On the Percentage of Water in the Brain and in the Spinal Cord of the Albino Rat

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CORRECTIONS

Page 122, line 23
For "15 to 16," read "17 to 18"

Page 138, line 5
For "P. 19" read "P. 134"

Page 143, next to bottom line
For "constituents the" read "constituents of the"

LIMENTS OF

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THE WISTAR INSTITUTE
PHILADELPHIA

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WITH FIVE FIGURES

The object of this study has been to obtain a continuous record of the change in the percentage of water in the central nervous system of the albino rat during its life cycle, and to correlate this with the other important changes in the nervous system which are commonly recognized. These results in turn should put us in a position to determine to what extent and in what way this character may be modified.

Although it has long been known that at birth the percentage of water in the central nervous system was much greater than at maturity, yet the change in this character through the life cycle has never been systematically followed, and it thus happens that there are no other extensive records with which to make comparison. The relations of existing data to this investigation will be discussed later on.

The data used for the following study were largely obtained from the same animals which furnished the records employed for the two previous researches on the weight of the brain and of the spinal cord of the albino rat under different conditions of age, body-weight and body-length (Donaldson '08 and '09) although many cases have been necessarily excluded because the percentage of water had not been determined. On the other hand, a few new records have been added to the original series.

In carrying on this work, which has extended through a number of years, I have been greatly assisted by Dr. Hatai, as well as by two of my former students, Dr. Polkey and Dr. Whitelaw, both of whom made a number of the determinations of water under my directions, and to all of these gentlemen I wish here to express my obligations for assistance.

Technique. The determination of water has been made for the entire encephalon severed from the cord at the level of the first spinal nerve, and for the entire cord, the spinal nerves having been clipped away at their origin from the cord. The rats used were chloroformed, eviscerated and rapidly dissected. No special device for preventing evaporation during dissection was used.

The percentage of water applies therefore to the nerve structures proper, surrounded by the meninges and containing such blood as usually remains after the foregoing treatment.

The details of the technique according to which the brain and spinal cord were removed have been already given (see Donaldson '08, p. 346). Each brain or cord was placed in a small glass-stoppered weighing bottle, and after being weighed in the fresh state, was dried in a closed water bath which had a temperature ranging from 85°–95° C. and then was cooled in a dessicator over sulphuric acid, and reweighed.

The brain took somewhat longer to dry as a rule than the spinal cord, but usually seven days in the water bath served to bring it to a constant weight. At various times objections have been raised to the determination of the percentage of water by the use of heat. The other method which is most approved is that of drying the material at the room temperature or somewhat above, in a vacuum over sulphuric acid.

A comparison of these two methods has been made for the brain and cord of the rat, but no significant differences have thus far been found. I shall, however, reserve the discussion of the data on which this statement is based for another occasion.

The percentage of water in the brains of albino rats of different body weights. The number of cases is 409 males and 212 females. The mean values for the percentage of water in the brain for given body weights differing by 10 grams, as determined by a correlation table, are entered in table 1.

The examination of table 1 shows for the brain a relative loss of water amounting to about ten units between birth (body weight 5 grams) and the end of the series. This loss is most

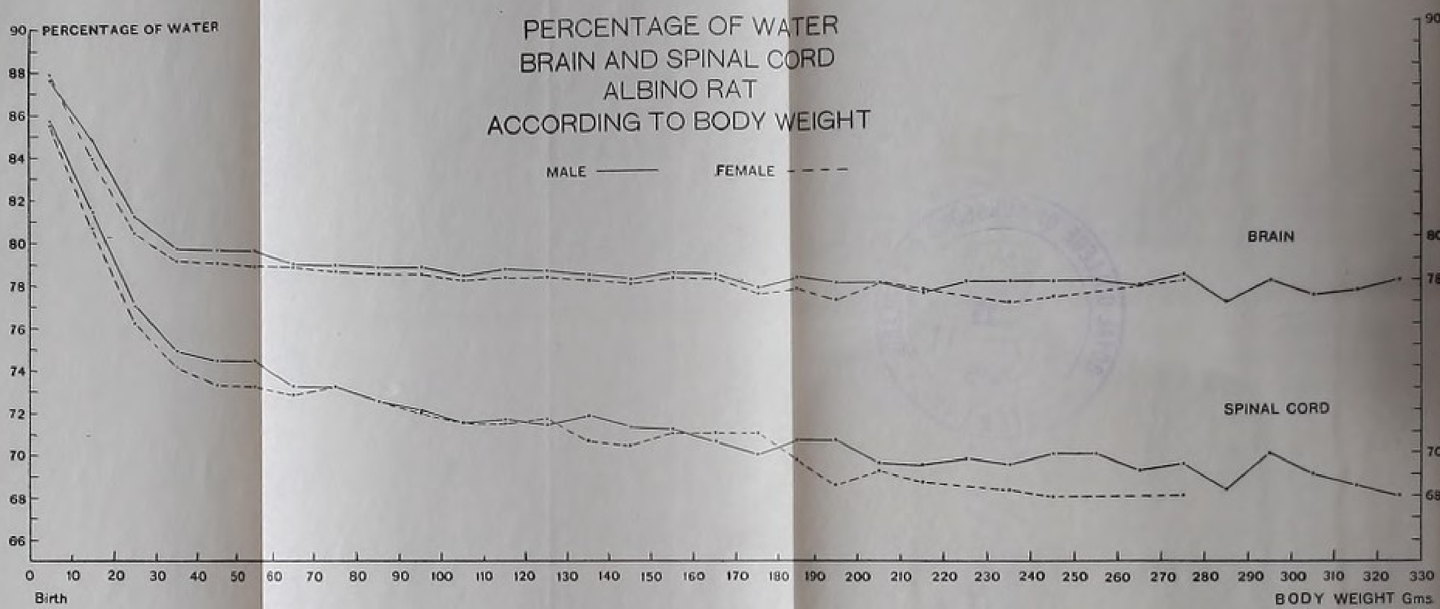

CHART 1

To show the changes in the percentage of water in the brain and in the spinal cord of the albino rat of different body weights. The data for the two sexes are plotted separately.

TABLE I.

The mean values of the percentage of water in the brain and spinal cord of the albino rat.[1] *Both sexes arranged according to body weights, increasing by 10 gram increments.*

BODY WEIGHT	PERCENTAGE OF WATER			
	BRAIN		SPINAL CORD	
	Male	Female	Male	Female
Grams.				
5	87.6	87.9	85.7	85.5
15	84.8	83.9	81.4	80.7
25	81.2	80.4	77.0	76.2
35	79.7	79.1	74.9	74.1
45	79.6	79.0	74.4	73.3
55	79.5	78.8	74.4	73.2
65	78.9	78.8	73.2	72.8
75	78.9	78.6	73.2	73.2
85	78.8	78.5	72.5	72.5
95	78.8	78.5	72.1	72.0
105	78.4	78.2	71.5	71.5
115	78.7	78.3	71.7	71.5
125	78.6	78.3	71.4	71.7
135	78.4	78.2	71.8	70.6
145	78.2	78.0	71.3	70.4
155	78.5	78.3	71.2	71.0
165	78.4	78.2	70.6	71.0
175	77.8	77.5	70.0	71.0
185	78.3	77.8	70.7	69.8
195	78.0	77.2	70.7	68.6
205	78.0	78.0	69.6	69.3
215	77.5	77.7	69.5	68.7
225	78.0		69.8	
235	78.0	77.0	69.5	68.3
245	78.0	77.3	70.0	68.0
255	78.0		70.0	
265	77.8		69.2	
275	78.3	78.0	69.5	68.0
285	77.0		68.3	
295	78.0		70.0	
305	77.3		69.0	
315	77.5		68.5	
325	78.0		68.0	

[1] For reasons similar to those previously given (see Donaldson '08, pp. 156–157), the individual records are not printed. These however are on file and copies of them may be had by application to the Director of the Wistar Institute.

rapid at the time when the brain is growing most actively. Table 1 further shows that the percentages for the females are in general slightly less than those for the males of the same body weights. Chart 1, which is based on table 1, exhibits this relation.

As we shall see later, the percentage of water in the central nervous system is more closely correlated with age than with the body weight or brain weight. Nevertheless, it will most often occur that it is desired to estimate the probable percentage of water in cases where the weight of the body or brain alone are known, and the foregoing table 1 furnishes the means of doing this for animals which have been grown under the ordinary normal conditions.

It has been already demonstrated (Donaldson '06) that for a given age, the body weight of the female is less than that of the male, consequently the comparison in each case is here between males that are younger than the females with which they are contrasted, and as increasing age is an important factor tending to reduce the percentage of water, it follows that the males, which are younger, should show, as they do, a slightly greater percentage of water.

Percentage of water in the spinal cord. In the spinal cord the relative loss of water with increasing body weight is greater than in the brain, being from 15 to 16 units. Although the initial percentage is somewhat less, yet the subsequent loss is regularly more rapid than that in the brain. The percentage of water in the two sexes is related in the same way as in the brain. The observations are given in table 1 and in chart 1.

Percentage of water in relation to age. To support the suggestion that the males in the foregoing tables show a greater percentage of water, because they are younger than the females, the data have been rearranged according to age. In many cases the age was not known, and this reduces the number of records to 358 males and 169 females. The results in the form of mean values, based on a correlation table are given in table 2 and plotted in chart 2, the entries being made for ten day intervals. When thus arranged, it appears that in the brains of males and females of like age, the percentage of water is similar.

For the brain, the records show in both sexes ranges in the percentage of water in the different age groups as follows:–

AGE			PERCENTAGES
0–10 days	total range	3 units	86–89
10–20 days	total range	5 units	82–87

From 20 to 100 days the range diminishes, and after this latter age it does not amount to more than one unit. The ranges for the spinal cord are less than those for the brain.

It will naturally be asked whether among individuals belonging to the same litter, reared under similar conditions and killed at exactly the same age there is any difference in the percentage of water between those having relatively heavy brains and spinal cords and those in which these organs are relatively light. This question seems to be answered in the negative by the result of 25 pairs of observations recently made.

The figures are as follows:—

	PER CENT OF WATER	PER CENT OF WATER	
Heavy brains	78.651	72.436	Heavy cords
Light brains	78.649	72.465	Light cords

In both instances as is seen, the differences found are too small to be significant. It may be added that the weight of the light brains was about 96 per cent that of the heavy, and similarly the weight of the corresponding light spinal cords about 93 per cent. Such differences as we find therefore among specimens of the same age must depend on some other cause than the individual variations in the weight of the central nervous system.

I feel sure that the irregularities seen in the curve for the cord, chart 2, 95–115 days, are purely incidental and would not appear on repeating the observations.

At the same time it is seen that the percentage of water in the female spinal cord after the period of rapid growth, is in general a trifle higher than in the male. This is an unexpected result. The mean difference as determined from those entries in table 2 where there are data for both sexes at a given age (i. e., up to 230–240 days) is 0.36 per cent. At the moment this difference is most readily explained as one effect of the passive lengthening

TABLE 2

The mean values of the percentage of water in the brain and spinal cord of the albino rat. Both sexes arranged according to age, increasing by 10 day increments.[2]

AGE IN DAYS	PERCENTAGE OF WATER			
	BRAIN		SPINAL CORD	
	Male	Female	Male	Female
0–10	87.4	87.4	84.8	84.8
10–20	83.7	83.4	80.5	80.3
20–30	81.3	81.6	77.2	77.1
30–40	79.4	80.0	74.3	74.8
40–50	79.2	79.0	73.9	73.7
50–60	79.0	79.3	72.9	74.2
60–70	79.3	78.8	74.5	73.2
70–80	78.9	78.8	72.9	73.8
80–90	78.3	78.8	72.8	73.8
90–100	78.7	79.0	73.0	74.1
100–110	78.3	78.0	70.0	70.8
110–120	78.6	78.7	71.3	72.5
120–130	78.3	78.2	71.6	71.7
130–140	78.2	78.0	70.0	71.0
140–150		78.0		72.0
150–160	78.1	78.0	70.6	70.8
160–170	78.2	78.3	71.0	71.3
170–180		78.0		71.0
180–190	78.0	79.0	71.0	71.5
190–200				
200–210	78.0	79.0	71.0	72.0
210–220	78.3	78.3	71.0	71.7
220–230	78.7	78.3	72.2	71.0
230–240	78.5	78.0	71.0	71.0
240–250				
250–260				
260–270				
270–280				
280–290				
290–300	78.5		72.0	
300–310		77.4		68.2
310–320		77.3		68.0

[2] Note that the values here given begin with 0–10 days, i..e, a mean age of *five days after birth.* Hence the initial percentages are less than those in table 1 which gives the values at 5 grams, approximately the weight at birth.

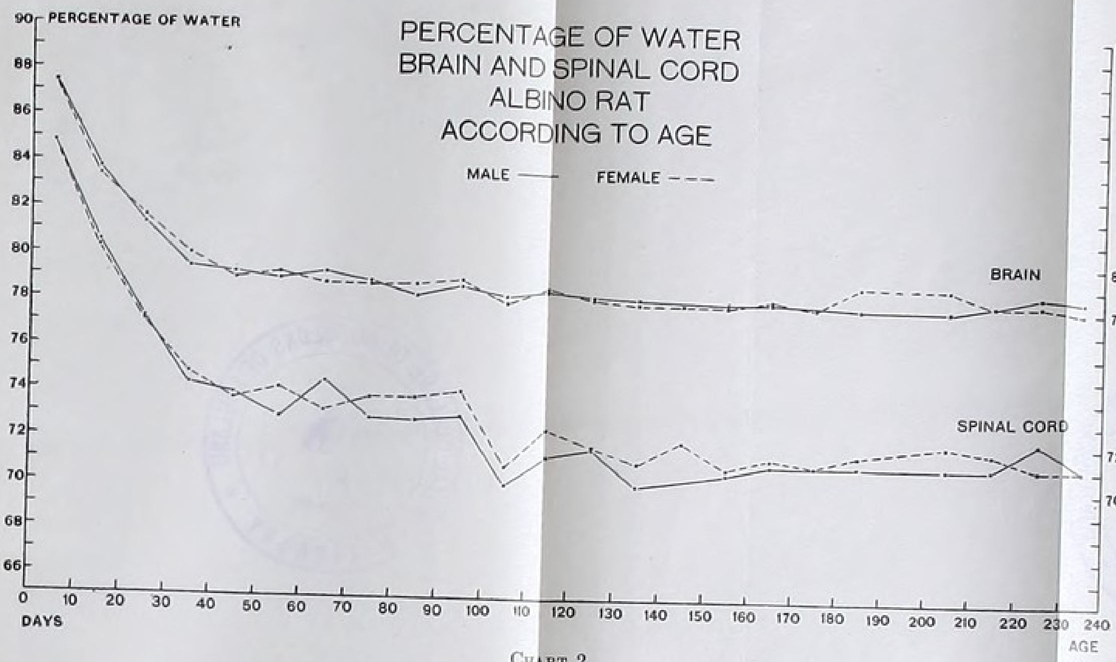

CHART 2

To show the changes in the percentage of water in the brain and in the spinal cord of the albino rat at different ages. The data for the two sexes are plotted separately. It is to be noted that the first entry is at the mean age of five days.

1:

Th… …nal cord of the alb…
…0 day increments.[2]

SPINAL CORD
Female
84.8
80.3
77.1
74.8
73.7
74.2
73.2
73.8
73.8
74.1
70.8
72.5
71.7
71.0
72.0
70.8
71.3
71.0
71.5
72.0
71.7
71.0
71.0
68.2
68.0

2 … …s, a mean age of *five*
day… …those in table 1 which
giv… …birth.

of the spinal cord which for a given age is relatively somewhat greater in the male than in the female (Donaldson, '09 pp. 163–164). The effect of this lengthening would be to diminish the percentage of water. The influence of passive lengthening is discussed more fully later on.

Theoretic curves. When we take the more extensive series of mean values which is that for the males as given in table 1, and draw the theoretic curves based on them, we obtain the relations shown in chart 3, the entries being arranged according to body weight. The data for this chart are given in table 3. For the formulas for these curves, I am indebted to Dr. Hatai.

The formulas for the percentage of water in the brain of the male albino rat are as follows:

Up to a body weight of 30 grams

$$y = 99.5 - 12.6 \log (x + 3.5) \quad [1]$$

and from a body weight of 30 grams on

$$y = 82.62 - 2 \log (x - 10) \quad [2]$$

In the case of the percentage of water in the spinal cord of the male albino rat we have for body weights up to 35 grams

$$y = 94.9 - 12.8 \log (x) \quad [3]$$

and from a body weight of 35 grams on

$$y = 85.2 - 6.5 \log (x) \quad [4]$$

In all these formulas y = the percentage of water and x = the weight of the body in grams.

The formulas are of the same type as those used to express the growth changes described in several previous investigations (Donaldson '08, '09; Hatai '09), and have their main value as convenient expressions of the several series of observations.

Calculations (based on table 1, down to and including the entries for 275 grams body weight) show that in general for given body weight, the females which are under these conditions relatively older as compared with the males, have a percentage of water lower by 0.37 per cent in the brain and 0.60 per cent in the spinal cord. The theoretic values for the female can therefore be obtained approximately by applying these corrections to the determinations here given for the males.

Having thus presented the data on the percentage of water

TABLE 3

Giving the values of the percentage of water in the brain and spinal cord of the male albino rat, calculated according to the formulas given above. Brain: formulas 1 and 2; spinal cord: formulas 3 and 4. For comparison the observed values for the male, taken from table 1, are repeated here. Arranged according to body weights

BODY WEIGHT	PERCENTAGE OF WATER			
	BRAIN MALE		SPINAL CORD MALE	
	Calculated	Observed	Calculated	Observed
grams				
5	87.79	87.6	85.96	85.7
10	85.26		82.10	
15	83.50	84.8	79.80	81 4
20	82.24		78.26	
25	81.17	81.2	76.98	77.0
30	80.22		75.96	
35	79.83	79.7	75.16	74.9
45	79.53	79.6	74.45	74.4
55	79.31	79.5	73.89	74.4
65	79.14	78.9	73.42	73.2
75	78.99	78.9	73.01	73.2
85	78.87	78.8	72.66	72.5
95	78.76	78.8	72.34	72.1
105	78.66	78.4	72.06	71.5
115	78.58	78.7	71.81	71.7
125	78.50	78.6	71.57	71.4
135	78.43	78.4	71.35	71.8
145	78.36	78.2	71.15	71.3
155	78.30	78.5	70.96	71.2
165	78.24	78.4	70.79	70.6
175	78.19	77.8	70.62	70.0
185	78.13	78.3	70.46	70.7
195	78.09	78.0	70.31	70.7
205	78.04	78.0	70.17	69.6
215	78.00	77.5	70.04	69.5
225	77.96	78.0	69.91	69.8
235	77.92	78.0	69.79	69.5
245	77.88	78.0	69.67	70.0
255	77.84	78.0	69.56	70.0
265	77.81	77.8	69.45	69.2
275	77.77	78.3	69.34	69.5
285	77.74	77.0	69.24	68.3
295	77.71	78.0	69.15	70.0
305	77.68	77.3	69.05	69.0
315	77.65	77.5	68.96	68.5
325	77.62	78.0	68.87	68.0
470	77.30		67.80	

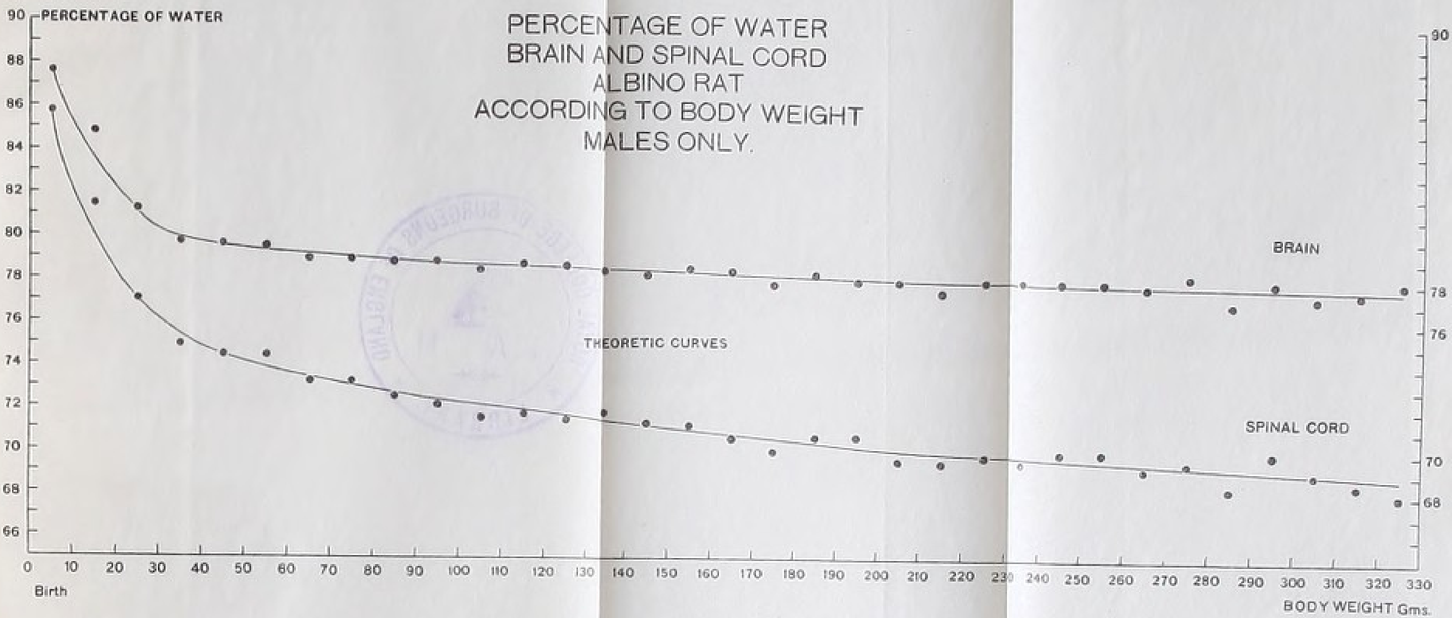

CHART 3

Theoretic curves showing the changes in the percentage of water in the brain and in the spinal cord of the male albino rat at different body weights. The dots ● show the observed mean values.

in the brain and cord of rats according to age and to the normal body weight, we pass to the question of the extent to which the percentage of water may be modified experimentally under special conditions. The amount of modification which has been experimentally induced is thus far extremely slight, nevertheless some deviation seems to occur. The evidence is as follows:

(*a*) *Some conditions which increase the percentage of water in the brain and cord.* Dr. Watson ('05) when working on the effects of the bearing of young on the weight of the central nervous system in the albino rat, noted that the mated animals had both heavier brains and heavier cords. He noted also that the mated rats, as compared with the unmated of like age, had the following percentages of water:

	NO. OF CASES	PERCENTAGE OF WATER Brain	Cord
Female mated	(8)	77.47	68.51
Female unmated	(10)	77.37	68.29

This shows that the mated rats had in the brain 0.10 per cent more water than the unmated, and in the spinal cord 0.22 per cent more. Thus, even though the brain and cord in the mated series were absolutely heavier, yet if the higher percentage of water be taken as an index of a lesser maturity, the central nervous system of the mated rats must be regarded as physiologically younger. Such slight differences would, of course, not be worthy of remark if they had been obtained merely by the averaging of widely varying data, but in this case comparisons were made by Watson in five different groups for the brain, and five for the cord, and in only one (in the cord) out of the ten comparisons, did the mated rats show a smaller percentage of water. Thus though the difference is small, it was found to occur in the same sense in nine cases out of the ten. This seems to justify the conclusion which Watson drew that mated female rats had a slightly higher percentage of water in the brain and spinal cord than the unmated females belonging to the same litters.

Hatai ('07) also has made observations on the modifications of body growth as the result of which the percentage of water in the central nervous system was slightly increased.

When young rats were underfed for three weeks and then returned to a normal diet, Hatai found that their subsequent increase in body weight was somewhat more rapid than that of the control group, and in the case of the males, the final weight even greater. Hatai's table IV ('07) is here repeated.

TABLE 4.

	ENCEPHALON PER CENT	SPINAL CORD PER CENT
Male controls	77.50	69.71
Male experimented	77.75	70.05
Female controls	77.50	69.40
Female experimented	77.75	70.10

Taking both sexes together, the experimented groups, as shown in the above table 4, had on the average a percentage of water in the brain greater by 0.25 per cent and in the cord by 0.52 per cent. As will be observed, this treatment produced a rather greater alteration in the percentage of water than was obtained by Watson in the case of the mated and unmated females.

In the foregoing instance there were fourteen pairs of brains between which comparisons were made, and in thirteen of these the experimented rats show a greater percentage of water. In the case of the spinal cord, eleven pairs out of a total of fourteen show the experimented rats to have the greater percentage of water, so that here again although the variation induced by the treatment is not great, yet a slight change seems to be really effected.

In another series of observations Hatai ('08) got still more marked differences in the percentage of water. In this case there were seven pairs of contrasted individuals. Seven individuals were used as controls and seven others, from the same litter, fed with small quantities of a varied diet and thus stunted. When these latter had attained an average age of about 140 days, they were put on a full normal diet for thirty days and then both lots were killed and examined at the same time.

During the thirty days of normal feeding, the stunted rats grew in weight and length. When killed at this time it was found that the stunted rats had in both brain and cord a distinctly greater percentage of water than did the controls. The difference is in the same sense in all the pairs and for both the brain and spinal cord. The average figures are as follows.—

		PERCENTAGE OF WATER	
AVERAGE AGE	NO. OF CASES	Brain	Cord
170 days	7 stunted	78.618	72.613
170 days	7 controls	78.378	71.076

As the figures show, the percentage of water in the stunted group is greater by 0.24 per cent in the brain and 1.53 per cent in the cord.

The difference in the case of the brain is about that found in the preceding investigation, but that in the cord is much greater. The reason for the greater percentage of water in the case of the spinal cord requires still to be investigated.

The foregoing conditions are the only ones which at the moment have been shown to increase the percentage of water in the central nervous system of the rat, and in all cases this increase seems to be associated with more vigorous growth processes.

(*b*) *Some conditions which decrease the percentage of water in the brain and spinal cord.* On the other hand, in 1904 Hatai determined that in rats killed at the end of three weeks of underfeeding the experimented rats, though initially heavier, had on the average only about 44 per cent of the body weight of the controls.

This result was due not only to an arrest of growth, but to an actual loss, as measured by changes in the weight of the entire body and also of the brain. At the termination of the experiment, the brain weight in the underfed group was about 11 per cent less than in the controls, approximately two thirds of this deficiency being due to the arrest of growth, and one third (4.3 per cent) to actual loss (see table IV, Hatai '04). On the other hand, the percentage of water in the brain was

79.11 per cent in the controls
78.91 per cent in the experimented,

thus showing a deficiency of 0.2 per cent in the latter. If the process of the *reduction* of the percentage of water had been *stopped* by the underfeeding, which stops the growth as indicated by the body weight and the brain weight, we should have found the higher percentage in the experimented rats.

As further evidence that the disturbance of the growth process involves but slightly the changes in the percentage of water correlated with increasing age, we have the data in this same paper by Hatai given in Table IV, series II where the control group was killed and examined at the beginning of the experiment. Here the percentages are

79.01 for the control rats
78.71 for the experimented rats

giving a difference of 0.3 per cent.

The difference in this case is greater than in the preceding because not only is the percentage of water in the experimented group slightly diminished by the treatment, but also because the experimented group was three weeks older than the controls at the time of killing, thus giving a total loss of 0.3 per cent in series II against 0.2 per cent in series I, where both controls and experimented rats were killed at the same time. This again supports the view that underfeeding does not arrest the changes in the percentage of water characteristic for advancing age, but may rather hasten them.

The weight of water in the brain and spinal cord. The preceding descriptions have been given in the terms of the percentage of water. A better view of the changes taking place can be obtained however by following the suggestion of my colleague, Dr. Hatai, and showing the changes in the absolute weight of the water in the brain and cord at different weights of these parts. This eliminates the time factor which has modified the previous forms of presentation, and gives a simple and suggestive picture of the changing relations between the water and the solids.

The determinations thus made are given in table 5 and have been also plotted in charts 4 and 5

The following table 5 shows that for the successive increments of weight, the female brain has less water than the male brain of like weight. This is undoubtedly due to the fact that under the conditions of comparison, the female brains are the older. Owing however to the relatively large interval of brain weight used in the correlation tables, from which the means in table 5 were obtained, the absolute weights for the amounts of water increase irregularly, and this in turn makes the progressive per-

TABLE 5

The weight of water present in the brain and in the spinal cord according to the absolute weight of these organs. Sexes distinguished. Based on the entire series of records for both sexes. Mean values determined from correlation tables.

BRAIN WEIGHT	AMOUNT OF WATER — BRAIN		SP. CD. WEIGHT	AMOUNT OF WATER — SPINAL CORD	
	Male	Female		Male	Female
grams	*grams*	*grams*	*grams*	*grams*	*grams*
0.25	0.208*	0.175*	0.03	0.028	0.027
0.35	0.325	0.290	0.07	0.067	0.062
0.45	0.350	0.400	0.11	0.085	0.083
0.55	0.510	0.450	0.15	0.116	0.110
0.65	0.600		0.19	0.147	0.146
0.75	0.650	0.650	0.23	0.176	0.183
0.85	0.736	0.700	0.27	0.199	0.191
0.95	0.817	0.800	0.31	0.230	0.226
1.05	0.860	0.850	0.35	0.250	0.248
1.15	0.950	0.938	0.39	0.280	0.275
1.25	1.025	1.012	0.43	0.308	0.308
1.35	1.088	1.067	0.47	0.340	0.318
1.45	1.150	1.143	0.51	0.354	0.358
1.55	1.234	1.232	0.55	0.390	0.390
1.65	1.304	1.294	0.59	0.412	0.398
1.75	1.359	1.355	0.63	0.434	0.430
1.85	1.450	1.444	0.67	0.465	0.450
1.95	1.530	1.520	0.71	0.473	0.470
2.05	1.636	1.550	0.75	0.520	
2.15	1.650				

*Not plotted.

centages still more irregular. However, a second series of calculations based on the theoretic curve for the percentage of water (see table 3 and chart 3) agree so well with the observed results here given that the general correctness of the latter may be accepted.

The significance of table 5 is made more evident by plotting the data on a base line giving either the weight of the brain or of the spinal cord. It is then seen that the records for the weight of water lie in an approximately straight line.

Weight of water in the brain. Beginning with the brain, chart 4, it is seen that when the lines representing the actual weight of water are contrasted with the dotted line, showing the amount of water necessary to maintain the percentage constant at its initial value, the former ascend less rapidly. Further inspection shows that the lines representing the increments of water as observed are slightly convex. This is true for both sexes. We will first consider in detail the relations as thus shown for the males.

A straight line drawn between the terminals for the male curve corresponds to an average of 73.6 per cent of water in the increments of weight after a brain weight of 0.35 grams. Since, however, the curve is slightly convex, it is better represented by two straight lines, one drawn from the initial entry to the entry above the brain weight of 1.05 grams, and the second from this latter to the final entry at 2.15 grams. The angle of the former line corresponds to 76.4 per cent. of water and that of the latter to 71.8 per cent.

From this it appears that the earlier increments of brain weight have a somewhat greater percentage of water than those acquired later.

It is to be noted however that the earlier period comes to an end when the animal weighs only 17 grams, and is about 15 days old (see chart 4) although by this age the very rapid growth of the brain in weight has been completed. (See Donaldson '08, plate III, chart 3.)

With slight differences, which are not significant, the relations here described for the males hold for the females also, but it is hardly necessary to give the determinations in detail.

Such are the general relations of the increase in the weight of water with the increase in brain weight. By these relations several facts are shown.

First. The proportion of water in the brain diminishes with increasing brain weight; a fact already demonstrated by the previous tables and charts.

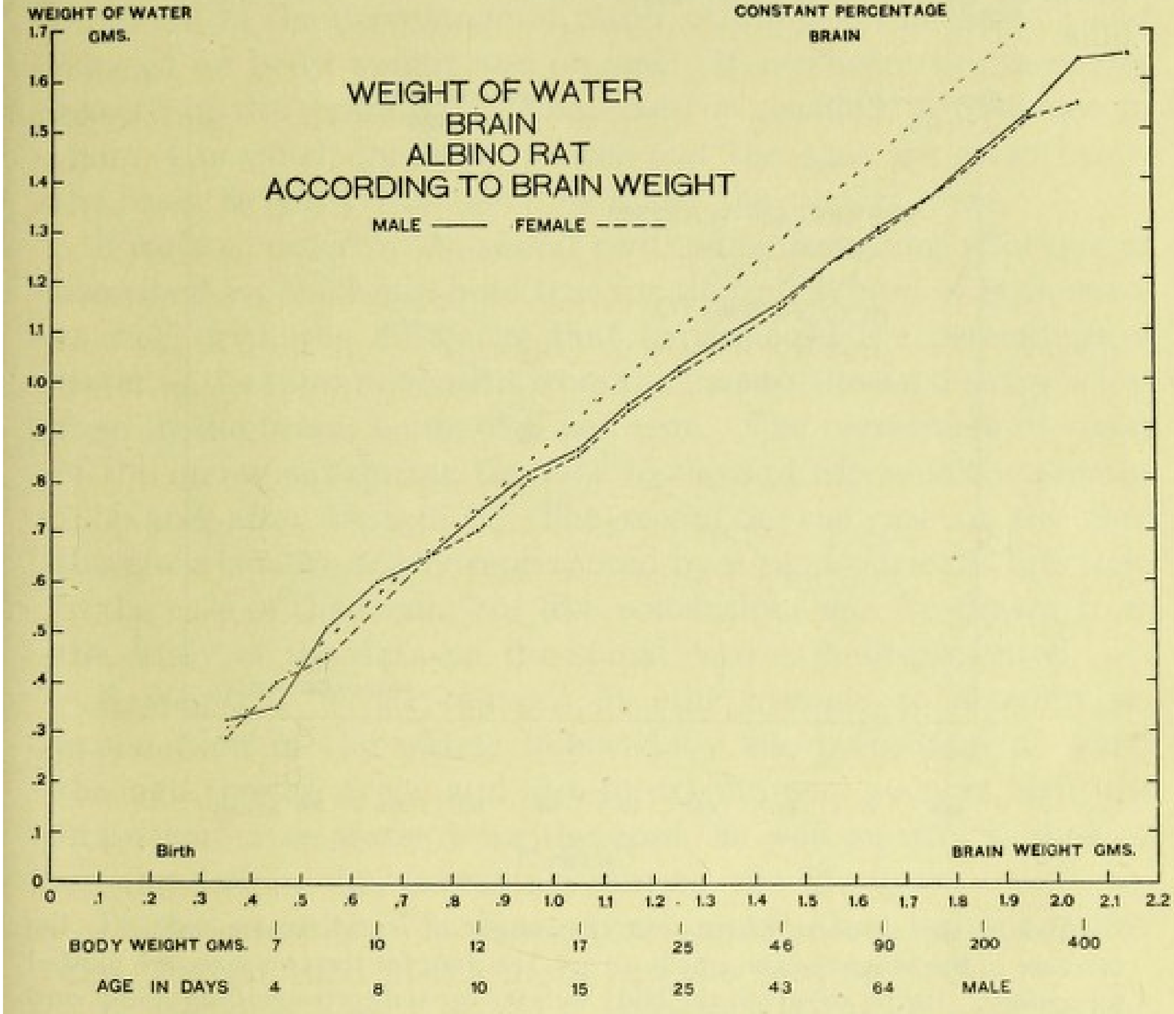

CHART 4

To show the absolute increase in the weight of water corresponding to the increase in brain weight. The data for the two sexes plotted separately. The first entry is for a brain weight of 0.35 grams. Below are given the body weights and the ages in days for the several brain weights. The dotted line indicates the amount of water which would be required to maintain the percentage at the initial value.

Second. The increments of brain weight are characterized by a continuous though small diminution in the percentage of water in the successive increments, the more rapid diminution occurring after the first fifteen days of life.

Third. After the rat has attained about fifteen days of age, the percentage of water in the increment of weight becomes approximately constant for the remainder of the life cycle, having an average value of 71.8 per cent. This value forms a limit towards which the percentage of water in the entire brain slowly falls.

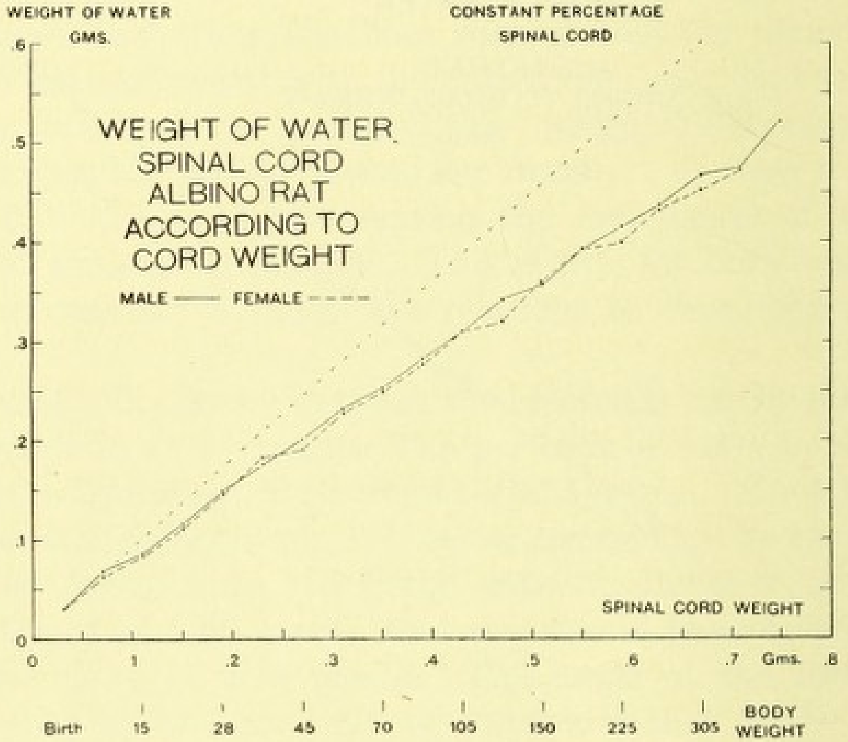

CHART 5

To show the absolute increase in the weight of water corresponding to the increase in the weight of the spinal cord. The data for the two sexes are plotted separately. Below are given the body weights for the corresponding spinal cord weights. The dotted line indicates the amount of water which would be required to maintain the percentage at the initial value.

Fourth. During the period of most active medullation, i. e., from 20–100 days, the percentage of water in the increments of brain weight does not indicate that the medullary sheaths which are being rapidly formed, possess a percentage of water less than that of the axones on which they appear.

It follows from the foregoing that as the amount of water in the brain at any time after birth is the sum of the amount present at birth (a constant) plus the successive increments, the percentage of water will diminish most rapidly at first. As the brain becomes heavier, and the increments form a greater proportion of the total weight, the rate at which the percentage of water diminishes will become slower and slower. At first glance it may be difficult to harmonize these data on the absolute weight of water with the rapid fall in the percentage of water as it appears in charts 1 and 2 based on body weight and on age. If, however, the precocious growth of the brain and spinal cord is recalled, a reference to chart 4 in which the body weight and the ages are given below the brain weights, will serve to make the matter clear.

Weight of water in the spinal cord. The foregoing relations as described for the brain hold true for the spinal cord of both sexes as well, with the difference that in the cord the percentage of water in the total increment from the first to the final entry is less than in the brain, being 68.3 per cent. The percentage of water in the increment during the first 15 days of life is on the average 70.4 and after that 67.9. The record in the case of the cord therefore is more nearly represented by a single straight line than in the case of the brain, but like conclusions can be drawn from the study of the data on the spinal cord as here presented.

Explanation of the change. It still remains to attempt an explanation of the course followed by the percentage of water through the life cycle, and also to explain why even at birth the brain has more water than the cord, as well as why it shows a smaller fall in this percentage during the life cycle.

In the interests of such a general explanation, let us consider first the condition of the brain and the cord at birth.

In the albino rat at birth, both brain and spinal cord are unmedullated, and both are very watery. Both are composed of gray matter in the strict sense, and growing axones, also gray in color. The nerve elements are enmeshed in supporting tissues and vessels.

In the brain the probability is that the supporting tissues, as well as the vessels, form a slightly smaller fraction of the total mass than in the cord. Cell division in the brain is continued longer after birth than in the cord, while medullation in the brain begins later than in the cord, and is less rapid. During subsequent growth, medullation is most actively carried on from the age of about twenty to one hundred days.

Between birth and maturity the proportional increase in the weight of the brain is only about two fifths that of the spinal cord (Donaldson '08, p. 355 and p. 358) and at maturity the relative amount of white matter in the brain is much less than in the spinal cord (Donaldson and Davis '03; Watson '03). Such are the characteristics of these two portions of the central nervous system which are of interest to us in connection with the percentage of water.

Explanation of the greater percentage of water in the brain at birth. The greater percentage of water in the brain at birth may be connected with some of the facts just enumerated, namely, the lesser maturity of the brain, as indicated by the longer continuance of cell division, by the later onset of medullation, and by the lesser proportion of supporting tissues and other non-nervous constituents. All of these conditions would tend to give the brain a higher percentage of water.

During the subsequent growth, the slower diminution of the percentage of water in the brain is due to the fact that the relative increment of water is greater than in the case of the cord (see charts 4 and 5). This however is again no explanation and leaves the conditions which control the increment of water in each division of the system still to be described.

As can be seen from inspecting chart 4 it is possible to express the events taking place by assuming that the initial weight of material in the brain maintains its initial percentage of water and that each of the subsequent increments in weight from just after birth to old age has a relatively low and slightly diminishing percentage of water. Such a statement however is purely formal.

What probably takes place is this: Starting with a given percentage of water in the brain or cord, this percentage continually diminishes as the formed material becomes older—at the moment of formation, however, the young material subsequently added most probably has a relatively high percentage of water, and the percentage we obtain at any given age is therefore the mean of these several values. The rate at which the percentage is falling off at any moment, together with the general slowing of the growth process—requiring a longer and longer time to add the same increment of weight to the brain the older the brain becomes—is so adjusted as to yield after the period of more rapid growth of the brain, the rather simple relations of a nearly constant weight of water for the same increment of total weight.

In this connection the analysis of the brain and cord should however be carried one step further. Both are composed of gray matter (substantia grisea) and axones, plus the supporting elements, the axones being more or less medullated according to locality and age. In the case of the rat, it has not been possible to study the changes in the percentage of water in the gray matter alone. We know however from a number of studies on man—on the cortical gray and the gray of the corpus striatum—that the change in the percentage of water in the substantia grisea with age, is much less—less than one-half—that in the axones (white matter). This has a bearing on the percentage of water in the brain as contrasted with the cord, because the brain has relatively less axone substance in it. Moreover the maturing of this substance is slower in the brain than in the cord. It is worthy of note as bearing on this last point that according to Watson ('03, p. 91 and 105) medullated fibers in the spinal cord of the rat are first found on the second day after birth, while in the cerebrum, they are not found until the eleventh day. At that age—eleven days—the percentage of water in the brain has fallen to that of the cord at the second day, and it thus appears that the medullation of axones begins in both divisions of the central nervous system when these have acquired the same percentage of water.

This suggestion, that the onset of medullation is closely related to the percentage of water in the axones, fits with the common observation that the fibers first medullated in any locality become the largest (because they have the longest time to grow after reaching the condition in which they can become medullated) and that in any nerve containing medullated and non-medullated fibers, it is the smaller (or younger) fibers which lack the sheath (Boughton '06). Also, as the portion of the axone nearest the cell body is the older, and hence would have the lower percentage of water, this should be the portion first medullated; a conclusion which fits with the observations.

It is hardly necessary to remark that these last two facts when interpreted in this way, constitute indirect evidence for the view that the axone is an outgrowth from the cell body.

The medullation process as such does not reduce the percentage of water. This statement, already made in the "fourth" conclusion on p. 19 is here repeated because there is a more or less widely diffused opinion that the medullary sheath is a structure containing less water than the axones, and that it is the addition of the myeline, as it appears in the medullary sheaths, which largely serves to reduce the percentage of water in the white substance, and thus in the entire mass of the central system. For this there is no evidence. Charts 4 and 5, exhibiting the increase in the weight of water with increasing brain weight and cord weight, show no changes in the increment of water which would warrant such an explanation. It appears most probable therefore that the medullary sheaths when first formed have approximately the percentage of water characteristic for the axones at the time of their myelination, and after that, in company with the axones, they undergo a slow but steady diminution in water content.

A few separate determinations of the percentage of water have been made by various investigators on the white and gray substances of man and other larger mammals. These show without exception that between birth and maturity there is a greater loss of water in the white substance than in the gray. In these cases of course the white substance at maturity is always medullated, and thus the results do not answer the question whether the formation of the medullary sheaths has contributed to the diminution in the percentage of water. That the axones previous to medullation do show a reduction in the percentage of water with advancing age, is indirectly indicated by my own observations in the following way:

At birth (i. e., 5 grams body weight) the average percentage of water in the rats' brains of both sexes is 87.8 per cent (table 1). At eleven days of age, as shown in chart 2, it is about 84.8 per cent, a loss of three units, yet it is not until after the eleventh day that medullation in the brain begins. The percentage of water in the brain therefore falls off before medullation begins, and the nerve substance, cell bodies and axones, are the portions in which this diminution chiefly occurs.

As there is every reason to think from what we know concerning the relatively small reduction in the gray substance that the percentage of water in the cell bodies in this case is not progressing more rapidly than it does in the entire brain, it follows that in the remaining nerve structure—the axones—the percentage of water is reduced at least an equal amount. Since however the diminution in the percentage of water is found to be much greater in the mature white substance than in the mature gray, it seems probable that the axones are subject to a more extensive reduction in the percentage of water than are the cell bodies.[3]

From this it follows that the greater proportion of gray substance in the brain would tend to maintain in that organ a higher percentage of water at maturity, and the lesser proportion of gray in the cord, a lower percentage (see the measurements on the areas of the gray and white matter in the spinal cord as given by Watson, '03, p. 101).

But there is still one more peculiarity of the spinal cord which is important in this connection. This I have called (Donaldson '09, pp. 166–167) *passive lengthening*. The segments of the cord, especially in the thoracic region, undergo during growth a lengthening which is largely passive, and which does not imply any marked increase in the structural complexity of the cord, but serves mainly to keep the spinal nerves nearly opposite to their intervertebral foramina.

In the course of this lengthening, we have evidence that the volume of the gray substance is but slightly increased, while the proportions of the gray column are much modified in the sense that the diameter alters but slightly (it may even diminish) while the length is correspondingly increased (see the measurements on the areas of the gray and white matter in the spinal cord of the rat, Watson '03, p. 101, and Donaldson and Davis '03).

At the same time that this is occurring in the gray columns, the white tracts not only lengthen (passively) but also increase in the area of their cross sections, and thus at the end of any step

[3] The question whether a growing fiber at any age of the animal becomes medullated as soon as its percentage of water falls below the value at which medullation first begins after birth, cannot at the moment be answered. It is conceivable however that with advancing age this critical point for medullation is lowered.

in this transformation, we find a larger proportion of white substance than at the beginning. The white substance having a lower percentage of water than the gray, tends of course to bring down the general average. We know from previous studies that in the albino rat the weight (and length) of the spinal cord increases so long as the animal grows (Donaldson '09).

It is therefore the relative increase in the white substance due to this continuous passive lengthening—which is so marked in the cord—that can justifiably be held responsible for the more rapid decrease in the percentage of water in the cord after maturity.

In brief then, the more rapid diminution in the percentage of water in the cord up to maturity, and the greater rate of diminution after maturity, are due, aside from the excess of supporting tissues and vessels, to the greater amount of axone substance in the cord and the peculiar form of growth designated as passive lengthening.

General significance of this change. If we are correct in concluding that in the percentage of water we have a character correlated very closely with the age of the animal, and but slightly influenced by the conditions which modify general growth, it follows that this change must depend on processes intimately associated with the span of life or longevity of the animal concerned.

Broadly speaking, the changes in the percentage of water indicate progressive chemical modifications which take place in those constitutents of the cell that are most stable.

A comparison of the albino rat with man in respect to the percentage of water in the brain. In connection with such a comparison, I have examined the entire literature on the percentage of water in the nervous system. This literature needs to be summarized, but for such a summary, this is not the occasion. Out of the data available, I have selected however the findings of Weisbach ('68) and of Koch ('09) to be used in the present instance, as from these we get the best series of determinations of the water in the human brain at different ages. The data from Weisbach are as follows:

He determined the percentage of water in each case for six different localities in the encephalon: (1) white substance (callosum); (2) gray substance (corpus striatum); (3) gyrus (white and gray mixed); (4) cerebellum; (5) pons; (6) medulla oblongata.

For the percentage of water in the human encephalon at birth, the determinations for these several localities are averages from three male and five female newborn infants.

A series of tests applied by me to Weisbach's data for mature brains have shown that the percentage of water in the entire encephalon is approximately equal to the sum of four times that in the white substance (1); five times that in the gray substance (striatum) (2); and once that in the cerebellum (3) divided by 10.

This procedure gives for the percentage of water in the human brain at birth 88.34 per cent. The value thus obtained is probably nearly correct.

By the same procedure I obtained from Weisbach's data for children between three and fourteen years of age (2 males: 3 years and 8 years; 2 females: 4 years and 14 years) a mean value for the entire encephalon of 79.2 per cent at 9.5 years. Finally, Weisbach's records for 64 males and 17 females, 20–30 years of age, give a mean value of 77.0 per cent.

Turning now to the determinations of Koch ('09) we find his average determination of the percentage of water in five human encephala at maturity to be 77.8 per cent. In a female brain of two years, he gives the percentage of water in the cortex of hemispheres as 84.49 per cent and in the callosum as 76.45 per cent.

In a male of 19 years, the cortex was found to have 83.17 per cent and the callosum 69.67 per cent. This last case may be taken to represent the conditions at maturity. This being assumed, it was found that combining the determination for the cortex in the proportion of 603 times to 397 times of that for the white substance gave a mean percentage of 77.8, which is Koch's determination for the water in the entire encephalon at maturity.[4]

Using the same proportions as those just given for the gray and white substances at maturity and applying them to the data for the brain at two years, mentioned above, we obtain as a mean

[4] The proportional abundance of the gray and white substance in the encephalon is not to be inferred from the numbers given above. Each investigator has used more or less arbitrary criteria for the gray substance, and a treatment of the results of an author in the manner here followed, has a value for the determinations by that author alone.

value for the percentage of water in the encephalon at two years 81.1 per cent. Thus we are able to obtain approximate values for the percentage of water in the human encephalon at birth, two years, nine and one-half years and at maturity, twenty-five years.

TABLE 6.

Comparison of the percentage of water in the encephalon of man and the albino rat at corresponding ages

MAN		RAT	
Age Years	Percentage of Water	Percentage of Water	Age Days
Birth	88.3	87.7	Birth
2 years	81.1	81.3	26 days
9.5 years	79.2	78.6	115 days
25 years maturity	77.0	78.0	290 days

In order to compare these determinations, it is necessary to recall that the span of life in man is about thirty times as long as that in the rat, and if this relation holds throughout the life cycle, it follows that each determination for man is to be compared with that for the rat having one thirtieth the human age taken.

The data for the rat are based on the entries in table 2 giving the percentage of water according to age.

This table shows that when we compare brains of corresponding ages, the diminution in the percentage of water in the two forms has similar limits, and would be expressed by a curve of like form in both instances.

When we examine the records for other mammals, we find almost no determinations for the water in the encephalon at birth, but we do find determinations for this character at maturity, and the values are very similar to those for man and the rat. Remembering that the relative amount of white matter in the encephalon varies somewhat in different species, and must therefore modify this result, we reach the interesting conclusion that probably in all mammals we shall find approximately the same range in the percentage of water between birth and maturity, and that the loss of water in them occurs in the same manner but that the time required for the successive steps is determined by the intensity of the growth process characteristic for each species. (Rubner '08 and '08a).

CONCLUSIONS

1. In the albino rat between birth and maturity, the percentage of water in the brain diminishes from 87.8 to 77.5 and in the spinal cord from 85.6 to 68.0. Table 1.

2. The progressive diminution of the percentage of water is a function of age and is not significantly modified by any conditions to which the animals have been thus far experimentally subjected.

3. The diminution in the percentage of water is most rapid during the first twenty-five days of life; the period at which the central nervous system is growing most actively.

4. The maturing of the axone substance is characterized by a greater diminution in the percentage of water than is the maturing of the gray substance.

5. Medullation begins when the percentage of water in the brain and cord has diminished to about 85.3 per cent (second day in the spinal cord; eleventh day, in the brain).

6. The process of medullation itself as indicated by the formation of the medullary sheaths, is not a controlling factor in reducing the percentage of water in the central nervous system.

7. The range and course of the diminution of the percentage of water in the brain are similar in man and in the albino rat. The rapidity of change agrees with the intensity of the growth processes in each of the two species, and is therefore about thirty times more rapid in the rat than in man. This point has not been tested for the spinal cord.

8. It is probable that the same limits in the percentage of water and the same course of diminution will be found to occur in other mammals.

9. The progressive diminution of the percentage of water in the central nervous system with advancing age, is to be regarded as an index of fundamental chemical processes, which take place in the more stable constituents the nerve cells.

These processes are but little modified by changes in the environment and taken all together constitute a series of reactions which express not only the intensity of the growth process in the nervous system, but also the span of life characteristic for any given species.

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