A CORRELATION OF MYELINIZATION WITH THE RESULTS OF OSCILLOGRAPHIC INVESTIGATION OF THE CORPUS CALLOSUM AND FRONTO-PONTO-CEREBELLAR TRACT IN ONE TO FIVE DAY OLD RABBITS

by

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(Dean, Graduate Division)

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TABLE OF CONTENTS

INTRODUCTION

This investigation was undertaken, (1) to study the development of functional connections in the central nervous system in immature mammals as determined by oscillographic methods; (2) to correlate this with the weight, age and state of myelinization of those tracts and centers under consideration; and (3) to determine whether or not conduction, as measured by oscillographic methods, is found in fiber tracts prior to their medullation.

That the relationship of myelogeny to function, as suggested by Flechsig in 1876, is still not a settled question, will be seen by a review of the literature. The pathways selected for consideration were the corpus callosum and the fronto-ponto-cerebellar tract, as these are readily available from an operative standpoint and because oscillographic studies of these tracts have been made in other, adult mammalian forms.

MYELOGENY AS RELATED TO FUNCTION IN THE DEVELOPING MAMMAL

Meckel(1), in 1815, recognized the gradual development of myelin in the central nervous system and stated that different parts of the neuraxis become medullated at different times.

Flechsig(2), in a series of studies started in 1876, first suggested a palingenetic interpretation of medullation. Flechsig's fundamental myelinogenetic law states that "the myelinization of nerve fibers in the developing brain follows a definite chronologic sequence, such that those fibers belonging to particular functional systems mature at the same time". He presented the belief that projection paths were myelinated before association, sensory before motor, and peripheral before central. Later he modified this to the statement that, in regard to any one projection center, myelinization proceeded in the order: sensory, efferent, and then association.

Tilney and Casamajor(3) studied the development of the central nervous system of the cat, establishing a chronologic sequence of behavioral reactions in the first days of life. An examination of Pal-Weigert sections of the brains of these cats, during the first 14 days of life, led them to the conclusion that the deposition of myelin, in the cat, is coincidental with the establishment of function in definite fiber systems. By assuming a functional capacity established in those fiber tracts myelinized at birth these authors were able to hypothesize an explanation of early behavioral reactions in terms of stimuli, received over these tracts.

Langworthy (1927)$^{(4)}$, investigating the response to electrical stimulation of the motor cortex in young kittens from six hours after birth up to the forty-seventh day, found functional response to stimulation in all the kittens used in the experiment. As no medullation was visible in the pyramidal tracts until after the first nine or ten days of life, and as medullation was not complete in these tracts until about the fiftieth day, he was able to conclude that the functional response to electrical stimulation of the cerebral cortex of the kitten occurred prior to medullation of the cortico-spinal fibers necessary for the response of the fore leg musculature. He did find, however, that responses to electrical stimulation of the hind leg and facial centers appeared about the time that myelinization began.

In 1926 Langworthy$^{(5)}$ published his study on the reaction of decerebrate rigidity in the guinea pig, kitten and rabbit. He found a correlation between myelinization of the rubro-spinal tract and the occurrence of decerebrate rigidity. Prior to medullation of these tracts in kittens and rabbits, he found that decerebration, instead of producing rigidity, served only to increase the activity of the animals. After medullation of the rubro-spinal tract had commenced, typical decerebrate rigidity following decerebration was also present from birth.

This work on medullation is of interest, despite the fact that decerebrate rigidity has been demonstrated to occur in earlier fetal stages(6,7), and that the importance of the red nucleus in the mechanism of decerebrate rigidity has been questioned by several workers(8,9,10).

In 1928 Langworthy(11) studied the process of myelinization in the pouch young opossum. This animal is particularly well adapted for this type of study due to the fact that such animals are available to behavioral examination at a time when there is no evidence of myelin (Pal-Weigert method) in the neuraxis.

Langworthy found that these animals were capable of performing many complicated acts, such as entering a pouch, finding a nipple and obtaining food from the mother, before there was any sign of myelinization of nerve fibers.

Again in 1929, Langworthy(12) published observations in this field in the form of a study of the reflex activity in fetal and young kittens, correlated with the myelination of tracts in the nervous system. He concluded: (1) that ventral spinal roots myelinate before dorsal; (2) that myelinization occurs in the cervical portion of the cord first and proceeds caudally; (3) that pathways appear to become myelinated in the order in which they developed phylogenetically; (4) that, in general, nerve tracts tend to become myelinated at a time when they become functional; and (5) that bilateral movements of the extremities begin to coordinate when the ventral commissural fibers of the cord receive their myelin sheaths.

Keene and Hewer(13), from a study of human fetal and post-natal material, arrived at the conclusion that there are four definite periods at which the myelination process in the human appears to receive an impetus. These are: (a) about the 14th week of gestation; (b) the 22nd-24th week of gestation; (c) just before full term; (d) about 8 months after birth. These workers found myelination to occur first in the sensory paths together with the motor cranial and spinal nerve roots and medial longitudinal bundle. They were impressed by the fact that the sensory fibers of the V and the cochlear fibers of VIII nerve took longer to receive myelin than any other of the nerve roots. Finding that the column of Goll was slower in myelination than that of Burdach, these authors tentatively suggested that, since the rate of growth of the hinder parts of the body lags behind that of the remainder, there may be some relationship between the rate of growth and the myelination of afferent fibers. Observing some acceleration of the myelination process in the central nervous system in material obtained from a child born prematurely at seven months, that had survived for nearly 3 weeks, they felt that this study lent further weight to the assumption that myelination and functional activity are related.

Larsell(14), in summarizing the process of myelination, states that "as indicated by myelination those axons which enable the cord to function as an organ per se, that is, the axons making possible the simpler reflex activities, complete their development before those axons that involve the brain with the activities of the cord".

Flechsig's concepts were first assailed by such workers as Westphal, Monakow and Vogt. Later, in 1907, Watson (15) came to the conclusion that the general correlation of Flechsig was not applicable to the white rat, for he found that a rat 24 days of age, when myelination was just beginning in the higher centers, was capable of solving satisfactorily as complicated a problem as can be solved by an adult rat.

More recently, Angulo y Gonzalez(16) has pointed out that Flechsig's concept should be regarded in more of a general nature than some workers have been wont to do. Not denying the importance of this concept of phylogeny in determining the appearance of myelin in each fiber path, this worker points out the necessity of bearing in mind the fact that, phylogenetically speaking, myelin is one of the last components to be added to the neuron. Angulo quotes the work of Swenson(17, 18) and his own work, in which it was found that motility of the rat fetus occurs many days before myelinization can be observed. Angulo(19) takes issue with Tilney and Casamajor concerning their postulation that the postural reaction of the kitten comes into being suddenly. He claims that their observations do not preclude the possibility that the cat may be capable of performing the considered reactions previous to myelination of the pathways under discussion, and points out further that in the rat, at least, such postural reactions are the result of "an evolutive process which has its inception in the first feeble lateral flexion of the neck", which action spreads in a cephalocaudal direction similar to the early flexure of Amblystoma as described by Coghill(20). He discusses the findings of Minkowski, who has found movement to occur in human fetuses before myelination has taken place. Minkowski feels that the fetus at this period moves as a whole, and that this is the result of spread of the nervous impulse over the whole central nervous system, and that later the myelin sheath, acting as an insulator, allows for specific reflexes. Angulo, however, points out that for the rat this latter hypothesis is not true, for in that animal discrete reflexes demonstrate a selectivity in the conducting mechanism prior to myelination.

Similarly the work of Langley(44) has shown that regenerating cat sympathetic nerve is able to function prior to attainment of the myelin sheath.

Langworthy(21), in 1932, published observations on the condition of myelinization in the human fetus. He came to the conclusion that reflex activity may be observed for a considerable period before any pathways are myelinated in the nervous system. He points out that there is not sufficient proof that the deposit of myelin is coincident with the development of function in the neuron.

Windle (7,22,23) has shown that sensory, motor and integrative pathways in cat fetuses and embryos are capable of functioning before they become myelinated. He, however, leaves open the question as to the efficiency of such function as compared to the function of these same pathways after medullation has occurred. Windle furthermore showed that the order of appearance of myelin in the cat was not strictly a consequence of the order of appearance of neurons of the embryo.

C. and O. Vogt(24) caution against the too ready acceptance of the idea of correlating function with myelinization. These authors state that myelinization depends upon the number and size of the fibers in the path under consideration. In 1924, however, Tilney and Casamajor(3) found, among the early myelinized systems, fibers of every size, from the smallest to the largest, and hence were unable to lend support to this point of view of the Vogts.

Speidel(25) has shown that a nerve fiber presents a characteristic thickening of the axon before myelinization occurs.

Duncan(26) presents evidence that in mammals (cow, cat and rat) a diameter of 1.5 micra (axon plus myelin sheath) is critical, below which all axons are unmyelinated. Seemingly myelinated one-micron fibers, he found, if followed in section, will be seen to be merely constricted portions of larger fibers. Different critical diameters were demonstrated for different phyla. He further observed that: (1) nerve fibers myelinate in order of their appearance and that the first fibers to myelinate are the largest in the adult and, (2) the order of fiber size for the various functional groups is the same in different mammals.

Gerin(27), in studying progressive myelinization in the sciatic nerve of young rabbits, found that although in fetuses removed 8 days before term the average size of fibers to first show myelin was 1.5-2 micra, some fibers as small as 1 micron were myelinated.

Von Monakow, 1910(28), believed that vascularization of brain areas played the important role in determining the sequence of myelinization. From the scattered distribution of myelinized fibers at birth, as observed in their sections, Tilney and Casamajor(3) were unable to corroborate this point of view. However, the work of Craigie(29), who showed that vascular richness is related to functional activity, may indicate that the last word has not as yet been said in regard to this theory.

Hermann, 1897(30), described the migration of myelin in an electric field and pointed out that it collects at the end of the nerve fiber to the extent that "Macroscopisch nimmt das Hervenende eine pilzformige Gestalt an". Kappers(31), carried this observation further to suggest that the accumulation of myelin around nerve fibers may be the result of just such currents flowing in a peripheral direction. The implication from this is that myelinization of the nerve fiber occurs at a time when impulses first begin to travel along the fiber.

MATERIALS AND METHOD

Young rabbits from the first to the fifth day of life were used. Sixty-three animals were used in the investigation of the corpus callosum; fifty-four in the work on the cortico-ponto-cerebellar tract. The rabbits for several age groups were usually obtained from the same litter, and it was found that as the litter diminished in size the stomachs of the remaining animals suffered a progressive dilatation caused by accumulation of milk curd. Hence the stomachs of the animals were removed post mortem and weighed. The weight of the stomach was then subtracted from the total weight of the live rabbit, thus rendering truer weights for rabbits of the different age groups.

The animals were anesthetized with Nembutal using 1 cc. of a 0.6% solution for every 100 grams body weight.

Stimulation was produced by a single condenser discharge of 0.3 msec. duration. The strength of the shock was variable up to 140 volts, peak voltage. The stimulating electrode consisted of a glass bead in which two wires were buried. The ends of the wires were flush with the contact surface.

The lead electrode was a pointed cotton wick moistened with Ringer's solution and applied to the brain surface. An indifferent electrode was placed on the skull.

The action potentials were amplified by condenser coupled amplifiers and recorded by a cathode-ray oscillograph.

HISTOLOGICAL TECHNIQUE

A Weigert modification method commonly in use at the histological laboratories of the University of Oregon

Medical School was tried without success in an attempt to show the early myelinization in the brains of these young rabbits.

Several reasons for this failure may be suggested. The cell nuclei in fetal material have been shown to retain hematoxylin as tenaciously as do the young myelin sheaths(23); and during the period here under consideration, the water content of the brain tissue is undergoing a change that is not encountered in more mature material(32). Suitsu(33) found difficulty in obtaining good results with the Pal-Weigert method and used the Kultschitzky-Wolter method to bring out the very fine fibers.

After many trials, the modification of the Weigert method as presented here was found to be satisfactory.

HISTOLOGICAL TECHNIQUE

1. Place the hemisected brain immediately into a solution of 5% bichromate of potassium.
2. Change this solution every two days for three changes, again after a month; and leave in the final solution for six additional weeks.
3. Imbed in pyroxylin over a period of from three to four months.
4. Section tissue at 20 micra.
5. Store sections in 70% alcohol.
6. Place sections in solution I for three and one-half hours.
   Solution I: One part of a saturated solution of copper acetate and one part of distilled water.
7. Place in 70% alcohol for twenty-four hours.

8. Place in solution II at room temperature for twenty-four hours and then leave for four additional hours at 40° C.
   Solution II: one gram of hematoxylin, ten cc. of absolute alcohol, one cc. of saturated solution of lithium carbonate and ninety cc. of distilled water.

9. Rinse the sections in water for twelve hours.

10. The sections are placed in solution III for a variable length of time, usually one to four hours. The process of differentiation is watched under the microscope until the background tissue is pale brown and the myelin tracts are a deep black.
    Solution III: two and one half grams of ferricyanide of potassium, two grams of borax and two hundred cc. of distilled water.

11. Wash in water for 24 hours.

12. 70% alcohol for 24 hours.

13. 80% alcohol for 4 hours.

14. 95% alcohol for 15 minutes.

15. Carbol-xylol for 15 minutes.

16. Clear in xylol for 15 minutes.

17. Mount

Sections were cut at 20 micra. After staining, every tenth section was mounted for microscopical examination.

TABLE I

RANGE OF WEIGHTS IN ONE TO FIVE DAY OLD RABBITS

1 day

Mean: 49.6 Grams
Range: 22 - 74 Grams

2 day

Mean: 58.9 Grams
Range: 35 - 85 Grams

3 day

Mean: 67.3 Grams
Range: 44 - 90 Grams

4 day

Mean: 89.6 Grams
Range: 49 - 120 Grams

5 day

Mean: 93.8 Grams
Range: 55 - 120 Grams

RESULTS OF STIMULATION OF THE CORPUS CALLOSUM

In the investigation of callosal potentials the stimulating electrode was moved over one hemisphere of the cerebral cortex. The lead electrode was kept at symmetrical points on the contralateral hemisphere in order to record the strongest possible potentials. (Curtis(34))

All available parts of the exposed cortex were systematically explored until it was decided whether or not the callosal system of each animal was as yet capable of mediating potentials.

In one of the ten one-day rabbits a callosal response was obtained (Figure 1.). This animal was the largest in that group and weighed in excess of the mean weight for three-day animals (Table I.). An equal percentage of the twenty two-day animals gave positive results. It happened that these two animals weighed less than the mean weight for the one-day group.

The smallest animal to respond was a 44 gram three day old rabbit. There was no significant difference in correlation between callosal responses with age (.89) and the correlation of callosal responses with weight (.82). (Figure 1.)

Analysis of the potential waves revealed a comparable type of wave throughout the age range studied. (Figure II.) An initial negative spike of approximately 15 msec. duration and a positive spike of 15-45 msec. were followed by a large negative wave of 100 or more msec., which, in

Figure 1.

Percentage of response over fibers of the corpus callosum plotted against increasing age (days), and increasing weight (grams). The row of numbers, A, above each figure shows the number of animals used. Row B shows the number of animals giving positive responses.

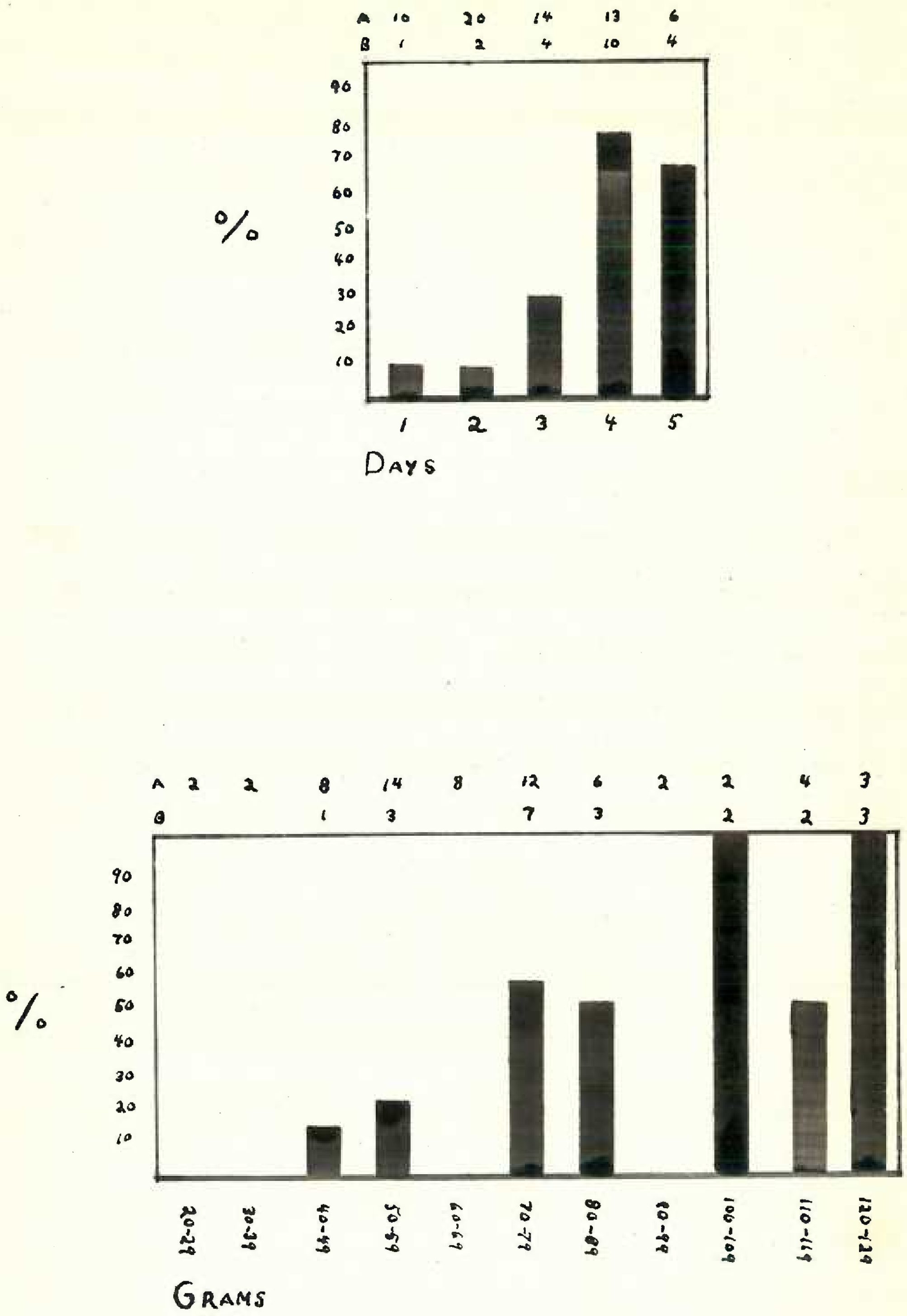
A 10 20 14 13 6
B 1 2 4 10 4
90
80
70
60
50
40
30
20
10
%
1 2 3 4 5
DAYS
A 2 2 8 14 8 12 6 2 2 4 3
B 1 3 7 3 2 2 3
90
80
70
60
50
40
30
20
10
%
20-29
30-39
40-49
50-59
60-69
70-79
80-89
90-99
100-109
110-119
120-129
GRAMS

FIG. 1

some of the records was of such duration as not to be completely recorded and suggest a possible long duration artifact.

Curtis$^{(35)}$ investigated callosal potentials in the cat and studied a model of the callosal system. This model consisted of a frog nerve suspended in Ringer's solution, both ends of the nerve just reaching the surface a few mm. apart. He came to the conclusion that the positive potentials he obtained were due to impulses traveling towards the electrode but not reaching it, (i.e., nerve fibers ending before reaching the surface).

This author interprets the negative phase as due to impulses, initiated in the first cortical layer, traveling to the deeper layers.

If we assume this hypothesis to be correct, there must enter the possibility that our first component is due to such an impulse moving away from the electrode. Curtis, upon moving his microelectrode lead closer to the surface of the cortex, found a reversal of spike to occur when he reached layer I. This he attributed to final termination of some of the callosal fibers in this layer. It seems possible that the callosal fibers may not reach this layer in the animals here studied, but rather may terminate in a lower layer. Kappers$^{(36)}$ has stated that callosal fibers all terminate in layer III. It seems, therefore, that after a synaptic delay of less than 1 msec. (Lorente de No$^{(37)}$) a transference to the cells with

Figure 2.

Potentials mediated by the corpus callosum, obtained by leading from the cerebral cortex in one to five day old rabbits. a. One day old rabbit. b. Two day old rabbit. c. Three day old rabbit. d. Four day old rabbit. e. Five day old rabbit. f. Typical callosal spike as seen by Curtis(34). An upward deflection is negative.

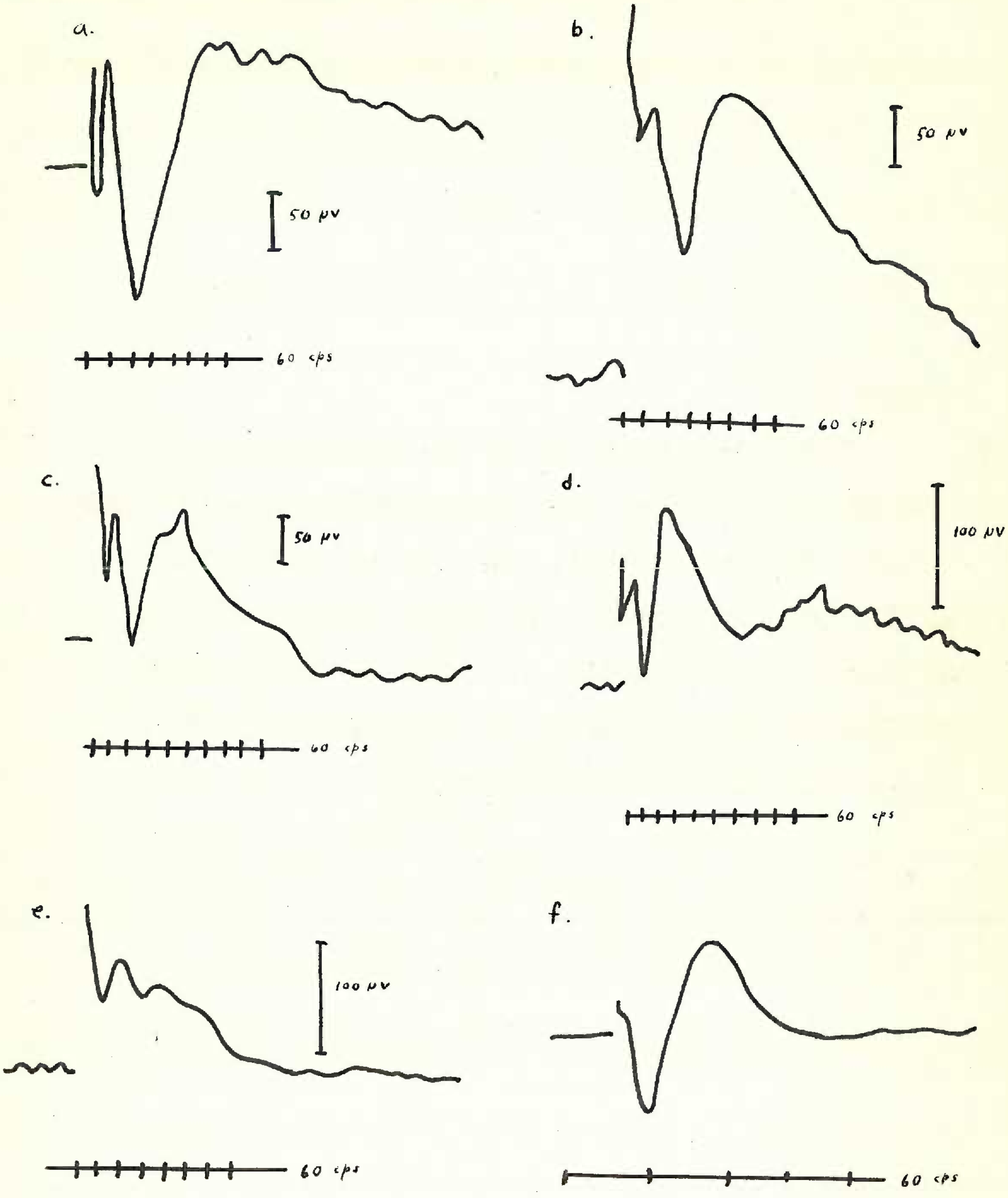
a.
50 μv
60 cps
b.
50 μv
60 cps
c.
50 μv
60 cps
d.
100 μv
60 cps
e.
100 μv
60 cps
f.
60 cps

FIG 2

Figure 3.

The cerebellum of the rabbit. a. Lateral view. b. Dorso-ventral projection (after Brodal(45), modified by Larsell).

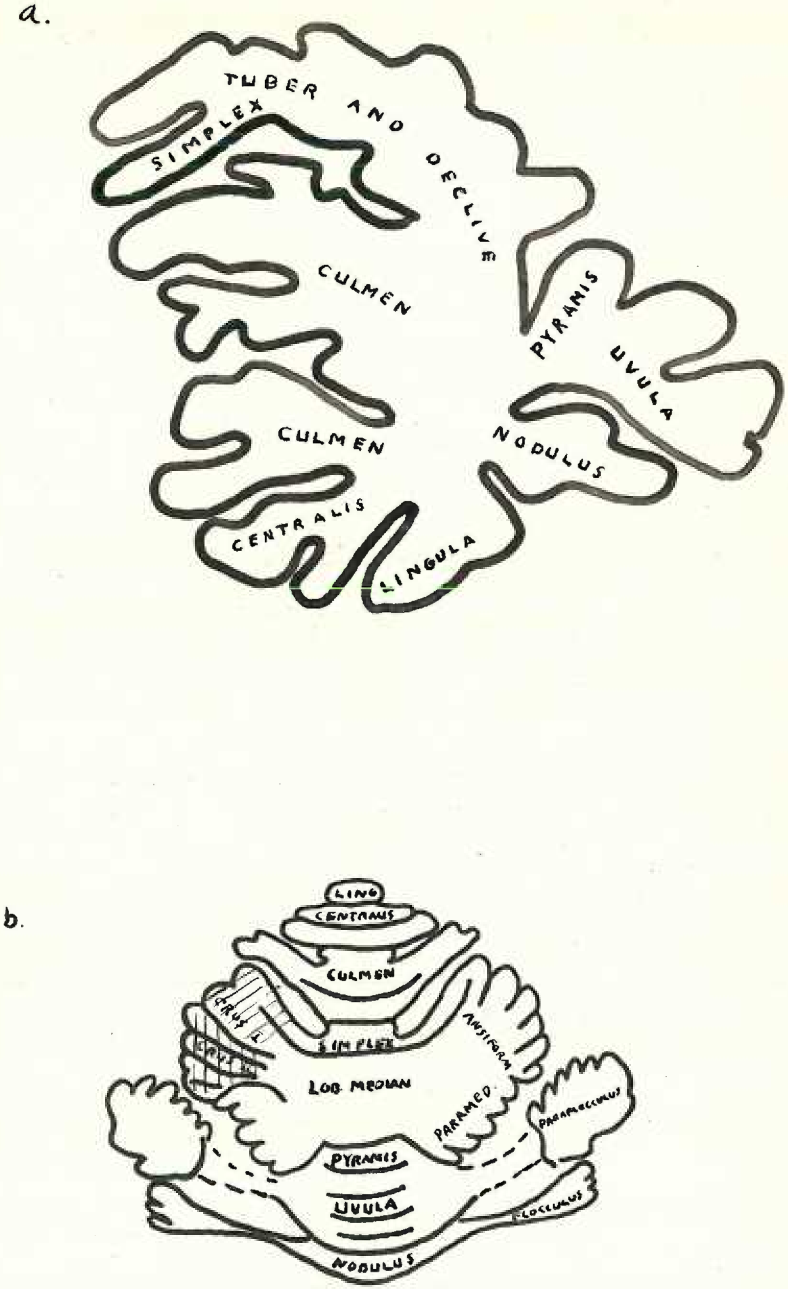
a.
TUBER AND DECLIVE
SIMPLEX
CULMEN
CULMEN
CENTRALIS
LINGULA
PYRAMIS
UVULA
NODULUS
b.
LING
CENTRALIS
CULMEN
CRUS I
CRUS II
SIMPLEX
ANSIFORM
LOB. MEDIAN
PARAMED.
PARAFLOCCULUS
PYRAMIS
UVULA
FLOCCULUS
NODULUS

FIG. 3

ascending axons could account for the later appearance of the positive potentials as seen here.

The use of strychnine to ascertain whether or not the first negative spike was influenced by synaptic transmission, and the histological demonstration of callosal fiber endings might add light to this question.

Also, the difference in wave form here seen might be accounted for by the findings of Curtis and Bard(38), who, in an earlier work on monkeys, stated, "the wave form is .. ... variable". In his later work, however, Curtis(36) made no comment on variability and presumably found the wave form to be constant throughout this series of experiments.

No consistent progressive change in latency with increasing age or weight could be found, and although this may have been due to a lack of comparability of loci of stimulation and differences in brain size, and hence length of fiber tracts in the animals studied, it should be noted that Curtis and Bard(38) found in adult animals a variable latency of from 10-40 msec., a range comparable to that found in our experiments.

MYELINIZATION OF THE CORPUS CALLOSUM

There was no trace of myelin found in the callosal system in any of the rabbits studied. In fact, the only trace of myelination found in this region of the brain was in the vestigium indusium griseum where a few myelinated fibers were seen first in the four-day rabbits.

These findings are in keeping with the late myelinization of the callosal system in the rat (Watson(15)), the cat (Tilney and Casamajor(3)), and the human (Flechsig(39), Langworthy(21)).

RESULTS OF STIMULATION OF THE CORTICO-PONTO-CEREBELLAR PATHWAY

Point to point relationships of cerebral cortex and cerebellum have been studied by electrical methods in larger animals (Curtis(40), Dow(41)). The diminutive morphological relationships of the cerebellum, together with the poor tenacity of life in the newborn rabbits under the conditions of these experiments, prohibited such investigations here. Hence, the stimulating electrode was gross in comparison with the small cerebrum studied. It was moved to various points on the frontal lobe (Mettler(42), Levine(43)) in an attempt to stimulate pontine afferent fibers. The lead electrode was routinely placed on the folium and tuber vermis or pyramis, on the contralateral cerebellar cortex and on the paramedian lobe. The lead electrode was moved about over the exposed area of each cerebellum until it was ascertained whether or not potentials could be evoked. An attempt was made to cover as much as possible of the portion of the cerebellum which corresponds to that demonstrated by Dow(41) in the cat and macaque to respond to cerebral stimulation. Figure 3, however, shows how the proximity of the posterior colliculus to the anterior surface of the cerebellum prevented exploration of the cerebellum in these young forms. It is possible then that stimulation of other areas, including the simplex and culmen, might have yielded potentials at an even earlier date than those seen in this experiment.

Response to cortical stimulation of the frontal lobe was seen in the vermis of only one of the twelve two-day old rabbits (Figure 5). The animal in which this occurred was the heaviest in that age group. Weighing 80 grams, this animal exceeded the mean weight of the two-day rabbits by 22 grams, and had a weight lying between the mean of the three and four day rabbits (Table I). Placing this animal in a group of rabbits of similar weight, regardless of their age, would put this animal in a group in which three out of four yielded positive results.

In the third day of life, three of eight animals gave positive responses. The smallest of these weighed only 44 grams, 5 grams below the mean for the one-day rabbits. A progressively greater number of positive responses occurred with increasing age. But the weight of the individual rabbit giving a positive response was not always near the mean weight for its age group.

Figure 6, showing responses obtained in leading from the paramedian lobe shows similar results.

Hence, it appears that weight and age need not go hand in hand as indicators of the maturity of the central nervous system. Yet both are equally potent factors in determining whether or not cortical stimulation will yield cerebellar potentials. This was shown by a correlation of .99 of total cerebellar responses with age and a correla-

Figure 4.

Percentage of response, as recorded from the cerebellum, (both paramedian and vermian recordings) to stimulation of the cerebral cortex, plotted against increasing age (days), and increasing weight (grams). The row of numbers, A, above each figure shows the number of animals used. Row B shows the number of animals giving positive responses.

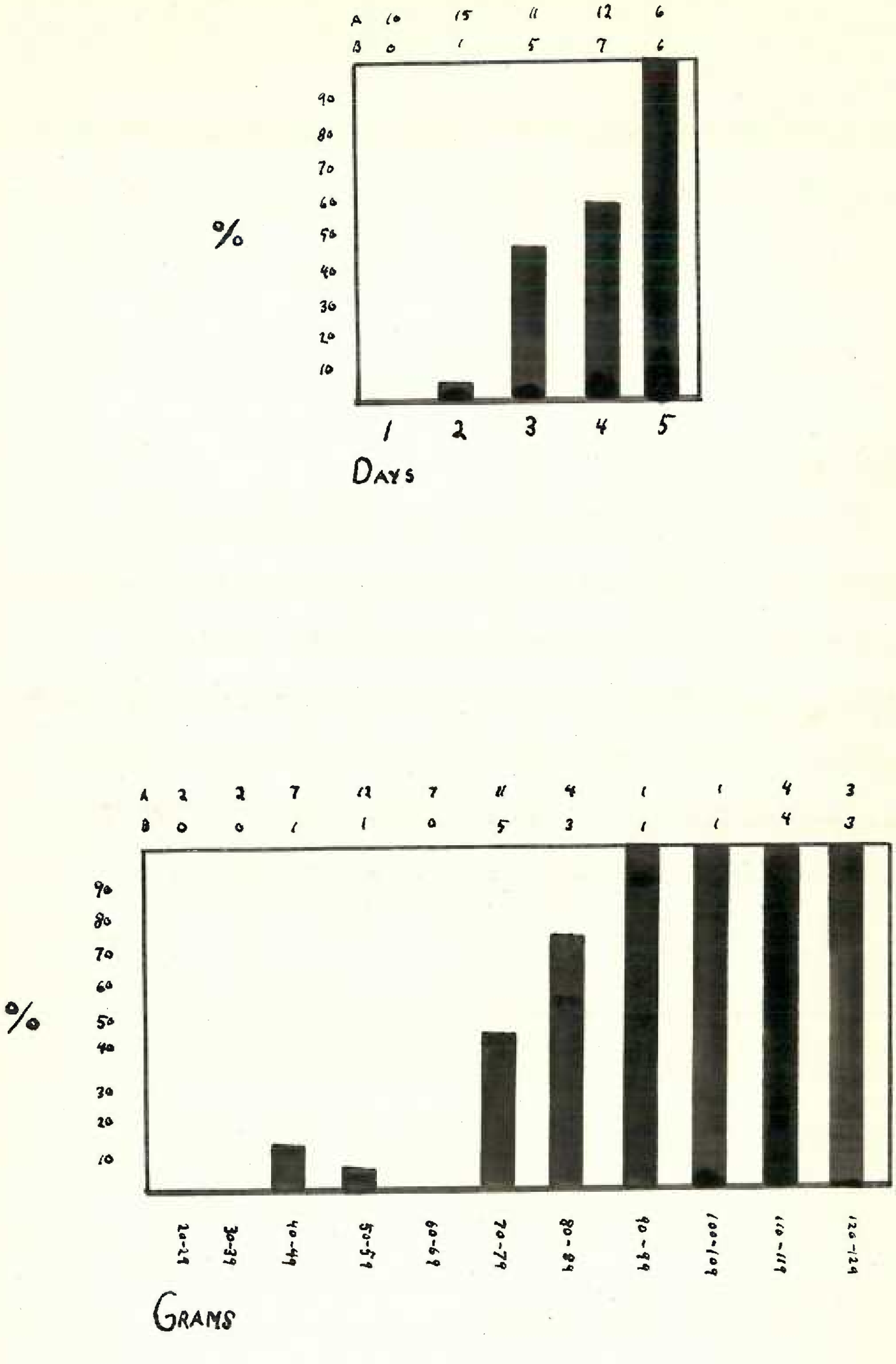
A 10 15 11 12 6
B 0 1 5 7 6
%
90
80
70
60
50
40
30
20
10
1 2 3 4 5
DAYS
A 2 2 7 12 7 11 4 1 1 4 3
B 0 0 1 1 0 5 3 1 1 4 3
%
90
80
70
60
50
40
30
20
10
20-29
30-39
40-49
50-59
60-69
70-79
80-89
90-99
100-109
110-119
120-129
GRAMS

FIG. 4

Figure 5.

Percentage of response, as recorded from the vermis, to stimulation of the cerebral cortex plotted against increasing age (days), and increasing weight (grams). The row of numbers, A, above each figure shows the number of animals used. Row B shows the number of animals giving positive responses.

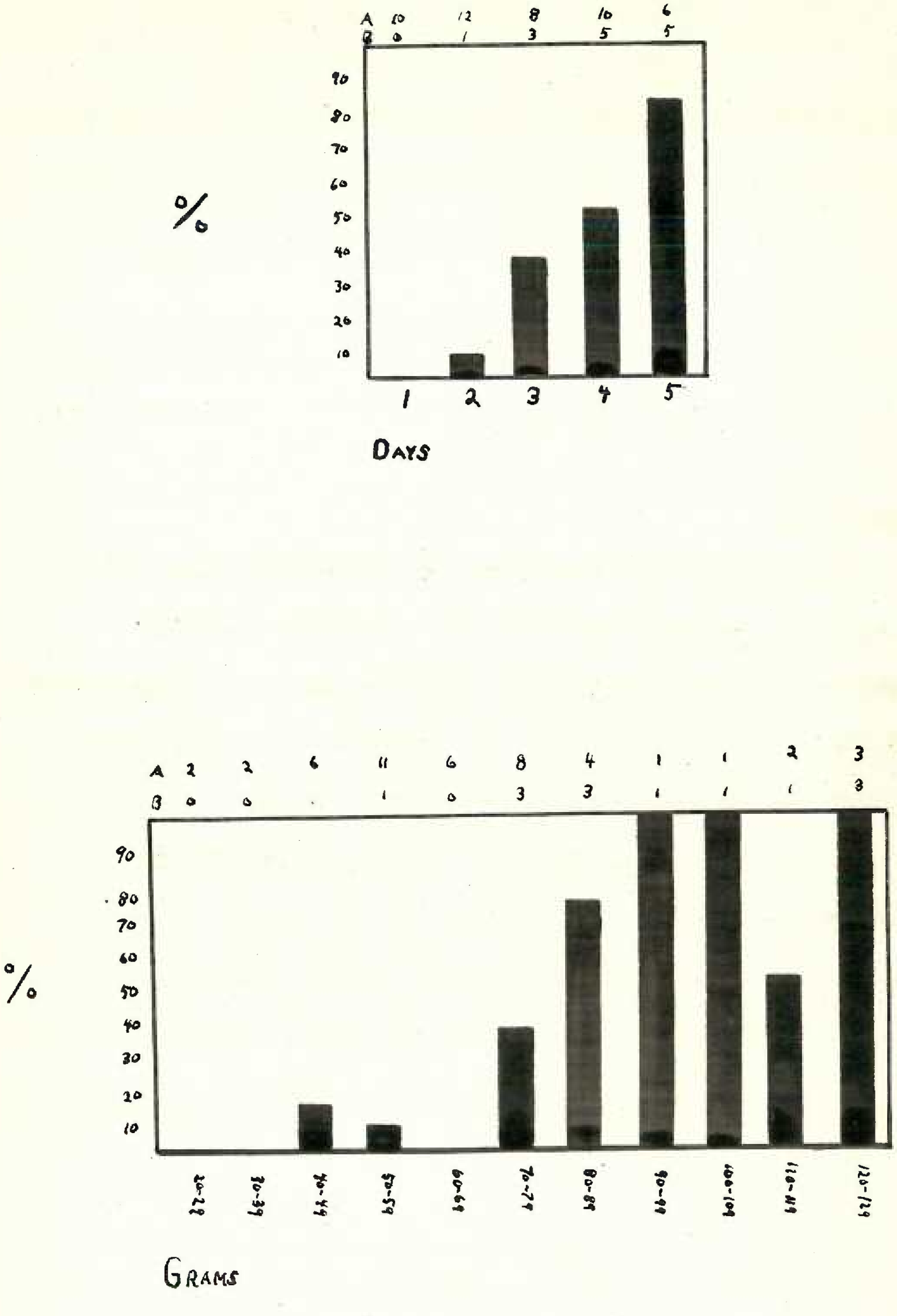
A 10 12 8 10 6
B 0 1 3 5 5
90
80
70
60
50
40
30
20
10
%
1 2 3 4 5
DAYS
A 2 2 6 11 6 8 4 1 1 2 3
B 0 0 1 0 3 3 1 1 1 3
90
80
70
60
50
40
30
20
10
%
20-29
30-39
40-49
50-59
60-69
70-79
80-89
90-99
100-109
110-119
120-129
GRAMS

FIG. 5

Figure 6.

Percentage of response, recorded from the paramedian lobe, to stimulation of the cerebral cortex plotted against increasing age (days), and increasing weight (grams). The row of numbers, A, above each figure shows the number of animals used. Row B shows the number of animals giving positive responses.

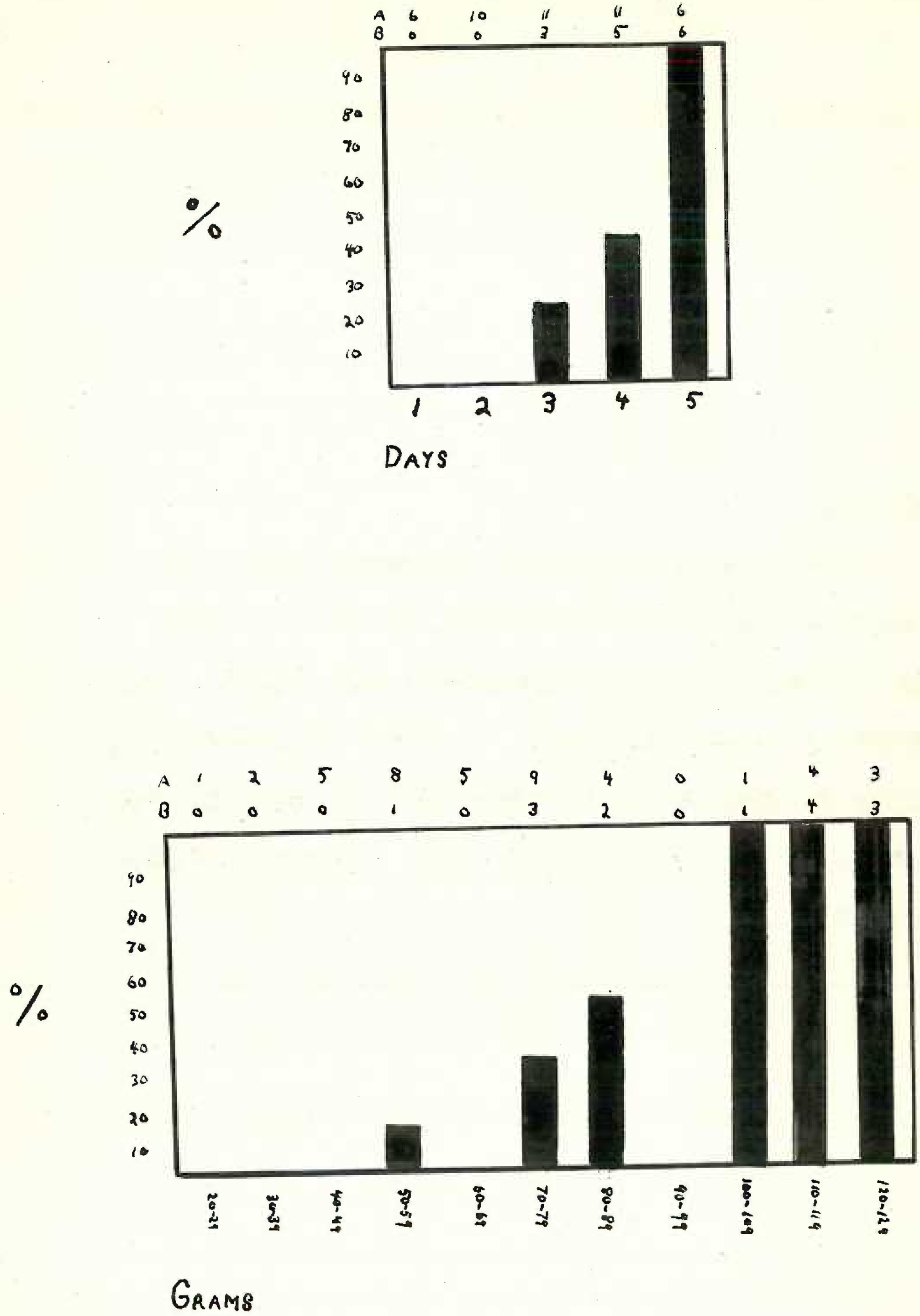
A 6 10 11 11 6
B 0 0 3 5 6
90
80
70
60
50
40
30
20
10
%
1 2 3 4 5
DAYS
A 1 2 5 8 5 9 4 0 1 4 3
B 0 0 0 1 0 3 2 0 1 4 3
90
80
70
60
50
40
30
20
10
%
20-29
30-39
40-49
50-59
60-69
70-79
80-89
90-99
100-109
110-119
120-129
GRAMS

FIG. 6

Figure 7.

Potentials obtained from the vermis after stimulation of the cerebral cortex. a. Two day old rabbit. b. Three day old rabbit. c. Four day old rabbit. d. Five day old rabbit. e. Response from the l. simplex to cortical stimulation (Dow(41)). An upward deflection is negative.

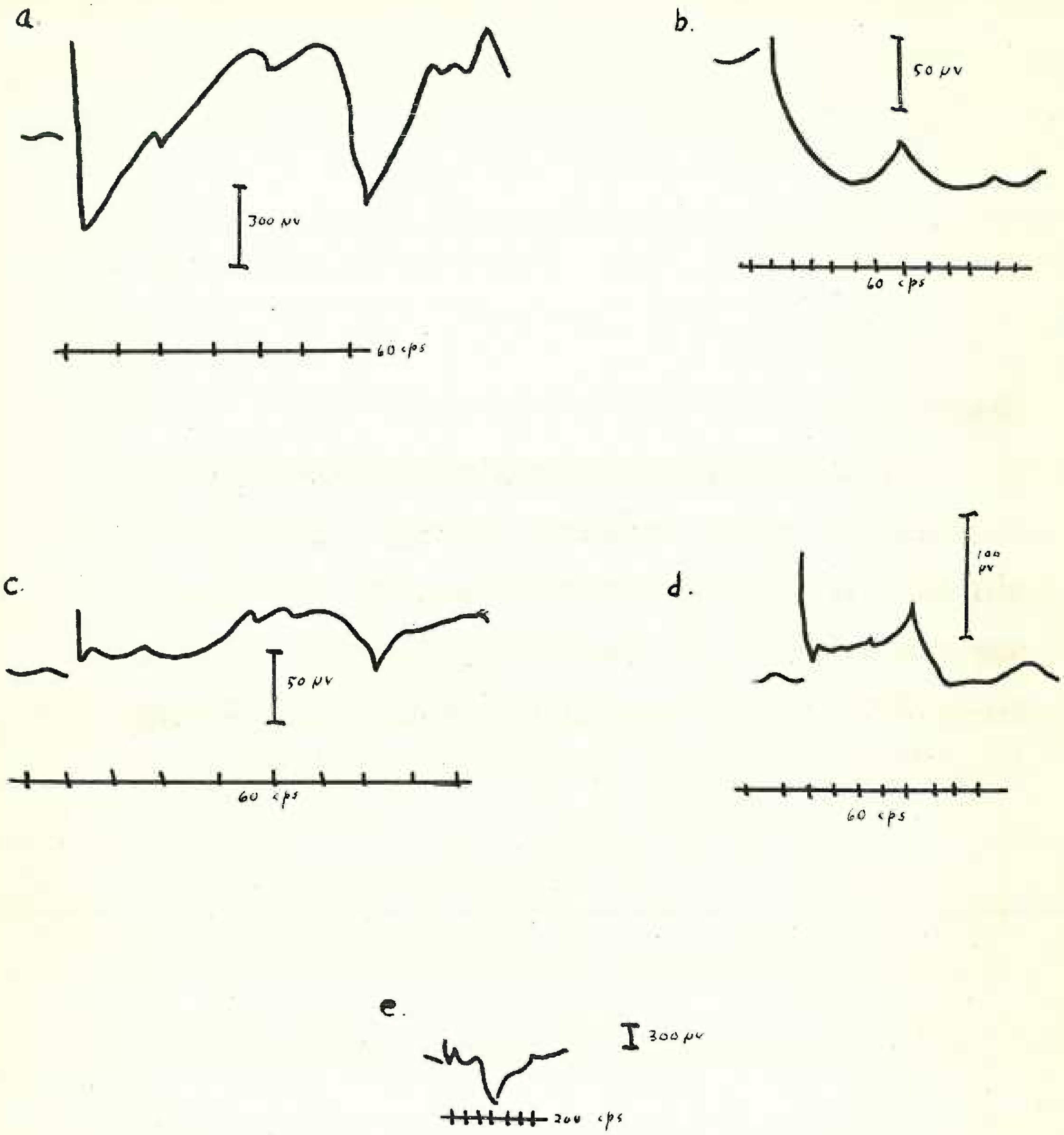
a.
300 µv
60 cps
b.
50 µv
60 cps
c.
50 µv
60 cps
d.
100 µv
60 cps
e.
300 µv
200 cps

FIG. 7

tion of .93 of total cerebellar responses with weight.

In this study responses were obtained from the mid vermis on the second day. The paramedianus gave no response until the third day. The accompanying study of myelin deposition showed medullation occurring in the medial portions of the cerebellum prior to the lateral portions. This might seem significant save for the fact that in none of the stages studied was there myelinization of the cortico-pontine or ponto-cerebellar fibers, and that such myelin as is seen in the cerebellum appears traceable to the phylogenetically older spino- and vestibulo-cerebellar connections.

Analysis of the action potentials in the vermis following cortical stimulation showed that they were unpredictable as to sign. This is in agreement with work in adult animals by Dow(41). In the experiments under consideration there were as many responses with negative sign as with positive. A biphasic potential occurred in the case of an 87 gram, five day old rabbit.

The latency of the response measured from shock artifact to the crest of the wave gave a mean of about 108 msec. for vermian responses, with a range of from 60 - 110 msec. No constant waves were noted at other latencies. Paramedian responses showed a similar lability of sign, a slightly greater tendency to biphasicity, and a mean latency of about 77 msec., with a range of from 40 - 180 msec. There was noted a tendency towards a

Figure 8.

a. Mean latencies of the response, as recorded from the paramedian lobe, to stimulation of the cerebral cortex (millesseconds) plotted against increasing age (days), and increasing weight (grams).

b. Mean latencies of the response, as recorded from the vermis, to stimulation of the cerebral cortex (millesseconds) plotted against increasing age (days), and increasing weight (grams).

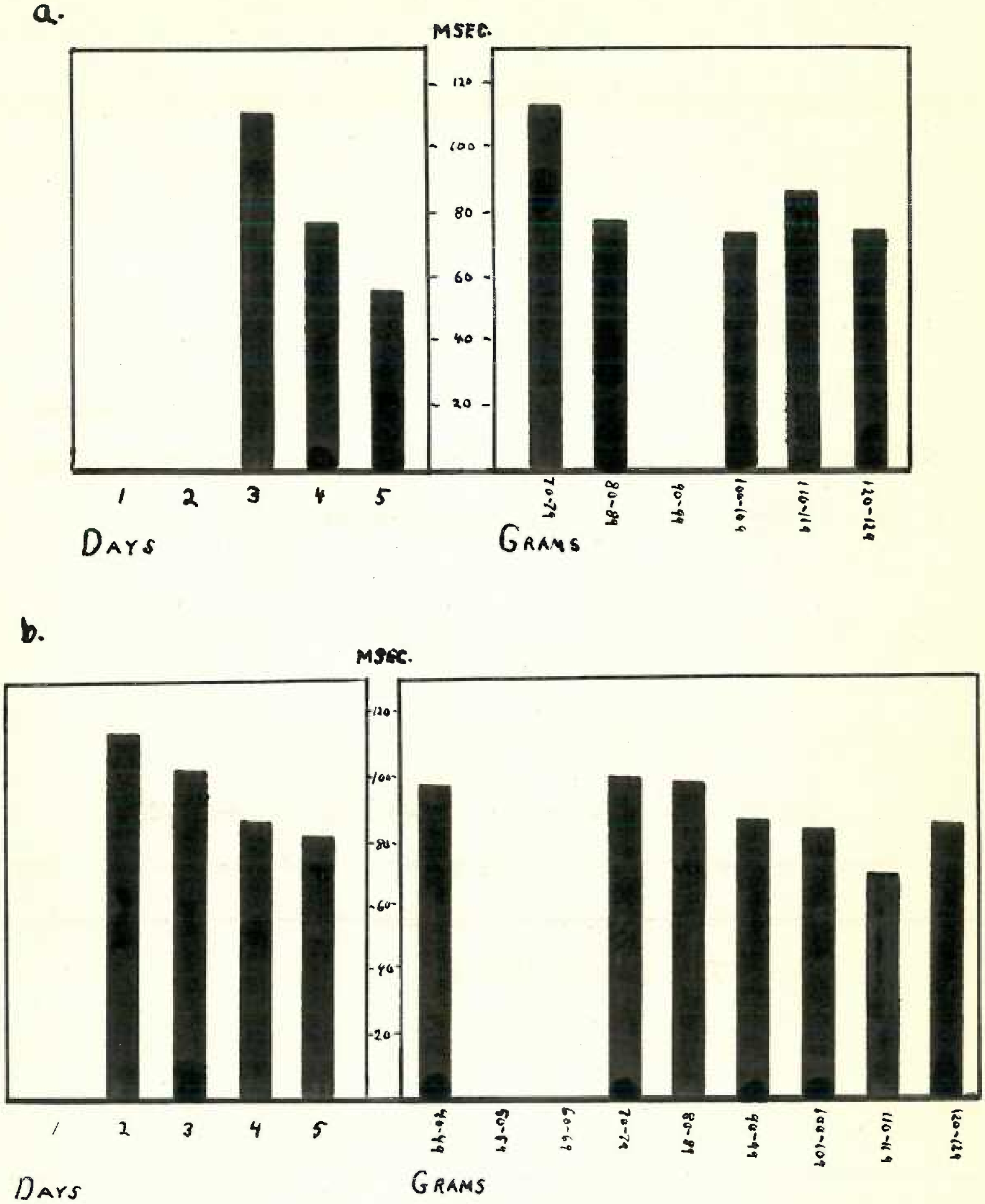
a.
MSEC.
120
100
80
60
40
20
1
2
3
4
5
DAYS
70-79
80-89
90-99
100-109
110-119
120-129
GRAMS
b.
MSEC.
120
100
80
60
40
20
1
2
3
4
5
DAYS
40-49
50-59
60-69
70-79
80-89
90-99
100-109
110-119
120-129
GRAMS

Fig. 8

shortening of this latency both with increasing age and increasing weight (Figure 8). Inconsistencies in this trend may be accounted for on the basis of the variable placement of the lead and stimulating electrodes which brought about differences in the length of the conducting pathway.

Dow(41) in his work on the adult cat and macaque, found latencies of 18-30 msec. In the light of this, and in view of the shortening of the latency periods found in the young rabbits, it would be of interest to compare similar responses in the adult rabbit. One might thus determine if maturation, including the appearance and completion of myelinization, would shorten the period of latency over these tracts, despite their increase in length due to enlargement of the maturing brain.

MYELINIZATION OF THE CORTICO-PONTO-CEREBELLAR TRACTS

A study of Weigert preparations in the rabbit brains of from one to five days revealed no trace of myelinization in the cortico-pontine connections. No myelinated fibers were to be seen connecting the pons with the cerebellum in any of the animals studied, and it was only in one five-day rabbit that some short, incompletely myelinated fibers were to be seen, in the base of the pons.

In the literature on myelinization, description of that process in the rabbit has not been extensive (Langworthy(12)) and a description of the fiber systems under investigation was not found in the literature. From the work in other mammalian forms (Langworthy[11,48], Tilney and Casamajor[3], and Keene and Hewer[43,47], however, it appears that this tract receives its component of myelin at a relatively late time.

An examination of these sections for the purpose of describing the process of myelinization in the cerebellum was attempted. It was found, however, that complete serial sections would be required for this purpose.

Suffice it to say that the more medial portions of the cerebellum appeared to become medullated prior to the more lateral portions. The vestibulo-cerebellar connections were seen in the one-day animal as were also the dorsal and ventral spino-cerebellar pathways. Of these, the dorsal tract was the heavier, but examination of the individual fibers under higher magnification failed to reveal any difference in maturity of the myelin sheath as judged by the amount of beading, segmentation and vacuolation of the myelin (Gerin[27]). The brachium conjunctivum was well shown in the one day rabbits.

SUMMARY AND CONCLUSION

1. The fibers of the corpus callosum in one to five day old rabbits are capable of mediating nerve impulses evoked by electrical stimulation. The responses were obtained in rabbits weighing over 40 grams, and an investigation of the one and two day old rabbits below this weight failed to yield positive results. Correlations of positive responses with increasing age and weight were similar.

2. No myelinization was seen in the corpus callosum throughout the series studied.

3. The fibers of the cortico-ponto-cerebellar tract of two to five day old rabbits are capable of mediating nerve impulses evoked by electrical stimulation. These impulses were recorded from the vermis. Responses were not obtained from the paramedian lobe until the third day. Correlations of positive responses with increasing age and weight were similar.

4. No myelinization of the cortico-pontile tracts were seen in this series.

5. It is concluded that myelinization of the fibers of the corpus callosum and cortico-ponto-cerebellar tracts is not essential for the mediation of nerve impulses produced by electrical stimulation.

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