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THE FUNCTIONAL DEVELOPMENT OF THE CEREBRAL CORTEX IN DIFFERENT GROUPS OF ANIMALS

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I.—*The Functional Development of the Cerebral Cortex in Different Groups of Animals.*

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In connection with my investigations on the psychic development o young animals,[1] it seemed important, in regard to the question of physical correlation, to ascertain, in so far as that is possible by experimental methods, at what period the cortex of the brain becomes functionally active. Nothing, to my knowledge, has been done of late years on this subject. I determined, therefore, to give it as complete an investigation as possible; accordingly I have lost no opportunity during the past two to three years to secure the newly-born young of several groups of animals, being those usually kept in confinement or inhabiting our dwellings. Realizing that breadth of investigation was important, as well as thoroughness, the experiments have not been confined to one or two groups of animals but cover several. This, together with the desire to report only what was thoroughly well determined, has extended these investigations over a long period and involved much labour.

METHODS.

Only those individual animals have been used the exact age of which was known, and, as a matter of fact, most of them were born and kept under my own observation, so that their exact age and, in many cases, their breeding, etc., were known.

ANÆSTHETICS.

Anæsthetics were used in all cases, and invariably by inhalation, as by this method alone can nice gradations in the depth of the anæsthesia be made in young animals. The young animals of all the species that have been the subjects of my experiments have taken anæsthetics well—much better, in fact, as a rule, than the adults of the same groups.

Throughout, ether has been used, as the most satisfactory, for several reasons. It is safer, though in the case of the young animal this applies with less force than for older ones But it is, to my mind, the most desirable, chiefly because the degree of anæsthesia can be so quickly

[1] Transactions of the Royal Society of Canada, 1894 and 1895.

varied. This is a matter of great moment, seeing how sensitive the cortex is to injury from exposure to the air, loss of blood, etc. It is unfortunate that ether favours hæmorrhage perhaps more than some other anæsthetics, but I think the advantage just referred to outweighs all its disadvantages.

Objections to other methods of producing narcosis will be considered later.

Experience alone determines that degree of anæsthesia in each animal which is most favourable for the experiment. During a certain depth of anæsthesia it is impossible to get any response by electrical excitation by any reasonable strength of current; on the other hand, all my experience is against placing any reliance on results obtained from animals when not under the influence of an anæsthetic to some extent, the degree, as before mentioned, being determined by experience. If there be a reaction from one part of the cortex, one may assume, of course, as a general rule, that the rest of the cortex is in an equally favourable condition to respond, if it be natural for it to do so.

Operative Procedure.

It matters little, it has been found, how the brain is laid bare, provided it be not injured. I have generally opened the skull over a certain area with a trephine, and then proceeded to remove a sufficiency of bone with a small bone forceps. In the case of very small and young animals a sharp knife and a dressing forceps were the only instruments found necessary.

Methods of Examination.

In a few cases the area usually responsive to electrical excitation has been removed, the wound carefully closed with regard to antisepsis, and the young one returned to its mother. Reference will be made to this subject again. In by far the greater number of cases electrical excitation of the cortex was the sole method employed to determine the question of its functional activity. Of necessity, this can reveal only the presence or absence of motor centres in a functionally active condition. While such centres are known to be confined in the mature animal to certain definite regions of the cortex, in practice it was not found wise to limit explorations to such areas, and, as a matter of fact, almost, if not quite, the whole cortical surface of the cerebrum was made the subject of examination.

Apparatus Used.

Only the rapidly interrupted current of a Du Bois-Reymond inductorium was employed. Electrodes ending in small blunt points (knobs), and with a distance between their extremities varying with the size of the brain to be stimulated—this distance never being greater than a few millimetres—were used to convey the stimulus to the brain.

It was found desirable to use about four different strengths of current: (1) A current felt distinctly on the tongue, but easily tolerated; (2) a current readily felt on the lips, but tolerable; (3) a current not to be borne on the lips without inconvenience; (4) a current too strong to be borne on the lips at all without positive pain. These will be designated currents A, B, C, D, respectively.

Occasionally a current stronger still was employed, such as could not be borne on the skin anywhere. This will be designated "strongest current," as it was the strongest to be obtained by the use of one Daniell's cell or its equivalent. Such a current is generally useless, however, in brain work, on account of the readiness with which it passes beyond the area of stimulation; nevertheless, as will appear later, it has sometimes served a good purpose.

Difficulties.

So delicate, ill-organized, unstable are the motor centres of the very young animal that it requires great care to get at the exact state of affairs and avoid fallacies.

In my experience, hæmorrhage is the greatest difficulty and source of fallacy. Sometimes a very moderate loss of blood seems to suffice to ruin the activity of a centre; at other times the centre remains functionally active in spite of hæmorrhage, exposure to the air, etc.

In some cases a few stimulations seem to exhaust, if not to destroy, the centre, even when very moderate currents are used.

Naturally, the younger the animal the greater the difficulties and the more carefully the source of fallacy must be guarded. The longer I continued my researches the more I became impressed with this, as well as with the wide margin of individual difference in animals, and this accounts in part for the large number of experiments I have been obliged to make to satisfy myself as to the correctness of my results. In not a few cases no positive conclusions could be drawn at all.

EXPERIMENTAL RESULTS.

I.—The Dog.

A number of puppies, some of them pure-bred St. Bernards (bitches), others cross-bred, were tested when very young, viz., from 36 hours up to the 8th day. The result, no matter what strength of current was used, was absolutely negative as regards both the cortex and the white matter beneath, except in one case, to which I now refer in detail.

Unless otherwise stated, the movements will be understood to be on the opposite side in all cases.

CASE I.—*Cross-bred puppy; 6th day of life.*—Eyes not open. Ether.

Right side of brain exposed.

With any but the strongest current no movement. One movement of the hind-leg with strongest current. The same result for the other side of brain. There is also one movement when sharp-pointed electrodes are pushed into the brain to the depth of 3-6 mm. After this no positive result to be obtained. The result for stimulation of the white matter is in no wise more marked than in the case of the cortex.

Though no one of these very young animals had reached the eighth day of life, the results were absolutely negative for both cortex and medulla (white matter) with any strength of current.

The result of testing older dogs will now be given.

CASE II.—*Mongrel puppy; 10 days old.*—Eyes slightly opened. Ether.

Only the strongest current applied to cortex gave any positive result, but with such a current the hind-leg and the head moved, the latter to the opposite side. This applies to both sides of the brain.

The surface of the brain over the area stimulated with the above result, together with considerably more, is sliced away. On one side no result on stimulation with any strength of current.

On sinking the electrodes into the brain to the depth of one-half inch, the fore-leg, both hind-legs and the head move.

CASE III.—*Mongrel bitch puppy; 11 days old.*—Eyes partly open. Ether.

With current C get movement of hind-leg alone when deeply under ether. Later, when slightly anæsthetized, get movement of head, fore-leg and hind-leg, by stimulation of the areas which in the main correspond to those of the mature dog; but by using a somewhat stronger current over any one of these areas movements of all the three parts mentioned occur; with a slightly weaker current both the fore-leg and the hind-leg are moved.

It is impossible to decide that one leg is made to move more readily than the other.

The advance in one day in a puppy of the same litter seems to be well illustrated in this case.

CASE IV.—*Cross-bred bitch puppy; 11th day.*—Eyes open. Ether. Considerable hæmorrhage.

Stimulation on right side with current B produces only movement of hind-leg; on opposite side the same result, also movement of the fore-leg once. Medulla (white matter), negative.

CASE V.—*Cross-bred bitch puppy; 10th day.*—Eyes not open. Ether. Negative to stimulation of cortex on both sides till current C used, when the hind-leg is moved; result the same when the medulla is stimulated. No real localization with moderate currents.

CASE VI.—*Cross-bred dog puppy of same litter; 12th day.*—Eyes half open. Ether.

Can get no positive results with B and C, but with D get the following: Hind-leg, head and fore-leg (once) movements. There is in this case localization, though apparently the head movement is the most perfect.

CASE VII.—*Cross-bred dog puppy of same litter; 15th day.*—Eyes well open. Ether.

With current B movement of the hind-leg; with C, of both fore-leg and hind-leg on stimulating adjacent areas; head movements with only the strongest current.

In this case there seemed to be rough localization, though a very strong current is required; the hind-leg responds most readily; in fact, the fore-leg is uncertain.

CASE VIII.—*Cross-bred dog puppy of same litter; 17th day.*—Ether.

With current B get decided movement of fore-leg and head, but can not get these repeated; hind-leg movement distinct. Remove cortex over one motor area (and more) thoroughly, then, on stimulation with the same current, get movement of fore-leg twice, but after these it is impossible to get movement with any strength of current. The wound is closed by sutures and with some regard to antisepsis. These the dam removes the same evening. There is later some suppuration and granulations appear. The puppy could suck, lap milk, and never at any time manifested signs of paralysis, etc. It seemed to move as usual. Four days later (*i. e.*, when 21 days old), the skull is again opened, when, on stimulated over the motor area of the till now intact side, movements of the fore-limb and head are readily produced, but of the hind-limb somewhat indifferently. These movements may be more fully described thus:

1. With current B head is moved upward (or backwards), and, of course, to the opposite side. This results with this strength of current over an area extending in a curve around the outer extremity of the crucial sulcus.

2. Movements of the fore-leg, both extension and flexion of the paw, *i. e.*, sometimes one and sometimes the other, when an area a little more extensive than the original one is stimulated.

3. To get movement of the hind-leg in this case a stronger current is required, and the result follows whether the stimulus be applied to the crucial sulcus itself or behind it and as near the middle line as the centre for the fore-limb.

CASE IX.—*Mongrel puppy; 10th day.*—Eyes not open. Ether.

No reaction to any strength of current applied over the greater part of the cortex of both sides. On removal of the cortex over the motor area very freely movements of the hind-leg are produced by stimulation on three successive trials; after this, no result of a positive kind.

CASE X.—*Mongrel puppy of the same litter; 12th day.*—Eyes open.

With current B, movement of the hind-leg; no other movements with any strength of current and none when the cortex removed. The animal, however, was then considerably depressed.

CASE XI.—*Mongrel puppy of same litter as last; 13th day.*—Eyes open. Ether.

With current C get movements of the hind-leg, but no others till the cortex is removed; then hind-leg movements were again produced, and movements of the toes of the fore-leg. On trying the opposite side (cortex), with the same rather strong current applied to adjacent areas, movements of both the fore-leg and the hind-leg follow. In this case the movements are equally good for both legs at first, but they persist longest for the hind-leg.

CASE XII.—*Mongrel puppy; 14th day.*—Eyes open. Ether.

With current B, movement of the hind leg; the same result on stimulating the opposite side of the brain; after a few stimulations, no movement. The cortex is removed; movement of the hind-leg is then produced. At a point more forward get movement of the head to the opposite side; and further to one side, movement of the fore-leg.

CASE XIII.—*Mongrel puppy; 20th day.*—Ether.

Much hæmorrhage when attempting to reach the right side of the cortex. This side refractory to stimulation. Then quickly exposed the left side; brain is very pale; can get movement of the hind-leg only. No result on sinking the electrodes into the white matter through the cortex.

CASE XIV.—*St. Bernard puppy; 15th day.*—Eyes open. Ether.

Negative to any strength of current: this applies to both cortex and medulla; both sides of brain tested.

CASE XV.—*St. Bernard puppy, same litter; 28th day.*—Ether.

With current C get movements of head, of fore-leg and of hind-leg when different areas are stimulated. The order given serves to indicate the readiness and perfection of the different movements in this case.

CASE XVI.—*Gordon Setter bitch-puppy; 22nd day.*—Ether.

With current B, movement of the fore-legs; with a slightly stronger current, movement of the hind-leg; where the strongest current used, both legs at times move together, and the head is also moved (to the opposite side).

GENERAL REMARKS ON THE EXPERIMENTS ON DOGS.

In these and cases of other animals used, only those have been reported in which the conditions were favourable, unless it has been otherwise stated. Results, or the lack of positive results, are, as before mentioned, of no moment when hæmorrhage is excessive, when the narcosis is very profound, or when all but absent, speaking generally. Occasionally I have noticed that movements may be obtained in spite of severe hæmorrhage, prolonged exposure of the brain, frequent stimulation, etc., and while such results are highly instructive, they do not bear so directly on the questions—At what period is there first cortical localization of any kind? and In what order are the centres functionally developed?—which were the main problems of this research.

The experiments reported are against any sort of cortical localization before about the tenth to the thirteenth day, though Case I. seems to be an exception, unless we assume that the result was owing to the conduction of the current to the white matter beneath. This subject will be considered later.

Case II. seems to show an advance in the cortex. The result on sinking the electrodes deeply into the brain is one to which I should hesitate to attach much importance as indicating the superior functional activity of the medulla at this period, considering the strength of the current.

Case III. is interesting in illustrating the advance made in a single day. It also seems to indicate that some of the results are due to diffusion of the current.

The medulla giving a negative reaction in this case is to be explained, I think, wholly on the ground of unfavourable conditions, such as hæmorrhage, trial after the brain had been exposed for some time, etc.

From such a case as V., taken by itself, it is impossible to come to any conclusion as to localization; for the movement resulting from stimulation seemed to be in no wise better when the medulla was in question than when the cortex was tested.

Case IV. includes both an advance and fairly distinct localization;

but the fact that so strong a current is necessary to get the result in this and other very young animals is suggestive.

Case VI. falls under the same remarks as the last, but seems to be an instance in which the hind-leg centre is not clearly in advance of the head. This is so rare that it is likely not actually so, but owing in this case to some peculiar conditions of the moment. The very next case (VII.) appears to bear out this view. It also seems to indicate that the hind-leg centre is the first developed in this particular animal.

Case VIII. is especially instructive. There is clearly a well-defined cortical localization in this animal on the seventeenth day, and, notwithstanding unfavourable circumstances, this localization is preserved.

It is noteworthy that ablation of the area around the crucial sulcus produces no paralysis, and, so far as can be readily observed, no change whatever in the movements of the animal, though it must be remembered that a puppy's movements at this age are still but moderately well co-ordinated; nevertheless paralysis would undoubtedly be shown by the leg bending under, etc., were it present even in moderate degree.

Case IX. is apparently clearly in favour of the earlier functional development of the medulla.

Case X. speaks for an earlier development of the centre for the hind limb.

Case XI. is clearly one in which the centre for the hind-limb is best developed. This case also points to an earlier development of the medulla.

Case XII. is in favour of the earlier activity of the centre for the hind-limb.

Case XIII. I consider important, not only because it illustrates perfectly the disastrous effect of hæmorrhage, but because it seems to show clearly that at an early period the centre for the hind-leg is the best organized.

Case XIV. is an example of my experience with St. Bernard puppies. The motor cortical centres seem to develop later, which is in harmony with the generally slower somatic and psychic development of the larger breeds of dogs.

Case XVI. is apparently one in which the centre for the hind-leg was not in advance of that for the fore-limb.

General Conclusions.

The following conclusions seem to be warrantly based on the foregoing:

There is no proper functional cortical development in dogs before the eyes open, *i. e.*, before about the tenth to the thirteenth day of life.

An advance in development is sometimes to be observed in a single day.

In by far the greater number of cases examined the cortical centre for the hind-leg was functionally active at a somewhat earlier date than that for the fore-limb.

The centres for movements of the head as a whole and of its various parts are developed later than those for the limbs.

In the case of large breeds of dogs the cortical motor centres become functionally active at a later date than in small breeds or in mongrels.

All the principal motor centres are functionally active within about the first thirty days of life; most of them earlier.

Removal of those parts of the cortex producing movements when electrically excited does not prevent those movements being caused by the animal itself, such movements being executed about as well as before the cortical ablation, even when that involves an area more extensive than that marked out by stimulation.

The medulla is functionally active in most instances somewhat earlier than the cortex, but never at birth nor for several days afterwards.

EXPERIMENTAL RESULTS.

II.—The Cat.

Case I.—*Kitten of 4 to 8 hours.*—Ether. All conditions favourable.

Results negative as regards both cortex and medulla to any strength of current.

Case II.—*Kitten; 6th day.*—Eyes closed. Ether.

With current C, movement of fore-leg; this is very distinct and is repeated half a dozen times. The same result on the opposite side, though there is considerable loss of blood on that side. Removal of cortex over the motor area on the side first opened and stimulation in the same manner results in movements of both fore-leg and hind-leg.

Case III.—*Kitten; 5th day.*—Eyes closed. Ether.

With current B, on stimulating two areas adjacent to each other, movements in the one case of the fore-leg, in the other of the hind-leg. When th· electrodes are placed between these areas there is a tendency to movement in both legs. The same applies to the opposite side.

On cutting away the cortex, get movements of both legs with best localization for hind-leg.

Case IV.—*Kitten; 7th day.*—Eyes unopened. Ether.

With current B, get movements of fore-leg by stimulation of each side of the brain; soon leads to exhaustion; not very well localized, but is best marked when a certain limited area, adjoining the crucial sulcus, and not far from the middle line, is stimulated. In this case both areas for some distance around the crucial sulcus removed deeply and the wound closed.

Case V.—*Kitten; 7th day.*—Eyes unopened. Ether.

With strongest current get movement of the fore-leg, but no other.

Case VI.—*Kitten; 7th to 8th day.*—Eyes beginning to open. Ether.

With current B get movement of fore-leg and both hind-legs.

Case VII.—*Kitten; 8th day.*—Eyes open. Ether.

On stimulating different brain areas with current B get the movement of both the fore-leg and the hind-leg, but the former responds distinctly better, and in this case all the conditions are favourable for a clear judgment. The cortex is removed over a large area around the crucial sulcus. On using the same current the movements are produced more readily than when the cortex is stimulated. When the current is increased in strength there is a tendency to movement of both fore-legs. Can get only three distinct movements of the fore-legs before exhaustion sets in; the same applies to the hind-leg.

CASE VIII.—*Kitten; 8th to 9th day.*—Eyes unopened. Ether.

With current C get on stimulation of definite regions around the crucial sulcus movements of the fore-leg and the hind-leg. In this case there seems to be distinct localization. On cutting away the cortex in this region get similar results. These results are very transient, exhaustion soon setting in.

CASE IX.—*Kitten; 9th day.*—Eyes unopened. Ether.

No certain positive results with any current. The same applies to the medulla, though I get the impression that movements are incipient, so to speak.

CASE X.—*Kitten; 9th day.*—Eyes opening. Ether.

With current C get movement of both fore-legs. Later, with current B, one only moves, but most distinctly. After removal of the cortex around the crucial sulcus for some considerable distance, stimulation results in the same movement.

In this case the wound is closed; some antiseptic precautions. Movements on recovery from anæsthesia much, if not quite, as before; no clear evidence of any unilateral weakness.

CASE XI.—*Kitten; 10th to 11th day.*—Eyes open. Ether.

With currents B, C and D movement of the fore-leg, and somewhat better with the stronger currents.

On removal of the cortex, the movements of the fore-leg are very marked, of the hind-limb less so.

CASE XII.—*Kitten; 11th day.*—Eyes open. Ether.

With current B movement of the fore-leg; with current C get movement of the hind-leg and both fore-legs, but the movement on the opposite side is much more pronounced. A distinct advance in the character of the fore-leg movement as compared with any yet noticed; the response is more prompt and the movement more elaborate and perfect in every way.

CASE XIII.—*Kitten; 13th or 14th day.*—Eyes open. Ether.

With current B, movement of the fore-leg and later of the hind-leg on stimulation of different areas; with current C, both fore- and hind-legs move together; but there is localization, and the area for the fore-leg seems to be more readily roused to action and the most resisting.

CASE XIV.—*Kitten; 14th or 15th day.*—Eyes open. Ether.

Get movement of fore-leg with much weaker current than hitherto gave positive results, viz., with current A. To get movement of the hind-leg a stronger current must be used. On using a very strong current (D), get movement of both fore-legs.

REMARKS ON THE EXPERIMENTS ON CATS.

The first case is given as an example of what I have invariably found—that in very young cats both cortex and medulla are absolutely inexcitable, no matter what the strength of the current employed.

In Case II., though the cat is only six days old and the eyes unopened, with a strong current movements of the fore-leg are produced, and these are repeated a good many times—in fact, a great number, considering how young the animal is ; and such a case contrasts strongly with the rapid exhaustion in the young dog.

It is noteworthy that movements of the hind-leg can be induced only after removal of the cortex.

Case III. seems to be better pronounced still as an example of very early cortical development—in fact, of localization. In this case also the medulla seems to be in advance of the cortex.

Case IV. points to the presence of an indistinctly defined motor area for the fore-limb.

Case V. is in favour of primary development of the centre for the fore-limb.

Case VI. is one of a class not very readily explained, and will be discussed later.

Case VII. is especially valuable, as it points clearly not only to localization but to the better development of the centre for the fore-limb at this age. This case also seems to be distinctly in favour of an earlier functional development of the white matter of the brain.

Case VIII. is an example of fairly definite localization of motor areas for both limbs.

Case IX. and Case III. illustrate the great difference in individuals. Case III. is one of very early and Case IX. of a somewhat delayed cortical development.

In Case X. we get an illustration of the great difference in results according to the strength of current used.

Removal of the motor area, as in the case of the puppies, did not give rise to paralysis.

Case XI. illustrates the earlier development of the centre for the fore-limbs and also of the medulla.

Case XII. shows that in a very short time there may be a distinct advance in the development of a centre.

Case XIII. points to distinct localization and to the more advanced development of the centre for the fore-limb.

Case XIV. is an example of the same features as Case XIII.

Conclusions.—The Dog and the Cat Compared.

At birth and for several days after the cortex does not respond to electrical stimulation ; but in the cat the cortex usually responds at an earlier date than in the dog, and is functionally active in some cases before the eyes open.

The centre for the fore-limb is responsive earlier than that for the hind-limb.

Head movements, as in the case of the dog, can be induced only at a later date than movements of the limbs.

The white matter lying beneath the cortex is usually responsive earlier than the cortex, and this has been more clearly marked in the case of the cat.

The functional activity of the brain of the very young cat persists longer under the ordinary conditions of experiment than in the dog.

The same remarks as to distinct advance in a very short period, and negative results of ablation of the cortex, hold for the cat equally with the dog.

Upon the whole the motor centres in the cat are developed somewhat earlier than in the dog.

EXPERIMENTAL RESULTS.

III.—The Rabbit.

Case I.—*Belgian Hare rabbit; 7th or 8th day.*—Eyes unopened. Ether.

The most that can be said is that with a very strong current (D), there is the suspicion of incipient movement of the fore-leg.

Case II.—*Belgian Hare rabbit of same litter; 10th day.*—Ether.

With a very strong current no distinct localized movement. The medulla seems to be somewhat more responsive than the cortex, but no very definite statements can be made.

Case III.—*Belgian Hare rabbit of same litter; 13th day.*—Eyes open. Ether.

With current B, get movement of fore-leg and mouth parts; on increasing the strength of current, grinding of the teeth is produced. On the opposite side, get fore-leg and head movement (to opposite side). These movements are all distinct and follow on stimulation of different parts of the cortex—a clear case of localization. Similar results follow on stimulating the medulla. In neither case are there movements of the hind-leg.

Case IV.—*Rabbit; 10th day.*—Ether.

No movement with any strength of current. Cortex removed over a large area. With current B, get movement of the fore leg and head to opposite side, but with no very clear localization.

Case V.—*Rabbit; 12th day.*—Eyes open. Ether.

Both sides of the brain exposed with but little loss of blood. Strong current (C), used on both sides of the brain with negative results so far as the limbs are concerned, but with slight turning of the head to the opposite side on stimulating each side of the brain.

On removal of the cortex and stimulating with the same strength of current, the same result follows, and, in addition, chewing movements.

Case VI.—*Rabbit; 15th day.*—Ether.

With current B, only movement that of head to opposite side; with somewhat stronger current, get, in addition, chewing movements and movement of the fore-leg. The cortex is now excised. The movements are more marked, especially as regards the fore-limb. No movement of the hind-limbs under any circumstances.

EXPERIMENTAL RESULTS.

IV.—The Cavy (Guinea-pig).

As is well known, the cavy is born in an advanced condition of development. In a few hours it can run about, eat, etc. Its eyes are open at birth, and it sees and hears well; if not then, at least in a few hours.

In a cavy, twenty-six to thirty hours after birth, I had no difficulty in getting movements of both the fore-limb and the hind-limb with a current of very moderate intensity.

In a cavy eight days old, movements of the limbs, head (to opposite side) and eyes almost, if not quite, as perfect as in older specimens.

V.—The Rat and the Mouse.

I have been able to make but few experiments on young rats and mice, but, so far as they go, they point clearly to the same conditions as in the rabbit, *i. e.*, while their eyes are unopened the cortex is inexcitable, but very soon after the reverse. Rats, mice and rabbits are born naked (comparatively hairless), and with closed eyes, but both develop rapidly, physically and psychically when the eyes do open.

Remarks on the Experiments Made on Rabbits.

Cases I. and II. show that it is some time before there is any distinct reaction to stimulation of either the cortex or the medulla.

Case III. seems to be a clear instance of cortical localization, and that head (neck) and face movements should be induced thus early is noteworthy.

Case IV. points to earlier development in the medulla.

Case V. illustrates the late development of the cortex and indicates that in this case also the white matter is somewhat in advance.

Case VI. seems to indicate an earlier development of the centre for movement of the head and advance in the medulla over the cortex.

Neither in these nor in older rabbits have I been able to get movements of the hind-leg on stimulation of the cortex under the same circumstances as those under which the centres for other movements reacted.

Remarks on the Experiments Made on Other Rodents.

The Cavy.—There is little additional to be said. It is plain, from the sample experiments reported, that the motor centres in this animal, at all events the principal ones, are practically functionally active at birth, though there is a progressive development of a kind reaching a high degree of perfection when the animal is but a few days old.

Rats and Mice.—They seem, so far as the brain is concerned, to develop in the same way as the rabbit, all three groups contrasting strongly with the cavy.

Conclusions Regarding Rodents.—Comparisons.

In rabbits, rats and mice the cerebral cortex is not functionally active at birth, nor long, if at all, before the eyes open.

The early development of the cortical centres presiding over the movements of the head, as a whole, and of its different muscles, is a feature contrasting in the rabbit very strongly with the condition in the dog and the cat.

These movements in the rabbit occur at a date almost, if not quite, as early as those of the fore-limbs.

Equally noteworthy is the fact that in very young rabbits in which the movements referred to above occur, movements for the hind-limbs cannot be induced under similar circumstances.

The cavy contrasts strongly with the rodents mentioned above, as well as with the dog and the cat, by the fact that there is good cortical localization at or within a few hours after birth.

Examination of the Work of Others, etc.

When my own investigation was well advanced, and I had obtained results unbiassed by the conclusion of others, I undertook a careful examination of the important research of Soltmann,[1] which is about the oldest and best on this subject.

This investigator experimented on dogs and rabbits. He tried chloroform and ether as anæsthetics, but abandoned them for subcutaneous injections of morphia. As he points out, the first two, as compared with the latter, are open to the objection of favouring hæmorrhage. Morphia, however, seems to me to be very unsatisfactory, as it is difficult to produce by it the exact degree of narcosis required, and in all experiments of this kind it is important to be able to vary the depth of the narcosis. With a certain degree of narcosis it is impossible, as has been the experience of many workers on the brain, to get a reaction with any strength of current. There is a definite degree of anæsthesia which is essential to enable one to draw correct conclusions. I place no reliance on results obtained without anæsthesia, and experience enables one to determine when reactions are reliable. I have in all cases used ether, because by it the depth of the narcosis can be rapidly and nicely varied—a most important matter, as before stated, when one has to deal with the brain of a very young animal, so readily is it exhausted or in some way injured. As previously indicated, many experiments have been rejected as unreliable from hæmorrhage, etc. Nevertheless my results in a large degree are in accord with those of Soltmann, as I shall now proceed to show. He found that in dogs the cortex was not excitable in the "newly-born," but that the fibres of the internal capsule were; that the fore-limb was the first to respond to electrical excitation of the cortex, then the hind-limb, and later the face. If it be true that morphia heightens the excitability of the white fibres, as some affirm,[2] this may explain the greater readiness of Soltmann to claim a much earlier activity

[1] Jahr. f. Kinderheilkunde u. Phys., Erziehung, 1876.

[2] Bubnoff and Heidenhain, Pflüger's Archiv. f. Physiologie, 1881.

for them. My experiments show that in dogs, cats and rabbits the cortex is inexcitable at birth and for some days afterwards; that the same applies to the white matter, so that if by "newly-born" Soltmann means animals just born or only a few days (two to four) old, I cannot agree with him; but he is correct in stating that the white matter is, as a rule, earlier functionally active than the cortex. To these remarks, as I have shown, the cavy is an exception, as its cortex responds to stimulation at or a few hours after birth.

While in the rabbit and the cat my experiments show already that the centre for the fore-limb is responsive before that for the hind-limb, this does not apply to my experiments on dogs. It can scarcely be an experimental coincidence that in by far the greater number of my cases the hind-limb in dogs was the first to react. It may, however, be that this divergence from Soltmann's results is to be explained by individual differences.

I am very glad to find Soltmann recognizing differences for "individuals and races" as regards the exact site of early localization. I am certain that this individually applies not only to this point, but also to the date at which the centres first became functionally active, etc., and I strongly suspect that in dogs there is no fixed rule as to which limb first responds to electrical excitation of the cortex. It must be borne in mind that the fore-limb is much more and much earlier used well by the rabbit and the cat than by the dog.

My results are also in entire agreement with those of Soltmann, in that they show that the centres for the face and neck are of later development than those for the limbs, though in the case of the rabbit there is very little, if any, difference as regards the face and the fore-limb.

Soltmann's work on ablation of the cortex, carried out under great difficulties, as I well know from experience (for, as he points out, the mother interferes in a most troublesome way with the wound), are quite in accord with my results as far as they go, *i. e.*, ablation of the cortex does not lead to paralysis or any decided alterations in the movements of very young animals.

Soltmann is also correct in stating that localization is at first somewhat indefinite, but gradually gets better defined.

I have also found, as he states, that stimulation of an area lying between, say that for the fore-leg and that for the hind-limb, gives rise to movements of both legs. This is not, however, a very frequent result with weak currents and is still rarer in animals in which the localization is well defined.

In some cases in my experience, as noted in using a strong current, both limbs move together and perhaps also the head. No doubt, difference of current may explain some of these cases. Occasionally both fore-limbs move on stimulating one side of the brain. It is more difficult to explain this by diffusion from the use of any moderate current.

The advance in the readiness with which a centre can be stimulated noticed in my record of cases seems to me to indicate in the clearest way that there is a process of development in the brain cortex. When the centre is less developed it requires a stronger stimulus, in some instances a very strong one, and it is not satisfactory to assume that when on stimulating the cortex no result follows till a strong current has been used that the result is owing to diffusion of current unless it can be shown that in the same subject the white matter reacts easier, and as this has not been my experience in many instances on very young animals, I have been strongly impressed with this gradual development of centres, rapid as it is. The difficulties in the cases just referred to will not be entirely removed until the histological development of the brain is better worked out.

As Dr. Ferrier's work[1] is so well known, I quote in part the paragraph which bears on this subject of the early condition of the cortex: "It is not until after the opening of the eyes—usually about the eighth day in dogs—that the limbs can be excited to action by electrical stimulation of the sigmoid gyrus. Generally the cortical centres do not react till about the tenth day, the centres for the fore-limb becoming excitable before those of the posterior limb. Similar conditions obtain in rabbits and guinea-pigs."

Opening of the eyes on the eighth day in dogs must be of the rarest. It seldom occurs before the tenth to the thirteenth day. It is, however, quite correct that in dogs the cortex is rarely, if ever, excitable before the eyes do open.

I, as already stated, have not found that in dogs the centre for the fore-limb is the first to develop, so that this statement must be modified. The guinea-pig (cavy) must also be excluded from Ferrier's generalization.

I think my researches are the only ones carried out in connection with an extensive study of the psychic[2] development of the same creatures, and that more groups of animals have been compared than by any previous investigator.

I give below the conclusions that I believe may be relied on as regards the functional development of the brain in the dog, the cat, the rabbit and the cavy. As to rats and mice I must express myself with more hesitation.

Though I have made a series of experiments on the domestic fowl and the pigeon, chiefly the latter, I have never been able to get movements of any part (the eyes excepted) on stimulating the cortex in mature animals, consequently did not try young ones. I believe the

[1] The Functions of the Brain, second edition. London, 1886.
[2] See these Transactions for 1894 and 1895.

statements of Ferrier[1] to the effect that the cortex of the pigeon is excitable to be erroneous.

The brain of the bird will be further referred to in another paper.[2]

General Conclusions.

In the dog, cat, rabbit (and in so far as the writer's experiments go in the rat and the mouse) neither the brain cortex nor the underlying white matter is excitable by electrical stimulation at birth or for some days afterwards.

The cortex is usually not excitable till about the period when the eyes open, though there are exceptions to this rule, most frequent in the writer's experience in the cat, in favour of an earlier date.

The white matter of the brain just beneath the cortex is generally excitable either at an earlier date than the cortex, or with a weaker stimulus.

The reaction for the limb movements is obtainable invariably somewhat earlier in the dog and the cat, and generally so in the rabbit, than those for the neck, face, etc.

Localization for the cortex and still more for the white matter is at first ill-defined, but gradually, though rapidly, becomes more definite.

In the cavy (guinea-pig) the cortex and the white matter beneath are electrically excitable either at birth or a few hours afterwards, and perfection of reaction and localization is reached in a few days.

Before the brain cortex responds to electrical excitation, ablation of the motor area (centres) leads to no appreciable interference with movements.

The younger the animal the stronger the current required to produce reaction up to the time that localization is well established, *i.e.*, the weakness of the current required to cause a movement is an indication of the degree of development of the centre in question.

Differences for breeds and individuals exist and constitute to some extent exceptions to the above general statements.

In the above "cortex" refers to the gray matter in or near the motor area and "white matter" to the brain substance immediately beneath.

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[1] The Functions of the Brain, second edition, London, 1886, p. 262.

[2] These Transactions, 1896.