

Supplementary Table 1. Demographic characteristics of FTO genotype groups (*rs1421085* SNP) in BMI, impulsivity, and dietary analyses in the BLSA

	BMI analysis		P value	Impulsivity analysis		P value	Dietary analysis		P value
	FTO+ (N = 471)	FTO- (N = 226)		FTO + (N= 468)	FTO - (N= 224)		FTO + (N= 373)	FTO - (N= 185)	
Age at baseline, years	45.8 (17.3)	45.6 (15.7)	0.848	55.3 (16.2)	54.8 (15.1)	0.751	52.8 (17.1)	52.2 (16.1)	0.710
Female, n(%)	216 (45.8)	109 (48.2)	0.557	215 (45.9)	109 (48.7)	0.502	173 (46.4)	85 (45.9)	0.923
Education, years	16.6 (2.3)	16.7 (2.1)	0.969	16.7 (2.3)	16.7 (2.1)	0.991	16.7 (2.3)	16.8 (2.0)	0.544
Mean follow-up visits	10.3 (6.0)	10.8 (6.1)	0.338	4.1 (2.6)	4.5 (2.6)	0.072	3.0 (2.0)	3.1 (1.9)	0.879
Mean follow-up years, mean (SD)	22.8 (12.1)	23.8 (11.8)	0.278	9.7 (5.9)	10.7 (5.7)	0.040	11.1 (11.1)	12.3 (11.6)	0.207

Supplementary Table 2. Demographic characteristics of *FTO* genotype groups (*rs1421085* SNP) in the ¹⁵[O] water PET study.

	Whole sample (N=69)	FTO + (N= 41)	FTO - (N= 28)	P value
Sex (female), N (%)	26 (37.7)	14 (34.2)	12 (42.9)	0.46
Age at first PET scan, years, mean(SD)	69.0 (7.3)	69.5 (7.2)	68.3 (7.5)	0.50
Hypertension, N(%)	35 (50.7)	21 (51.2)	13 (50)	0.92
Diabetes, N(%)	8 (11.6)	3 (7.3)	5 (17.9)	0.18
Current/former smoker, N(%)	44 (63.7)	28 (68.3)	16 (57.1)	0.55
Hypercholesterolemia, N (%)	10 (14.5)	5 (12.2)	5 (17.9)	0.51
History of angina, N(%)	16 (23.2)	8 (19.5)	8 (28.6)	0.38
History of MI	9 (13.4)	5 (12.2)	4 (14.3)	0.80
History of TIA	4 (5.8)	3 (7.3)	1 (3.6)	0.51
Mean BMI during PET scans, kg/m ² , mean(SD)	27.4 (3.8)	27.3 (3.6)	27.5 (4.2)	0.84
BMI at age 50, kg/m ² , mean(SD)	25.2 (3.5)	24.5 (2.8)	26.1 (4.1)	0.066

Supplementary Table 3. Local maxima of regions showing greater longitudinal decreases and increases in rCBF in the *FTO+* (*rs1421085* SNP) group

Region	Side	Coordinates			T value	P value	Number of voxels
		x	y	z			
Decreases in rCBF							
Anterior cingulate gyrus (32)	L	-12	46	14	3.54	<0.001	116
Medial orbitofrontal gyrus (11)	R	10	34	-12	3.32	<0.001	260
Anterior cingulate gyrus (24)	R	2	30	4	3.28	0.001	
Inferior parietal gyrus(40)	R	42	-60	42	3.12	0.001	56
Superior temporal gyrus (21)	R	64	-16	2	3.58	<0.001	96
Parahippocampal gyrus(35)	L	-22	-24	-16	3.21	0.001	117
Occipital/peristriate (19)	R	28	-84	24	3.38	0.001	87
Cerebellum	L	-34	-94	-20	4.59	<0.001	375
Cerebellum	R	8	-44	-24	3.22	0.001	108
Increases in rCBF							
Inferior frontal gyrus (45)	L	-32	36	2	3.30	0.001	69
Middle temporal gyrus (21)	L	-58	-50	0	4.07	<0.001	331
Cuneus (18)	R	10	-72	24	3.36	<0.001	87
Brainstem	R	6	-24	-14	3.26	0.001	81

Supplementary Table 4. Longitudinal change of (A) impulsivity-related traits (N=692) and (B) food intake (N=558) for number of obesity-related risk C alleles of *FTO* (*rs1421085*)

(A)

	TT slope (SE) [†]	TC slope (SE)	CC slope (SE)	Differences in slopes	p-value	Effect size
Impulsivity (N5)*	-0.07 (0.07)	-0.06 (0.07)	-0.05 (0.08)	0.007 (0.03)	0.809	0.23
Excitement-seeking (E5)	-0.19 (0.07)	-0.13 (0.06)	-0.07 (0.07)	0.06 (0.03)	0.027	2.0
Self-Discipline (C5)	-0.09 (0.08)	-0.10 (0.07)	-0.11 (0.08)	-0.01 (0.03)	0.740	0.33
Deliberation (C6)	0.08 (0.07)	0.07 (0.07)	0.06 (0.07)	-0.007 (0.03)	0.808	0.23

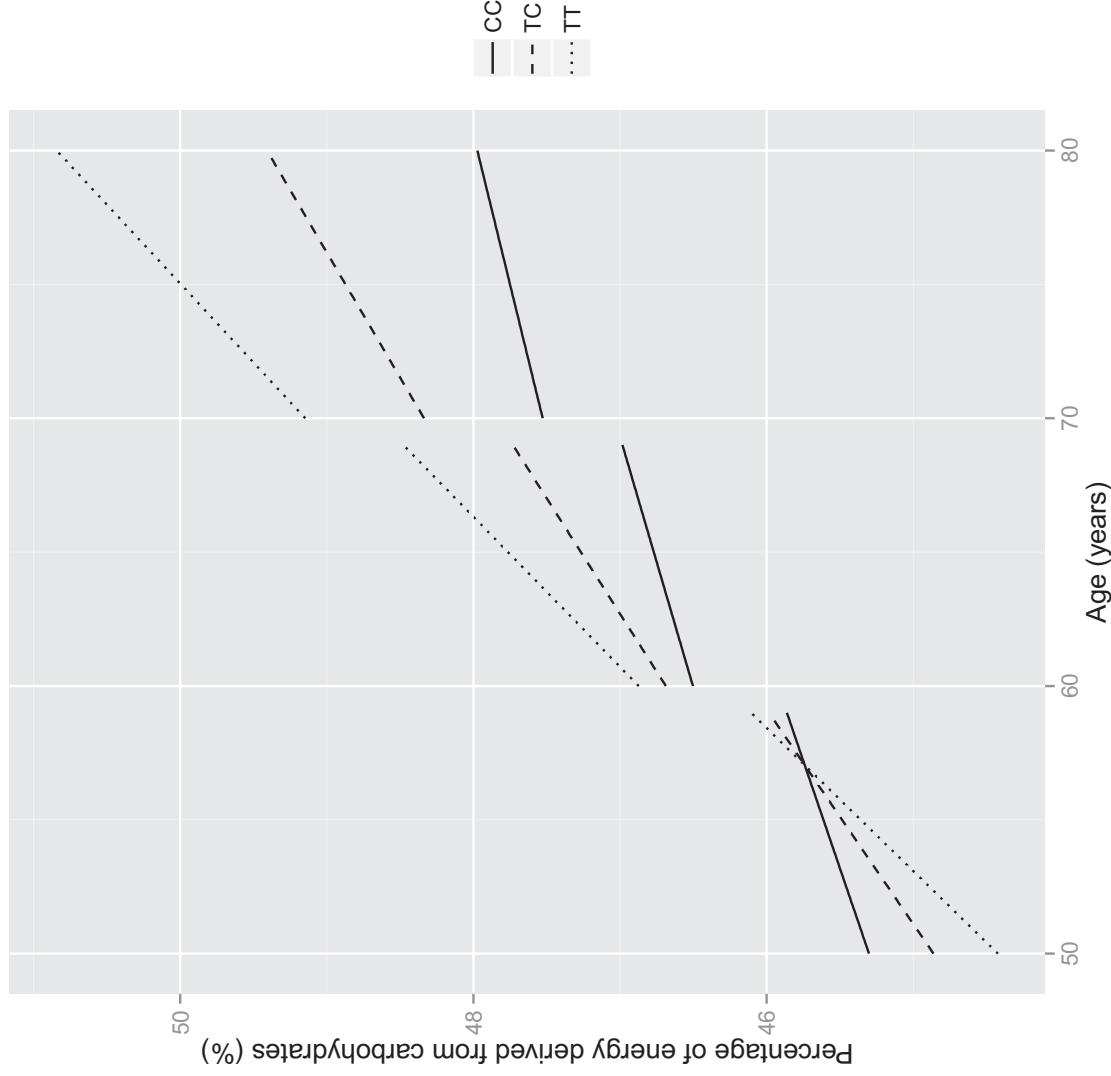
(B)

	TT slope (SE) [†]	TC slope (SE)	CC slope (SE)	Differences in slopes	p-value	Effect size
Fat intake (%)§	-0.14 (0.04)	-0.08 (0.03)	-0.02 (0.04)	0.06 (0.03)	0.016	2.0
Carbohydrate intake (%)	0.18 (0.05)	0.12 (0.04)	0.06 (0.05)	-0.06 (0.03)	0.06	2.0
Protein intake (%)	-0.002 (0.01)	-0.004 (0.01)	-0.006 (0.02)	-0.002 (0.01)	0.848	0.2

* All impulsivity-related traits were standardized T score. All models were adjusted for baseline age (centered at 60), sex, baseline age×time, sex×time, years of education (centered at 16 years)

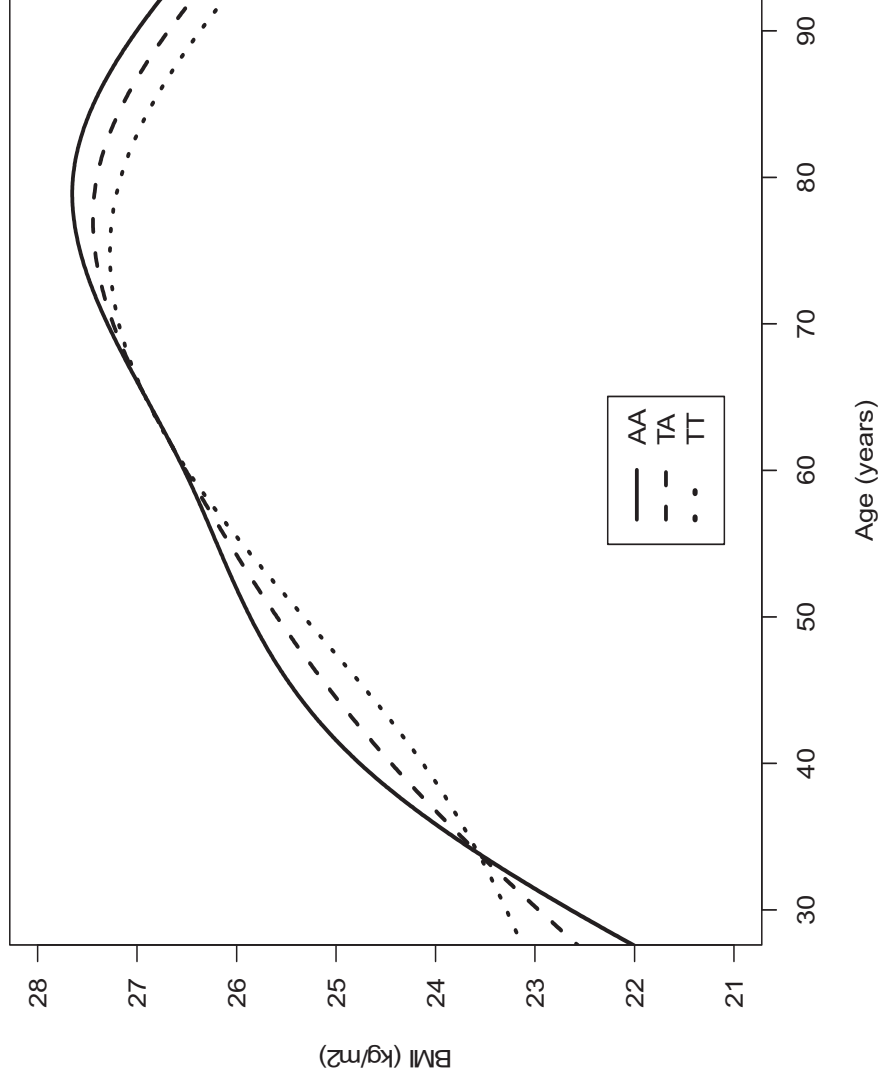
[†] SE: standard error

§ Macronutrient intakes were calculated as the percentages of energy derived from macronutrient intakes. All models were adjusted for baseline age (centered at 60), sex, baseline age×time, sex×time and year of baseline visit (centered at year 1980)



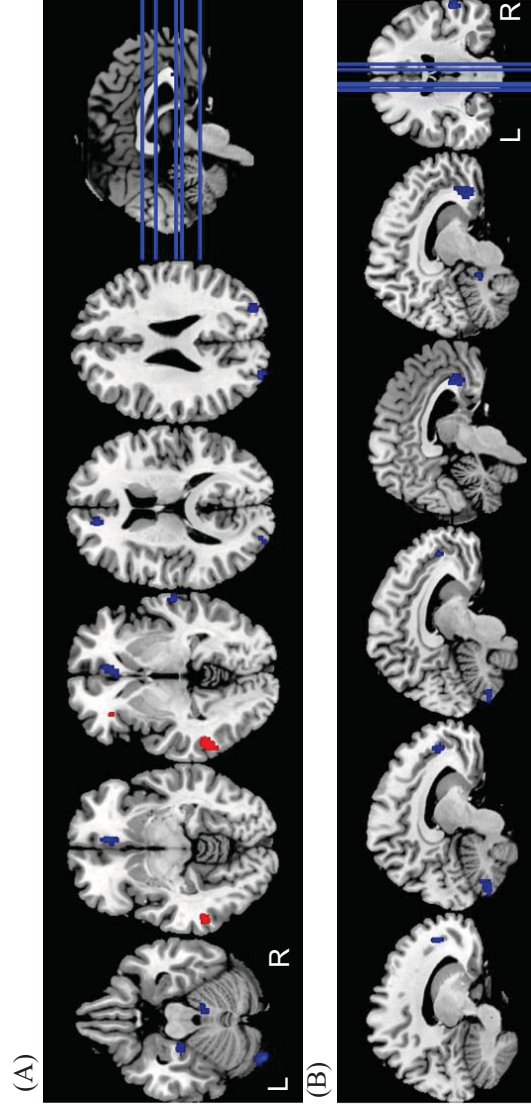
Supplementary Fig. 1

The effect of *FTO* genotype (rs1421085 single nucleotide polymorphism; obesity-risk allele-C) on carbohydrate intake during aging from the mixed-effects models. The trajectories were presented at 3 different baseline age periods: 50-60, 60-70, 70-80 years of age. In general, carbohydrate intake increased as age increased. The presence of obesity risk alleles was associated with less increase in carbohydrate intake over time.



Supplementary Fig. 2

The effect of *FTO* genotype (*rs9939609* single nucleotide polymorphism; obesity-risk allele-A) on age- and sex-adjusted trajectories of body mass index (BMI) during aging. Trajectories of BMI over time were significantly different between obesity risk allele non-carriers, heterozygous and homozygous individuals (likelihood ratio test: $\chi^2=13.4$, $df=4$, $p=0.0096$)



Supplementary Fig. 3

Differences in longitudinal changes in regional resting state cerebral blood flow (rCBF) between obesity risk allele carriers (*FTO*+) and non-carriers (*FTO*-) (*rs9939609*). Blue areas indicate brain regions that show significantly greater longitudinal decreases in rCBF in the *FTO*+ group; red areas indicate brain regions that show greater longitudinal increases in rCBF in the *FTO*+ group. (A) axial view (B) sagittal view.

Supplementary Table 5. Local maxima of regions showing greater longitudinal decreases and increases in rCBF in individuals with *FTO+* gene (*rs9939609*)

Region	Side	Coordinates			T value	P value	Number of voxels
		x	y	z			
Decreases in rCBF							
Anterior cingulate gyrus (32)	L	-12	46	16	3.54	0.001	69
Medial orbitofrontal gyrus (11)	R	8	34	-10	3.30	0.001	223
Anterior cingulate gyrus (24)	R	4	30	0	3.21	0.001	
Superior temporal gyrus (39)	R	44	-53	30	3.16	0.001	55
Superior temporal gyrus (21)	R	64	-16	2	3.46	<0.001	77
Parahippocampal gyrus(35)	L	-22	-24	-18	3.20	0.001	117
Occipital/peristriate (19)	R	28	-84	24	3.07	0.001	55
Cerebellum	L	-32	-96	-18	4.71	<0.001	304
Cerebellum	R	8	-44	-22	2.93	0.001	53
Increases in rCBF							
Middle frontal gyrus (10)	L	-30	46	4	3.21	0.001	132
Inferior frontal gyrus (45)	L	-32	36	2	3.14	0.001	
Middle temporal gyrus (21)	L	-56	-46	2	3.45	<0.001	184

Supplementary Table 6. Longitudinal change of (A) impulsivity-related traits (N=692) and (B) food intake (N=558) for number of obesity-related risk A alleles of *FTO* (*rs9939609*)

	TT slope (SE) [†]	TA slope (SE)	AA slope (SE)	Differences in slopes	p-value	Effect size
Impulsivity (N5)*	-0.06 (0.07)	-0.06 (0.07)	-0.07 (0.08)	-0.002 (0.03)	0.950	0.07
Excitement-seeking (E5)	-0.18 (0.07)	-0.13 (0.06)	-0.08 (0.07)	0.05 (0.03)	0.073	1.67
Self-Discipline (C5)	-0.08 (0.08)	-0.11 (0.07)	-0.13 (0.08)	-0.02 (0.03)	0.471	0.67
Deliberation (C6)	0.07 (0.07)	0.07 (0.07)	0.07 (0.07)	-0.0001 (0.03)	0.997	0.003

(B)

	TT slope (SE) [†]	TA slope (SE)	AA slope (SE)	Differences in slopes	p-value	Effect size
Fat intake (%)§	-0.14 (0.04)	-0.08 (0.03)	-0.01 (0.04)	0.07 (0.03)	0.013	2.3
Carbohydrate intake (%)	0.19 (0.05)	0.11 (0.04)	0.04 (0.05)	-0.07 (0.03)	0.03	2.3
Protein intake (%)	-0.006 (0.02)	-0.003 (0.01)	0.0005 (0.02)	0.003 (0.01)	0.777	0.3

* All impulsivity-related traits were standardized T score. All models were adjusted for baseline age (centered at 60), sex, baseline age×time, sex×time, years of education (centered at 16 years)

† SE: standard error

§ Macronutrient intakes were calculated as the percentages of energy derived from macronutrient intakes. All models were adjusted for baseline age (centered at 60), sex, baseline age×time, sex×time and year of baseline visit (centered at year 1980)