

eTable 1 Demographic and clinical characteristics of the participants

Patient	Age(years)	Gender	Days Since Stroke	Fazekas scores	FMA scores	Location side
1	68	F	3	1	42	L
2	47	F	4	1	40	R
3	55	F	3	1	55	R
4	74	F	4	1	53	L
5	77	M	5	1	36	L
6	48	M	3	1	54	L
7	46	M	4	1	22	L
8	54	M	3	1	11	L
9	52	M	4	1	31	R
10	35	M	3	1	62	R
11	25	M	4	1	18	R
12	68	M	3	1	52	R
13	69	M	5	2	0	L
14	68	F	4	1	55	R
15	33	F	5	1	55	R
16	62	F	3	1	21	R
17	50	F	4	2	5	R
18	63	F	5	1	55	R
19	67	F	4	1	63	R
20	68	M	3	1	52	L
21	61	M	5	1	58	L
22	70	M	4	2	9	L
23	60	M	5	1	15	R
24	40	M	4	1	15	R
25	44	M	3	1	55	L
26	37	M	4	1	33	L
27	68	F	5	1	13	L
28	43	F	6	1	56	L
29	61	F	3	2	10	L
30	70	F	4	1	35	R
31	61	F	5	1	38	R
32	42	M	6	1	38	R
33	27	M	4	1	62	R
34	65	M	3	1	63	R
35	62	M	5	1	28	L
36	58	M	4	1	28	R
37	73	M	4	1	58	R
38	74	M	3	1	44	R
39	75	M	3	1	37	L
40	70	M	4	1	32	L
41	51	M	5	1	46	L

42	69	F	4	1	7	L
43	51	F	5	2	9	L
44	59	F	4	1	30	R
45	62	F	3	1	28	R
46	75	M	4	1	66	R
47	63	M	3	1	60	R
48	62	M	5	1	33	R
49	54	M	3	1	68	R
50	62	M	4	2	5	L
51	60	M	3	1	68	L
52	59	M	4	1	61	R
53	32	M	3	1	65	R
54	63	M	5	1	15	R
55	64	M	3	1	65	R

Abbreviations:y=years; M=male;F=female;FMA=Fugl-Meyer assessment;L=left; R=right.

eTable 2 Statistical Comparison of Mean SC between PA and HC

SC	PA vs. HC (flipped)	PA vs. HC (non-flipped)
PoCG_ipsi and SPG_ipsi	<0.001***	<0.001***
PreCG_ipsi and PoCG_ipsi	<0.001***	<0.001***
PreCG_contra and PoCG_contra	<0.001***	<0.001***
PoCG_contra and SPG_contra	<0.001***	<0.001***
PoCG_contra and THA_contra	<0.001***	<0.001***
PreCG_contra and SPG_contra	<0.001***	<0.001***
SPG_ipsi and PoCG_contra	<0.001***	<0.001***
SPG_ipsi and SPG_contra	<0.001***	<0.001***
PoCG_ipsi and SPG_contra	<0.001***	<0.001***
PoCG_ipsi and THA_contra	<0.001***	<0.001***

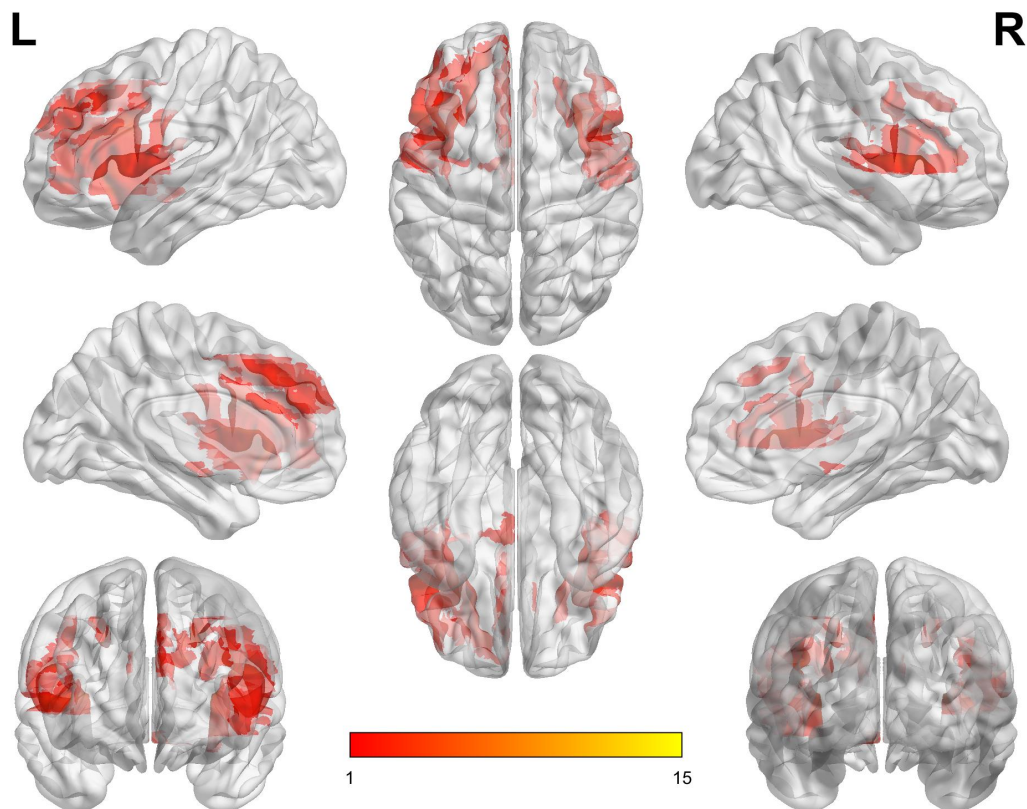
Abbreviations:SC=structural connectivity; PA=Stroke Patients; HC=Healthy Controls; PoCG=Postcentral gyrus;SPG=Superior parietal gyrus;PreCG=Precentral gyrus;THA=Thalamus; ipsi = ipsilesional; contra = contralesional.

eTable 3 Statistical Comparison of Mean FC between PA and HC

FC	PA vs. HC (flipped)	PA vs. HC (non-flipped)
PUT_ipsi and PUT_contra	<0.001***	<0.001***
PoCG_ipsi and PoCG_contra	<0.001***	<0.001***
PoCG_ipsi and PreCG_contra	<0.001***	<0.001***
PoCG_ipsi and SPG_ipsi	<0.001***	<0.001***
THA_ipsi and THA_contra	<0.001***	<0.001***
PreCG_contra and THA_contra	0.02*	0.02*
THA_ipsi and PreCG_contra	0.04*	0.04*
SPG_ipsi and SPG_contra	0.04*	0.04*
THA_ipsi and PoCG_contra	0.04*	0.04*
PreCG_ipsi and PreCG_contra	0.05*	0.05*
PoCG_contra and THA_contra	0.05*	0.05*

Abbreviations:FC = functional connectivity; PA=Stroke Patients; HC=Healthy Controls; PUT=Lenticular nucleus, putamen; PoCG=Postcentral gyrus;PreCG=Precentral gyrus; SPG=Superior parietal gyrus; THA=Thalamus;ipsi = ipsilesional;contra = contralesional.

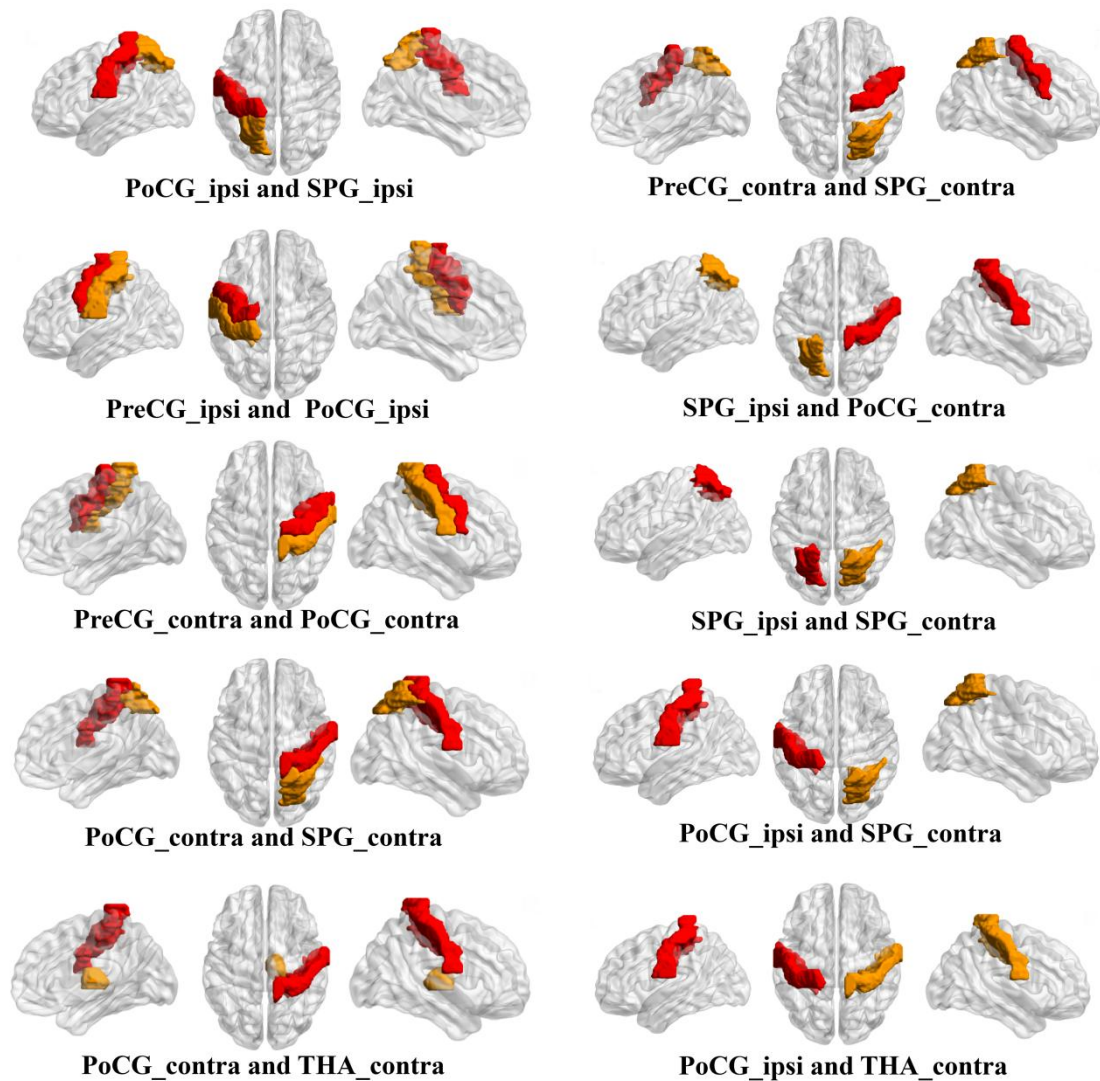
eFigure 1
Distribution of the lesion areas in patients



Note:The lesion areas overlapping across patients were rendered on the brain. Group-level lesion overlap map showing the spatial distribution of ischemic lesions in 55 patients. The color bar represents the number of patients with a lesion at each voxel.

Abbreviations: L=left; R=right.

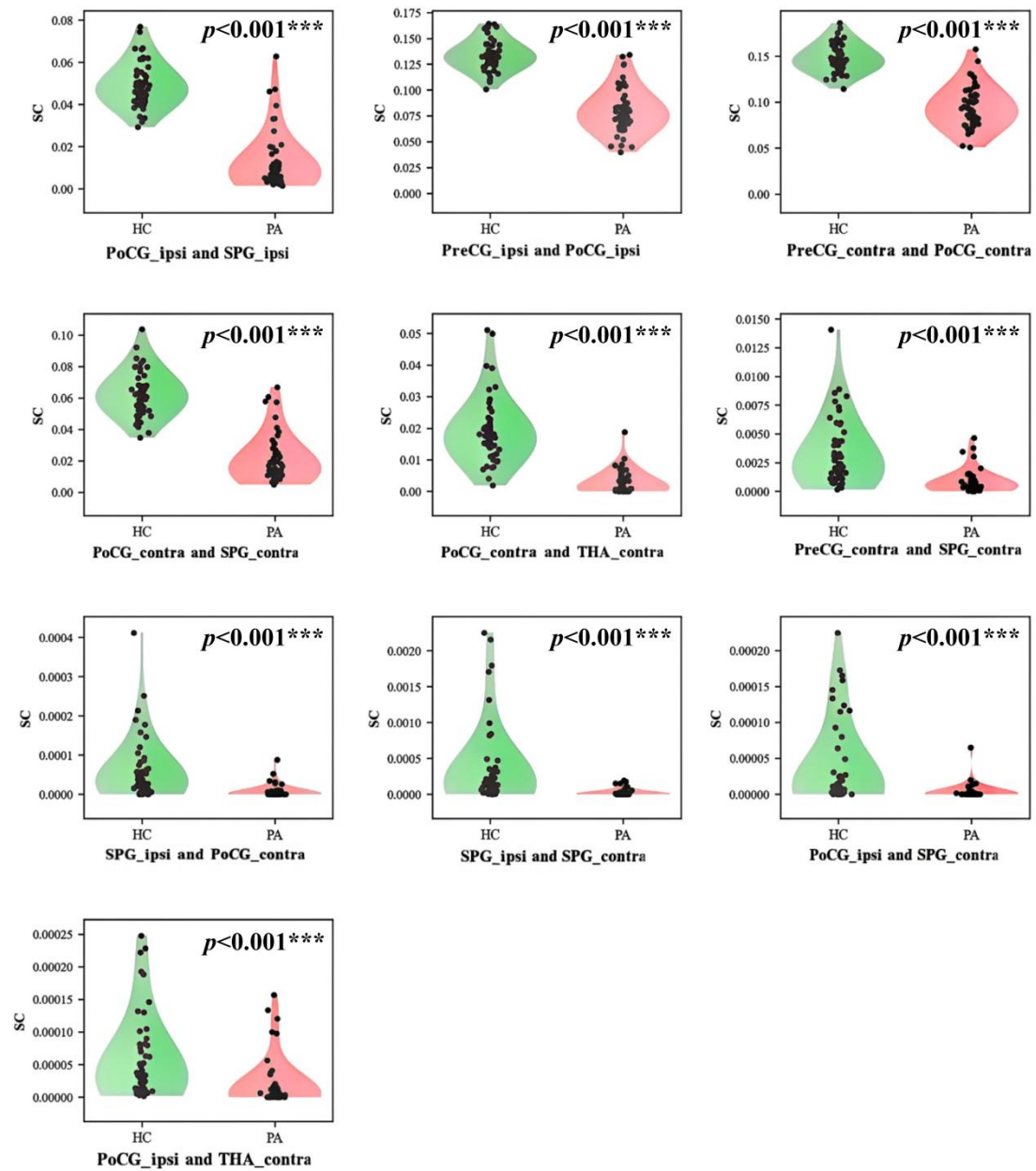
eFigure 2
The anatomical locations of SC regions



Abbreviations: SC=structural connectivity; PoCG=Postcentral gyrus; SPG=Superior parietal gyrus; PreCG=Precentral gyrus; THA=Thalamus; ipsi = ipsilesional; contra = contralesional.

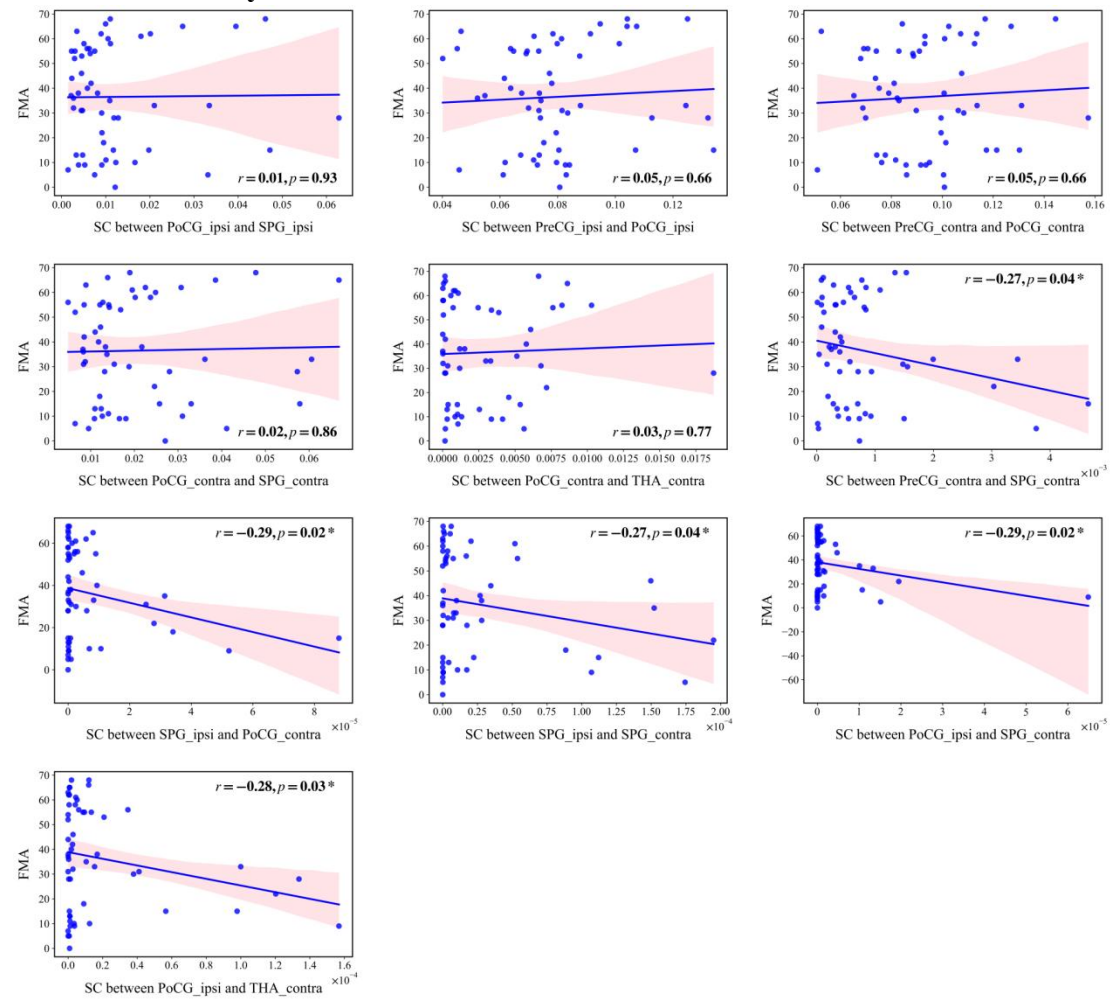
eFigure 3

The mean SC of WM in PA and HC



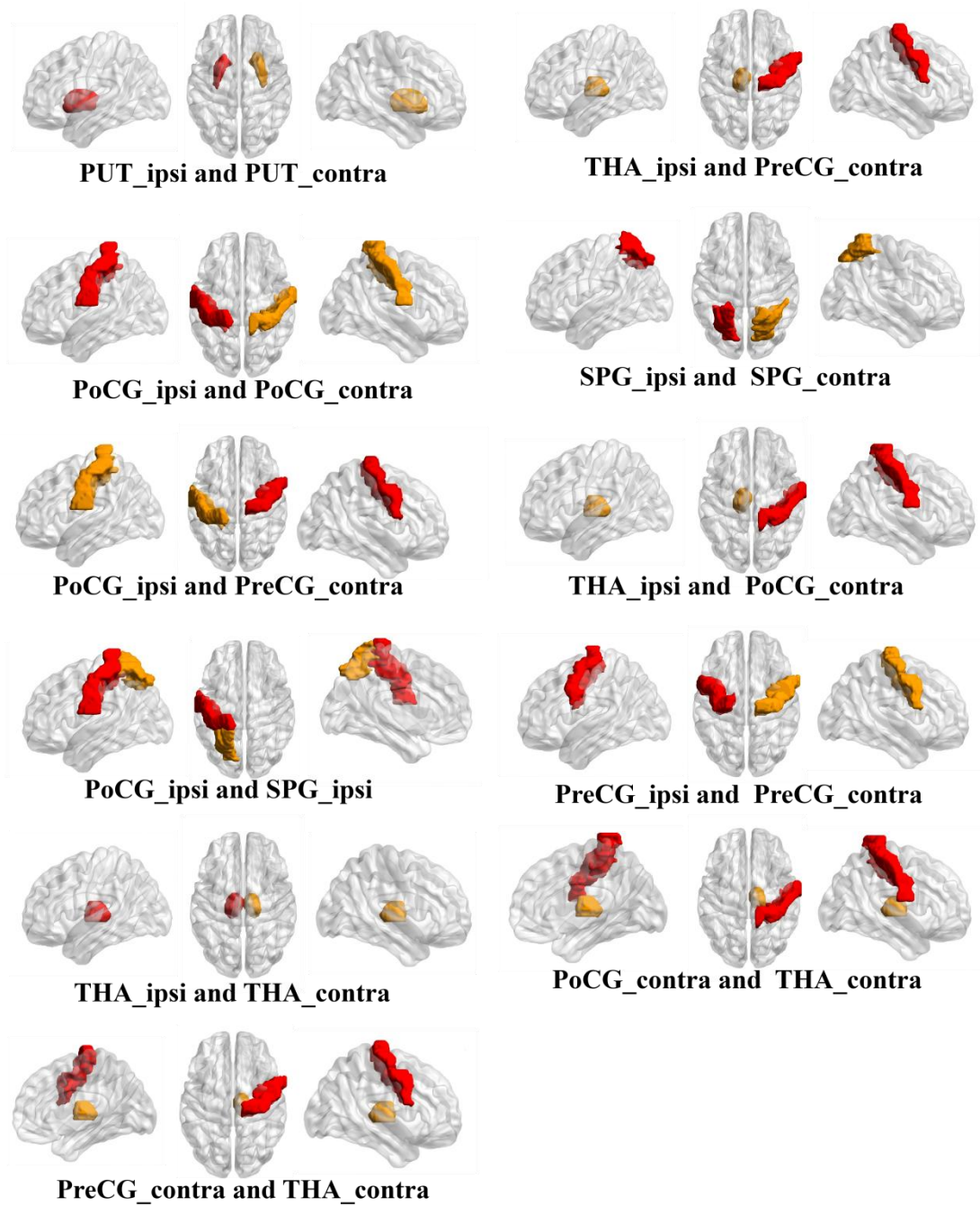
Abbreviations: SC=structural connectivity; WM = white matter; PA= patients; HC = healthy controls; PoCG=Postcentral gyrus; SPG=Superior parietal gyrus; PreCG=Precentral gyrus; THA=Thalamus; ipsi = ipsilesional; contra = contralesional.

eFigure 4
Correlation Analysis Between SC and FMA Scores



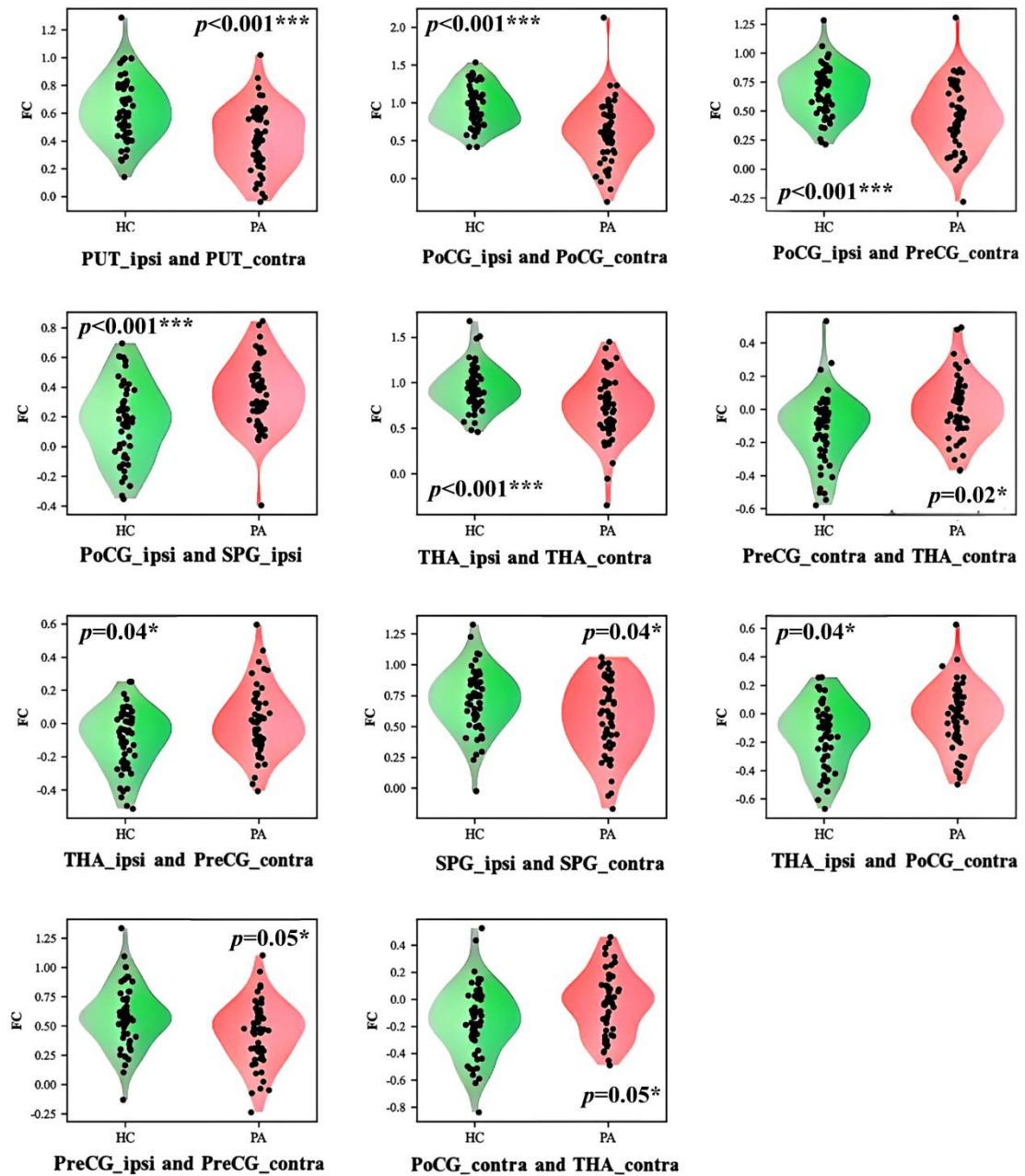
Abbreviations: SC=structural connectivity;FMA = Fugl-Meyer assessment; PoCG=Postcentral gyrus;SPG=Superior parietal gyrus;PreCG=Precentral gyrus; THA=Thalamus; ipsi = ipsilesional;contra = contralesional.

eFigure 5
The anatomical locations of FC regions



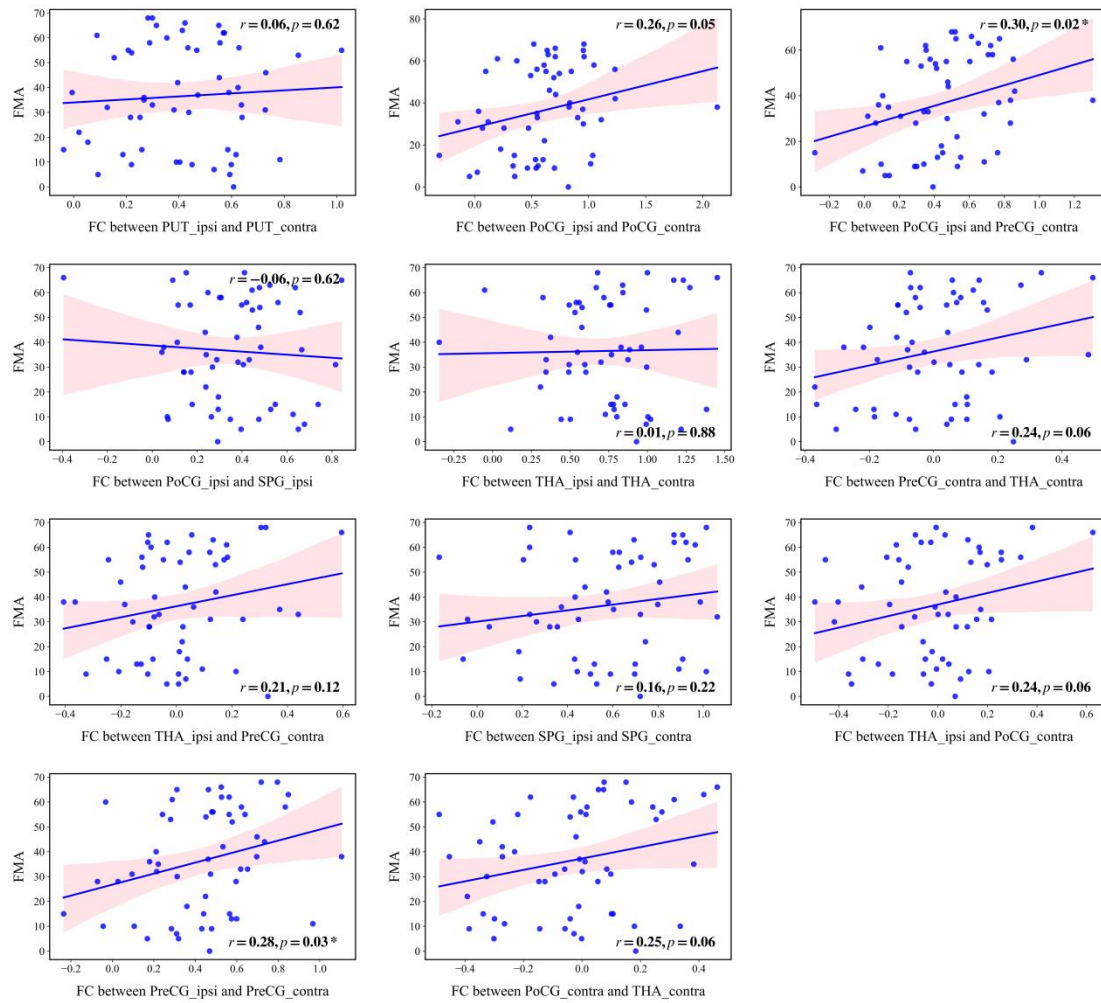
Abbreviations: FC = functional connectivity; PUT=Lenticular nucleus, putamen; PoCG=Postcentral gyrus; PreCG=Precentral gyrus; SPG=Superior parietal gyrus; THA=Thalamus; ipsi = ipsilesional; contra = contralesional.

eFigure 6
The mean FC in PA and HC



Abbreviations: PA=patients; HC = healthy controls; FC = functional connectivity; PUT=Lenticular nucleus, putamen; PoCG=Postcentral gyrus; PreCG=Precentral gyrus; SPG=Superior parietal gyrus; THA=Thalamus; ipsi=ipsilesional; contra = contralesional.

eFigure 7
Correlation Analysis Between FC and FMA Scores



Abbreviations: FC=functional connectivity;FMA = Fugl-Meyer assessment; PUT=Lenticular nucleus, putamen;PoCG=Postcentral gyrus;PreCG=Precentral gyrus; SPG=Superior parietal gyrus;THA=Thalamus;ipsi = ipsilesional;contra = contralesional.

Supplementary materials on mediation analysis for Structural–Functional Connectivity Coupling in Motor–Brain Networks Following Acute Ischemic Stroke

Mediation Analysis

To assess FC as a mediator of the relationship between SC and motor functional outcome, we considered all possible mediation models where the FC feature could serve as a mediator between the SC feature and the behavioral outcome (FMA). To account for the issue of multiple testing arising from the evaluation of multiple SC–FC mediation models, we applied false discovery rate (FDR) correction to the mediation analyses. Specifically, for each candidate mediation model, the significance of the indirect effect was evaluated using a bootstrap-based test, yielding an associated P value. These P values from all the tested mediation models were then jointly corrected using the Benjamini–Hochberg procedure to control the FDR at $q = 0.05$. A mediation analysis was performed using a bootstrap method within the PROCESS macro of SPSS (*Brain Behav.* **2020**;10). A bootstrap sample size of 10,000 was used to estimate the significance of the indirect or mediating effect, yielding an estimated β coefficient and confidence interval (CI). The indirect effect was considered significant if the 95% CI did not include zero. Mediation analysis involves testing five pathways (**sFigure 1**): (1) Path c , the total effect of SC on motor function; (2) Path a , the effect of SC on FC; (3) Path b , the effect of FC on motor function controlling for SC; (4) Path c' , the direct effect of SC on motor function controlling for FC; and (5) the indirect effect ($a \times b$), the product of paths a and b . The total effect (c) is the sum of the indirect effect ($a \times b$) and the direct effect (c').

These causal pathways are estimated using the following set of three linear regression models:

$$(1) Y = i_1 + cX + \epsilon_1$$

$$(2) M = i_2 + aX + \epsilon_2$$

$$(3) Y = i_3 + c'X + bM + \epsilon_3$$

where in Equation 1, the coefficient c represents the total effect (Path c) of SC (X) on motor outcome (Y), without accounting for the mediator. In Equation 2, the coefficient a represents the effect of SC (X) on the mediator, FC (M) (Path a). In Equation 3, the coefficient b represents the effect of the mediator, FC (M), on motor outcome (Y) after adjusting for the independent variable, SC (X) (Path b). The coefficient c' represents the direct effect (Path c') of SC on motor outcome that is not accounted for by the mediator. In all the equations, i_1 , i_2 , and i_3 denote intercept terms, whereas ϵ_1 , ϵ_2 , and ϵ_3 denote residual error terms.

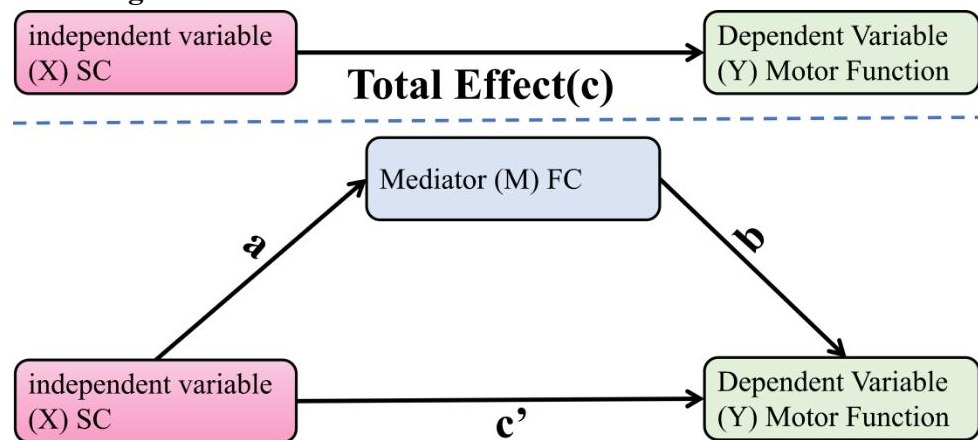
Mediation Analysis of Structural Connectivity, Functional Connectivity, and Motor Function

We investigated the relationships among SC, FC, and motor function in AIS patients using multimodal fMRI and mediation analysis. However, unfortunately, no significant results were found after the mediation analysis in the original manuscript

underwent rigorous correction (sTable 1) .

sFigure 1

Path diagram of mediator model



$$c = \frac{\text{Total Effect of SC on Motor Function}}{\text{SC}}$$

$$a = \frac{\text{Effect of SC on FC}}{\text{SC}}$$

$$b = \frac{\text{Effect of FC on Motor Function}}{\text{FC} | \text{SC}}$$

$$c' = \frac{\text{Direct Effect of SC on Motor Function}}{\text{SC} | \text{FC}}$$

$$\text{Indirect Effect} = a \times b = \frac{\text{Effect of SC on FC}}{\text{SC}} \times \frac{\text{Effect of FC on Motor Function}}{\text{FC} | \text{SC}}$$

Note: Variables in the left of | represent the variables, and in the right of | represent the controlling variables.

Abbreviations: SC=structural connectivity; FC=functional connectivity.

sTable 1 Results of mediation analysis after multiple corrections

SC	FC	Path a (Beta)	Path a (<i>P</i>)	Path a (95% CI)	Path b (Beta)	Path b (<i>P</i>)	Path b (95% CI)	Direct c' (Beta)	Direct c' (<i>P</i>)	Direct c' (95% CI)	Total c (Beta)	Total c (<i>P</i>)	Total c (95% CI)
PreCG_contra and SPG_contra	SPG_ipsi and PUT_contra	-0.058	0.674	[-0.247, 0.330]	0.381	0.003	[0.145, 0.618]	-0.21	0.097	[-0.397, - 0.026]	-0.232	0.088	[-0.409, 0.012]
PreCG_contra and SPG_contra	PreCG_contra and PoCG_ipsi	-0.04	0.774	[-0.371, 0.182]	0.296	0.025	[0.097, 0.546]	-0.22	0.092	[-0.375, 0.061]	-0.232	0.088	[-0.408, 0.028]
PoCG_ipsi and THA_contra	SMA_ipsi and SMA_contra	-0.099	0.47	[-0.402, 0.073]	0.266	0.047	[0.014, 0.520]	-0.206	0.121	[-0.363, 0.012]	-0.232	0.088	[-0.379, - 0.042]
PoCG_ipsi and THA_contra	SPG_contra and PUT_contra	-0.048	0.726	[-0.189, 0.126]	0.281	0.035	[-0.002, 0.569]	-0.219	0.097	[-0.362, - 0.040]	-0.232	0.088	[-0.381, - 0.041]
PoCG_ipsi and THA_contra	SPG_contra and PUT_ipsi	0.126	0.361	[-0.010, 0.328]	0.339	0.01	[0.051, 0.574]	-0.275	0.036	[-0.404, - 0.121]	-0.232	0.088	[-0.372, - 0.043]
PoCG_ipsi and THA_contra	PreCG_contra and PoCG_ipsi	-0.163	0.235	[-0.538, 0.032]	0.275	0.041	[0.064, 0.539]	-0.188	0.159	[-0.344, 0.083]	-0.232	0.088	[-0.378, - 0.039]
PoCG_ipsi and THA_contra	SPG_ipsi and PUT_contra	-0.035	0.797	[-0.229, 0.163]	0.385	0.003	[0.166, 0.621]	-0.219	0.084	[-0.366, - 0.020]	-0.232	0.088	[-0.377, - 0.040]
PoCG_ipsi and SPG_contra	PreCG_ipsi and PreCG_contra	-0.137	0.32	[-1.081, 0.064]	0.254	0.057	[0.011, 0.506]	-0.221	0.097	[-0.677, - 0.066]	-0.256	0.06	[-0.789, - 0.151]
PoCG_ipsi and SPG_contra	SMA_ipsi and SMA_contra	-0.057	0.678	[-0.905, 0.276]	0.272	0.039	[0.033, 0.510]	-0.24	0.068	[-0.683, - 0.079]	-0.256	0.06	[-0.813, - 0.143]
PoCG_ipsi and SPG_contra	SPG_contra and PUT_contra	-0.067	0.627	[-0.362, 0.174]	0.275	0.037	[-0.012, 0.564]	-0.237	0.071	[-0.752, - 0.111]	-0.256	0.06	[-0.789, - 0.139]
PoCG_ipsi and SPG_contra	SPG_contra and PUT_ipsi	0.027	0.842	[-0.175, 0.487]	0.312	0.018	[0.031, 0.537]	-0.264	0.042	[-0.789, - 0.178]	-0.256	0.06	[-0.780, - 0.142]
PoCG_ipsi and SPG_contra	PreCG_contra and PoCG_ipsi	-0.072	0.603	[-1.376, 0.043]	0.288	0.029	[0.080, 0.529]	-0.235	0.073	[-0.583, 0.093]	-0.256	0.06	[-0.808, - 0.139]
PoCG_ipsi and SPG_contra	SPG_ipsi and PUT_contra	0.044	0.747	[-0.310, 0.438]	0.405	0.002	[0.191, 0.643]	-0.274	0.029	[-0.859, - 0.131]	-0.256	0.06	[-0.795, - 0.135]
SPG_ipsi and SPG_contra	PreCG_ipsi and PreCG_contra	-0.165	0.23	[-0.509, 0.060]	0.256	0.059	[0.011, 0.510]	-0.175	0.192	[-0.381, 0.060]	-0.217	0.111	[-0.441, 0.019]
SPG_ipsi and	SMA_ipsi and	-0.115	0.403	[-0.393,	0.265	0.049	[0.010,	-0.187	0.16	[-0.424,	-0.217	0.111	[-0.434,

SC	FC	Path a (Beta)	Path a (P)	Path a (95% CI)	Path b (Beta)	Path b (P)	Path b (95% CI)	Direct c' (Beta)	Direct c' (P)	Direct c' (95% CI)	Total c (Beta)	Total c (P)	Total c (95% CI)
SPG_contra	SMA_contra			0.366]			0.504]			0.032]			0.021]
SPG_ipsi and SPG_contra	SPG_contra and PUT_contra	-0.056	0.687	[-0.214, 0.158]	0.28	0.036	[0.000, 0.563]	-0.202	0.126	[-0.438, 0.029]	-0.217	0.111	[-0.446, 0.015]
SPG_ipsi and SPG_contra	SPG_contra and PUT_ipsi	-0.073	0.596	[-0.259, 0.091]	0.29	0.03	[-0.002, 0.510]	-0.196	0.136	[-0.430, 0.040]	-0.217	0.111	[-0.448, 0.025]
SPG_ipsi and SPG_contra	PreCG_contra and PoCG_ipsi	-0.23	0.091	[-0.575, 0.008]	0.269	0.05	[0.064, 0.530]	-0.155	0.251	[-0.376, 0.094]	-0.217	0.111	[-0.445, 0.026]
SPG_ipsi and SPG_contra	SPG_ipsi and PUT_contra	0.006	0.967	[-0.188, 0.276]	0.394	0.002	[0.167, 0.625]	-0.22	0.082	[-0.489, 0.009]	-0.217	0.111	[-0.443, 0.025]
SPG_ipsi and PoCG_contra	PreCG_ipsi and PreCG_contra	-0.431	0.001	[-0.717, - 0.236]	0.215	0.145	[-0.045, 0.528]	-0.16	0.276	[-0.393, 0.097]	-0.253	0.062	[-0.467, - 0.093]
SPG_ipsi and PoCG_contra	SMA_ipsi and SMA_contra	-0.055	0.691	[-0.753, 0.229]	0.273	0.039	[0.017, 0.536]	-0.238	0.07	[-0.437, 0.011]	-0.253	0.062	[-0.470, - 0.090]
SPG_ipsi and PoCG_contra	SPG_contra and PUT_contra	-0.071	0.605	[-0.198, 0.338]	0.275	0.038	[0.002, 0.568]	-0.233	0.076	[-0.491, - 0.067]	-0.253	0.062	[-0.469, - 0.102]
SPG_ipsi and PoCG_contra	SPG_contra and PUT_ipsi	0.078	0.571	[-0.092, 0.246]	0.326	0.013	[0.049, 0.550]	-0.278	0.032	[-0.484, - 0.123]	-0.253	0.062	[-0.476, - 0.083]
SPG_ipsi and PoCG_contra	PreCG_contra and PoCG_ipsi	-0.366	0.006	[-0.679, - 0.027]	0.245	0.086	[0.023, 0.542]	-0.163	0.249	[-0.433, 0.102]	-0.253	0.062	[-0.474, - 0.095]
SPG_ipsi and PoCG_contra	SPG_ipsi and PUT_contra	-0.015	0.911	[-0.308, 0.141]	0.389	0.003	[0.172, 0.625]	-0.247	0.05	[-0.473, - 0.018]	-0.253	0.062	[-0.478, - 0.085]
PreCG_contra and SPG_contra	PreCG_ipsi and PreCG_contra	-0.033	0.812	[-0.314, 0.151]	0.277	0.037	[0.035, 0.535]	-0.223	0.091	[-0.362, 0.017]	-0.232	0.088	[-0.406, 0.015]
PreCG_contra and SPG_contra	SMA_ipsi and SMA_contra	-0.171	0.213	[-0.393, 0.114]	0.254	0.061	[-0.007, 0.524]	-0.189	0.159	[-0.385, 0.041]	-0.232	0.088	[-0.410, 0.009]
PreCG_contra and SPG_contra	SPG_contra and PUT_contra	-0.072	0.604	[-0.245, 0.277]	0.276	0.038	[-0.006, 0.567]	-0.212	0.107	[-0.400, - 0.009]	-0.232	0.088	[-0.403, 0.028]
PreCG_contra and SPG_contra	SPG_contra and PUT_ipsi	-0.066	0.632	[-0.323, 0.260]	0.29	0.029	[0.007, 0.517]	-0.213	0.105	[-0.376, - 0.021]	-0.232	0.088	[-0.405, 0.010]
PoCG_ipsi and THA_contra	PreCG_ipsi and PreCG_contra	-0.242	0.075	[-0.591, - 0.000]	0.242	0.078	[0.003, 0.518]	-0.174	0.204	[-0.328, 0.075]	-0.232	0.088	[-0.376, - 0.048]

Note:Path a: the effect of structural damage on altered functional connectivity; Path b: the effect of structural damage on motor impairment; Path c': the direct effect of structural damage on motor outcome after controlling for the mediator; $a \times b$ effect, referred to as the indirect effect of the mediator. The total effect (c) is the sum of the indirect effect ($a \times b$) and the direct effect (c').

Abbreviations:SC = structural connectivity; FC = functional connectivity; PoCG=Postcentral gyrus; PreCG=Precentral gyrus; THA=Thalamus; SPG=Superior parietal gyrus; SMA=Supplementary motor area; PUT=lenticular nucleus, putamen; ipsi = ipsilesional; contra = contralesional.

