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Supplementary Material

Article Title: Polygenic Effects of the Lipid Metabolic Pathway Accelerated Pathological Changes and Disrupted Default Mode Network Trajectory Across the Alzheimer's Disease Spectrum

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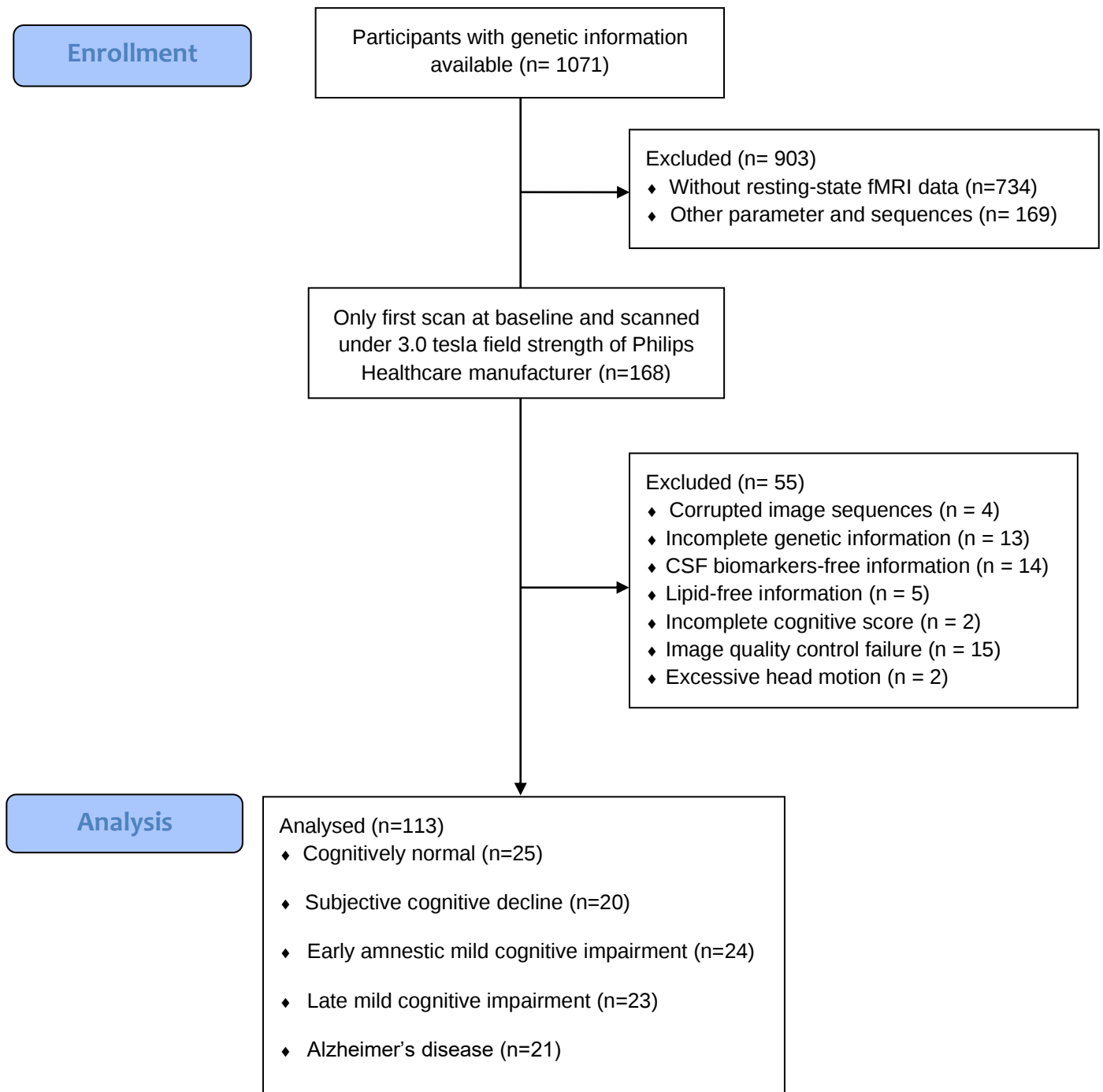
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Supplementary Figure 1. Participant flow



Supplementary Table 1. Summary information of lipid metabolic pathway related multiple genes.

SNP	Chr.	Position	Closest gene	Allele change	GMAF	OR	HWE		Function
							X ²	p	
rs11136000	8	27607002	CLU	T>C	0.3848	0.86	0.974	0.324	CLU is related to cholesterol reverse transporting. ¹
rs5930	19	11113589	LDLR	A>G	0.3450	0.85	0.071	0.791	Elevated level of LDLR in the brain promotes extracellular Aβ clearance. ²
rs1799986	12	57141483	LRP1	C>T	0.1047	0.92	0.293	0.588	Blood brain barrier-associated pericytes internalize and clear aggregated Aβ through LRP1-dependent APOE subtype-specific mechanism. ³
rs3851179	11	86157598	PICALM	T>C	0.3297	0.85	1.440	0.230	PICALM participates in receptor-mediated endocytosis as lipid internalization and transport mediated by lipoprotein particles containing APOE and CLU. ⁴
rs2070045	11	121577381	SORL1	T>G	0.3214	1.13	0.381	0.537	SORL1 can bind lipoprotein particles containing APOE and mediate their endocytosis. ⁵
rs5882	16	56982180	CETP	G>A	0.4481	1.11	0.043	0.836	CETP mediates the transfer of cholesterol esters from HDL to VLDL, thus promoting the balanced exchange of triglycerides and regulating HDL levels. ⁶
rs2230808	9	104800523	ABCA1	T>C	0.4109	1.10	0.870	0.351	ABCA1 regulates APOE levels, lipidation, and APOE-mediated cholesterol transfer from glial cells to neurons. ⁷
rs744373	2	127137039	BIN1	A>G	0.3714	1.17	0.227	0.634	BIN1 is also associated with receptor-mediated endocytosis. ⁸
rs429358	19	45411941	APOE	-	-	-	1.391	0.238	APOE is a major cholesterol carrier and APOE isoforms differentially regulate Aβ aggregation and clearance in the brain. ⁹
rs7412		45412079		-	-	-			

Abbreviations: Chr. = chromosome; GMAF = global minor allele frequency reported from 1000Genome genotype data; HWE = Hardy-Weinberg equilibrium; OR = odds ratio for the minor allele; SNP = single nucleotide polymorphism.

Supplementary References

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