Fatty Acid Compositions of Human Brain Lecithin and Sphingomyelin in Normal Individuals, Senile Cerebral Cortical Atrophy, Alzheimer's Disease, Metachromatic Leucodystrophy, Tay-Sachs and Niemann-Pick Diseases

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Abstract

The fatty acid compositions of whole brain lecithin and sphingomyelin were determined. Brain specimens from normal adults, a normal infant, and several disease states were examined. Normal adult brain lecithin has a very simple fatty acid composition (palmitic, stearic, and oleic acids) and infant brain lecithin contains more palmitic acid and less oleic acid than adult brain. The whole brain lecithin fatty acid compositions from metachromatic leucodystrophy, and Tay-Sachs and Niemann-Pick diseases are intermediate between that of normal infant and normal adult brain and no characteristic features attributable to specific disease states were detected. The fatty acids of whole brain lecithin from senile cerebral cortical atrophy and Alzheimer's disease were similar to normal adult brain except that a greater variety of fatty acids was seen in both pathological states. No characteristic features attributable specifically to either pathological state were detected. The fatty acid composition of normal adult brain sphingomyelin differs from that of the normal infant in that longer chain fatty acids are more abundant in adult brain. The fatty acid compositions of whole brain sphingomyelins from Niemann-Pick disease and metachromatic leucodystrophy differed from that of normal infant and adult brain in that C_{24} acids were not detected. No characteristic features attributable to a specific disease were detected. Fatty acid compositions of whole brain sphingomyelins in senile cerebral cortical atrophy and Alzheimer's disease were found to be very similar to those of the normal adult.

Introduction

THE DETERMINATION of the fatty acid composition of lipid classes in normal and disease states defines the normal condition and may disclose abnormalities in disease states. This report presents the fatty acid compositions of normal adult and infant brains and the findings in several pathological states. The lipid class compositions of the same brain specimens are presented by Rouser et al. (1).

Methods

The brain specimens were obtained and the lipids extracted as described by Rouser et al. (1,2). The fatty acid compositions of lecithin and sphingomyelin were determined on samples separated by thin-layer chromatography (TLC) by the method of Feldman and Rouser (3).

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Results and Discussion

The fatty acid compositions of the eight brain lecithin samples studied are shown in Table I and the values for the sphingomyelin fatty acid compositions from the same brain samples are shown in Table II.

Several important observations are immediately apparent from the lecithin values. From the values in columns 1 and 2 it is apparent that the normal adult male and female brain are very similar and have a very simple fatty acid composition. These findings are in agreement with previous reports (4,5) except that a somewhat simpler picture of fatty acid composition was obtained in the present studies. This may be related to the fact that previous investigators examined brain specimens from older persons. Comparison of columns 2 and 3 with column 5 shows that while the immature normal brain of a 5-month-old infant has a relatively simple fatty acid distribution similar to that of the normal adult brain, infant brain lecithin contains more palmitic acid and less oleic acid.

The values for palmitic, stearic, and oleic acids of the brain lecithins from senile cerebral cortical atrophy and Alzheimer's disease (columns 3 and 4) are very similar to those of the two normal brains (columns 1 and 2), but a greater variety of fatty acids is evident in both pathological states. The presence of small amts of other fatty acids appears to be the only distinctive feature of both abnormal brain samples.

The brain lecithin samples from Niemann-Pick and Tay-Sachs diseases and metachromatic leucodystrophy (columns 6, 7 and 8) are intermediate between the infant (column 5) and normal adult (columns 1 and 2) with regard to percentages of 16:0 and 18:1. The samples from the three pathological states have a greater variety of fatty acids than the normal specimens in keeping with the findings in adult brains.

Table II shows the brain sphingomyelin samples from a normal adult male and female to be very similar (columns 1 and 2). The findings are in agreement with the reports of earlier investigators (4). The samples show the presence of longer chain (C_{22} and C_{24}) fatty acids not present in lecithin. The longer chain fatty acids are decreased in infant brain (column 5). The occurrence of more longer chain fatty acids appears to be a reflection of increased myelination. Our findings with infant brain are in agreement with those of Svennerholm (6) who reported the fatty acid compositions of brains of fetuses and infants.

The fatty acid compositions of sphingomyelin from senile cerebral cortical atrophy and Alzheimer's disease are very similar to the two normal adult samples.

The fatty acids of sphingomyelins of Niemann-Pick disease, Tay-Sachs disease and metachromatic leucodystrophy (columns 6, 7 and 8) are intermediate be-

TABLE I
Brain Lecithin Fatty Acids [a]

Fatty Acid	1 NAM	2 NAF	3 CAAF	4 AlzAF	5 NI	6 NP	7 TS	8 MLD
12:0	.....	.....	.....	0.78	.....	.....	.....	.....
14:0	.....	.....	0.80	0.88	.....	0.82	1.09	0.91
15:0	.....	.....	0.21	.....	.....	.....	0.18	.....
16:0	47.58	44.38	41.59	43.89	60.60	52.85	51.57	52.32
16:1	.....	.....	2.47	2.45	.....	3.48	3.59	1.80
17:0	.....	.....	0.51	.....	.....	.....	.....	.....
18:0	12.09	13.88	11.88	13.00	11.27	8.65	7.16	12.63
18:1	40.33	41.74	35.88	37.17	23.27	29.47	31.94	27.29
18:2	.....	.....	1.29	0.74	2.23	.....	1.06	.....
20:0	.....	.....	.....	.....	.....	0.57	.....	.....
20:1	.....	.....	1.06	.....	2.63	0.98	0.68	.....
21:0	.....	.....	0.86	.....	.....	.....	.....	.....
22:0	.....	.....	0.46	1.08	.....	3.18	1.83	5.05
22:1	.....	.....	2.36	.....	.....	.....	.....	.....
(?)	.....	.....	0.32	.....	.....	.....	0.89	.....

[a] Values expressed as relative percent. Blank spaces indicate the failure to detect a fatty acid or detection of a trace amt only.
NAM, normal adult male; NAF, normal adult female; CAAF, senile cerebral atrophy, adult female; AlzAF, Alzheimer's disease, adult female; NI, normal infant (5 months of age); NP, Niemann-Pick disease; TS, Tay-Sachs disease; MLD, metachromatic leucodystrophy.

TABLE II
Brain Sphingomyelin Fatty Acids [a]

Fatty acid	1 NAM	2 NAF	3 CAAF	4 AlzAF	5 NI	6 NP	7 TS	8 MLD
12:0	.....	.....	2.75	.....	.....	.....	.....	.....
14:0	.....	.....	0.34	0.67	0.75	.....	0.79	.....
15:0	.....	.....	.....	0.62	.....	.....	.....	.....
16:0	6.42	6.79	7.62	6.82	7.30	5.89	11.93	15.80
16:1	1.35	0.45	.....	0.61	.....	0.37	.....	0.57
18:0	47.04	45.80	42.78	42.40	70.33	85.63	64.84	79.58
18:1	3.23	.....	3.81	2.26	1.97	.....	3.21	2.32
18:2	.....	.....	0.59	.....	.....	.....	.....	.....
20:0	1.04	1.48	1.91	1.83	2.62	3.70	3.47	1.71
22:0	3.63	2.35	2.11	2.58	3.65	4.24	3.88	.....
22:1	1.89	.....	.....	.....	.....	.....	.....	.....
23:0	.....	3.10	1.89	4.37	2.67	.....	.....	.....
24:0	4.52	6.69	7.63	9.89	4.46	.....	4.12	.....
24:1	30.86	31.71	28.55	27.14	8.39	.....	7.78	.....
(?)	.....	1.62	.....	.....	.....	.....	.....	.....

[a] Values expressed as relative percents. Abbreviations as for Table I.

tween those of normal infant and normal adult brain in some respects. The C_{24} fatty acids characteristic of the normal brain are present only in the sample from Tay-Sachs disease. This large change in C_{24} acids is not a specific feature of one disease. Svennerholm (6) has reported a decrease in longer chain fatty acids of sphingomyelin in metachromatic leucodystrophy.

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Speculations on the Nature of the Metabolic Defects in Tay-Sachs, Niemann-Pick, Gaucher's and Alzheimer's Diseases, and Metachromatic Leucodystrophy

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Abstract

It is concluded that the defect in Tay-Sachs disease is for an enzyme degrading a monosialoganglioside, in Niemann-Pick disease for an enzyme degrading sphingomyelin or possibly ceramide, in chronic Gaucher's disease for an enzyme degrading a glucocerebroside, and in metachromatic leucodystrophy for an enzyme for degradation of sulfatide. Alzheimer's disease does not appear to involve any specific changes in lipid composition. An hypothesis to explain the findings in Alzheimer's disease is presented.

Introduction

PATHOLOGICAL PROCESSES affecting lipids can be classified as primary or secondary events. Secondary changes in lipids brought about by some other primary event such as an infectious disease, a disturbance in carbohydrate or amino acid metabolism, or a structural defect of the vascular system are important, but the primary changes involving lipids directly are particularly interesting. We have sought to avoid the inadvertent study of lipid changes secondary to other processes by studying hereditary metabolic diesases where histological