On the chemical pathology of the brain / by Adam Addison.

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Publication/Creation

[Place of publication not identified] : [publisher not identified], [1866] (London : J.E. Adlard.)

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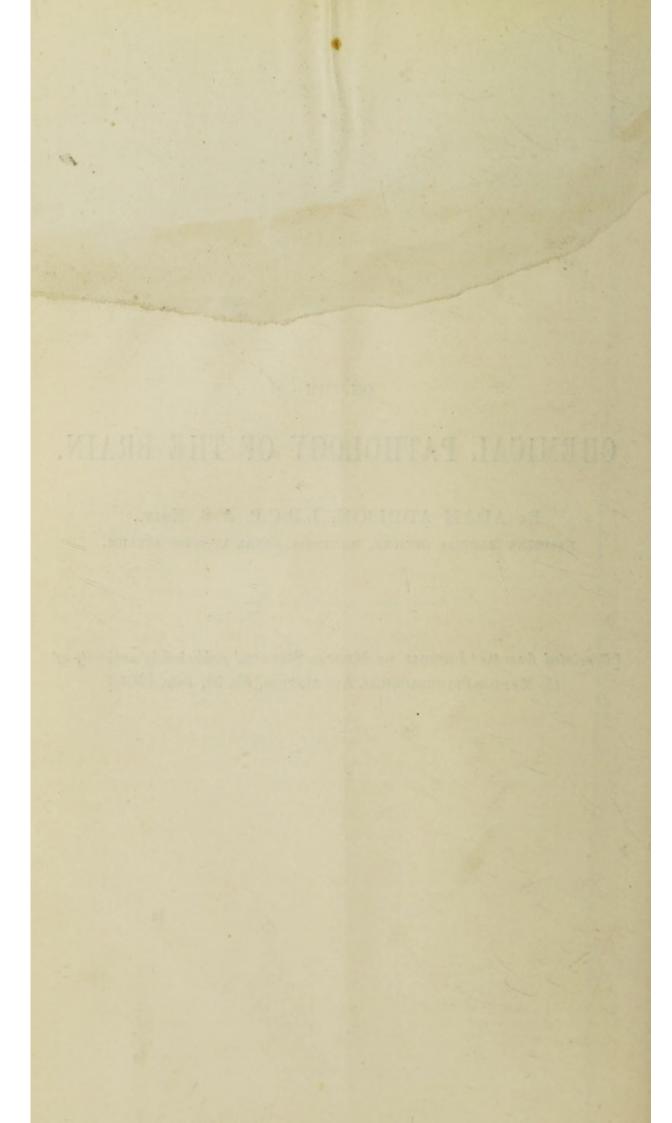


ON THE

CHEMICAL PATHOLOGY OF THE BRAIN.

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[Reprinted from the 'Journal of Mental Science,' published by authority of the Medico-Psychological Association, No. 58, July, 1866.]



CHEMICAL PATHOLOGY OF THE BRAIN.

THE chemistry of the nervous system is a subject to which little attention has been given by British authors, but their place has been creditably supplied by several foreign chemists, conspicuous among whom are Couërbe, Fremy, Von Bibra, Hauff, Walther, and Schlossberger. These writers have effected something as regards the chemical pathology of the brain in persons dying sane, but with the exception of a few isolated analyses whose results are sadly in want of confirmation, by Lassaigne, Couërbe, and L'Héritier, it may be said that absolutely nothing has been done in the case of the insane. In fact, the field is a terra incognita of unknown extent. I purpose, therefore, to devote some attention to this subject, and to communicate to the profession from time to time the results of such chemical analyses of insane brains as it may be in my power to make. this view I shall take my starting-point from the results obtained by Bibra and others; and in order to present a standard for comparison, I shall give an abstract of what has been effected by these chemists. I find that this has been so thoroughly done by Von Gorup-Besanez ('Lehrbuch der Pathologischen Chemie') that I shall not hesitate to make a free translation of his chapter on this subject, criticising and adding where I think it necessary.

Quantitative analyses of the brain, having for their object the determination of the water, of the matters extractable by alcohol and ether, the albumen and salts, have been made at different times and by different chemists. We shall give some of these tabularly arranged.

SETT SETTION	LASS	AIGNE.	V. BIBRA.					
In 100 parts.	Whole brain.	Gray substance.	White substance.	I. Cerebrum.	II—Medullary substance.			
Water	77.0	85.0	73.0	77.26	84.39			
Solid matters	23.0	15.0	27.0	22.74	15.61			
Albuminates	9.6	7.5	9.9	9.62	8.01			
Fat and fatty phos-	10.3	4.7	14.8	12.00	6.10			
phatic matters		1.4		1:12	1.50			
Extractive matters	2.0		1.0	1.17	1.90			
Inorganic salts	1.1	1.2	1.3	-	-			

The analyses of Lassaigne were made upon the brain of a lunatic; Analysis I by Bibra upon a sane brain (the convolutions of the cerebrum), II upon that of a cretin. The following by L'Héritier are those of the brain and spinal marrow of men of different ages, but without reference to any definite anatomical parts.

In 100 norts			Brain.			Spinal cord
ln 100 parts.	Child.	Youth.	Adult.	Old man.	Cretin.	Adult.
Water	82.79	74.26	72:15	73.85	70.93	71.05
Solid matters	17.21	25.74	27.85	26.15	29.07	28.95
Albuminates	7.00	10.24	9.40	8.65	8.40	7.30
Fats, &c	4.25	6.95	7.90	5.32	5.85	10.15
Extractive matters and salts	5.96	8.59	10.19	12.18	14.82	11.50

These analyses were made after a very imperfect method, and it is certain that in consequence of this a considerable part of the phosphatic fatty matter has been collectively reckoned with the extractives. In recent years the comprehensive investigations of Bibra and Schlossberger as to the quantities of water, fat, and other solid matters in the different anatomical regions of the brain, have led to some important results. Von Bibra did not confine his observations to the brain of man at different periods of life, but also extended them to many of the lower animals. We shall give here some of those analyses which have reference to the human brain, and shall state the results of the analyses of the nervous system of the other classes only in so far as is required to explain the deductions to be drawn from them.

A Woman, at. 19 (Typhus).

				1.5			
In 100 parts.	Medulla oblongata.	Cerebellum and pons Varolii.	Crura cerebri.	Hemi- spheres.	Corpora striata.	Thalami optici.	Average of whole.
Water Solid matter Fats	72·90 27·10 18·39	76·82 23·18 12·00	76·02 23·98 12·42	76·40 23·60 9·31	77.69 22.31 9.36	80·26 19·74 6·80	76.68 23.32 11.38
Albuminates, extractive matters, and salts		11.18	11.56	14.29	12.95	12.94	11.94

A Man, at. 21 (Tuberculosis).

In 100 parts.	Medulla oblongata.	Cerebellum and ponsVarolii.	Crura cerebri.	Hemi- spheres.	Corpora striata.	Thalami optici.	Average of whole.
Water Solid matter Fats Albumen, &c.	74·73	76·17	76·97	79·01	78·16	82·91	77·99
	25·27	23·83	23·03	20·99	21·84	17·09	22·01
	15·09	14·28	14·18	12·38	11·80	8·76	12·75
	10·18	9·95	8·85	8·61	10·04	8·33	9·26

A Woman, at. 35 (Tuberculosis).

In 100 parts.	Medulla oblongata.	Cerebellum and ponsVarolii.	Crura cerebri.	Hemi- spheres.	Corpora striata.	Thalami optici.	Average of whole.
Water Solid matter Fats Albumen, &c	75·13 24·87 17·99 6·88	76·98 23·02 14·53 8·49		75·69 24·31 17·69 6·62	70·11 29·89 12·55 17·34	79·82 20·18 11·09 9·09	75·55 24·45 14·77 9·68

A Man, æt. 65 (Marasmus).

In 100 parts.	Medulla oblongata.	Cerebellum and ponsVarolii.	Crura cerebri.	Hemi- spheres.	Corpora striata.	Thalami optici.	Average of whole.
Water Solid matter Fats Albumen, &c.	74·46	75·82	76·30	74:43	77:38	80·00	76·39
	25·54	24·18	23·70	25:57	22:62	20·00	23·61
	15·43	13·29	13·60	14:46	9:91	80·20	12·44
	10·11	10·89	10·10	11:11	12:71	11·80	11·17

A Man, æt. 41 (Typhus).

In 100 parts.	Medulla oblongata.	Cerebellum and pons Varolii.	Crura cerebri.	Hemi- spheres.	Corpora striata.	Thalami optici.	Average of whole.
Water Solid matter Fats Albumen, &c.	73:08	76·52	76·49	74·24	78·56	79·82	76·44
	27:00	23·48	23·51	25·77	21·44	20·18	23·56
	18:33	14·27	14·89	15·25	12·22	10·78	14·29
	8:67	9·21	86·20	10·52	9·22	9·40	9·27

A Man, æt. 80 (Marasmus).

In 100 parts.	Medulla oblongata.	Cerebellum and ponsVarolii.	Crura cerebri.	Hemi- spheres.	Corpora striata.	Thalami optici.	Average of whole,
Water Solid matter Fats Albumen, &c.	72·03	72·30	72·38	80·00	75·64	73·44	74·58
	27·97	27·70	27·62	20·00	24·36	26·56	25·42
	16·77	13·33	15·72	8·45	11·70	14·53	13·41
	11·20	14·37	11·90	11·55	12·66	12·03	12·01

From these analyses by Bibra of the brains of those who have died of the most dissimilar diseases it appears, first of all, that the quantity of fat in the brain is always to a certain extent individual, and that diseases which are attended by general emaciation do not alter the amount of cerebral fat. It must not, however, be forgotten that what we designate as cerebral fats are proper fats only to a very small extent; in short, that they are peculiar matters of a fatty nature containing a large quantity of phosphorus, whose chemical constitution is not sufficiently known, though it is certain that

they differ essentially from the proper fats. So, when we find that in diseases which produce a great emaciation of the body the cerebral matters soluble in ether are not lessened in quantity, it is not so very wonderful, because it is only the fat proper which suffers loss.

Among the different anatomical regions of the brain the medulla oblongata contains the largest quantity of cerebral matter soluble in ether. This is also the result of the analyses of Hauff and Walther. On the other hand, the thalami optici and the corpora striata appear to contain least fat, but this rule appears to have more or less nume-

rous exceptions, according to individual conditions.

Age appears to be not without influence upon the quantity of fat in the brain, which seems to decrease in advanced life. As regards the quantity of water, no general laws can be deduced from Bibra's analyses; it appears to vary much within certain limits. In general, it may be assumed that those parts of the brain which have most fat give the smallest quantity of water, and vice versa. Age appears to exercise no considerable influence upon the quantity of water, but, on the other hand, the albuminates, &c., appear to increase somewhat in old age. Von Bibra, Walther, and Hauff have also made observations upon the relation of the water, the fats, and other solid matters in the gray and white substance. They agree in stating that the fatty contents of the gray substance are much smaller in quantity than those of the white, and that the former contains more water than the latter, and, what is very remarkable, in almost the same proportion as it is poorer in fat. These conditions supply a general confirmation of the results of Lassaigne's analyses previously given.

BIBRA.

	Male, æt. 21. Typhus.			Male,	et. 59. I Disease.	Bright's	Male, æt. 30. Tuberculosis.		
In 100 parts.	Gray sub- stance of hemispheres.	White sub- stance of hemispheres.	White sub- stance of corpus callo- sum.	Gray sub- stance of hemispheres.	White sub- stance of hemispheres.	White sub- stance of corpus cal- losum.	Gray sub- stance of hemispheres.	White sub- stance of hemispheres.	White sub- stance of corpus cal- losum.
Water Fat Albumen, &c.	87·00 5·97 7·03	71·82 19·73 8·45	65·37 20·33 14·30	88·22 5·46 6·32	72·15 20·39 7·46	63·54 21·18 15·28	83·57 6·43 10·00	69·19 20·43 10·38	71·55 14·67 13·78

WALTHER AND HAUFF.

	Corpus callosum.		Corticals	Cortical substance.		oblongata	Arbor vitæ.		
In 100 parts.	Male, æt. 60.	?	Male, æt. 60.	5	Male, æt. 60.	9	Male, æt. 60.	9	
Water Fat	70·61 15·41	70·81 14·90		85·00 4·86	69·74 15·21	72·48 15·12	81·36 6·06	79·94 5·96	

The investigations of Bibra and Schlossberger have shown some remarkable deviations from the adult normal in the constitution of

the brain of embryos and new-born children.

The cerebral fat, in the case of embryos and new-born children, is much smaller in quantity than in the adult; on the other hand, the quantity of water is greater; but in the new-born child the fatty matters are remarkably greater than in the embryo, and increase with considerable rapidity as age advances to maturity.

Then Schlossberger's experiments bring out the remarkable result that the difference in the quantitative distribution of the fat in the gray and white substances does not exist in the embryo. The fol-

lowing tables give a few of these relations.

BIBRA.

		TI TI	os.			
In 100 parts.	Of 10	Of 12	Of 14	Of 18	Of 20	Of 22
	weeks.	weeks.	weeks.	weeks.	weeks.	weeks.
Water	85·10	86·71	86·24	86·90	86:33	85·93
Fats	1·26	0·99	1·53	1·16		1·23
Albumen, &c.	13.64	12.30	12.23	12.04	12.60	12.84

Embryo of 37 weeks.						Female child, 6 months. Pneumonia.				
In 100 parts.	Medulla oblongata.	Cerebellum and pons Varolii.	Crura cerebri.	Hemi- spheres.	Medulla oblongata.	Cerebellum and pons Varolii.	Crura cerebri.	Hemi- spheres.		
Water Fats Albumen, &c.	87·72 4·20 8·18	88·62 2·94 8·40	87·65 3·95 8·40	91·06 2·36 6·58	82·00 8·50 9·50	83·18 3·92 12·90	81·87 7·79 10·34	81·87 7·79 10·34		

From these figures it will be seen that the medulla oblongata is also richest in fat in embryos and new-born children—

SCHLOSSBERGER.

		New-bo	rn child.	
In 100 parts.	Gray substance of hemispheres.	Corpus striatum.	Corpus callosum.	Thalamus opticus.
Water	88·56 3·82	88·04 4·57	89·12 3·85	87·73 4·74

In embryos the quantity of water in the gray and white substances is equally high, and there is no remarkable difference in the amounts of fat in these parts. Accurate methods of separation available for the quantitative determination of the cerebrine, cholesterine, of the proper, and of the phosphatic fats, are still wanting, but

Bibra believes it may be concluded from his observations that in adult men 100 parts of the fatty matters soluble in ether consist of from about 20 to 21 per cent. of cerebrine, 30 to 33 of cholesterine, and 46 to 50 of the other fats and fatty matters.

The gray substance of the brain contains least cerebrine, a medium quantity of cholesterine, and a greater quantity of the other fats.

The white substance contains more cerebrine and cholesterine than

the gray, and therefore less of the other fats.

The general result of the comprehensive inquiries of Von Bibra, Schlossberger, Walther, and Hauff, into the quantities of water and fat in the brains of the lower animals, is that there is an increased quantity of water the lower we descend in the vertebral kingdom. The brain of the lower mammalia approaches, as to its quantity of water, to the undeveloped feetal brain of the higher mammalia and of man.

Experiments made on animals also confirmed the fact that the different anatomical parts of one and the same brain contain very different proportions of the matters soluble in ether. As in man, so also in animals, the gray substance is far poorer in fatty matter than the white, and these also stand in an inverse relation to the quantity of water, while the medulla oblongata is also in almost every case richest in the so-called fats. The brain of the mammalia contains far more fat than that of the other classes. As to the distribution of the cerebrine, cholesterine, &c., the mammalia differ from the condition found in man in that the brain contains a less quantity of cerebrine; the phosphatic fats in the lower animals, as in the embryo of man, are present in less quantity than in the higher vertebrata and adult men.

The experiments of Bibra also show that starvation produces no essential change in the weight of the brain of an animal, nor in the relation of its chemical constituents, and that in processes which call into sympathy the whole bodily organism, tissue-change in the brain undisturbedly pursues its course.

Quantitative relations of the inorganic constituents of the Brain.—
We possess only one complete analysis of the ash of the whole brain, made by Breed. But it may be questioned whether this gives a correct idea of the distribution of the constituents of the ash in the brain, since, on the one hand, it is a very difficult matter to reduce the brain completely to an ash, in consequence of the great quantity of phosphoric acid and phosphatic salts which prevent the incineration of the carbon, by which they may also be to some extent reduced, and because it is not stated whether he made use of one brain only or several. However, it appears from Breed's analysis that the ash of the brain shares with that of the muscular tissue and of the yolk of egg great richness in phosphoric acid and a great superabundance

of potassium as compared with sodium, and therefore presents a greater similitude to the ash of milk than to that of the blood. For the sake of comparison we place beside Breed's analysis of the brain that of the ash of blood, flesh, yolk of eggs, and milk.

In 100 parts,	Brain. BREED.	Calves'flesh STAFFEL.	Yolk of egg. Poleck.	Human milk. WILDEN- STEIN.	Human blood. VERDEIL.
Potassium	32.42	34.40	8.93	21.44	11.24
Sodium	10.69	2.35	5.12		6.27
Magnesia	1.23	1.45	2.07	0.87	1.26
Lime	0.72	1.99	12.21	18.78	1.85
Chloride of sodium	4.74	10.59		10.73	55.63
Chloride of potassium		1		26.33	
Phosphate of iron	1.23			0.21	
Phosphoric acid (combined) .	39.02	48.13	63.18	19.00	11.10
Free phosphoric acid	9.15		5.70		
Sulphuric acid	0.75			2.64	1.64

There are also some other analyses of the ash-constituents of the cerebrum, but the most comprehensive observations made in this direction—those of Von Bibra—were made upon brains which had been deprived of their fat, and therefore do not give the whole weight of the cerebral ash, but only that of those salts which have not passed over in the ether-extract. The latter, however, has also been determined separately by the same observer, and he has added some analyses of the phosphatic constituents of the ether-extract made from different parts of the brain.

	10 File 1810 BN 107 TO EL	0 parts brain.	O parts C. and Of fat.	Ash in 1	00 parts.
Individuals.	Regions of brain.	Ash in 100 parts of fresh brain.	Ash in 100 of brain at 100° C deprived of	Soluble salts.	Insolu- ble salts.
Male, æt. 21	Hemispheres	0.190	2.20	72.75	27.25
,, ,,	Cerebellum and pons Varolii .	0.317	3.47	74.90	25.01
, 33	Medulla oblongata	0.349	3.46	61.10	38.90
), ,,	Cerebellum and pons Varolii .	0.328	3.30	85.70	14.30
,, ,,	Crura cerebri	0.230	2.30	75.00	25.00
,, ,,	Hemispheres	0.361	3.52	86.50	13.50
Female, æt. 33	Medulla oblongata	0.348	3.76	75.00	25.00
,, ,,	Cerebellum and pons Varolii .	0.193	5.72	89.80	10.20
,, ,,	Crura cerebri	0.488	4:83	84.10	15.90
,, ,,	Hemispheres	0.509	4.99	86.60	13.40
Male, æt. 86	Medulla oblongata	1.072	9.43	80.00	20.00
,, ,,	Cereb., crura, hemispheres	0.449	4.37	72.70	27.30
,, 36	Medulla oblongata	0.557	6.27	56.30	43.70
,, ,,	Cerebellum and pons Varolii .	0.652	5.73	88.80	11.20
,, ,,	Crura cerebri	0.571	5.14	81.50	18.50
), ,, ,,	Hemispheres	0.559	4.64	90.30	9.70
" " …	Corpora striata	0.304	4.68	86.60	13.40

No general conclusions can be drawn from these results except in the case of the medulla oblongata, which appears to contain more insoluble salts (phosphatic earths) than the other parts of the brain. Similar analyses made upon the brains of different of the lower animals showed that the cerebral ash of the bird is greater than that of man and the mammalia, generally that of the brain of the amphibia and fishes larger than that of all other classes, and also that in the amphibia and fishes the quantity of the phosphatic earths is more considerable than in the other orders.

Some comparative analyses of the ash of the gray and white substances have been made by Schlossberger. He confirms the statement of Lassaigne, that the ash of the gray substance has an alkaline reaction, but that of the white is decidedly acid, which, without doubt, is explained by the fact that the white substance contains more of the phosphatic fats.

Schlossberger found in 100 parts of fresh brain-

In the gray substance—

1. Of a man æt. 74. . . 1.00 per cent of ash.

2. Of a calf . . . 1.16 ,

In the white substance—

1. Of a man æt. 74. . . 1.82 ,, 2. Of a calf . . . 1.72 ,,

The white substance, therefore, contains more inorganic salts than the gray.

The following are Von Bibra's analyses of the ash of the etherextract and the constituents of the cerebral fats of man:

Individuals.	In 100 parts of ether-extract:	In 1	00 parts of	In 100 parts of ash : rela tion of Potassium and Sodium.		
	per-centage of ash.	Dhambania			Potassium.	Sodium.
Female, æt. 21 Male, " 30 " " 27	4·46 5·27 5·45	10·0 12·7 13·1	17·0 18·1 9·1	73·0 69·2 77·8	37·0 41·2 58·8	63·0 58·8 41·2

From these figures it is apparent that in the ether-extract a distribution of the bases exists which does not correspond to their relation in the whole ash, in which the potassium so considerably overweighs the sodium.

The determination of the quantity of phosphorus in the brain has been an object of considerable interest in consequence of the important rôle it was supposed to play in the activity of the nervous system, and also in consequence of the conflicting results which several analysists have published. Schlossberger points out that the old analyses by Vauquelin, who found one and a half per cent. of phosphorus in fresh brain, evidently rest upon an error (and in this opinion Berzelius concurs); for assuming the brain substance to contain on an average 80 per cent. of water, these results would give 7 per cent. of phosphorus in dried cerebral matter. And equally incomprehensible are the more recent (1843) analyses of L'Heritier, who would appear to have found analogous numbers, namely, in the brain of the child, 0.80; of the adult, 1.80; youth,

Schlossberger further remarks that Couërbe's ideas as to the connection of certain mental disturbances with an increase or diminution of the normal quantity of phosphorus must be regarded as chimerical so long as they do not rest upon confirmed facts; L'Heritier also finds a minus quantity of phosphorus in the brains of idiots, but does not agree with Couërbe that the quantity is greater than normal in the case of maniacal patients. Indeed, the only trustworthy analyses are those of Von Bibra, who made use of the ether-extract for the determination of the quantity of phosphorus in the belief that it belongs to one of the cerebral fats, and of course the numbers must be regarded as giving the weight of the phosphates of the fats only. They are as follow:

In 100 parts of Ether-extract.

Male,	æt.	59.	Medulla	oblong	ata	1.65	Lunati	c,æt	.38.	In whole brain 1.93
			Cerebelly	ım a	and		,,	,,	52.	" " … 1.75
			pons	Varolii		1.83	Male,			Gray substance of
	-		Crura ce	rebri		1.76				hemispheres 1.88
			Hemisph	eres		1.83				Corpus callosum 1.54
			Corpora							White substance 1.54
			Thalami	optici		1.54	,,	,,	59.	Gray substance of
			Corpus c	allosun	1	1.54	Mark San	199		hemispheres 2.33
			Average			1.68				White substance of
Female,	,,	19.	In whole	brain		2.53				hemispheres 1.82
Male,	,,	56.	,,	,,		1.72				Corpus callosum 1.36
		80.				1.83	,,	,,	38.	Gray substance of
		25.	"			1.89				hemispheres 2·10
Lunatic,				,,		1.75				White substance 1.62
F	mh	rvo	of 87 wee	ks.			in w	hol	e bre	in 2·09
			abryos fro			e mool		,		1.68

From these figures it appears that the fat of the gray substance contains somewhat more phosphorus than that of the white, but as a general rule the deviations above and below the average are included within very narrow limits, and experiments made on the lower classes show that in animals of a very low grade as to intellectual capacity, in the more intelligent orders, and lastly in man, there are no remarkable differences in the quantity of phosphorus in the brain. The natural conclusion follows, that the quantity of this cerebral constituent does not stand in a parallel connection with the development of the intellectual faculties.

Gorap Besanez, in summing up, observes, that the foregoing quantitative analyses present no deductions of definite value bearing upon pathological conditions or mental diseases. Perhaps not, but when we find that Bibra's analyses of insane brains were limited to three or four cases at most, it seems to me inexpedient and baneful to the progress of exact knowledge that the inquiry should be closed. It is by no means impossible that deviations from the normal quantitative composition will be found in diseased conditions and functions of the brain, and in many cases of paralysis and other diseases limited to definite parts of the cerebrum it will be interesting to ascertain the difference between the healthy and unhealthy parts. It is with this view that I communicate the results of my own work.

I shall first state the processes by which my results were obtained. As soon as possible after removal from the calvaria the brain was stripped of its membranes, and portions of the different regions weighed on watch glasses, on a balance turning with 100th of a grain. The anatomical parts analysed are the same as in Bibra's cases; but it appeared to me more correct to examine the gray and white substance of the hemispheres separately, so that I have one column more than this author has. The gray matter was carefully scraped off the white with a scalpel. The weighed portions were then dried at a temperature of 230° Fahrenheit, until after repeated weighings

they ceased to lose weight. The loss was deducted as water.

After the calculation of the water the fats were extracted from the dried portions of brain in an apparatus recommended by Bibra. Into a small glass flask of suitable size an air-tight cork is fixed, through which a strong glass tube, about six or seven inches in length and half an inch in diameter, reaches half way down into the flask. This tube, at its lower end, is furnished with a small opening 3—5 lines in size; into its upper end a perforated cork is fitted, through which another tube, bent twice at a right angle, connects the apparatus with a second flask. The bent tube leads through a perforated cork, not quite air-tight, to the bottom of the second flask, which should be well cooled in water. Into the strong tube, which reaches half-way down into the first flask, the substance to be extracted is placed, and the extracting material (the ether) in the flask below.

When the ether is warmed and brought to boiling by a lamp, the hot vapours ascend through the small opening in the end of the tube, soften the substance there, dissolve as much as they are able to take up, and remain partly concentrated and fully saturated in the tube, while the superfluous ether is distilled through the bent pipe into the second flask. When a certain quantity has collected into this the lamp is removed, and the natural consequence is that the distilled ether returns with some force into the first flask and carries with it the fat which has been concentrated in the tube. Bibra says that

when this is done ten or twelve times the extraction is generally complete, but I have had to do it nearer twenty times; at any rate, it must be done until it is seen by its colour that the ether does not take up any more fat. As it is impossible to remove the dried brain substance from the watch glasses without loss, the quantity to be used must again be weighed. After the fat is thoroughly extracted, the ether is evaporated to dryness and the solid residue weighed. The brain substance should not be powdered, but placed in the tube in lumps; otherwise light floating particle will be carried down by the returning ether, and give too high a result. The advantage of this method is that a very small quantity of ether suffices to exhaust the brain substance of the fat, and no filtration is required if it is properly done.

The brain fats are all soluble in boiling ether; if alcohol is employed, a not inconsiderable quantity of extractive substances

which are soluble in this fluid are obtained with the fats.

Owing to the want of an accurate method of separation, it did not appear to me that I could undertake the analysis of the fat into cerebrine, cholesterine, &c., with any hope of success. The albuminates, extractives, &c., were reckoned by deducting the amount of fat from the total solids. It has already been stated that Bibra made use of the ether-extract for the determination of the phosphorus. This method did not appear suitable for my purpose. In the first place the quantities of fat extracted were generally very small, and then I was by no means sure that it would contain the absolute amount of phosphorus in the regions from which it was taken. Consequently I preferred to operate on the fresh brain, and then, in order to give an unvarying standard of comparison, to calculate the quantity in 100 parts of dried cerebral substance, making use for this purpose of the previous determination of the per-centage of solids.

The following method was recommended to me by Dr. Stevenson Macadam, of Edinburgh. The weighed brain substance was drenched with lime water, evaporated to dryness, and charred in a crucible. The charred mass digested with heat in diluted hydrochloric acid, filtered, and ammonia added, which precipitated alumina, iron, and phosphoric acid. The precipitate dissolved in a little hydrochloric acid; a solution of tartaric acid added; rendered alkaline by ammonia; and a stream of sulphuretted hydrogen passed through. Heated very gently, filtered, and evaporated to small bulk. A solution of sulphate of magnesia and ammonia added, which precipitated the phosphorus as phosphate of magnesia and ammonia. The precipitate was then washed with water containing ammonia, dried, burned, and weighed, the ash of the filter being deducted, and the phosphorus determined in the form of phosphate of magnesia.

In the carrying out of the foregoing processes all the little chemi-

cal minutiæ were attended to, such as the thorough washing of filters, cooling over sulphuric acid, &c.

The cases now follow. I shall give only those points in the

autopsies which have a bearing upon the analysis.

I.—Elizabeth S—, æt. 75. A case of senile insanity, manifested by apparent want of comprehension and incoherent muttering. Died of an attack of diarrhæa, after she had been insane about a month.

Autopsy.—Body emaciated. Membranes of the brain apparently normal, with the exception of some milky opacity of the arachnoid. Three ounces of clear fluid were found in the arachnoid sac, and one ounce in the lateral ventricles. There were no granulations on the living membrane of the ventricles. The brain substance was ædematous; intestines ulcerated.

						Hemis		
In 100 parts.	Medulla oblongata.	Cerebellum and Pons varolii.	Crura cerebri.	Corpora striata.	Thalami optici.	Gray sub- stance.	White	Average.
Water Solids Fats Albumen, &c	75·87 24·13 16·31 7·82	75·04 24·96 13·82 11·18	74·19 25·81 15·00 10·81	80·27 19·73 8·74 10·99	79.66 20.34 15.58 4.76	85·10 14·90 5·68 9·22	76·47 23·53 11·90 11·63	78·09 21·91 12·43 9·48

In this case the results correspond very nearly with many of Bibra's; nor is this surprising, seeing that she had been only a month insane.

II.—Charles F—, æt. 30. Had been several years demented;

died of tubercular pneumonia.

Autopsy.—Scalp thin, and poor in fat. Dura mater normal; arachnoid thin and transparent. A considerable quantity of fluid in arachnoid sac; rather more than normal in the lateral ventricles. On making a section of the hemispheres, a large quantity of fluid exuded from the brain-substance. Puncta vasculosa in white substance large and purple-coloured. The gray substance of the hemispheres was of a dark leaden colour. Under the microscope some of the cells and most of the vessels were seen surrounded by granular deposits. In some of the capillaries large and abnormally numerous nuclei were observed in the coats. In the outer layer of the cortical substance the corpora amylacea were exceedingly numerous.

The lungs were full of tubercle.

There is nothing peculiar in this case.

		m iii.				Hemis	pheres.	
In 100 parts.	Medulla oblongata.	Cerebellum and Pons varolii.	Crura	Corpora striata.	Thalami optici.	Gray sub- stance.	White	Average.
Water	73·74 26·26 16·47 9·79	74·17 25·83 17·28 8·55	79·93 20·07 7·19 12·88	82·01 17·99 10·36 7·63	71:80 28:20 11:24 16:96	85·19 14·81 4·64 10·17	69·92 30·08 18·21 12·87	76·68 23·32 12·19 11·13

III.—John D—, æt. 52. A person of weak mind, with several delusions; many years resident in the asylum; died of tubercular

pneumonia.

Autopsy.—The membranes of the brain appeared normal. The cerebral substance itself was pale; otherwise there was nothing abnormal. Under the microscope the cells were observed to be surrounded by granular deposit. The lungs were full of tubercle, and partially hepatized.

In 100 parts.	Medulla oblongata.	Cerebellum and Pons varolii.	Crura cerebri.	Corpora striata.	Thalami optici.	Gray sub- stance.	White substance	Average.
Water Solids Fats Albumen, &c. Phosphorusin 100 parts, dried at 230° Fahr.	76·17 23·83 12·83 11·00 0·441	79·00 21·00 6·56 14·44 0·550	77·26 22·74 11·98 10·76 0·282	81·38 18·62 5·67 12·95 0·913	81·77 18·23 5·98 12·25 0·659	86·23 13·77 2·50 11·27 0·653	71·20 28·80 17·72 11·08	79·01 20·99 9·03 20·99

The quantity of fat generally is small, and in the gray matter it is less than what Schlossberger found in the new-born child. If we accept Bibra's view, that the phosphorus belongs to the fat, the relation of the average quantity of phosphorus to the average quantity of fat in the whole brain would be 1.52 per cent.

IV.—Magdaline D—, æt. 37. Many years demented, latterly quite unable to comprehend what was said to her. Died of

phthisis.

Autopsy.—Body much emaciated. Dura mater normal, vessels of the arachnoid over the posterior lobes filled with firm clots, of a white fibrinous aspect, and the membrane was of a rusty hue, most intense in the immediate vicinity of the vessel. Fluid in ventricles three drachms.

Lungs contained tubercular deposits.

	4 4	B ::	3/4			Hemis	pheres.	
In 100 parts.	Medulia oblongata.	Cerebellum and Pons varolii.	Crura cerebri.	Corpora striata.	Thalami optici.	Gray sub- stance.	White	Average.
Water	73·37 26·63	78·04 21·96	73·88 26·12	81·50 18·50	77·27 22·24	86·42 13·58	69·62 30·38	77·22 22·78
Albumen, &c Phosphorusin 100	9°16 17·48	6·04 15·92	11·53 14·59	6·23 12·27	6·46 15·78	9·48	12·21 18·17	7·96 14·82
parts, dried at }	0.991	0.380	0.751	0.728	0.896	0.620	0.421	0.698

Phosphorus in fat of whole brain, according to Bibra, 1.99.

V.—William McK—, æt. 19. A congenital idiot, without power of speech or manifestation of the slightest intelligence; dirty in his

habits; died of phthisis.

Autopsy.—Body emaciated. Membranes of brain apparently normal. A small quantity of fluid escaped on opening the arachnoid sac. Three drachms of fluid were found in the lateral ventricles. The convolutions were numerous, and beautifully developed. The lungs were tubercular.

		H H				Hemis	pheres.	
In 100 parts.	Medulla oblongata.	Cerebellum and Pons varolii.	Crura	Corpora striata.	Thalami optici.	Gray sub- stance.	White	Average.
Water	78.90	79.30	75.70	82.83	81.01	85.88	71.45	79.16
Solids	21.10	20.70	24.30	17.17	19.19	14.12	28.55	20.84
Fats	9.81	7.80	13.74	7.13	8.23	3.80	16.97	9.64
Albumen, &c	11.29	16-90	10.36	10.04	11.76	11.32	11.58	11.20
Phosphorus in 100]						1 114		
parts, dried at }	1.548	1.301	1.717	1.851	1.173	0.693	0.441	1.246
230° Fahr]	Alexandra (A CHARLES	Harden L	639213	la sur	The state of		No. of the

Relation of phosphorus to fat 2.69 per cent. It will be seen that in this case the quantity of phosphorus is large, not in one region only, but in all, and is probably accounted for by his youth. It may not be unworthy of mention, that the analysis of this lad's urine, published in the 'British and Foreign Medico-Chirurgical Review,' for April, 1865, showed that he was then passing a larger than the average quantity of phosphoric acid, according to body weight. I do not, however, regard the two facts as other than a coincidence. I have again to direct attention to the fact that the fat in the gray matter is very small.

VI.—Alexander D—, æt. 50. A congenital imbecile; had much difficulty in expressing himself. Died of phthisis.

Autopsy.—Body emaciated; membranes of the brain apparently

normal. The brain-substance was pale, but otherwise normal to the

unassisted eye.

Under the microscope, the cells and vessels were seen surrounded by large quantities of granular deposit. The lungs contained tubercle.

In 100 parts.	Medulla oblongata.	Cerebellum and Pons varolii.	Crura cerebri.	Corpora striata.	Thalami optici.	Gray sub- stance.	White substance	Average.
Water Solids Fats Albumen, &c. Phosphorusin 100 parts, dried at 230° Fahr.	73·85 26·15 	78·52 21·48 8·85 12·63 0·552	74·24 25·76 11·42 14·34 0·416	81·07 18·93 5·30 13·63 0·368	78·04 21·96 9·57 12·39 0·388	86·04 13·96 1·65 12·31 0·650	69·21 30·79 18·77 12·02 0·163	77·28 22·72 9·26 13·46 0·423

The quantity of fat in the gray matter is here again excessively small, being only about half the amount found in the new-born child, and corresponding pretty nearly with the quantity obtained from embryos of an early stage. The relation of the phosphorus to the fat is 1.03 per cent.

VII.—Betsy K—, æt. 70. A case of dementia of many years' duration. Could comprehend what was said to her, and answered

with coherence occasionally. Died of general decay.

Autopsy.—Body in fair condition. Membranes of brain apparently normal. On removing the dura mater a considerable quantity of straw-coloured fluid escaped. The brain-substance was very pale, and anæmic. The lateral ventricles contained four drachms of fluid, and a few crystalline granulations were seen on their lining membrane. Microscopic examination showed that the cells and vessels were surrounded by large quantities of granular deposit. The heart, liver, and kidneys were found to be intensely fatty under the microscope.

	,	B :;				Hemis	pheres.	
In 100 parts.	Medulla oblongata.	Cerebellum and Pons varolii.	Crura cerebri.	Corpora striata.	Thalami optici.	Gray sub- stance.	White	Average.
Water	82.78	78.99	77.10	82.19	81.32	86.08	74.20	80.38
Solids	17.22	21.01	22.90	17.81	18.68	13.92	25.80	19.62
Fats	5.07	6.74	8.45	5.44	5.59	4.10	12.12	7.07
Albumen, &c	12.15	14.27	14.45	12.37	13.09	9.82	13.68	12.55
Phosphorusin 100			Take !					
parts, dried at }	1.845	0.494	0.787	0.935	0.934	0.740	0.399	0.833

The most striking peculiarity of this case is the small quantity of fat in the medulla, which is so unusual that it may be regarded as pathological. The relation of the phosphorus to the fat is 2.31 per cent.

VIII.—Robert McD—, æt. 29. Three months resident in the asylum. During that time it was observed that he was very irritable in his temper, and continually made mistakes as to the identity of persons; occasionally he was excited, and talked incoherently. Habits dirty; paralysed on the left side, and on several occasions he had epileptiform attacks, during which the convulsions were confined to the paralysed side. The paroxysm did not last more than five minutes, and was not followed by coma. It was stated that, before admission, he had been very violent and unmanageable for six weeks, and that for three years previously he had suffered from diabetes insipidus (which, however, did not exist during his residence in the asylum); that he was greatly troubled with frontal headache, and that these paroxysms of pain alternated with the diabetes; that is to say, that when he suffered from his head the quantity of urine was not abnormally great, and vice versā. He

died suddenly while sitting in his seat.

Autopsy.—On cutting through the scalp the temporal muscles of the right side were found to be edematous. The dura mater was adherent to the calvaria, on the right side, but not on the left. It was also redder on the right than on the left side. On attempting to remove the dura mater, it was found adherent over the anterior lobe of the right side, and on breaking up this adhesion a small quantity of fluid, of the colour and consistence of pus, escaped. arachnoidal surface of the dura mater was much thickened, congested over the middle and posterior lobes, and over the anterior lobe there adhered to it a portion of the superior surface of the hemisphere, of a rich yellow pus colour. The superior surfaces of both hemispheres were flattened. The left ventricle was opened, and two ounces of clear fluid removed, the whole superior surface of the right anterior lobe was of a yellow pus colour, and in cutting into it, it was found to be quite hard and solid, the hardness extending into the white The extreme anterior point of the lobe was softened, and was removed piece by piece. The base of the brain, the corpus striatum, and optic thalamus, were much softer on the right than on the left side. The right hemisphere weighed 22 oz.; the left, 181. A portion of the altered structure placed under the microscope presented cells of various sizes, some round, some oblong, and some angular, filled with granular matter, some being very similar to compound granular corpuscles, but surrounded by a cell-wall. While parts of the altered brain-substance were abnormally hard, others were undergoing softening. It was regarded as a case of cancer cerebri.

In 100 parts.	Left corpus striatum.	Left thalamus opticus.	Left hemisphere. Gray substance.	Right hemisphere. Cancerous mass.	
Water	81.82	77.13	83.51	84:01	
Solids	18.18	22.87	16.49	13.99	
Fats	4.48	9.87	7.13	5.72	
Albumen, &c	13.70	13.00	9.36	10.27	

The altered structure contained a little more water, less fat, and more albuminates than the normal gray substance.

IX.—Margaret S—, æt. 65. Several years paralysed on the left side; subject to attacks of excitement; had persistent delusions as to being under electric influence. Died comatose during an attack of diarrhœa. Autopsy. Body in fair condition. Calvaria very soft and spongy. With the exception of a large quantity of fluid in the arachnoidal sac, two ounces in the lateral ventricles and some cysts in the choroid plexus, the membranes and substance of the brain appeared normal. The lower intestine was ulcerated.

The state of the s		Right hemisphere.				Left hemisphere.				
In 100 parts.	Corpus striatum.	Thala- mus opticus.	Gray sub- stance.	Average.	Corpus striatum.	Thala- mus opticus.	Gray sub- stance.	Average		
Water Solids Fats Albumen, &c	80·90 19·10 6·24 12·86	77.55 22.45 9.59 12.86	83·22 16·78 4·63 12·15	80·55 19·45 6·82 12·63	79·48 20·52 9·45 11·07	76·67 23·33 12·66 10·67	83·53 16·47 5·35 11·12	79·89 20·11 9·15 10·96		

It will be seen that the right side, or the side opposite the paralysis, contains more water, less fat, and more albuminates than the left.

X.—Julia W—, æt. 68. A case of chronic melancholia with hypochondriasis. Died comatose and paralysed on the left side after

an illness of eight hours.

Autopsy.—Body emaciated. Dura mater presents on its internal aspect a rusty appearance on the right side, owing to numerous minute pin-point extravasations of blood. The left side presents the same appearance to a less extent, the dura mater surrounding the cerebellum is not coloured rusty. The arachnoid likewise presents multitudes of pin-point extravasations, which, under the microscope, are distinctly seen embedded in its substance. Lateral ventricles contained four drachms of turbid serum, and their lining membranes were studded with a few crystalline granulations. Cerebral substance apparently normal. The right side, that is, the affected side, contains a smaller quantity of fat and phosphorus than the left.

		Right hemisphere.				Left hemisphere.				
In 100 parts.	Corpus striatum.	Thala- mus opticus.	Gray sub- stance.	Average.	Corpus striatum.	Thala- mus opticus.	Gray sub- stance.	Average.		
Water	80.91	79.28	88.70	82.96	80.54	78.12	86.12	81.59		
Solids	19.09	20.72	14.30	17.04	19.46	21.88	13.88	18.41		
Fats	3.27	9.35	1.76	4.79	7.89	7.59	4.19	6.45		
Albumen, &c	15.82	11.37	12.84	13.25	11.87	14.29	9.69	11.96		
Phosphorus in 100 parts, dried at 230° Fahr			0.536				0.594			

XII.—Mary M—, æt. 65. Several years paralysed on the right side. Admitted in consequence of an attack of excitement. Died

comatose during an attack of diarrhœa.

Autopsy.—Dura mater greatly congested. The vessels of the arachnoid were injected, otherwise it was normal. The whole left hemisphere was softened and disorganised. The right hemisphere appeared normal. The vessels of the base of the brain were intensely atheromatous. Large intestine ulcerated.

-		Right hemisphere.				Left hemisphere.				
In 100 parts.	Corpus striatum.	Thala- mus opticus.	Gray sub- stance.	Average.	Corpus striatum.	Thala- mus opticus.	Gray sub- stance.	Average.		
Water	82.05	80.09	86.25	82.79	86.05	82.13	85.38	84.52		
Solids	17.95	19.91	13.75	17.21	13.95	17.87	14.62	15.48		
Fats	4.81	7.94	3.77	5.51	5.03	5.71	4.55	5.10		
Albumen, &c	13.14	11.97	9.98	11.70	8.92	12.16	16.07	10.38		
Phosphorus in 100 parts, dried at 230° Fahr			0.782				0.497			

In the case of the left hemisphere the brain-substance was so much softened that it was found impossible to separate the gray matter from the white, and a portion of both were taken; yet, not-withstanding the great additions made to the fat by the admixture of medullary substance, as in the two foregoing cases, the average amount of fat in the left hemisphere is not equal to that of the right It remains now to sum up and compare the results with those of other observers.

1. Water. Bibra reckons his average maximum, mean, and minimum quantity of water, in brains of persons from 19—48, at the following per-centage:

Maximum.	Mean.	Minimum.
77-99	75.66	73.25

My average per cent. for seven cases is—

Maximum.

80.38

Mean.

76.68

A comparison of the different quantities found in different regions of the brain with those of other authors is instituted in the next table.

	Schlossberger.		Hauff and Walther.			
The second second		and the		Max.	Mean.	Min.
Medulla oblongata		69.72	72.9	82.78	76.68	73.37
Cerebellum and pons		72.75	74.76	79.30	77.72	74.17
Crura cerebri .		_	-	79.93	76.04	73.88
Corpus striatum		80	82:85	82.83	81.60	80.27
Thalamus opticus		75·78 77·78	78.80	81.77	78.69	71.80
Cortical substance		84.84-	86.64	86.42	85.56	85.10
Medullary substance		69.64-	70.68	76.47	71.73	69.21

My results are about 3 per cent. higher than Bibra's; this in part is explained by the fact that I examined the gray and white matter separately, and thus obtained a higher figure for the hemispheres; but it will be found that they agree pretty closely with Schlossberger's, though generally they are a little higher. This is not surprising when we consider how often in cases of insanity we have to deal with effusions of fluid into the brain which may have existed for months before death. Then, again, slight variations will be caused by the length of the interval between death and the autopsy. It does not appear that the water of the cerebral substance directly

plays any important part in its function.

2. Fats.—Bibra's average per-centage of the fats for eleven brains is 14.44 per cent.; mine is only 9.66, making a difference of more than four parts. In phthisis he found 16.40, 12.75, 16.16, 15.30, and 14.77 per cent. In five cases of the same disease I obtained 12.19, 9.03, 7.96, 9.64, and 9.26. These numbers are low, but it must be borne in mind that, though phthisis does not appear to diminish the quantity of fat in the brain, yet it can scarcely be doubted that insanity, as a pathological process, can fail to be attended by very great alterations in the nutrition and composition of the brain. Bibra gives analyses of three insane brains, one a case of general paralysis with 13.25 per cent. of fat, another of chronic mania with 12.39, and a third of melancholia with 13.54. I do not doubt that these high results can be obtained; I have two with 12.43 and 12.19 per cent.; but I am sure that cases will be found at the other extreme, and it is absurd to build pathological conclusions upon three cases. The following tables will serve still further to contrast my figures with those of other writers.

Cort. sub.	Medullary sub.	Corp. striat.	Thal. opt.	Arbor vitæ.	Med. oblong.	Corp. callos.
Hauff 4·8—5 Bibra 6·7	14·9—16·9 Hauff.			6-7 H. 7-8 B.		18 B. 16·9 H.

The next columns contain still higher results:

	n individuals rom 19—38 years. (Bibra.)	b. In persons from 59—86 years. (Bibra.)	c. In persons of middle age. Hauff.		d. In	persons f —75 years Addison.	
Medulla oblongata Cerebellum Crura cerebri Corpora striata Thalami optici	17 15·9 14·9 12·8 12·8	17 12 13·8 11·7	15·5 11—14 7—8 9—11	rev sub.	Max. 16:47 17:28 15:00 10:36 15:58 5:68	Mean. 11.60 9.55 11.33 6.98 8.95 3.78	Min. 5·07 6·04 7·19 5·30 5·98 1·65
Hemispheres	16.0	13.9	$14-16$ $\left\{ {rac{G}{W}} \right\}$	hite "	18.77	15.41	11.90

It will be seen that my numbers are, as a whole, considerably lower than those of the others. I have generally found, not the medulla oblongata, but the common medullary substance, richest in the fats, and the gray substance poorest. In four cases the fat in the last stood respectively at 1.65, 1.76, 2.50, and 3.80 per cent., quantities unusually below the average, and comparable only with the results obtained in the case of the new-born child and in embryos (see Bibra's and Schlossberger's tables). This fact is very suggestive when we consider the mental condition of the patients. The first and last were found in the cases of congenital idiots, whose mental faculties had never undergone any change from birth; the second belonged to a cerebral hemisphere disorganised by paralysis. The third was obtained in the case of a dement. Nor less significant is the fact that in the three cases of paralysis the average quantity of fat was less on the diseased side than on the healthy. If these results should be confirmed by subsequent analyses something will have been achieved, even though they give but a pathological proof of what was physiologically assumed, namely, the great importance of the cerebral fats for the nutrition and function of the brain.

3. Phosphorus. The average quantity of phosphorus for five brains was 0.556 per cent. of cerebral substance dried at 230° Fahr. The amounts for the different regions are as follow:

	Maximum.	Mean.	Minimum.
Medulla oblongata .	. 1.548	1.131	0.441
Cerebellum and pons	. 1.301	0.675	0.480
Crura cerebri	. 1.717	0.564	0.282
Corpora striata	. 1.851	0.959	0.368
Thalami optici	. 1.173	0.870	0.388
Gray substance .	. 0.740	0.711	0.620
Medullary substance .	. 0.441	0.356	0.163

The corpus striatum contained the largest quantity of phosphorus, and the difference between the gray and white substances, in this respect, is notably to the advantage of the former.

Having ascertained its relation quantitatively to the fat, I shall

now compare my numbers with Bibra's:

BIBRA.					ADDISON.					
A girl,	æt.	19,	in whole bra	ain 2.53	A boy,	æt.	19, for	whole brain	2.69	
A man,		56,			A man	,,	52,	,,	1.52	
A ,,	,,	80,	,,		A woman		70,	,,	2.31	
A lunatic	,,	36,	,,		A ,,		37,	,,	1.99	
A ,,	,,	52,	,,	1.87	A man	,,	50,	"	1.03	

The differences are trifling; it must not, however, be forgotten that the figures, compared with Bibra's, are not the result of an analysis, but of a calculation. The maximum quantity was found in the case of a congenital idiot, which is not in accordance with the theory that dementia is connected with a minus quantity of phosphorus in the brain. Borsarelli ('Medical Times and Gazette,' August 31st, 1861) states that the amount of phosphorus in the brain varies from 1.352 to 1.790 per cent. I have not had an opportunity of consulting his communication in the original, and the translator does not mention what he means by per cent., whether recent or dried The same loose statement is also copied into the brain-substance. last edition of Carpenter's 'Physiology.' If fresh cerebral matter is meant, like all the earlier analyses of this substance, the results are incredible; if dried brain, he is not improbably correct. In that case my numbers generally would fall very far below the normal.

The results deducible from the whole foregoing observations are :-

1. A confirmation of the assertion that the different anatomical parts of one and the same brain present great differences in their quantities of water and fat (with the addition that these differences appear to be greater when complicated by insanity).

2. A confirmation of the fact that the gray substance is far poorer

in fat than the white.

3. A confirmation of the law that the quantity of matters soluble in ether stands in an inverse relation to the quantity of water.

4. That in the greater number of the foregoing cases the results as to the quantities of water were slightly higher than those of other

experimenters on sane brains.

5. That the quantities of fat were generally smaller, and that in two cases of idiocy, one of dementia, and one of chronic melancholia, they were below the quantity found in the new-born child, and in two cases not greater than the amount found in embryonal conditions of an early stage.

6. That the quantities of phosphorus did not have a parallel con-

nection with the degree of intelligence.

7. That in three cases of hemiplegia the average quantity of fat in the corpus striatum, optic thalamus, and gray substance of the hemisphere opposite the paralysis, was less than the average quantity in the same parts of the other side.

8. That in a case of cancer cerebri the cancerous mass contained less fat and more albuminates than the unaltered cerebral substance.

I have to thank my chief, Dr. Howden, for permission to make use of everything connected with these cases, and to acknowledge that the microscopical observations are his.