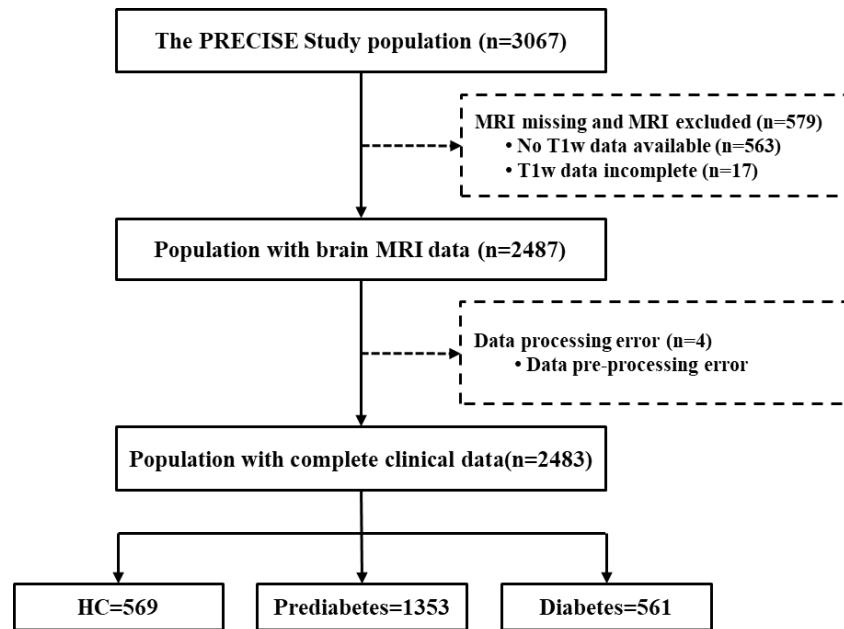
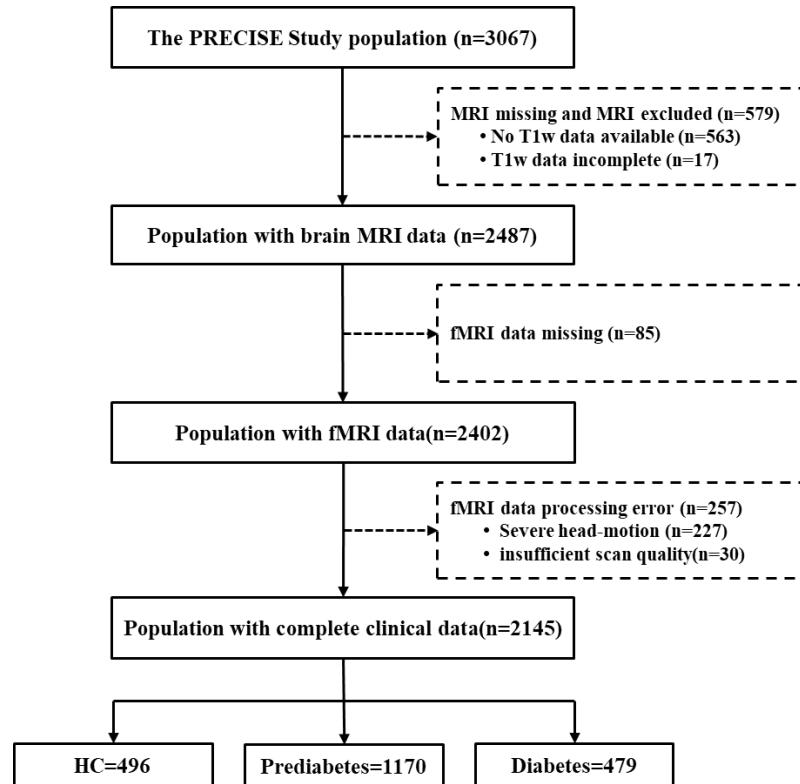


SUPPLEMENTARY DATA

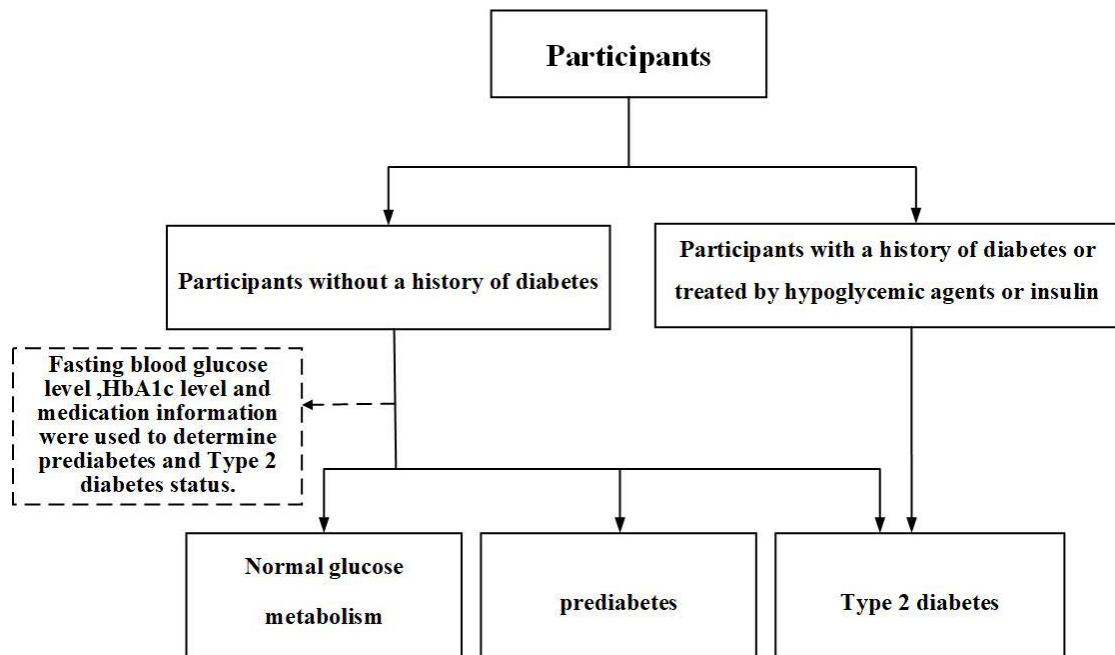
Supplementary Figure 1. Flowchart of the sMRI study population



Supplementary Figure 2. Flowchart of the fMRI study population



Supplementary Figure 3. Flowchart of the assessment of prediabetes and diabetes



Supplementary Table 1 Details of the 246 regions in Human Brainnetome atlas

Lobe	Gyrus	Left and Right Hemisphere	Anatomical and modified Cyto-architectonic descriptions	lh.MNI(X,Y,Z)	rh.MNI(X,Y,Z)
SFG, Superior Frontal Gyrus	SFG_L(R)_7_1		A8m, medial area 8	-5, 15, 54	7, 16, 54
	SFG_L(R)_7_2		A8dl, dorsolateral area 8	-18, 24, 53	22, 26, 51
	SFG_L(R)_7_3		A9l, lateral area 9	-11, 49, 40	13, 48, 40
	SFG_L(R)_7_4		A6dl, dorsolateral area 6	-18, -1, 65	20, 4, 64
	SFG_L(R)_7_5		A6m, medial area 6	-6, -5, 58	7, -4, 60
	SFG_L(R)_7_6		A9m, medial area 9	-5, 36, 38	6, 38, 35
	SFG_L(R)_7_7		A10m, medial area 10	-8, 56, 15	8, 58, 13
MFG, Middle Frontal Gyrus	MFG_L(R)_7_1		A9/46d, dorsal area 9/46	-27, 43, 31	30, 37, 36
	MFG_L(R)_7_2		IFJ, inferior frontal junction	-42, 13, 36	42, 11, 39
	MFG_L(R)_7_3		A46, area 46	-28, 56, 12	28, 55, 17
	MFG_L(R)_7_4		A9/46v, ventral area 9/46	-41, 41, 16	42, 44, 14
	MFG_L(R)_7_5		A8vl, ventrolateral area 8	-33, 23, 45	42, 27, 39
	MFG_L(R)_7_6		A6vl, ventrolateral area 6	-32, 4, 55	34, 8, 54
	MFG_L(R)_7_7		A10l, lateral area 10	-26, 60, -6	25, 61, -4
Frontal Lobe	IFG, Inferior Frontal Gyrus	IFG_L(R)_6_1	A44d, dorsal area 44	-46, 13, 24	45, 16, 25
		IFG_L(R)_6_2	IFS, inferior frontal sulcus	-47, 32, 14	48, 35, 13
		IFG_L(R)_6_3	A45c, caudal area 45	-53, 23, 11	54, 24, 12
		IFG_L(R)_6_4	A45r, rostral area 45	-49, 36, -3	51, 36, -1
		IFG_L(R)_6_5	A44op, opercular area 44	-39, 23, 4	42, 22, 3
		IFG_L(R)_6_6	A44v, ventral area 44	-52, 13, 6	54, 14, 11
OrG, Orbital Gyrus	OrG_L(R)_6_1		A14m, medial area 14	-7, 54, -7	6, 47, -7
		OrG_L(R)_6_2	A12/47o, orbital area 12/47	-36, 33, -16	40, 39, -14
		OrG_L(R)_6_3	A11l, lateral area 11	-23, 38, -18	23, 36, -18
		OrG_L(R)_6_4	A11m, medial area 11	-6, 52, -19	6, 57, -16
		OrG_L(R)_6_5	A13, area 13	-10, 18, -19	9, 20, -19
		OrG_L(R)_6_6	A12/47l, lateral area 12/47	-41, 32, -9	42, 31, -9
PrG, Precentral Gyrus	PrG_L(R)_6_1		A4hf, area 4(head and face region)	-49, -8, 39	55, -2, 33
		PrG_L(R)_6_2	A6cdl, caudal dorsolateral area 6	-32, -9, 58	33, -7, 57
		PrG_L(R)_6_3	A4ul, area 4(upper limb region)	-26, -25, 63	34, -19, 59
		PrG_L(R)_6_4	A4t, area 4(trunk region)	-13, -20, 73	15, -22, 71
		PrG_L(R)_6_5	A4tl, area 4(tongue and larynx region)	-52, 0, 8	54, 4, 9
		PrG_L(R)_6_6	A6cvl, caudal ventrolateral area 6	-49, 5, 30	51, 7, 30
PCL, Paracentral Lobule	PCL_L(R)_2_1		A1/2/3ll, area 1/2/3 (lower limb region)	-8, -38, 58	10, -34, 54
	PCL_L(R)_2_2		A4ll, area 4, (lower limb region)	-4, -23, 61	5, -21, 61
Temporal Lobe	STG, Superior Temporal Gyrus	STG_L(R)_6_1	A38m, medial area 38	-32, 14, -34	31, 15, -34
		STG_L(R)_6_2	A41/42, area 41/42	-54, -32, 12	54, -24, 11
		STG_L(R)_6_3	TE1.0 and TE1.2	-50, -11, 1	51, -4, -1
		STG_L(R)_6_4	A22c, caudal area 22	-62, -33, 7	66, -20, 6
		STG_L(R)_6_5	A38l, lateral area 38	-45, 11, -20	47, 12, -20
		STG_L(R)_6_6	A22r, rostral area 22	-55, -3, -10	56, -12, -5

	MTG_L(R)_4_1	A21c, caudal area 21	-65, -30, -12	65, -29, -13
MTG, Middle Temporal Gyrus	MTG_L(R)_4_2	A21r, rostral area 21	-53, 2, -30	51, 6, -32
	MTG_L(R)_4_3	A37dl, dorsolateral area37	-59, -58, 4	60, -53, 3
	MTG_L(R)_4_4	aSTS, anterior superior temporal sulcus	-58, -20, -9	58, -16, -10
ITG, Inferior Temporal Gyrus	ITG_L(R)_7_1	A20iv, intermediate ventral area 20	-45, -26, -27	46, -14, -33
	ITG_L(R)_7_2	A37elv, extreme lateroventral area37	-51, -57, -15	53, -52, -18
	ITG_L(R)_7_3	A20r, rostral area 20	-43, -2, -41	40, 0, -43
	ITG_L(R)_7_4	A20il, intermediate lateral area 20	-56, -16, -28	55, -11, -32
	ITG_L(R)_7_5	A37vl, ventrolateral area 37	-55, -60, -6	54, -57, -8
	ITG_L(R)_7_6	A20cl, caudolateral of area 20	-59, -42, -16	61, -40, -17
	ITG_L(R)_7_7	A20cv, caudoventral of area 20	-55, -31, -27	54, -31, -26
FuG, Fusiform Gyrus	FuG_L(R)_3_1	A20rv, rostroventral area 20	-33, -16, -32	33, -15, -34
	FuG_L(R)_3_2	A37mv, medioventral area37	-31, -64, -14	31, -62, -14
	FuG_L(R)_3_3	A37lv, lateroventral area37	-42, -51, -17	43, -49, -19
PhG, Parahippocampal Gyrus	PhG_L(R)_6_1	A35/36r, rostral area 35/36	-27, -7, -34	28, -8, -33
	PhG_L(R)_6_2	A35/36c, caudal area 35/36	-25, -25, -26	26, -23, -27
	PhG_L(R)_6_3	TL, area TL (lateral PPHC, posterior parahippocampal gyrus)	-28, -32, -18	30, -30, -18
	PhG_L(R)_6_4	A28/34, area 28/34 (EC, entorhinal cortex)	-19, -12, -30	19, -10, -30
	PhG_L(R)_6_5	TI, area TI (temporal agranular insular cortex)	-23, 2, -32	22, 1, -36
	PhG_L(R)_6_6	TH, area TH (medial PPHC)	-17, -39, -10	19, -36, -11
pSTS, posterior Superior Temporal Sulcus	pSTS_L(R)_2_1	rpSTS, rostoposterior superior temporal sulcus	-54, -40, 4	53, -37, 3
	pSTS_L(R)_2_2	cpSTS, caudoposterior superior temporal sulcus	-52, -50, 11	57, -40, 12
SPL, Superior Parietal Lobule	SPL_L(R)_5_1	A7r, rostral area 7	-16, -60, 63	19, -57, 65
	SPL_L(R)_5_2	A7c, caudal area 7	-15, -71, 52	19, -69, 54
	SPL_L(R)_5_3	A5l, lateral area 5	-33, -47, 50	35, -42, 54
	SPL_L(R)_5_4	A7pc, postcentral area 7	-22, -47, 65	23, -43, 67
	SPL_L(R)_5_5	A7ip, intraparietal area 7(hIP3)	-27, -59, 54	31, -54, 53
IPL, Inferior Parietal Lobule	IPL_L(R)_6_1	A39c, caudal area 39(PGp)	-34, -80, 29	45, -71, 20
	IPL_L(R)_6_2	A39rd, rostrodorsal area 39(Hip3)	-38, -61, 46	39, -65, 44
	IPL_L(R)_6_3	A40rd, rostrodorsal area 40(PFt)	-51, -33, 42	47, -35, 45
	IPL_L(R)_6_4	A40c, caudal area 40(PFm)	-56, -49, 38	57, -44, 38
	IPL_L(R)_6_5	A39rv, rostroventral area 39(PGa)	-47, -65, 26	53, -54, 25
	IPL_L(R)_6_6	A40rv, rostroventral area 40(PFop)	-53, -31, 23	55, -26, 26
Parietal Lobe	PCun_L(R)_4_1	A7m, medial area 7(PEp)	-5, -63, 51	6, -65, 51
	PCun_L(R)_4_2	A5m, medial area 5(PEm)	-8, -47, 57	7, -47, 58
	PCun_L(R)_4_3	dmPOS, dorsomedial parietooccipital sulcus(PEr)	-12, -67, 25	16, -64, 25
	PCun_L(R)_4_4	A31, area 31 (Lc1)	-6, -55, 34	6, -54, 35
PoG, Postcentral Gyrus	PoG_L(R)_4_1	A1/2/3ulhf, area 1/2/3(upper limb, head and face region)	-50, -16, 43	50, -14, 44
	PoG_L(R)_4_2	A1/2/3tonla, area 1/2/3(tongue and larynx region)	-56, -14, 16	56, -10, 15
	PoG_L(R)_4_3	A2, area 2	-46, -30, 50	48, -24, 48
	PoG_L(R)_4_4	A1/2/3tru, area1/2/3(trunk region)	-21, -35, 68	20, -33, 69

		INS_L(R)_6_1	G, hypergranular insula	-36, -20, 10	37, -18, 8
		INS_L(R)_6_2	vIa, ventral agranular insula	-32, 14, -13	33, 14, -13
Insular Lobe	INS, Insular Gyrus	INS_L(R)_6_3	dIa, dorsal agranular insula	-34, 18, 1	36, 18, 1
		INS_L(R)_6_4	vld/vIg, ventral dysgranular and granular insula	-38, -4, -9	39, -2, -9
		INS_L(R)_6_5	dIg, dorsal granular insula	-38, -8, 8	39, -7, 8
		INS_L(R)_6_6	dId, dorsal dysgranular insula	-38, 5, 5	38, 5, 5
Limbic Lobe	CG, Cingulate Gyrus	CG_L(R)_7_1	A23d, dorsal area 23	-4, -39, 31	4, -37, 32
		CG_L(R)_7_2	A24rv, rostroventral area 24	-3, 8, 25	5, 22, 12
		CG_L(R)_7_3	A32p, pregenual area 32	-6, 34, 21	5, 28, 27
		CG_L(R)_7_4	A23v, ventral area 23	-8, -47, 10	9, -44, 11
		CG_L(R)_7_5	A24cd, caudodorsal area 24	-5, 7, 37	4, 6, 38
		CG_L(R)_7_6	A23c, caudal area 23	-7, -23, 41	6, -20, 40
		CG_L(R)_7_7	A32sg, subgenual area 32	-4, 39, -2	5, 41, 6
Occipital Lobe	MVOcC, MedioVentral Occipital Cortex	MVOcC_L(R)_5_1	cLinG, caudal lingual gyrus	-11, -82, -11	10, -85, -9
		MVOcC_L(R)_5_2	rCunG, rostral cuneus gyrus	-5, -81, 10	7, -76, 11
		MVOcC_L(R)_5_3	cCunG, caudal cuneus gyrus	-6, -94, 1	8, -90, 12
		MVOcC_L(R)_5_4	rLinG, rostral lingual gyrus	-17, -60, -6	18, -60, -7
		MVOcC_L(R)_5_5	vmPOS, ventromedial parietooccipital sulcus	-13, -68, 12	15, -63, 12
	LOcC, lateral Occipital Cortex	LOcC_L(R)_4_1	mOccG, middle occipital gyrus	-31, -89, 11	34, -86, 11
		LOcC_L(R)_4_2	V5/MT+, area V5/MT+	-46, -74, 3	48, -70, -1
		LOcC_L(R)_4_3	OPC, occipital polar cortex	-18, -99, 2	22, -97, 4
	Cortex	LOcC_L(R)_4_4	iOccG, inferior occipital gyrus	-30, -88, -12	32, -85, -12
		LOcC_L(R)_2_1	msOccG, medial superior occipital gyrus	-11, -88, 31	16, -85, 34
		LOcC_L(R)_2_2	lsOccG, lateral superior occipital gyrus	-22, -77, 36	29, -75, 36
	Amyg, Amygdala	Amyg_L(R)_2_1	mAmyg, medial amygdala	-19, -2, -20	19, -2, -19
		Amyg_L(R)_2_2	lAmyg, lateral amygdala	-27, -4, -20	28, -3, -20
	Hipp, Hippocampus	Hipp_L(R)_2_1	rHipp, rostral hippocampus	-22, -14, -19	22, -12, -20
		Hipp_L(R)_2_2	cHipp, caudal hippocampus	-28, -30, -10	29, -27, -10
Subcortical Nuclei	BG, Basal Ganglia	BG_L(R)_6_1	vCa, ventral caudate	-12, 14, 0	15, 14, -2
		BG_L(R)_6_2	GP, globus pallidus	-22, -2, 4	22, -2, 3
		BG_L(R)_6_3	NAC, nucleus accumbens	-17, 3, -9	15, 8, -9
		BG_L(R)_6_4	vmPu, ventromedial putamen	-23, 7, -4	22, 8, -1
		BG_L(R)_6_5	dCa, dorsal caudate	-14, 2, 16	14, 5, 14
		BG_L(R)_6_6	dIPu, dorsolateral putamen	-28, -5, 2	29, -3, 1
	Tha, Thalamus	Tha_L(R)_8_1	mPFtha, medial pre-frontal thalamus	-7, -12, 5	7, -11, 6
		Tha_L(R)_8_2	mPMtha, pre-motor thalamus	-18, -13, 3	12, -14, 1
		Tha_L(R)_8_3	Stha, sensory thalamus	-18, -23, 4	18, -22, 3
		Tha_L(R)_8_4	rTtha, rostral temporal thalamus	-7, -14, 7	3, -13, 5
		Tha_L(R)_8_5	PPtha, posterior parietal thalamus	-16, -24, 6	15, -25, 6
		Tha_L(R)_8_6	Otha, occipital thalamus	-15, -28, 4	13, -27, 8
		Tha_L(R)_8_7	cTtha, caudal temporal thalamus	-12, -22, 13	10, -14, 14
		Tha_L(R)_8_8	lPFtha, lateral pre-frontal thalamus	-11, -14, 2	13, -16, 7

Supplementary Table 2. Clinical characteristics of the study population and the subjects excluded from the study

Characteristic	Study population (n = 2483)	Excluded from the study (n = 584)	P
Demographics			
Age (years)	61.4±6.6	60.2 ±6.9	<.001
Sex (% female)	53.4	53.6	0.979
Glucose metabolism			
Fasting glucose (mmol/L)	6.0 ±1.6	5.7±1.6	<.001
2-h post-load glucose (mmol/L) *	7.7±2.9	8.0±3.2	0.026
HbA1c (%)	6.0 ±1.0	5.8±0.8	<.001
HbA1c (mmol/mol)	41.8±10.6	39.5±9.1	<.001
Cardiovascular risk factors			
BMI (kg/m2)	24.0 ±3.0	22.9±3.0	<.001
Systolic BP (mmHg)	130.1±16.3	125.9±16.2	<.001
Diastolic BP (mmHg)	75.5±9.0	73.8±9.3	<.001
Hypertension (%)	44.3	37.8	0.004
Total-to-HDL cholesterol ratio	4.0±1.1	4.07±1.2	0.032
Triglycerides (mmol/L)	1.8±1.3	1.7±1.2	0.023
eGFR (mL/min/1.73 m2)	101.9±12.5	102.2±12.0	0.769
History of stroke (%)	2.7	3.3	0.500
History of heart disease (%)	8.6	5.8	0.024
Medication use (%)			
Lipid-lowering	4.5	1.4	<.001
Antihypertensive	27.0	26.4	0.700
MoCA	21.6±4.8	20.5±4.9	<.001
Lifestyle factors (%)			
Smoking, never/current/quit	64.4/22.8/12.7	61.0/25.2/13.9	0.289
Education illiteracy or elementary school / middle or high school / college or above	41.0/51.4/7.7	59.2/40.6/0.2	<.001

Data are presented as means ± SD or percentage. Fasting glucose values were available in n = 3065. 2-h post-load glucose values were available in n = 2760. Total-to-HDL cholesterol ratio values were available in n = 3065. Triglycerides values were available in n = 3065. eGFR values were available in n = 3065.

BMI, body mass index; BP, blood pressure; HDL, high-density lipoproteins; eGFR, estimated glomerular filtration rate.

Supplementary Table 3 Multivariable-adjusted associations of MoCA with the brain volume

Region volume	Model 1		Model 2	
	β (95%CI)	P	β (95%CI)	P
SUB	0.098 (0.058,0.137)	<0.001	0.098 (0.058,0.138)	<0.001
THA.L	0.112 (0.074,0.151)	<0.001	0.108 (0.070,0.147)	<0.001
THA.R	0.085 (0.046,0.124)	<0.001	0.082 (0.043,0.121)	<0.001
CAU.L	0.018 (-0.018,0.054)	0.329	0.021 (-0.015,0.057)	0.251
CAU.R	0.013 (-0.022,0.049)	0.454	0.019 (-0.017,0.054)	0.303
PUT.L	0.038 (0.001,0.074)	0.042	0.038 (0.001,0.074)	0.045
PUT.R	0.019 (-0.018,0.056)	0.309	0.021 (-0.016,0.058)	0.262
PAL.L	0.030 (-0.004,0.065)	0.086	0.031 (-0.004,0.066)	0.079
PAL.R	0.037 (0.002,0.072)	0.036	0.036 (0.002,0.071)	0.041
HIP.L	0.120 (0.083,0.157)	<0.001	0.120 (0.082,0.157)	<0.001
HIP.R	0.106 (0.070,0.142)	<0.001	0.104 (0.068,0.141)	<0.001
AMY.L	0.108 (0.072,0.144)	<0.001	0.111 (0.074,0.148)	<0.001
AMY.R	0.083 (0.047,0.120)	<0.001	0.084 (0.047,0.121)	<0.001
NAcc.L	0.032 (-0.003,0.067)	0.071	0.027 (-0.008,0.061)	0.132
NAcc.R	0.064 (0.029,0.099)	<0.001	0.059 (0.024,0.095)	0.001

Model 1: adjustment for age, sex, and education level. Model 2: model 1 additionally adjusted for BMI, hypertension, total-to-HDL cholesterol ratio, history of stroke, history of heart disease.

SUB, total subcortical gray matter; THA, thalamus; CAU, caudate; PUT, putamen; PAL, pallidum; HIP, hippocampus; AMY, amygdala; NAcc, nucleus accumbens; L, left; R, right.

Supplementary Table 4 Multivariable-adjusted associations of MoCA with the functional connectivity

Functional connectivity	Model 1		Model 2	
	β (95%CI)	P	β (95%CI)	P
THA.L and VIS	-0.040 (-0.076, -0.005)	0.027	-0.031 (-0.067, 0.005)	0.093
THA.R and VIS	-0.050 (-0.086, -0.014)	0.007	-0.041 (-0.077, -0.004)	0.029
THA.L and SMN	-0.052 (-0.088, -0.017)	0.004	-0.048 (-0.083, -0.013)	0.007
THA.R and SMN	-0.030 (-0.065, 0.006)	0.099	-0.029 (-0.064, 0.006)	0.107
THA.L and DAN	0.010 (-0.026, 0.046)	0.590	0.007 (-0.029, 0.043)	0.712
THA.R and DAN	-0.007 (-0.043, 0.029)	0.712	-0.008 (-0.043, 0.029)	0.666
THA.L and VAN	-0.045 (-0.08, -0.009)	0.013	-0.040 (-0.076, -0.005)	0.025
THA.R and VAN	-0.023 (-0.058, 0.012)	0.200	-0.020 (-0.055, 0.015)	0.261
THA.L and LIM	0.037 (0.002, 0.073)	0.037	0.040 (0.005, 0.075)	0.026
THA.R and LIM	0.022 (-0.013, 0.057)	0.219	0.024 (-0.011, 0.059)	0.178
THA.L and FPN	0.010 (-0.025, 0.046)	0.565	0.012 (-0.023, 0.047)	0.516
THA.R and FPN	0.011 (-0.024, 0.046)	0.540	0.013 (-0.022, 0.048)	0.463
THA.L and DMN	-0.018 (-0.054, 0.017)	0.319	-0.010 (-0.046, 0.026)	0.584
THA.R and DMN	-0.005 (-0.041, 0.030)	0.764	0.002 (-0.034, 0.037)	0.921

Model 1: adjustment for age, sex, and education level. Model 2: model 1 additionally adjusted for BMI, hypertension, total-to-HDL cholesterol ratio, history of stroke, history of heart disease.

THA, thalamus; L, left; R, right

Supplementary Table 5 Multivariable-adjusted associations of functional connectivity with the brain volume

Functional connectivity	Region volume	Model 1		Model 2	
		β (95%CI)	P	β (95%CI)	P
THA.L and VIS	THA.L	-0.076 (-0.125, -0.027)	0.002	-0.075 (-0.124, -0.026)	0.003
THA.R and VIS	THA.R	-0.064 (-0.113, -0.015)	0.010	-0.064 (-0.113, -0.015)	0.010
THA.L and SMN	THA.L	0.044 (-0.005, 0.094)	0.080	0.047 (-0.003, 0.097)	0.064
THA.R and SMN	THA.R	0.024 (-0.026, 0.074)	0.340	0.024 (-0.026, 0.074)	0.346
THA.L and DAN	THA.L	-0.012 (-0.061, 0.037)	0.621	-0.016 (-0.065, 0.033)	0.528
THA.R and DAN	THA.R	-0.003 (-0.053, 0.046)	0.895	-0.004 (-0.054, 0.045)	0.866
THA.L and VAN	THA.L	0.024 (-0.026, 0.073)	0.347	0.029 (-0.021, 0.079)	0.256
THA.R and VAN	THA.R	0.000 (-0.050, 0.050)	0.999	0.002 (-0.048, 0.053)	0.928
THA.L and LIM	THA.L	0.010 (-0.040, 0.060)	0.691	0.005 (-0.045, 0.055)	0.836
THA.R and LIM	THA.R	0.011 (-0.040, 0.061)	0.680	0.004 (-0.046, 0.054)	0.869
THA.L and FPN	THA.L	-0.010 (-0.060, 0.040)	0.692	-0.007 (-0.057, 0.043)	0.781
THA.R and FPN	THA.R	-0.004 (-0.055, 0.046)	0.861	-0.002 (-0.052, 0.049)	0.947
THA.L and DMN	THA.L	-0.047 (-0.096, 0.002)	0.062	-0.045 (-0.094, 0.005)	0.075
THA.R and DMN	THA.R	-0.040 (-0.090, 0.010)	0.116	-0.041 (-0.094, 0.009)	0.107

Model 1: adjustment for age, sex, and education level. Model 2: model 1 additionally adjusted for BMI, hypertension, total-to-HDL cholesterol ratio, history of stroke, history of heart disease.

THA, thalamus; L, left; R, right