Lipids of Peripheral Nerve

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In order to study experimentally the changes which occur in the distribution of the lipids in a peripheral nerve when it undergoes degeneration, methods had to be developed which demanded only a small sample of tissue. In this paper the application of the methods at present in use in this laboratory to normal peripheral nerve is described.

METHODS

Analyses were made on the sciatic nerves of 3 rabbits, 4 cats, 3 dogs and a beaver, and on the sciatic nerves or emoral nerves of a number of humans. The nerve was dissected out as soon as possible after death and the lipids were extracted and estimated by the methods described previously (Johnson, McNabb & Rossiter, 1948). The concentration of free cholesterol, total cholesterol, cerebroside, total phospholipid, monoaminophospholipid and lecithin was measured directly, and, from these figures, the values for ester cholesterol, sphingomyelin and kephalin were calculated.

RESULTS

The concentration of 'essential lipid', i.e. cerebroside, cholesterol and phospholipid, for each nerve studied is given in Table 1, and the concentration of lecithin, sphingomyelin and kephalin, the individual phospholipids which go to make up the total phospholipid fraction, in Table 2. The figures in each of these tables are in terms of mg./100 mg. fresh tissue. In Table 3, each of the lipid fractions is given as a percentage of the 'essential lipid', while in Table 4 each of the individual phospholipids—lecithin, sphingomyelin and kephalin—is given as a percentage of the total phospholipid.

DISCUSSION

The classical work on the distribution of the lipids in peripheral nerve is that of Falk (1908), who found the following relative concentrations of lipid in medullated nerve: cholesterol, 25·0; kephalin, 12·4; lecithin, 2·9; and cerebroside, 18·2. In the present investigation, in which more refined methods have been used for determining the distribution of the lipids, the results are considerably different.

Randall (1938), in a study of human nerve, found that the concentration of phospholipid was 4·5, cholesterol 1·5 and cerebroside 1·6%, referred to wet weight. In general our results for human nerve substantiate those of Randall, but the latter did not attempt to distinguish between the various phospholipid fractions. In most of the human nerves studied, the concentration of the various lipids was found to be slightly less than that reported by

Table 1. *Lipids in peripheral nerve* (*expressed as mg.*/100 *mg. fresh tissue*)

	Cerebrosides	Free cholesterol	Total cholesterol	Ester cholesterol	Total phospholipid	'Essential lipid'
Rabbit 1 (S)	2·94	2·68	2·70	0·02	5·21	10·85
Rabbit 2 (S)	2·61	2·67	2·80	0·13	5·79	11·20
Rabbit 3 (S)	3·23	3·65	3·69	0·04	6·81	13·73
Cat 1 (S)	2·88	3·19	3·23	0·04	6·21	12·32
Cat 2 (S)	1·48	3·56	3·64	0·08	5·88	11·00
Cat 3 (S)	2·82	3·74	3·75	0·01	7·27	13·84
Cat 4 (S)	1·99	2·87	2·89	0·02	6·28	11·16
Dog 1 (S)	2·88	3·07	3·10	0·03	5·39	11·37
Dog 2 (S)	4·15	2·78	2·78	0·00	5·14	12·07
Dog 3 (S)	1·97	2·43	2·43	0·00	5·62	10·02
Beaver 1 (S)	1·34	3·15	3·15	0·00	5·85	10·34
Patient 1 (S)	2·54	1·51	1·65	0·14	3·81	8·00
Patient 2 (F)	0·94	1·37	1·37	0·00	2·22	4·53
Patient 3 (S)	1·09	1·25	1·29	0·04	3·09	5·47
Patient 3 (F)	1·35	1·44	1·44	0·00	2·97	5·76
Patient 4 (S)	1·30	1·16	1·17	0·01	2·40	4·87
Patient 4 (F)	1·33	1·48	1·53	0·05	3·32	6·18

S = sciatic nerve; F = femoral nerve.

Table 2. *Phospholipids in peripheral nerve (expressed as mg./100 mg. fresh tissue)*

	Total phospholipid	Monoamino-phospholipid	Lecithin	Sphingomyelin (total phospholipid less monoamino-phospholipid)	Kephalin (monoamino-phospholipid less lecithin)
Rabbit 1 (S)	5·21	2·74	0·67	2·47	2·07
Rabbit 2 (S)	5·79	3·54	0·66	2·25	2·88
Rabbit 3 (S)	6·81	2·94	1·10	3·87	1·84
Cat 1 (S)	6·21	3·22	0·72	2·99	2·50
Cat 2 (S)	5·88	3·25	0·72	2·63	2·53
Cat 3 (S)	7·27	2·76	1·01	4·51	1·75
Cat 4 (S)	6·28	3·13	0·96	3·15	2·17
Dog 1 (S)	5·39	2·09	1·03	3·30	1·06
Dog 2 (S)	5·14	2·23	1·01	2·91	1·22
Dog 3 (S)	5·62	2·38	0·72	3·24	1·66
Beaver 1 (S)	5·85	2·68	0·72	3·17	1·96
Patient 1 (S)	3·81	1·49	0·64	2·32	0·85
Patient 2 (F)	2·22	0·89	0·31	1·33	0·58
Patient 3 (S)	3·09	1·23	0·35	1·86	0·88
Patient 3 (F)	2·97	1·28	0·43	1·69	0·85
Patient 4 (S)	2·40	0·76	0·35	1·64	0·41
Patient 4 (F)	3·32	1·61	0·46	1·71	1·15

S = sciatic nerve; F = femoral nerve.

Table 3. *Distribution of lipids in peripheral nerve (expressed as percentage of 'essential lipid')*

	Cerebroside	Total cholesterol	Total phospholipid	Lecithin	Sphingomyelin	Kephalin
Rabbit 1 (S)	27·1	24·9	48·0	6·2	22·8	19·0
Rabbit 2 (S)	23·3	25·0	51·7	6·0	20·3	25·4
Rabbit 3 (S)	23·6	26·8	49·6	8·2	27·9	13·5
Cat 1 (S)	23·4	26·2	50·4	5·8	24·1	20·5
Cat 2 (S)	13·4	33·1	53·5	6·6	23·9	23·0
Cat 3 (S)	20·6	26·5	52·9	7·4	32·8	12·7
Cat 4 (S)	17·8	25·9	56·3	8·5	28·4	19·4
Dog 1 (S)	25·3	27·3	47·4	9·1	29·0	9·3
Dog 2 (S)	34·4	23·0	42·6	8·4	24·1	10·1
Dog 3 (S)	19·7	24·2	56·1	7·2	32·4	16·5
Beaver 1 (S)	13·0	30·4	56·6	6·9	30·8	18·9
Patient 1 (S)	31·7	20·7	47·6	7·8	29·1	10·7
Patient 2 (F)	20·9	30·2	48·9	6·7	29·4	12·8
Patient 3 (S)	19·7	24·3	56·0	5·9	33·9	16·2
Patient 3 (F)	23·3	25·1	51·6	7·5	29·4	14·7
Patient 4 (S)	26·6	24·1	49·3	7·1	33·8	8·4
Patient 4 (F)	21·5	24·8	53·7	7·4	27·7	18·6

S = sciatic nerve; F = femoral nerve.

Randall. However, our material came from older patients, the ages of the four patients studied being 54, 68, 74 and 45 years. Randall has reported that, in diabetic and arteriosclerotic gangrene, there is a decrease in the concentration of each of the 'essential lipid' constituents of nerve, an observation confirmed by us for other degenerative conditions.

Another point to consider is that the material studied came from the proximal end of the nerve, where the nerve is large and the incorporated fibrous connective tissue much greater. This, we feel, explains why, on a wet weight basis, the concentration of 'essential lipid' in human nerve was found to be less than that of the rabbit, cat, dog and beaver, where the nerves were smaller and connective tissue less. Despite the fact that the concentration of each of the lipid fractions was found to be less in human nerves, the distributions of the three fractions which make up the 'essential lipids', and of the individual phospholipids, were very similar in the human and animal nerves.

There are few data in the literature for the distribution of the lipids in the peripheral nerves of the rabbit, cat, dog and beaver. Schmidt, Benotti, Hershman & Thannhauser (1946) estimated total phospholipid and monoaminophospholipid concentration in three cat nerves. They found 7·5, 8·6 and 8·3% phospholipid, of which 50, 44·5 and 44·5% was sphingomyelin; these figures are of the same order as ours. They also found that sphingomyelin formed only 20% of the total phospholipid in rat

nerve, a value lower than that for any of the species investigated in the present study.

Table 4. *Distribution of phospholipids in peripheral nerve (expressed as percentage of total phospholipid)*

	Lecithin (%)	Sphingomyelin (%)	Kephalin (%)
Rabbit 1 (S)	12·9	47·4	39·7
Rabbit 2 (S)	11·4	38·9	49·7
Rabbit 3 (S)	16·2	56·8	27·0
Cat 1 (S)	11·6	48·2	40·2
Cat 2 (S)	12·2	44·8	43·0
Cat 3 (S)	14·0	62·0	24·0
Cat 4 (S)	15·2	50·3	34·5
Dog 1 (S)	19·1	61·2	19·7
Dog 2 (S)	19·6	56·6	23·8
Dog 3 (S)	12·8	57·7	29·5
Beaver 1 (S)	12·3	54·4	33·3
Patient 1 (S)	16·5	61·1	22·4
Patient 2 (F)	13·6	60·2	26·2
Patient 3 (S)	11·3	60·2	28·5
Patient 3 (F)	14·5	57·0	28·5
Patient 4 (S)	14·5	68·4	17·1
Patient 4 (F)	13·8	51·5	34·7

S = sciatic nerve; F = femoral nerve.

The relative distribution of cerebroside, cholesterol and phospholipid was roughly 1 : 1 : 2 in peripheral nerves of all the species studied. This is also roughly the distribution of the 'essential lipids' in brain tissue of the same species (Johnson *et al.* 1948). When one examines the distribution of the various constituents of the phospholipid fraction, however, a difference between peripheral nerve and brain tissue becomes apparent. In all the species studied 50–70 % of the phospholipid of peripheral nerve is sphingomyelin, whereas the corresponding figure for whole brain tissue is 20%. The figure is 40 % for brain white matter, however, and in general the distribution of all the lipid constituents of peripheral nerve bears a much greater resemblance to the lipid distribution in the white matter of the brain than to either that of the grey matter or that of the brain as a whole. This is particularly apparent when the lipids are presented as percentages of total 'essential lipid', and it is, perhaps, hardly surprising when one considers that a high percentage of the lipids in both the white matter of the brain and in peripheral nerve go to make up the 'myelin' sheath. The chief difference between the lipid distribution in peripheral nerve and that in white matter of the brain is that, in peripheral nerve the percentage of sphingomyelin is somewhat greater, while the percentage of kephalin and cerebroside is somewhat less.

SUMMARY

1. The cerebroside, free cholesterol, total cholesterol, total phospholipid, lecithin, sphingomyelin and kephalin concentrations in peripheral nerves from the rabbit, cat, dog, beaver and man have been determined.

2. The distribution of the 'essential lipids' (cerebrosides, total cholesterol and total phospholipid) and of the individual phospholipids more closely resembles the distribution in the white matter of the brain than that in either the grey matter or whole brain. In peripheral nerve, however, there is relatively more sphingomyelin and less kephalin and cerebroside than in brain white matter.

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