table e-1. A. Linkage disequilibrium (LD) between *FTO* variants.

LD	*FTO* dbSNP ID	rs1421085 (1)	rs17817449 (2)	rs8050136 (3)	rs9939609 (4)	--
r^2, White						
	rs1421085	x	0.948	0.943	0.941	
	rs17817449	0.948	x	0.992	0.989	
	rs8050136	0.943	0.992	x	0.993	
	rs9939609	0.941	0.989	0.993	x	
r^2, African-American						
	rs1421085	x	0.166	0.137	0.112	
	rs17817449	0.166	x	0.832	0.689	
	rs8050136	0.137	0.832	x	0.827	
	rs9939609	0.112	0.689	0.827	x	

B. Haplotype association analysis for *FTO* variants and 6-year change in scores on three neuropsychological tests.

Haplotypes (Freq.) White	DWRT (Beta)	p	DSST (Beta)	p	WFT (Beta)	p
4-marker (1-2-3-4)						
TTCT (0.584)	0.075	0.002	0.113	0.261	0.077	0.536
CGAA (0.401)	-0.073	0.002	-0.091	0.371	-0.105	0.403
3-marker (1-2-3)						
TTC (0.584)	0.075	0.002	0.114	0.256	0.083	0.507
CGA (0.402)	-0.074	0.002	-0.091	0.369	-0.101	0.421
3-marker (2-3-4)						
TCT (0.593)	0.068	0.004	0.092	0.365	0.064	0.607
GAA (0.404)	-0.070	0.003	-0.081	0.422	-0.070	0.578
2-marker (1-2)						
TT (0.584)	0.074	0.002	0.113	0.266	0.072	0.569
CG (0.404)	-0.072	0.003	-0.105	0.304	-0.098	0.435
2-marker (2-3)						
TC (0.593)	0.069	0.004	0.112	0.270	0.063	0.616
GA (0.405)	-0.072	0.003	-0.096	0.349	-0.056	0.658
2-marker (3-4)						
CT (0.595)	0.067	0.005	0.120	0.237	0.059	0.639
AA (0.404)	-0.066	0.006	-0.120	0.237	-0.068	0.591
Haplotypes (Freq.) AA	DWRT (β)	p	DSST (β)	p	WFT (β)	p
4-marker (1-2-3-4)						
TTCT (0.522)	-0.070	0.187	0.404	0.135	0.283	0.267
TGAA (0.276)	0.056	0.347	-0.270	0.371	-0.086	0.763
CGAA (0.103)	0.099	0.270	-0.370	0.415	0.044	0.918
TTCA (0.048)	-0.037	0.775	-0.837	0.203	-0.314	0.612
TTAA (0.044)	-0.036	0.787	0.001	0.999	-0.767	0.226
3-marker (1-2-3)						
TTC (0.570)	-0.081	0.133	0.280	0.305	0.230	0.373
TGA (0.277)	0.046	0.437	-0.196	0.515	-0.122	0.668
CGA (0.103)	0.111	0.214	-0.389	0.389	0.018	0.967
TTA (0.045)	-0.020	0.879	-0.020	0.976	-0.727	0.248
3-marker (2-3-4)						
TCT (0.525)	-0.066	0.211	0.422	0.114	0.258	0.307
GAA (0.379)	0.080	0.140	-0.375	0.174	-0.052	0.844
TCA (0.048)	-0.039	0.765	-0.858	0.191	-0.269	0.665
TAA (0.044)	-0.007	0.959	0.078	0.906	-0.673	0.284
2-marker (1-2)						
TT (0.614)	-0.089	0.109	0.294	0.296	0.135	0.610
TG (0.278)	0.055	0.363	-0.195	0.521	-0.142	0.622
CG (0.104)	0.102	0.261	-0.416	0.363	-0.033	0.939
2-marker (2-3)						
TC (0.573)	-0.093	0.089	0.290	0.296	0.166	0.524
GA (0.382)	0.093	0.095	-0.305	0.281	-0.032	0.903
TA (0.045)	0.006	0.966	0.031	0.963	-0.700	0.263
2-marker (3-4)						
CT (0.525)	-0.061	0.255	0.430	0.115	0.204	0.426
AA (0.424)	0.070	0.200	-0.323	0.243	-0.117	0.654
CA (0.048)	-0.036	0.782	-0.992	0.134	-0.305	0.623

LD was estimated using the computer program Haploview version 4.2, and haplotype association analysis was performed using a sliding window approach with PLINK software.(1, 2) Phased haplotype frequencies were inferred from genotyping data using an expectation-maximization (EM) algorithm. The SNPs in each haplotype are indicated by the number assigned to each marker at the top of the table. SNP, single nucleotide polymorphism, Freq., frequency; AA, African-American; β, beta coefficient; p, p-value adjusted for age, gender, and education; References: 1. Barrett JC, Fry B, Maller J, Daly MJ. Haploview: analysis and visualization of LD and haplotype maps. Bioinformatics 2005;21:263-265; 2. Purcell S, Neale B, Todd-Brown K, et al. PLINK: a tool set for whole-genome association and population-based linkage analyses. Am J Hum Genet 2007;81:559-575.

table e-2. MRI Measurements of Brain Volume and *FTO* genotype. ARIC study (2004 – 2006)								
	rs9939609				rs17817449			
White	N	B	SE	p	N	B	SE	p
Brain Vol. (cm^3)	470	-0.82	3.05	0.79	467	-0.63	3.04	0.84
Hippocampal Vol. (log,)	457	0.00	0.01	0.72	454	0.00	0.01	0.75
Total Intracranial Vol. (cm^3)	471	-0.40	7.36	0.96	468	1.80	7.31	0.81
AA								
Brain Vol. (cm^3)	475	-4.42	3.34	0.19	474	-2.88	3.44	0.40
Hippocampal Vol. (log,)	467	-0.00	0.01	1.00	469	0.01	0.01	0.40
Total Intracranial Vol. (cm^3)	487	-1.78	6.53	0.78	486	0.54	6.80	0.94
	rs8050136				rs1421085			
White	N	B	SE	p	N	B	SE	p
Brain Vol. (cm^3)	464	-0.70	3.01	0.82	464	-0.64	3.06	0.83
Hippocampal Vol. (log,)	451	0.00	0.01	0.63	451	0.00	0.01	0.62
Total Intracranial Vol. (cm^3)	465	0.91	7.35	0.90	465	-0.11	7.35	0.99
AA								
Brain Vol. (cm^3)	481	-3.32	3.36	0.32	479	4.65	5.70	0.42
Hippocampal Vol. (log,)	475	-0.00	0.01	0.88	473	0.01	0.01	0.38
Total Intracranial Vol. (cm^3)	494	-2.35	6.60	0.72	491	10.51	11.12	0.34

At the third clinical examination (1993-1995), 1,920 participants aged 55 years and older from two of the ARIC study field centers (Forsyth County, NC and Jackson, MS) were invited to undergo cranial MRI. In 2004-2006, 1,134 participants completed a second brain MRI examination and measurements of brain volume, hippocampal volume, and total intracranial volume were performed. (1) General linear models were used to analyze the association between three measures of brain volume and *FTO* genotype under an additive genetic model after adjusting for age, sex, and total intracranial volume (brain volume and hippocampal volume), or age and sex (total intracranial volume). N, number; β, beta coefficient; SE, standard error; rs, reference SNP; Vol., volume; log, natural log-transformed hippocampal volume; p, p-value; References: 1. Knopman DS, Penman AD, Catellier DJ et al. Vascular risk factors and longitudinal changes on brain MRI: the ARIC study. Neurology 2011;76:1879-1885

table e-3. Proportion of variance in cognitive change explained by *FTO* variants detectable at 80% power		
FTO dbSNP ID	Cognitive Change Assessed by Neuropsychological Tests	
	R^2 (AA) N = 2,083	R^2 White N = 8,364
rs9939609	0.008	0.002
rs8050136	0.008	0.002
rs17817449	0.008	0.002
rs1421085	0.008	0.002

Power analyses were performed with the program Quanto (http://hydra.usc.edu/GxE/) using a fixed sample size for white and African-American study participants, cognitive change calculated as the difference between the scores on each neuropsychological test (Delayed Word Recall Test, Digit Symbol Substitution Test, Word Fluency Test) at the second administration and the first administration and modeled as a continuous variable, a p-value of 0.002, and the allele frequencies in the study sample. SNP, single nucleotide polymorphism; dbSNP, The National Center for Biotechnology Information's SNP database (http://www.ncbi.nlm.nih.gov/SNP); ID, identification; rs, reference SNP; AA, African-American; N, number