

Supplementary Material

Sphingolipids in Cerebrospinal Fluid and Plasma Lipoproteins of *APOE4* Homozygotes and Non-*APOE4* Carriers with Mild Cognitive Impairment versus Subjective Cognitive Decline

Supplementary Table 1. LC-MSMS specifications

Component	Ion transition (m/z)*	retention time (min)	CE (volts)
S1P(d18:1)	380.4 → 264.2	5.30	20
Cer(d18:1/14:0)	510.6 → 264.2	6.54	30
Cer(d18:1/16:0)	538.6 → 264.2	6.77	30
Cer(d18:1/18:0)	566.6 → 264.2	7.06	30
Cer(d18:1/20:0)	594.6 → 264.2	7.41	30
Cer(d18:1/22:0)	622.6 → 264.2	7.82	35
Cer(d18:1/24:0)	650.6 → 264.2	8.34	40
Cer(d18:1/24:1)	648.6 → 264.2	7.90	40
SM(d18:1/16:0)	706.6 → 186.2	6.66	40
SM(d18:1/18:0)	734.6 → 186.2	6.93	40
SM(d18:1/18:1)	732.6 → 186.2	6.73	40
SM(d18:1/20:0)	762.6 → 186.2	7.26	40
SM(d18:1/22:0)	790.6 → 186.2	7.61	40
SM(d18:1/24:0)	818.6 → 186.2	8.07	47
SM(d18:1/24:1)	816.6 → 186.2	7.38	47
<i>Internal standards</i>			
S1P(d18:1)-D7	387.4 → 271.2	5.30	20
Cer(d18:1/17:0)	552.6 → 264.2	6.91	30
Cer(d17:0/24:1)	634.6 → 250.2	7.70	35
SM(d18:1/17:0)	720.6 → 186.2	6.78	40

*SM species are analyzed at m+3 instead of m+1

Supplementary Table 2. Characteristics of patients from whom CSF or plasma was used in sphingolipid analysis.

	<i>APOE4</i> homozygotes with SCD			Non- <i>APOE4</i> carriers with SCD		
	CSF	plasma	p ^a	CSF	plasma	p ^a
N	10	10		10	10	
ApoE2/E3	4	1	0.154	3	2	1
Female (%)	2	4	0.628	6	4	0.656
Age (y)	54.9 ± 12.8	58.3 ± 8.3	0.609	69.2 ± 8.9	69.8 ± 9.1	0.891
MMSE	29 ± 1	28 ± 2	0.286	23 ± 2	23 ± 2	0.656
BMI (kg/m²)	24.3 ± 3.7	28.0 ± 5.5	0.091	25.1 ± 5.6	25.7 ± 2.6	0.772
Smoking, ever (%)	7	3	0.179	3	3	1
Smoking, current	3	0	0.211	2	2	1
Statin use (%)	0	2	0.474	1	2	1
CSF Aβ₄₂ (pg/mL)	1242 ± 270	1082 ± 291	0.219	799 ± 264	773 ± 275	0.835
CSF pTau (pg/mL)	52 ± 17	49 ± 31	0.811	81 ± 50	61 ± 25	0.278

	<i>APOE4</i> homozygotes with MCI			Non- <i>APOE4</i> carriers with MCI		
	CSF	plasma	p ^a	CSF	plasma	p ^a
N	9	9		10	10	
ApoE2/E3	-	-		-	-	
Female (%)	2	5	0.335	5	5	1
Age (y)	58.4 ± 7.3	60.5 ± 6.9	0.669	64.9 ± 10.5	67.9 ± 5.1	0.251
MMSE	29 ± 1	29 ± 1	0.642	24 ± 2	24 ± 2	0.644
BMI (kg/m²)	26.2 ± 3.6	26.7 ± 2.4	0.888	23.8 ± 3.4	25.1 ± 4.0	0.458
Smoking, ever (%)	3	3	1	1	4	0.303
Smoking, current	1	1	1	0	1	1
Statin use (%)	2	1	1	2	3	1
CSF Aβ₄₂ (pg/mL)	852 ± 361	914 ± 333	0.872	644 ± 86	566 ± 121	0.114
CSF pTau (pg/mL)	60 ± 27	53 ± 13	0.821	66 ± 28	60 ± 23	0.612

^aby Student's t-test for continuous data and Fisher exact test for categorical data.

Supplementary Table 3. Plasma lipids of non-*APOE4* carriers and *APOE4* homozygotes with SCD or MCI.

	Non- <i>APOE4</i> carriers		<i>APOE4</i> homozygotes		effect size (partial eta squared) ^a			
	SCD	MCI	SCD	MCI	Age ²	Sex	<i>APOE4</i> versus non- <i>APOE4</i>	MCI versus SCD
N	10	10	9	10				
Total cholesterol (mM) [#]	5.20 ± 0.66	5.29 ± 1.14	6.04 ± 1.07	5.82 ± 1.27	0.09	0.08	0.10	0.02
Triglycerides (mM) [#]	1.69 ± 0.67	1.18 ± 0.29	1.97 ± 0.93	1.72 ± 0.67	0.06	0.01	0.10	0.01
HDL-C (mM) ^{#,S}	1.09 ± 0.31	1.28 ± 0.27	1.12 ± 0.40	1.07 ± 0.36	0.08	0.25^{&}	0.05	0
HDL-TG (mM) ^{#,S}	0.16 ± 0.02	0.14 ± 0.04	0.16 ± 0.05	0.16 ± 0.03	0.03	0.02	0	0
LDL-ApoB100 (g/L) ^{#,S}	0.54 ± 0.11	0.54 ± 0.11	0.65 ± 0.17	0.67 ± 0.13	0.30^{&}	0	0.23^{&}	0.16^{&}
LDL-C (mM) ^{#,S}	2.33 ± 0.57	2.35 ± 0.71	2.73 ± 0.73	2.94 ± 0.78	0.14^{&}	0.05	0.15^{&}	0.07
LDL-TG (mM) ^{#,S}	0.22 ± 0.03	0.20 ± 0.02	0.24 ± 0.09	0.28 ± 0.07	0.03	0.02	0.15^{&}	0.05
VLDL-ApoB100 (g/L) ^{#,S}	0.05 ± 0.02	0.05 ± 0.02	0.06 ± 0.03	0.06 ± 0.02	0.07	0.06	0	0.02
VLDL-C (mM) ^{#,S}	0.37 ± 0.14	0.24 ± 0.14	0.40 ± 0.25	0.32 ± 0.13	0.10	0	0.04	0
VLDL-TG (mM) ^{#,S}	0.40 ± 0.20	0.34 ± 0.23	0.30 ± 0.16	0.49 ± 0.29	0.05	0.02	0	0.07

Data are displayed as mean ± SD; -C, cholesterol; -TG, triglycerides.^S data derived after density gradient centrifugation.

^aGeneral Linear model with age squared, sex, *APOE* genotype and cognitive category; [&]p < 0.05

Supplementary Table 4. Plasma sphingolipid levels in non-*APOE4* carriers and *APOE4* homozygotes with SCD or MCI.

Plasma	Non- <i>APOE4</i> carriers		<i>APOE4</i> homozygotes		effect size (partial eta squared) ^a			
	SCD (n=10)	MCI (n=10)	SCD (n=9)	MCI (n=10)	Age ²	Sex	<i>APOE4</i> versus non- <i>APOE4</i>	MCI versus SCD
Cholesterol (mM)	5.20 ± 0.66	5.29 ± 1.14	6.04 ± 1.07	5.82 ± 1.27	0.11	0.06	0.09	0.02
Triglycerides (mM)	1.69 ± 0.67	1.18 ± 0.29	1.97 ± 0.93	1.72 ± 0.67	0.10	0.02	0.09	0.02
S1P(d18:1) (μM)	2.80 ± 0.89	2.57 ± 0.97	2.46 ± 0.88	2.47 ± 0.41	0	0	0.02	0
Ceramides (μM)	14.94 ± 3.03	14.21 ± 5.15	15.16 ± 4.29	17.22 ± 4.88	0.17^s	0.09	0.01	0.08
Cer(d18:1/14:0)	0.03 ± 0.01	0.03 ± 0.01	0.03 ± 0.01	0.03 ± 0.01	0.18^s	0.01	0.01	0.02
Cer(d18:1/16:0)	0.22 ± 0.06	0.21 ± 0.07	0.21 ± 0.05	0.21 ± 0.03	0.10	0	0	0.04
Cer(d18:1/18:0)	0.19 ± 0.06	0.19 ± 0.09	0.20 ± 0.05	0.23 ± 0.07	0.01	0	0.04	0.02
Cer(d18:1/20:0)	0.61 ± 0.21	0.56 ± 0.27	0.63 ± 0.21	0.67 ± 0.16	0.07	0	0.02	0.02
Cer(d18:1/22:0)	6.20 ± 1.46	5.32 ± 2.23	6.25 ± 2.34	6.45 ± 2.16	0.23^s	0.07	0.02	0.05
Cer(d18:1/24:0)	6.03 ± 1.25	5.91 ± 2.22	6.03 ± 1.44	6.44 ± 1.60	0.12^s	0.15^s	0	0.07
Cer(d18:1/24:1)	1.67 ± 0.44	1.98 ± 0.78	1.80 ± 0.59	2.16 ± 0.52	0.02	0.01	0.01	0.10
Sphingomyelins (μM)	710.30 ± 86.62	684.73 ± 107.28	746.40 ± 120.16	730.70 ± 137.93	0.06	0.19^s	0.02	0
SM(d18:1/16:0)	156.63 ± 12.57	154.36 ± 13.72	157.82 ± 22.15	164.80 ± 29.22	0.06	0.08	0.01	0.04
SM(d18:1/18:0)	23.74 ± 4.96	24.16 ± 3.36	25.68 ± 5.45	28.53 ± 5.67	0.01	0.05	0.09	0.05
SM(d18:1/18:1)	12.04 ± 3.04	11.77 ± 2.34	12.13 ± 2.22	13.76 ± 2.73	0	0.29^s	0.03	0.03
SM(d18:1/20:0)	67.21 ± 14.99	63.60 ± 9.57	70.56 ± 14.08	71.58 ± 14.93	0.02	0.16^s	0.03	0
SM(d18:1/22:0)	134.93 ± 24.42	119.49 ± 26.78	142.90 ± 26.88	131.89 ± 33.09	0.13^s	0.14^s	0.03	0
SM(d18:1/24:0)	67.08 ± 13.04	57.32 ± 14.68	70.59 ± 13.72	62.39 ± 16.76	0.11^s	0.15^s	0.01	0.1
SM(d18:1/24:1)	248.67 ± 36.78	254.04 ± 48.38	266.71 ± 48.57	257.74 ± 53.37	0.01	0.18^s	0.01	0

Data are mean ± SD. ^aGeneral Linear model with age squared, sex, *APOE* genotype and cognitive category; ^sp < 0.05.

Supplementary Table 5. Sphingolipid levels in plasma HDL from non-*APOE4* carriers and *APOE4* homozygotes with SCD or MCI.

HDL	Non-<i>APOE4</i> carriers		<i>APOE4</i> homozygotes		effect size (paired eta squared)^a			
	SCD (n=10)	MCI (n=10)	SCD (n=9)	MCI (n=10)	Age²	Sex	<i>APOE4</i> versus non-<i>APOE4</i>	MCI versus SCD
Cholesterol (mM)	1.09 ± 0.31	1.28 ± 0.27	1.12 ± 0.40	1.07 ± 0.36	0.08	0.25^s	0.05	0
Triglycerides (mM)	0.16 ± 0.02	0.14 ± 0.04	0.16 ± 0.05	0.16 ± 0.03	0.03	0.02	0	0
S1P(d18:1) (μM)	1.38 ± 0.37	1.62 ± 0.78	1.70 ± 0.65	1.61 ± 0.55	0.01	0.04	0.01	0
Ceramides (μM)	1.00 ± 0.24	1.02 ± 0.25	0.97 ± 0.31	1.09 ± 0.27	0.08	0.19^s	0	0.
Cer(d18:1/14:0)	0.02 ± 0.01	0.02 ± 0.01	0.02 ± 0.01	0.03 ± 0.01	0	0.01	0.01	0.02
Cer(d18:1/16:0)	0.10 ± 0.03	0.10 ± 0.02	0.09 ± 0.04	0.10 ± 0.03	0	0.02	0.01	0
Cer(d18:1/18:0)	0.06 ± 0.02	0.07 ± 0.02	0.06 ± 0.02	0.09 ± 0.04	0.01	0	0.04	0,03
Cer(d18:1/20:0)	0.05 ± 0.02	0.06 ± 0.02	0.06 ± 0.02	0.06 ± 0.02	0.09	0.07	0.01	0
Cer(d18:1/22:0)	0.25 ± 0.07	0.25 ± 0.09	0.27 ± 0.09	0.29 ± 0.07	0.12^s	0.28^s	0.02	0.02
Cer(d18:1/24:0)	0.33 ± 0.10	0.29 ± 0.06	0.28 ± 0.11	0.30 ± 0.09	0.03	0.14^s	0.02	0.01
Cer(d18:1/24:1)	0.19 ± 0.06	0.24 ± 0.08	0.19 ± 0.09	0.22 ± 0.08	0.06	0.14^s	0.01	0.01
Sphingomyelins (μM)	134.43 ± 58.93	173.97 ± 48.34	153.05 ± 57.26	143.82 ± 41.27	0.20^s	0.34^s	0.04	0.02
SM(d18:1/16:0)	40.58 ± 16.91	52.11 ± 10.21	41.78 ± 14.03	44.69 ± 12.57	0.14^s	0.26^s	0.05	0
SM(d18:1/18:0)	7.60 ± 3.24	10.12 ± 2.41	8.14 ± 3.23	9.17 ± 3.56	0.10	0.20^s	0.01	0.01
SM(d18:1/18:1)	5.14 ± 2.24	6.14 ± 1.86	5.47 ± 2.26	6.08 ± 1.69	0.14^s	0.41^s	0.01	0
SM(d18:1/20:0)	19.41 ± 10.24	23.38 ± 7.14	21.42 ± 7.85	20.44 ± 6.30	0.15^s	0.22^s	0.01	0.02
SM(d18:1/22:0)	19.35 ± 8.76	25.23 ± 8.31	26.42 ± 11.42	19.69 ± 9.09	0.09	0.34^s	0	0.04
SM(d18:1/24:0)	5.27 ± 2.24	6.34 ± 2.84	6.22 ± 2.73	5.22 ± 1.85	0.20^s	0.30^s	0.02	0.07
SM(d18:1/24:1)	37.08 ± 19.18	50.65 ± 20.22	43.61 ± 21.04	38.54 ± 12.62	0.23^s	0.29^s	0.04	0.03

Data are mean ± SD. ^aGeneral Linear model with age squared, sex, *APOE* genotype, and cognitive category; ^sp < 0.05.

Supplementary Table 6. Relative sphingolipid levels in plasma LDL from non-*APOE4* carriers and *APOE4* homozygotes with SCD or MCI.

LDL	Non- <i>APOE4</i> carriers		<i>APOE4</i> homozygotes		effect size (partial eta squared) ^a			
	SCD (n=10)	MCI (n=10)	SCD (n=9)	MCI (n=10)	Age ²	Sex	<i>APOE4</i> versus non- <i>APOE4</i>	MCI versus SCD
ApoB100 (g/L)	0.54 ± 0.11	0.55 ± 0.11	0.65 ± 0.17	0.67 ± 0.13	0.30^S	0	0.23^S	0.16^S
Cholesterol (mM)*	4.29 ± 0.44	4.28 ± 0.73	4.41 ± 0.61	4.30 ± 0.48	0.02	0.15^S	0	0.01
Triglycerides (mM)*	0.42 ± 0.08	0.38 ± 0.06	0.36 ± 0.08	0.42 ± 0.11	0.16^S	0.02	0.01	0.03
S1P(d18:1) (μM)*	0.32 ± 0.15	0.46 ± 0.23	0.46 ± 0.29	0.48 ± 0.22	0.01	0.02	0.04	0.01
Ceramides (μM)*	6.77 ± 1.95	6.60 ± 1.68	5.65 ± 2.04	7.38 ± 2.20	0.03	0.13^S	0.01	0.01
Cer(d18:1/14:0)*	0.06 ± 0.02	0.05 ± 0.02	0.05 ± 0.02	0.06 ± 0.02	0.03	0.01	0	0.01
Cer(d18:1/16:0)*	0.33 ± 0.09	0.31 ± 0.06	0.27 ± 0.08	0.31 ± 0.07	0.05	0.02	0.04	0
Cer(d18:1/18:0)*	0.18 ± 0.05	0.20 ± 0.05	0.17 ± 0.05	0.26 ± 0.11	0.09	0.01	0.03	0.02
Cer(d18:1/20:0)*	0.18 ± 0.05	0.17 ± 0.04	0.16 ± 0.05	0.22 ± 0.07	0.14^S	0.02	0.02 [#]	0 [#]
Cer(d18:1/22:0)*	1.40 ± 0.30	1.41 ± 0.47	1.28 ± 0.54	1.76 ± 0.49	0.03	0.19^S	0.01	0.03
Cer(d18:1/24:0)*	3.62 ± 1.33	3.36 ± 1.02	2.81 ± 1.13	3.53 ± 1.33	0	0.09	0.03	0
Cer(d18:1/24:1)*	1.00 ± 0.36	1.10 ± 0.29	0.92 ± 0.34	1.24 ± 0.45	0.08	0.14^S	0	0.01
Sphingomyelins (μM)*	421.68 ± 125.24	450.58 ± 118.20	433.92 ± 211.65	454.86 ± 116.21	0.07	0.10	0	0
SM(d18:1/16:0)*	128.03 ± 35.64	146.00 ± 27.74	127.59 ± 64.47	143.01 ± 37.50	0.06	0.08	0.01	0
SM(d18:1/18:0)*	23.73 ± 7.82	28.15 ± 6.09	24.82 ± 8.27	29.13 ± 7.29	0.07	0.07	0	0.01
SM(d18:1/18:1)*	10.30 ± 3.45	11.56 ± 4.58	11.08 ± 4.36	12.69 ± 3.13	0.06	0.16^S	0.01	0
SM(d18:1/20:0)*	40.63 ± 12.03	44.08 ± 10.60	42.61 ± 13.15	46.90 ± 10.28	0.12^S	0.11	0	0
SM(d18:1/22:0)*	66.45 ± 20.61	69.90 ± 22.00	74.76 ± 33.79	71.26 ± 17.38	0.01	0.13^S	0	0
SM(d18:1/24:0)*	20.94 ± 6.33	21.77 ± 11.62	26.18 ± 15.84	24.43 ± 7.65	0.02	0.09	0.02	0.01
SM(d18:1/24:1)*	107.28 ± 34.64	129.11 ± 45.20	126.87 ± 74.50	127.44 ± 45.98	0.08	0.07	0	0

Data are mean ± SD. ^aGeneral Linear model with age squared, sex, *APOE* genotype, and cognitive category; ^Sp < 0.05; [#]significant interaction between *APOE* genotype and cognitive category (p<0.05). *Normalized to ApoB100 (g/L).

Supplementary Table 7. Sphingolipid levels in plasma VLDL from non-*APOE4* carriers and *APOE4* homozygotes with SCD or MCI.

VLDL	Non- <i>APOE4</i> carriers		<i>APOE4</i> homozygotes		effect size (partial eta squared) ^a			
	SCD (n=10)	MCI (n=10)	SCD (n=9)	MCI (n=10)	Age ²	Sex	<i>APOE4</i> versus non- <i>APOE4</i>	MCI versus SCD
ApoB100 (g/L)	0.05 ± 0.02	0.05 ± 0.02	0.06 ± 0.03	0.06 ± 0.02	0.06	0.06	0.01	0.03
Cholesterol (mM)*	6.21 ± 1.51	4.58 ± 1.89	7.45 ± 2.01	5.82 ± 1.63	0.01	0	0.11	0.13 ^s
Triglycerides (mM)*	10.91 ± 5.70	6.25 ± 3.03	9.54 ± 3.82	9.83 ± 4.42	0.01	0.03	0.03	0.05
S1P(d18:1) (μM)*	0.52 ± 0.57	0.32 ± 0.24	0.54 ± 0.67	0.36 ± 0.20	0	0.07	0.01	0.04
Ceramides (μM)*	16.61 ± 9.49	12.69 ± 3.30	14.81 ± 5.33	18.62 ± 6.24	0.02	0.01	0.08	0.01
Cer(d18:1/14:0)*	0.14 ± 0.08	0.13 ± 0.05	0.15 ± 0.07	0.15 ± 0.05	0	0.04	0.02	0.01
Cer(d18:1/16:0)*	0.63 ± 0.22	0.55 ± 0.13	0.58 ± 0.20	0.77 ± 0.33	0	0.06	0.03	0
Cer(d18:1/18:0)*	0.41 ± 0.15	0.48 ± 0.20	0.46 ± 0.19	0.57 ± 0.26	0	0.12	0.04	0.04
Cer(d18:1/20:0)*	0.47 ± 0.21	0.42 ± 0.19	0.51 ± 0.24	0.63 ± 0.24	0.01	0.01	0.08	0
Cer(d18:1/22:0)*	3.47 ± 1.74	2.86 ± 0.95	3.56 ± 1.30	4.53 ± 1.71	0.04	0	0.07	0.02
Cer(d18:1/24:0)*	6.62 ± 2.13	5.64 ± 1.47	6.64 ± 2.79	7.54 ± 2.17	0.03	0.02	0.05	0.01
Cer(d18:1/24:1)*	2.21 ± 0.69	2.61 ± 1.28	2.92 ± 2.02	2.97 ± 0.85	0	0	0.04	0
Sphingomyelins (μM)*	533.18 ± 183.82	462.95 ± 131.66	611.37 ± 177.23	588.59 ± 271.26	0.01	0.01	0.05	0.02
SM(d18:1/16:0)*	136.20 ± 55.14	143.98 ± 38.55	183.17 ± 76.84	146.75 ± 63.67	0	0.04	0.06	0.01
SM(d18:1/18:0)*	33.15 ± 12.45	31.23 ± 11.22	36.34 ± 8.22	34.71 ± 8.82	0	0	0.03	0
SM(d18:1/18:1)*	16.45 ± 6.73	13.86 ± 4.62	17.45 ± 5.43	17.55 ± 5.11	0	0.02	0.04	0.01
SM(d18:1/20:0)*	78.20 ± 39.25	62.93 ± 19.99	77.63 ± 25.61	71.29 ± 13.64	0.03	0.01	0.01	0.01
SM(d18:1/22:0)*	93.92 ± 45.52	71.61 ± 29.03	101.85 ± 23.15	79.83 ± 24.52	0.09	0	0.02	0.02
SM(d18:1/24:0)*	28.05 ± 16.77	18.44 ± 7.78	28.58 ± 10.47	23.78 ± 9.13	0.04	0	0.02	0.03
SM(d18:1/24:1)*	146.10 ± 69.07	120.89 ± 44.32	166.34 ± 62.15	144.79 ± 71.71	0	0	0.03	0.03

Data are mean ± SD. ^aGeneral Linear model with age squared, sex, *APOE* genotype, and cognitive category. *Normalized to ApoB100 (g/L).

Supplementary Table 8. Ceramide Cer(d18:1/16:0), Cer(d18:1/18:0), and Cer(d18:1/24:1) levels relative to Cer(d18:1/24:0) in plasma, and in HDL, LDL, and VLDL in plasma from non-*APOE4* carriers and *APOE4* homozygotes with SCD or MCI.

Normalized to Cer(d18:1/24:0)		Non- <i>APOE4</i> carriers		<i>APOE4</i> homozygotes	
		SCD (n=10)	MCI (n=10)	SCD (n=9)	MCI (n=10)
Plasma	Cer(d18:1/16:0)	0.04 ± 0.02	0.04 ± 0.01	0.03 ± 0.01	0.04 ± 0.01
	Cer(d18:1/18:0)	0.03 ± 0.01	0.03 ± 0.01	0.03 ± 0.01	0.04 ± 0.02
	Cer(d18:1/24:1)	0.29 ± 0.10	0.35 ± 0.11	0.29 ± 0.04	0.35 ± 0.08
HDL	Cer(d18:1/16:0)	0.32 ± 0.07	0.33 ± 0.06	0.32 ± 0.08	0.35 ± 0.10
	Cer(d18:1/18:0)	0.20 ± 0.07	0.24 ± 0.08	0.24 ± 0.08	0.30 ± 0.12
	Cer(d18:1/24:1)	0.61 ± 0.11	0.81 ± 0.21	0.64 ± 0.13	0.75 ± 0.21
LDL	Cer(d18:1/16:0)	0.09 ± 0.03	0.09 ± 0.03	0.11 ± 0.04	0.10 ± 0.04
	Cer(d18:1/18:0)	0.06 ± 0.02	0.06 ± 0.02	0.07 ± 0.02	0.08 ± 0.04
	Cer(d18:1/24:1)	0.29 ± 0.08	0.34 ± 0.08	0.33 ± 0.07	0.37 ± 0.11
VLDL	Cer(d18:1/16:0)	0.09 ± 0.02	0.10 ± 0.02	0.09 ± 0.02	0.11 ± 0.04
	Cer(d18:1/18:0)	0.06 ± 0.02	0.09 ± 0.05	0.07 ± 0.01	0.08 ± 0.03
	Cer(d18:1/24:1)	0.34 ± 0.08	0.48 ± 0.26	0.37 ± 0.08	0.41 ± 0.09

Ratios are mean ± SD.

Supplementary Figure 1. Correlation between the level of specific sphingolipid species in CSF with CSF- $A\beta_{42}$ in participants with SCD and MCI. Data of individual participants are given. The solid and broken lines indicate linear regression lines for participants with SCD and MCI, respectively. p-values indicate that regression lines were statistically different. Interactions between CSF $A\beta_{42}$, *APOE4* genotype and cognition state were not significant ($p=0.606$, 0.768 , and 0.645 for Cer(d18:1/18:0), Cer(d18:1/24:0), and SM(d18:0/24:0), respectively). See Table 4 for further details.

