaneous, because, although usually a cutaneous nerve below the elbow, it was thought that abnormal conditions might exist, whereby flexor muscles below the elbow would be innervated through this source; and the precaution proved to have been necessary, as the dissection showed that in this particular instance a considerable communicating branch passed from its peripheral segment to join the peripheral segment of the median, and the possibility of this conveying fibres to muscles cannot be excluded.

The physiological examination also showed that the cerebral centres for extension and flexion of the paw exhibited no diminution of irritability, but rather the reverse, and that the normal flexion centre had become the extension centre, and that the flexion centre lay in the position of the normal extension centre, although a point which gave on stimulation flexion quite free from contractions in the extensor muscles could not be found.

This experiment, therefore, shows conclusively that after effective crossing of the nerve supply of the flexor muscles with that of the extensor muscles, complete voluntary coordinated movements are regained, a conclusion which accords with that of Rawa and of Stefani, and opposes that of Cunningham, and also that under such circumstances the cerebral cortical centres of the groups of muscles in question interchange their position, a conclusion which confirms that of Cunningham, but is different from that of Stefani, who found that in such conditions the irritability of these centres was lost.

It is necessary now to consider what bearing this experiment has on the interpretation of Experiments I and II. It was shown from the microscopic examination in the two first experiments that although nothing in the way of a decussation of fibres was found in the cicatrix, such as would be expected on the view that the return of coordinated function was due to a reunion of the corresponding ends of the nerve fibres, yet that this possibility could not be excluded, as much convolution of the young nerve fibres was exhibited in the cicatrix. This last experiment on nerve crossing, however, shows that the two first experiments may be fully explained on the view that the central segments of nerve fibres had united with peripheral segments with which formerly they did not connect, and that the new paths thus established enabled voluntary coordinated function to be carried on. There was, it is true, a difference in time between the appearance of the first sign of returning function in the two experiments, but to account for this is the difference of the conditions of the two experiments. In the experiment on nerve crossing the operation necessary was much more extensive, and this might delay the recovery. More important, however, is the different effect of paralysing by nerve section the hind and the fore limb. In the case of the hind limb, section of the sciatic had the effect of abolishing voluntary movements below the knee joint, but the chief disability resulting was in the movements of the digits, as the movements at the tibio-tarsal articulation are so limited, and the amount of fixation by ligaments so great, that the chief defect to be overcome by recovery of function was the dragging of the paw dorsal surface down. When the animal stood on the dorsal surface of the paw, this was a rigid position, maintained at the tibio-tarsal articulation by the ligaments. In the case of the fore limb, however, the effect of the animal landing on the dorsal surface of the paw was necessarily that no rigid support was found, and passive flexion at the radio-carpal joint at once occurred, bringing the end of the forearm into violent contact with the ground. Before, therefore, the use of the fore limb could be regained, it was necessary that there should be regained not only power to place the palmar surface on the ground, but that there should also be recovery of power to effect and to maintain extension at the radio-carpal articulation. This I think may account for the earlier return of function in the two first experiments.

Experiment V has an important bearing on the question of the immutability of function of the cerebral cortical nerve centres. It shows that at least in the case of volitional centres interchange of function as regards coordination may be brought about by alteration of circumstances, and that this interchange of function may be so perfect that with such centres brought into connection with muscles with which formerly they did not connect, not only as Cunningham believes may voluntary movements in the muscles be possible, but voluntary movements may be carried out in as perfect coordination as under the old conditions. Thus the compensation for the altered conditions brought about by the nerve crossing, takes place in the cortical centres themselves, and not as Stefani believes in lower centres. This is proved from the results of cerebral stimulation, which I have recorded above; for the centre for flexion gave no other movement than extension, and while a pure flexion centre could not be found, yet the new flexion centre lay in the area in which on the opposite hemisphere was found the extension centre.

The return of voluntary coordinated movements, involving the interchange of function of the cerebral centres for flexion and extension might be explained as the result of a process of education of the animal, the source from which the animal is informed of the new conditions, and of the necessity for an alteration of its movements being as Schiff points out, the afferent impulses. Schiff takes these afferent impulses to be those which ascend from the radio-carpal joint and skin of the forearm, which were supplied from nerves which were not involved in his experiments, and he disregards the muscular sense. But the afferent impulses which are of educational value are probably conveyed along the crossed nerves after functional union has been effected, and will lead to a voluntary alteration of the function of the centres in the following way. When the animal allows the paw to touch the ground for the first time after restoration of conductivity of the nerves, contact on the palmar surface is felt as contact on the dorsum. The animal thus feels that the dorsal surface is directed downwards, and to correct this makes the movement, which before the crossing produced extension. This movement, however, now produces flexion, and the result is that placing its weight on the ground with the dorsal surface of the paw directed downwards, and finding no support in this position, it falls on the lower end of the forearm. It is therefore informed that something is wrong, and learns by repeated experiences that in order to attain a rigid position of the foot with the palmar surface down, the opposite movement of what was formerly flexion has to be made. When this is established then dorsal sensation will be recognised as palmar sensation and vice versâ, and localisation of sensation will be regained, and with it, coordination of movements.

Whether or not the above is the exact process by which compensation is brought about, yet there is little doubt that the afferent impulses play a very important rôle in the elaboration of coordinated movements. It is in obedience to them that the discharges from the motor centres which call forth coordinated movements takes place. This view receives support from the well known results of cutting the posterior spinal roots of the nerves supplying a limb; for under such circumstances, although the anterior roots are left intact, the animal loses all power of performing voluntary coordinated movements, while incoordinated movements may be observed. (4.) This applies to the case under consideration. All the nerves of the paw were cut, and on restoration, the afferent fibres regaining function at the same time as the efferent fibres, the animal is informed through the former of the results of its impulses transmitted through the latter.

Summary.

The object of this paper is to determine whether the perfect restoration of coordinated movements and of localised sensation, which obtains after successful réunion of a divided nerve, is the result of the nerve centres becoming again connected with the peripheral terminals with which they were formerly connected, or on the contrary, the result of a capacity of the nerve centres to carry on function perfectly, although connected

to peripheral terminals which formerly they did not innervate. In other words, after division of a nerve do the nerve fibres unite as before the division, the central segments uniting with their proper peripheral segments, or, admitting Ranvier's view of regeneration of nerves, do the central segments succeed in reaching in their growth their old peripheral terminals? Or, on the other hand, do those fibres which are brought by suture into juxtaposition simply unite, and serve for normal function?

To investigate this the sciatic nerve was divided in three dogs at the level of the trochanter. In two of the animals the peripheral segment was rotated on its long axis to the extent of a semicircle, and united by suture in this position, while in the third animal the nerve was united in the same position as before the division. In the former two cases, therefore, the nerve fibres of the one side of the central segment of the nerve were coapted with the nerve fibres of the opposite side in the peripheral segment, while in the latter case the two segments of each of the nerve fibres were coapted as accurately as possible.

The experiments were intended to decide the progress of and time taken for recovery of function in the two cases, and if there were any important differences in the arrangement of the young nerve fibres in the cicatrix.

In all three experiments

the result was a perfect recovery of coordinated movements, the progress of the recovery was practically the same, and the time taken for the appearance of the first signs of returning function also was the same.

The microscopic appearances presented in the three nerve cicatrices showed no important differences, presenting in each much convolution of the young nerve fibres, but in Experiments I and II, there was no resemblance to a decussation of the fibres. The impossibility of tracing the young nerve fibres across the cicatrix, taken with the exhibition of convolution prevented a decision from these experiments whether or not the return of function was the result of the old paths for impulses being reestablished.

It is noteworthy that although perfect restoration of movements was established by the third week, this was proved not to have been due to healing of the nerve by so-called first intention, as the peripheral segment exhibited no old nerve fibres, but in their place young nerve fibres, with the degeneration remains of the old nerve fibres.

Two experiments on nerve crossing are next recorded. The central segments of the median, ulnar, and musculo-cutaneous were united to the peripheral segment of the musculo-spiral and vice versâ. Thus, the entire supply of the flexor group of muscles in the forearm was crossed with the entire supply of the extensor group, the musculo-cutaneous being included in the crossing in case of any communicating branch between it and the median existing; and this was found subsequently to be the case.

The result of this experiment was perfect restoration of coordinated movements of the limb, and the physiological examination showed that the nerves had united in the position in which they had been placed, that stimulation of the musculo-spiral above its junction with the median, ulnar, and musculo-cutaneous gave contractions only in the flexor muscles, and that stimulation of the latter nerves also above their junction with the former nerve gave contractions only in the extensor muscles. Stimulation of the cerebral cortex also showed that there was no loss of irritability of the centres governing flexion and extension of the paw, but that their position had interchanged.

The conclusion, therefore, is that impulses discharged from nerve centres, which are brought by alteration of the course of the nerve fibres into connection with peripheral organs with which they did not at first connect, can effect perfect coordinated movements, and that the compensation for this alteration takes place in the cortical nerve centres themselves.

From this it is clear how after reunion of a divided nerve perfect return of function results, although the old paths for nervous impulses are not restored as before the division.

In conclusion I have to express my thanks to Professor McKendrick and to Professor Young for much valued counsel in connection with this research, and also to my friends Dr. J. H. Fullarton, late of the Fishery Board for Scotland, and Drs Brodie and Teacher of the Physiological Department of the University of Glasgow for their assistance in making and for corroborating the observations recorded.

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Plates

and

Explanation of Plates.

Plate I.

Experiment I. Division of left Sciatic Nerve, rotation of peripheral segment to extent of a semicircle, and suture in this abnormal relationship of the two segments. Shows the dog 31 days after the operation. The left leg is in the position in which the dog itself placed it. The normal position of the paw and at the tibio-tarsal articulation is exhibited. The cicatrix of the operation wound is indicated in the area which was shaved before operation, and on which the hair had not yet grown.

Plate II.

Experiment I. Longitudinal section of the nerve cicatrix 54 days after section. A fasciculus of nerve fibres of the central segment is shown at the upper part, and the corresponding fasciculus of the peripheral segment on the opposite side at the lower part of the section. In the middle line of the section, the fibres are almost traceable across the cicatrix, but in other parts the structure is that of a neuroma, and the course of the nerve fibres, therefore, not traceable. Zeiss Obj. a. $\frac{12}{1}$.

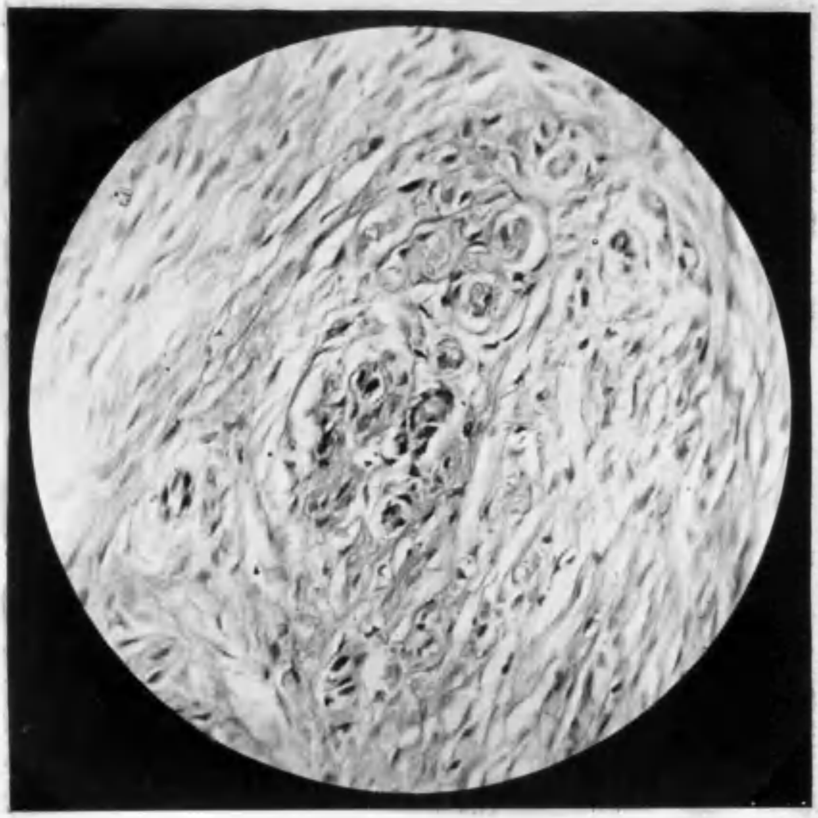

Plate III.

Experiment I. Portion of same longitudinal section from which Plate II was prepared. Shows the neuromatous structure displayed in a large part of the cicatrix in which the continuity of the nerve fibres across the cicatrix is not traceable. Shows some fibres longitudinally, but not traceable for any great distance, and others cut transversely.

Zeiss Obj. D. $\frac{300}{1}$

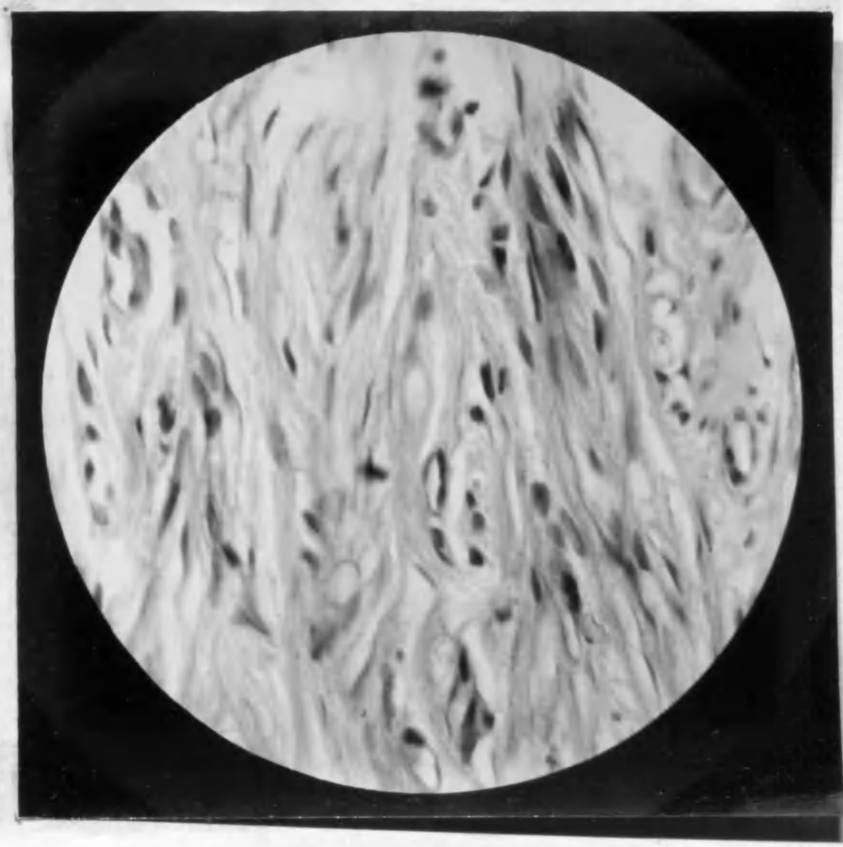

Plate IV.

Experiment III. Coaptation of the central and peripheral segments accurately i.e. without rotation of one segment in relation to the other. Histological appearances, 49 days after section, of a portion of the cicatrix, showing approximately the same structure as the cicatrix from Experiment I.

Zeiss Oil Imm. $\frac{1}{12}$. $\frac{600}{1}$.

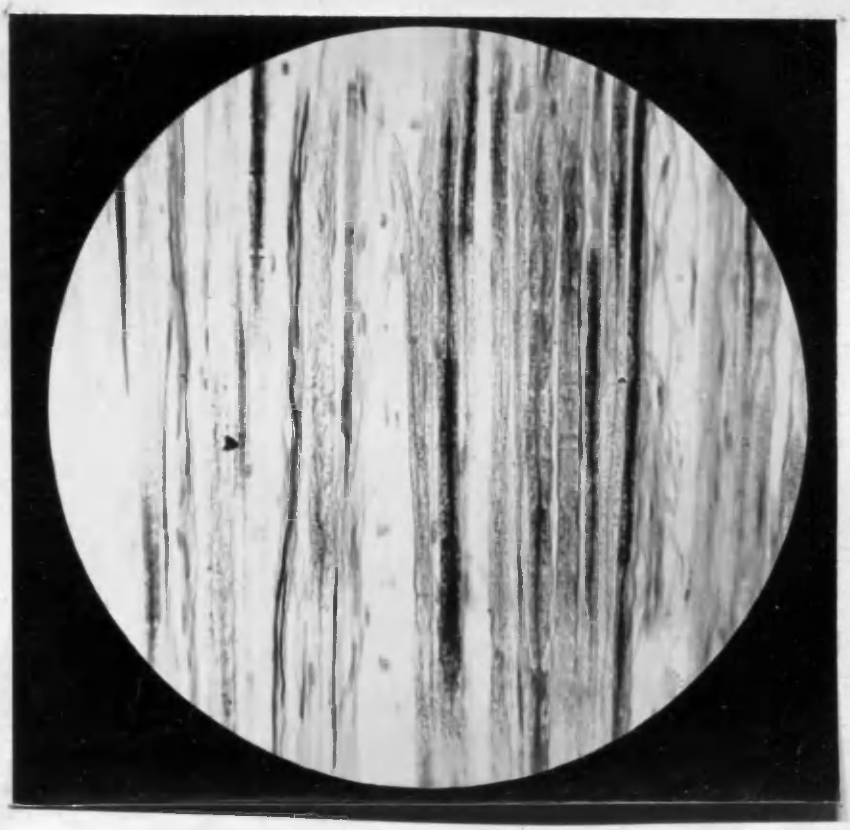

Plate V.

Experiment I. Longitudinal section of central segment of reunited sciatic, close to the cicatrix. Shows adult medullated nerve fibres.

Zeiss, Obj. D. $\frac{300}{1}$.

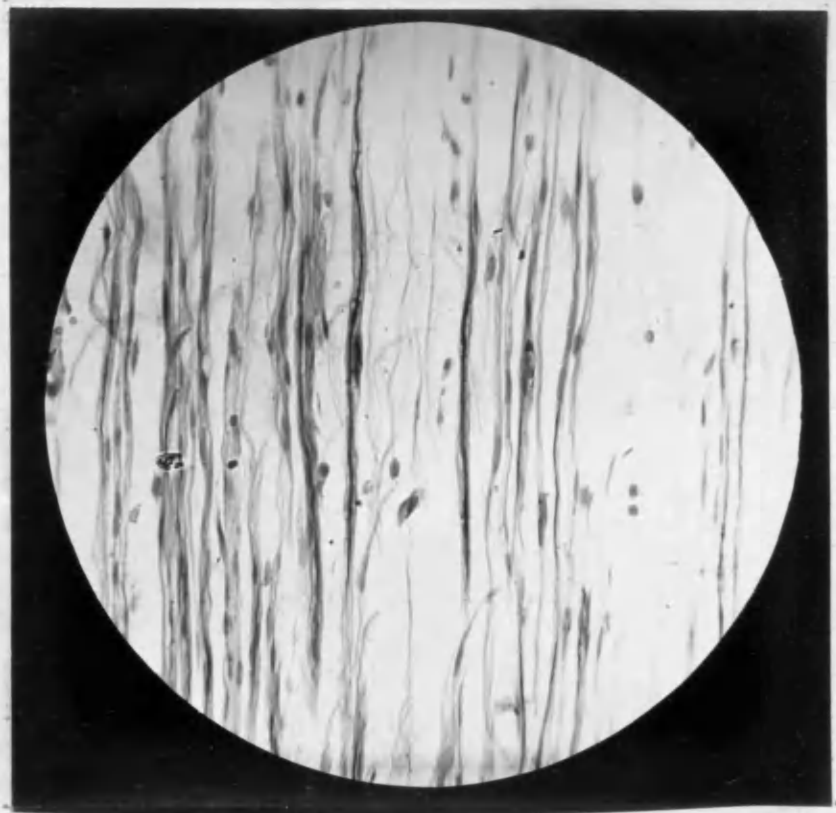

Plate VI.

Experiment I. Longitudinal section of peripheral segment of reunited sciatic, close to the cicatrix (from the same section as Plate V, but from the other side of the cicatrix, the section including the cicatrix with a portion of the central and peripheral segments). Shows young nerve fibres, and no adult medullated fibres, demonstrating that restoration of conductivity of the nerve was the result, not of union by first intention, but of regeneration of the peripheral segment. The same structure is exhibited also in the terminal divisions of the nerve. Zeiss, Obj. D. $\frac{300}{1}$.

Plate VII.

Experiment V. Crossing of the right Musculo-Spiral with the Ulnar, Median and Musculo-Cutaneous nerves. Shows the dog standing at the 93rd day after operation. There is no over-extension at the radio-carpal joint, and the paw is placed on the ground in the correct position. The limb is seen to be somewhat thinner than the ~~right~~ left limb.

Plate VIII.

Experiment V. Same as Plate VII, but with the left forelimb held up, so as to show that the animal could support the weight of the fore part of the body on the affected leg, and without production of over-extension at the radio-carpal joint.

Plate IX.

Experiment V. Shows dog 161 days after the operation. The position of the two forelimbs is seen to be the same, although there is still a difference in the thickness of the limbs. The animal had to be held by the collar as shown, as its movements were so active that restraint was necessary in order to obtain a photograph.

Plate X.

Experiment V. Dissection of the right forelimb seen from the inner side. Above can be seen running transversely a portion of the spinal cord lying in the vertebral column, and descending from the latter are seen the nerves of the brachial plexus from which may be traced the different nerves of the limb. The injected brachial artery is drawn forwards to allow the nerves to be seen. A piece of paper lies on the inner side of the anconeus internus muscle (inner head of the triceps), and resting on it can be seen the junction between the central segment of the musculo-spiral and the peripheral segments of the musculo-cutaneous, median, and ulnar, with a small subdivision which passes to supply the anconeus internus muscle. Above the piece of paper, passing over the edge of the anconeus internus muscle are seen the central segments of the musculo-cutaneous, median, and ulnar with its small subdivision. $\frac{2}{5}$ nat. size.

Plate XI.

Experiment V. Dissection of the forelimb seen from the outer side. The anconeus externus muscle (outer head of the triceps) is detached from its origin from the humerus and drawn backwards in order to show the deeper parts. On its deep surface, which is displayed, is seen entering the nerve supply from the central segment of the musculo-spiral, and from the same branch a division passes downwards to end in the anconeus quartus muscle. The central segment of the musculo-spiral can be seen coming into view above a narrow bridge of muscle between the anconeus internus and anconeus posterior, but instead of continuing its course, it disappears from view again, passing to the inner aspect of the limb. A piece of paper lies on the external side of the anconeus internus, and on this is resting the junction between the central segments of the musculo-cutaneous, median, and ulnar with the peripheral segment of the musculo-spiral, which at once is seen to divide into radial and posterior-interosseous nerves, and the terminal branches of the latter are displayed, entering the extensor muscles of the forearm.

$\frac{2}{3}$ nat. size.

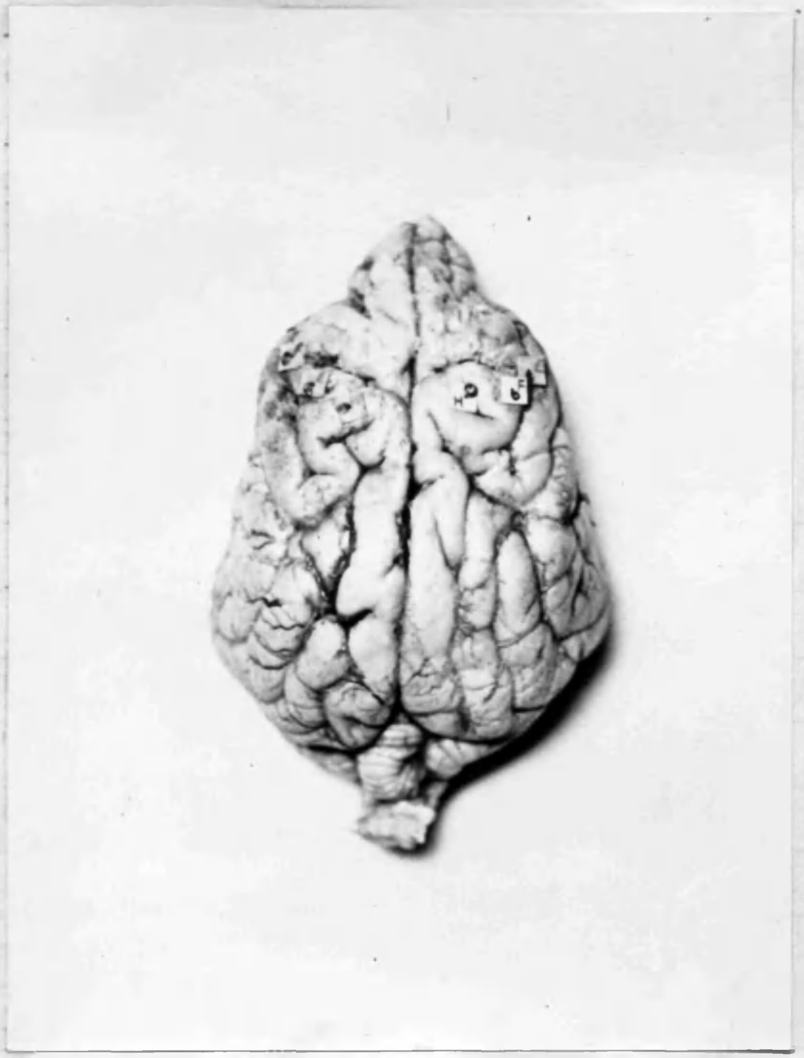

Plate XII.

Experiment V. Brain showing points at which stimulation gave the results described. The point marked by the innermost label on each side gave advancement of the hind limb. F on the right hemisphere gave flexion of the left fore paw and E on the left gave extension of the right fore paw. The centre marked E on the right hemisphere gave extension of the left fore paw, and contractions in the flexor muscles of the right forearm were obtained by stimulation at the point on the left hemisphere marked F. Natural size.