

### Table 1. Demographic, Behavioral, Genetic, and Molecular Biomarkers\*

Item	CN (n = 25)	SCD (n = 20)	EMCI (n = 24)	LMCI (n = 23)	AD (n = 21)	P Value
Age, y	74.64 ± 6.10	72.75 ± 5.73	69.96 ± 7.15	70.78 ± 6.99	71.81 ± 7.77	.147
Sex, male/female	12/13	9/11	11/13	14/9	12/9	.764**
Education, y	16.56 ± 2.22	16.65 ± 3.05	15.46 ± 2.50	16.52 ± 2.57	15.14 ± 2.76	.172
MMSE score	28.56 ± 1.33 <sup>a</sup>	29.15 ± 0.93 <sup>b,c,d</sup>	27.88 ± 2.12 <sup>e</sup>	27.83 ± 1.59 <sup>f</sup>	22.67 ± 2.50	< .001
ADAS-cog score	9.44 ± 3.43 <sup>a,g,h</sup>	8.65 ± 3.50 <sup>b,c,d</sup>	13.17 ± 5.68 <sup>e,i</sup>	16.87 ± 5.29 <sup>f</sup>	35.81 ± 8.99	< .001
Multiple protective genes, yes/no, n						
<i>CLU</i> rs11136000 T (TC + TT/CC)	17/8	16/4	16/8	15/8	13/8	.775**
<i>LDLR</i> rs5930 A (AG + AA/GG)	19/6	14/6	15/9	13/10	11/10	.452**
<i>LRP1</i> rs1799986 T (TC + TT/CC)	8/17	5/15	8/16	3/20	10/11	.152**
<i>PICALM</i> rs3851179 A (AG + AA/GG)	14/11	11/9	15/9	13/10	11/10	.972**
Multiple risk genes, yes/no, n						
<i>APOE</i> ε4 (±)	7/18	5/15	14/10	10/13	15/6	.008**
<i>SORL1</i> rs2070045 G (TG + GG/TT)	9/16	8/12	11/13	10/13	6/15	.785**
<i>CETP</i> rs5882 A (AG + AA/GG)	21/4	19/1	23/1	20/3	19/2	.631**
<i>ABCA1</i> rs2230808 G (AG + GG/AA)	21/4	19/1	23/1	19/4	19/2	.491**
<i>BIN1</i> rs744373 C (TC + CC/TT)	10/15	13/7	15/9	14/9	11/10	.407**
Cerebrospinal fluid metabolites, pg/mL						
Aβ	180.46 ± 48.60 <sup>a,j</sup>	211.25 ± 50.10 <sup>b,c,d</sup>	177.50 ± 47.77 <sup>e</sup>	167.60 ± 53.17	140.40 ± 43.59	< .001
Total tau	72.92 ± 38.50 <sup>a</sup>	67.33 ± 23.02 <sup>d</sup>	81.00 ± 53.68 <sup>e</sup>	85.17 ± 50.23 <sup>f</sup>	129.29 ± 61.42	< .001
p-tau	36.91 ± 19.13 <sup>a</sup>	31.32 ± 9.31 <sup>d</sup>	41.10 ± 25.19 <sup>e</sup>	44.48 ± 24.38	55.23 ± 26.13	.01
Serum lipid metabolites, mmol/L						
Medium VLDL particles	0.93 ± 0.39	0.93 ± 0.47	1.03 ± 0.47	1.04 ± 0.48	0.97 ± 0.40	.860
Small VLDL particles	1.05 ± 0.30	1.11 ± 0.37	1.18 ± 0.41	1.14 ± 0.35	1.12 ± 0.34	.783
Very small VLDL particles	0.96 ± 0.20	1.10 ± 0.22	1.02 ± 0.26	0.98 ± 0.21	1.01 ± 0.24	.346
IDL particles	2.13 ± 0.53	2.47 ± 0.51	2.25 ± 0.64	2.16 ± 0.53	2.24 ± 0.62	.350
Large LDL particles	2.53 ± 0.65	2.91 ± 0.63	2.70 ± 0.80	2.57 ± 0.65	2.66 ± 0.70	.417
Medium LDL particles	1.46 ± 0.39	1.66 ± 0.38	1.58 ± 0.49	1.49 ± 0.40	1.53 ± 0.39	.493
Small LDL particles	0.95 ± 0.24	1.07 ± 0.24	1.03 ± 0.30	0.96 ± 0.24	0.99 ± 0.24	.491
Large HDL particles	2.07 ± 0.68	2.03 ± 0.69	1.83 ± 0.79	1.85 ± 0.99	1.89 ± 0.72	.759
Medium HDL particles	2.27 ± 0.35	2.22 ± 0.33	2.26 ± 0.50	2.22 ± 0.47	2.15 ± 0.28	.886
Small HDL particles	2.62 ± 0.24	2.60 ± 0.20	2.72 ± 0.22	2.66 ± 0.20	2.61 ± 0.21	.352
Serum total cholesterol	3.65 ± 0.73	4.01 ± 0.68	3.79 ± 0.80	3.64 ± 0.72	3.72 ± 0.83	.497
Total cholesterol in VLDL	0.46 ± 0.14	0.53 ± 0.18	0.52 ± 0.20	0.51 ± 0.17	0.50 ± 0.17	.734
Remnant cholesterol (non-HDL, non-LDL cholesterol)	0.95 ± 0.25	1.11 ± 0.27	1.04 ± 0.34	1.01 ± 0.28	1.02 ± 0.30	.511
Total cholesterol in LDL	1.19 ± 0.35	1.38 ± 0.34	1.29 ± 0.43	1.21 ± 0.35	1.26 ± 0.36	.436
Total cholesterol in HDL	1.50 ± 0.25	1.52 ± 0.29	1.45 ± 0.35	1.43 ± 0.38	1.44 ± 0.28	.847
Total cholesterol in HDL <sub>2</sub>	1.03 ± 0.23	1.04 ± 0.27	0.98 ± 0.33	0.96 ± 0.35	0.97 ± 0.25	.839
Total cholesterol in HDL <sub>3</sub>	0.47 ± 0.02	0.48 ± 0.02	0.47 ± 0.03	0.47 ± 0.03	0.47 ± 0.02	.738
Esterified cholesterol	2.55 ± 0.53	2.82 ± 0.50	2.66 ± 0.58	2.55 ± 0.52	2.60 ± 0.59	.474
Free cholesterol	1.10 ± 0.20	1.19 ± 0.19	1.13 ± 0.22	1.09 ± 0.20	1.12 ± 0.24	.559
Serum total triglycerides	1.03 ± 0.35	1.01 ± 0.37	1.08 ± 0.37	1.10 ± 0.37	1.05 ± 0.33	.916
Triglycerides in VLDL	0.66 ± 0.28	0.63 ± 0.31	0.71 ± 0.30	0.73 ± 0.32	0.67 ± 0.27	.822
Triglycerides in LDL	0.15 ± 0.04	0.16 ± 0.03	0.15 ± 0.03	0.15 ± 0.03	0.15 ± 0.04	.948
Triglycerides in HDL	0.12 ± 0.03	0.12 ± 0.02	0.12 ± 0.03	0.12 ± 0.03	0.12 ± 0.03	.964
Total phosphoglycerides	1.72 ± 0.30	1.80 ± 0.27	1.73 ± 0.29	1.68 ± 0.31	1.70 ± 0.30	.748
Phosphatidylcholine and other cholines	1.65 ± 0.28	1.75 ± 0.26	1.66 ± 0.27	1.62 ± 0.29	1.64 ± 0.29	.635
Sphingomyelins	0.37 ± 0.05	0.39 ± 0.06	0.37 ± 0.07	0.36 ± 0.07	0.36 ± 0.07	.627
Total cholines	2.06 ± 0.30	2.16 ± 0.28	2.05 ± 0.30	2.00 ± 0.31	2.04 ± 0.33	.563
Total fatty acids	9.73 ± 1.85	10.30 ± 1.78	10.13 ± 1.83	9.87 ± 1.90	9.90 ± 1.92	.856
Docosahexaenoic acid	0.12 ± 0.04	0.13 ± 0.04	0.12 ± 0.03	0.12 ± 0.04	0.12 ± 0.04	.996
Linoleic acid	2.68 ± 0.46	2.85 ± 0.45	2.85 ± 0.48	2.73 ± 0.44	2.74 ± 0.59	.692
Omega-3 fatty acids	0.39 ± 0.14	0.40 ± 0.12	0.41 ± 0.10	0.40 ± 0.13	0.40 ± 0.13	.995
Omega-6 fatty acids	3.26 ± 0.53	3.48 ± 0.51	3.44 ± 0.54	0.30 ± 0.52	3.34 ± 0.64	.653
Polyunsaturated fatty acids	3.66 ± 0.64	3.88 ± 0.61	3.84 ± 0.62	3.70 ± 0.64	3.74 ± 0.75	.743
Monounsaturated fatty acids	2.56 ± 0.58	2.66 ± 0.58	2.69 ± 0.61	2.63 ± 0.62	2.60 ± 0.57	.946
Saturated fatty acids	3.51 ± 0.69	3.75 ± 0.64	3.59 ± 0.67	3.54 ± 0.69	3.56 ± 0.66	.796

\*Unless indicated, data are presented as mean  $\pm$  SD. Post hoc analyses were used with least significant difference (LSD) correction ( $P < .05$ ).  $P$  values obtained using the  $\chi^2$  test are indicated by a double asterisk (\*\*); other  $P$  values were obtained by 1-way ANOVA, but if the variance homogeneity test  $P < .05$ , the  $P$  value was acquired by Kruskal-Wallis test.

<sup>a</sup>Statistically significant difference was detected between CN group and AD group. <sup>b</sup>Statistically significant difference was detected between SCD group and EMCI group. <sup>c</sup>Statistically significant difference was detected between SCD group and LMCI group. <sup>d</sup>Statistically significant difference was detected between SCD group and AD group. <sup>e</sup>Statistically significant difference was detected between EMCI group and AD group. <sup>f</sup>Statistically significant difference was detected between LMCI group and AD group. <sup>g</sup>Statistically significant difference was detected between CN group and EMCI group. <sup>h</sup>Statistically significant difference was detected between CN group and LMCI group. <sup>i</sup>Statistically significant difference was detected between EMCI group and LMCI group. <sup>j</sup>Statistically significant difference was detected between CN group and SCD group.

Abbreviations: A $\beta$ =amyloid  $\beta$  peptides 1 to 42, *ABCA1*=ATP-binding cassette transporter A1, AD=Alzheimer's disease, ADAS-cog=Alzheimer's Disease Assessment Scale-13-item cognitive subscale, ANOVA=analysis of variance, *APOE*=apolipoprotein E, *BIN1*=bridging integrator 1, *CETP*=cholesterol ester transfer protein, *CLU*=clusterin, CN=cognitively normal, EMCI=early mild cognitive impairment, HDL=high-density lipoprotein (HDL<sub>2</sub> and HDL<sub>3</sub> indicate HDL subfractions), IDL=intermediate-density lipoprotein, LDL=low-density lipoprotein, *LDLR*=low density lipoprotein receptor, LMCI=late mild cognitive impairment, *LRP1*=low density lipoprotein receptor-related protein 1, MMSE=Mini-Mental State Examination, *PICALM*=phosphatidylinositol-binding clathrin assembly protein, p-tau=tau phosphorylated at the threonine 181 position, SCD=subjective cognitive decline, *SORL1*=sortilin-related receptor 1, VLDL=very low density lipoprotein.