Title： Alterations in static and dynamic functional network connectivity in subcortical vascular cognitive impairment

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The results of the altered connection strength among the four states in SVCI patients and HCs were shown in Figure 3

In State 1 (Figure 3A), the subcortical vascular cognitive impairment (SVCI) group was characterized by widespread reductions in connectivity. Specifically, the SMN showed weakened connections with multiple networks, including FPN, pDMN, and VN. Additionally, the ECN, SN, and lFPN had decreased connections with the rFPN and the VN. Connections between the pDMN and SN also decreased. However, the connectivity between the DMN and FPN increased, possibly reflecting a compensatory mechanism.

In State 2 (Figure 3B), the SVCI group exhibited more pronounced network connection changes, with both increases and decreases observed. Decreased connectivity was noted between several networks (e.g., AN, SMN, aDMN, FPN, ECN, SN, and DAN) and the VN. Additionally, connectivity between the aDMN and lFPN with the SMN, as well as the lFPN and ECN, also weakened. Conversely, some connections increased, including those between the SMN, aDMN, and SN with the ECN, and between the SN, DAN, pDMN, and lFPN with the SMN. Other increased connections were observed between VN and DAN, SN and pDMN, aDMN and lFPN, aDMN and ECN, and within-network connections of the ECN. These changes suggest that the SVCI group attempted to reconfigure their network to cope with disruptions.

In State 3 (Figure 3C), similar to State 1, the SVCI group was predominantly characterized by reduced connectivity with limited increases. SMN, aDMN, lFPN, and DAN showed decreased connections with the VN. Connectivity between the ECN and lFPN, as well as between the SMN and lFPN, also decreased. Additionally, connections between the AN and aDMN were reduced. However, there were increases in connectivity between the DMN and FPN, pDMN and SN, and DAN and SN. Furthermore, within-network connectivity of the SMN was enhanced. These patterns suggest impaired network integration in the SVCI group, with limited compensatory mechanisms.

In State 4 (Figure 3D), the SVCI group demonstrated far fewer network connection changes compared to the healthy controls (HCs), with a predominance of decreased

connectivity. Weakened connections were observed between the SMN and AN, SMN and lFPN, VN and lFPN, and DAN and aDMN, as well as decreased within-network connectivity of the SMN. Nevertheless, some inter-network connections were strengthened, including those between the pDMN and SMN, lFPN and DAN, and AN and ECN. These findings indicate a limited capacity for network interaction and a diminishing compensatory response in this state.

Reproducibility of SVCI in static and dynamic functional network connectivity

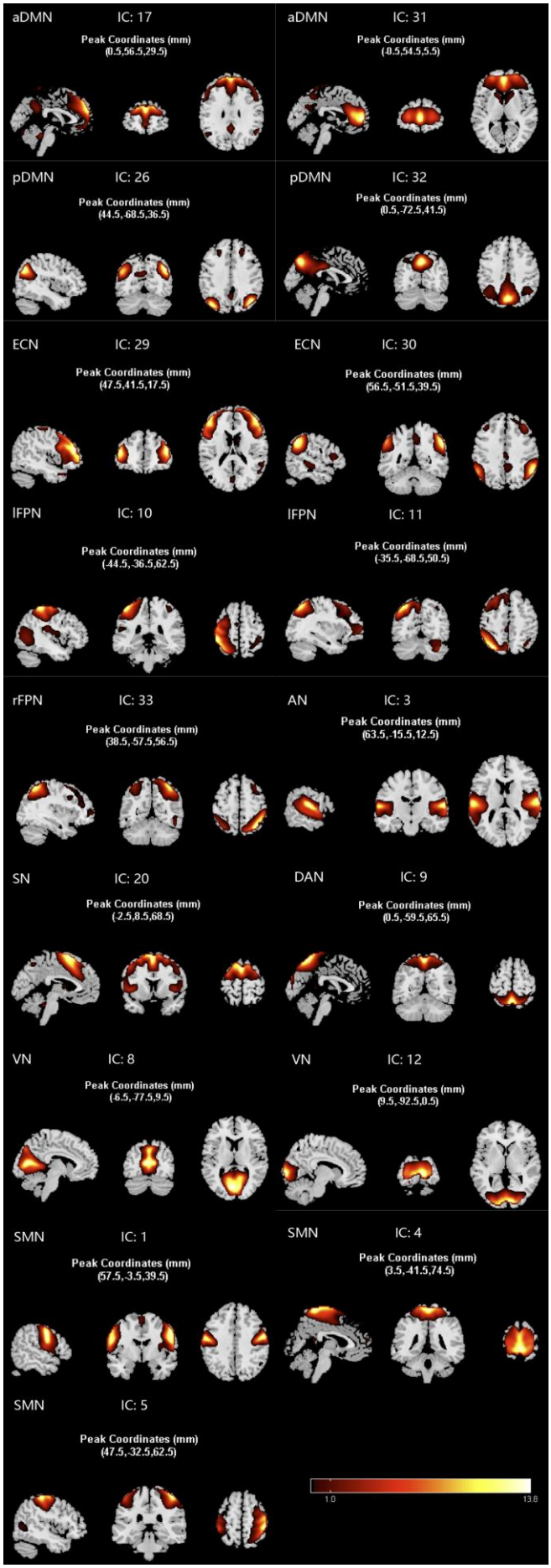
To verify the robustness of our findings with an independent dataset, we used newly included cases as the replication cohort. The replication cohort included individuals with SVCI (n = 36) and age-, sex-, and education-matched HCs (n = 36), recruited from October 2023 to November 2024.

We validated the static and dynamic functional network connectivity in SVCI in an independent replication cohort. There were no significant differences in age, sex, education, or history of hypertension, diabetes, or hyperlipidemia between the CSVD-MCI group and the HCs. However, significant differences were observed in cognitive assessment scores between the two groups (Supplemental Table 2).

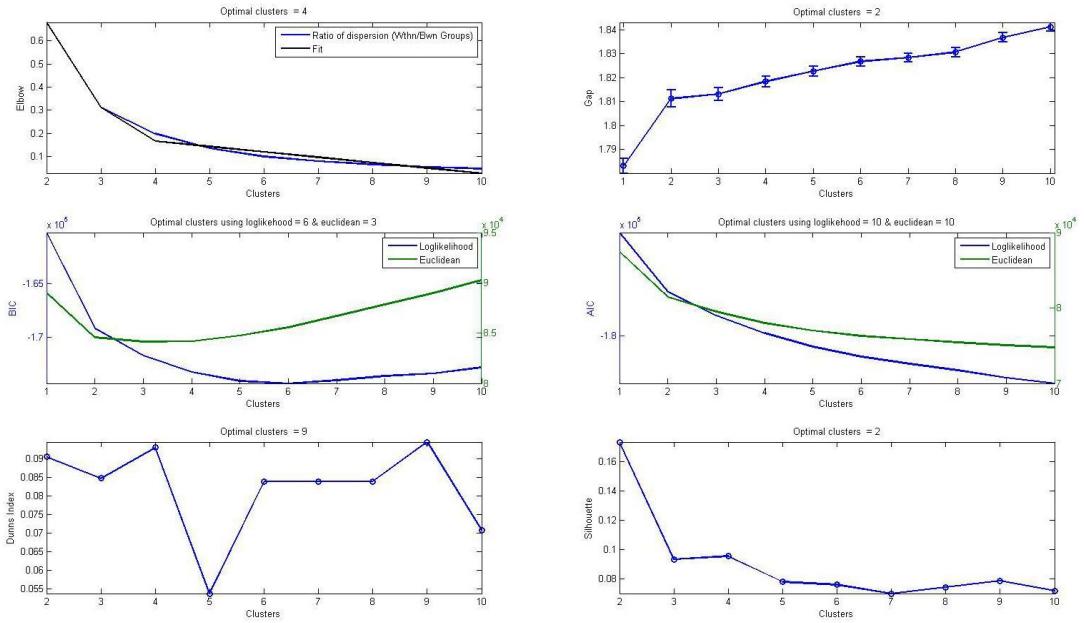
Supplemental Table 1 Demography and cognitive performance of SVCI and HCs of replication cohort

	HCs（n=83）	SVCI（n=80）	T value / χ^2 value	95% CI	*p*-value
Sex (male/ female)	13/23	19/17	1.406	[-0.091,0.371]	0.236
Age (years)	61.58±6.23	63.69±5.89	-1.461	[-4.921, 0.716]	0.149
Education (years)	11.00±8.58	9.79±3.83	0.826	[-1.733, 4.304]	0.412
Hypertension (Yes/No)	17/19	24/12	2.039	[-0.063,0.399]	0.153
Diabetes (Yes/No)	8/28	13/23	1.076	[-0.109, 0.353]	0.300
Hyperlipemia (Yes/No)	6/30	10/26	0.723	[-0.131,0.331]	0.395
MMSE	28.33±1.45	25.77±3.41	4.134	[1.335, 3.789]	< 0.001

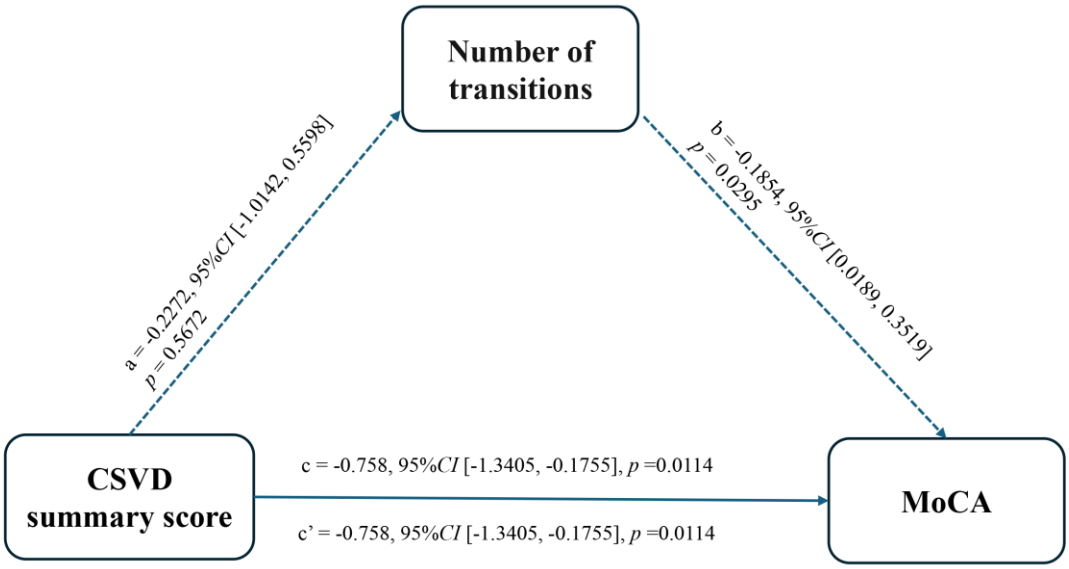
MoCA	28.30±1.44	21.03±3.78	10.347	[5.644, 8.353]	< 0.001
AVLT - IR	6.85±1.94	4.22±1.31	6.692	[1.866, 3.400]	< 0.001
AVLT - DR	7.08±2.50	2.54±2.58	7.528	[3.358, 5.723]	< 0.001
TMT - A	60.53±25.16	117.23±50.38	-6.024	[-75.307, -38.094]	<0.001
TMT - B	144.08±68.66	411.46±263.80	-5.881	[-357.602, -177.146]	<0.001
Stroop A	26.14±6.49	43.43±31.01	-3.273	[-27.78, -6.799]	0.003
Stroop B	44.22±10.97	71.08±43.30	-3.702	[-42.364, -12.791]	<0.001
Stroop C	77.78±21.80	199.26±122.78	-5.843	[-162.776, -80.183]	<0.001
DST - A	6.97±0.56	6.40±0.91	3.191	[0.218, 0.926]	0.003
DST - B	4.31±0.83	3.31±1.08	4.509	[0.558, 1.424]	<0.001
CDT	9.33±3.39	7.66±1.59	5.595	[1.084, 2.268]	0.037


aDMN IC: 17
Peak Coordinates (mm)
(0.5,56.5,29.5)
aDMN IC: 31
Peak Coordinates (mm)
(-0.5,54.5,5.5)
pDMN IC: 26
Peak Coordinates (mm)
(44.5,-68.5,36.5)
pDMN IC: 32
Peak Coordinates (mm)
(0.5,-72.5,41.5)
ECN IC: 29
Peak Coordinates (mm)
(47.5,41.5,17.5)
ECN IC: 30
Peak Coordinates (mm)
(56.5,-51.5,39.5)
lFPN IC: 10
Peak Coordinates (mm)
(-44.5,-36.5,62.5)
lFPN IC: 11
Peak Coordinates (mm)
(-35.5,-68.5,50.5)
rFPN IC: 33
Peak Coordinates (mm)
(38.5,-57.5,56.5)
AN IC: 3
Peak Coordinates (mm)
(63.5,-15.5,12.5)
SN IC: 20
Peak Coordinates (mm)
(-2.5,8.5,68.5)
DAN IC: 9
Peak Coordinates (mm)
(0.5,-59.5,65.5)
VN IC: 8
Peak Coordinates (mm)
(-6.5,-77.5,9.5)
VN IC: 12
Peak Coordinates (mm)
(9.5,-92.5,0.5)
SMN IC: 1
Peak Coordinates (mm)
(57.5,-3.5,39.5)
SMN IC: 4
Peak Coordinates (mm)
(3.5,-41.5,74.5)
SMN IC: 5
Peak Coordinates (mm)
(47.5,-32.5,62.5)
1.0
13.8

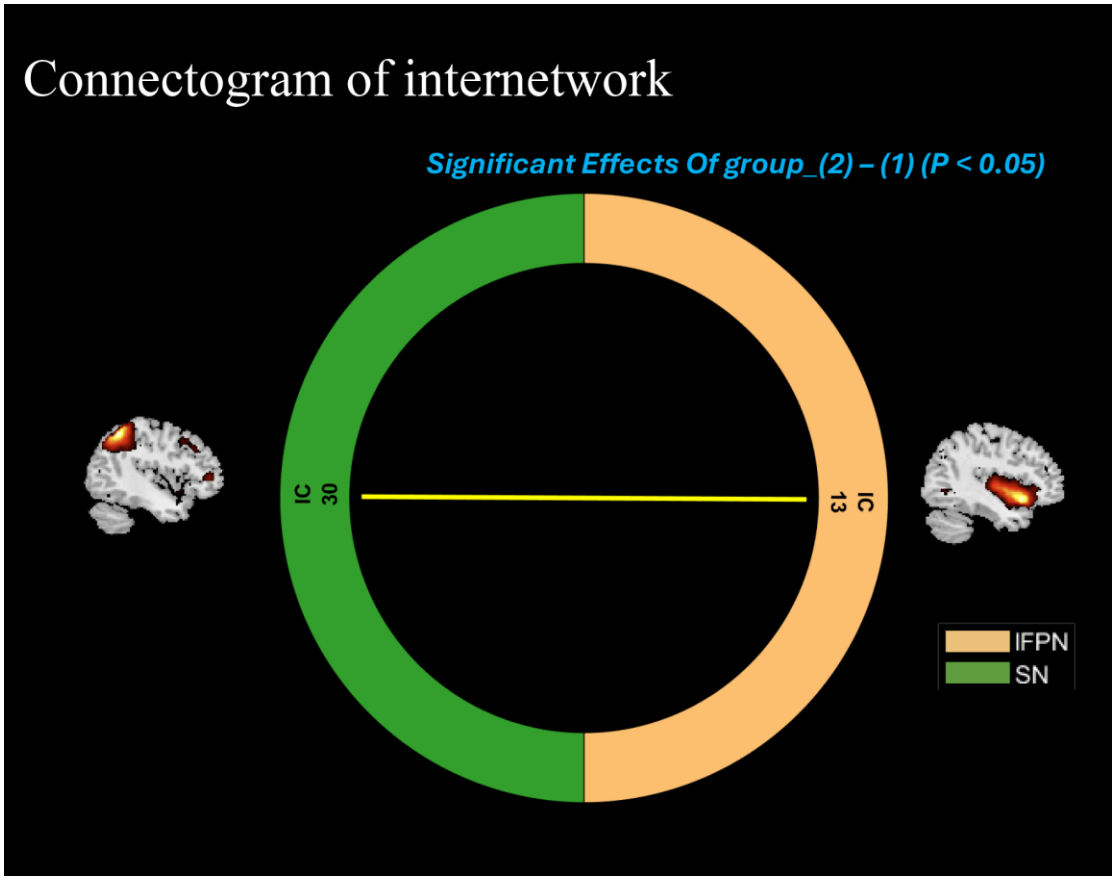
Supplementary Figure 1 Spatial maps (displayed at the three most informative slices) of 17 independent components (ICs) that were chosen as our networks of interest. aDMN, anterior default mode network; pDMN posterior default mode network; ECN executive control network; lFPN left frontoparietal network; rFPN, right frontoparietal network; AN, auditory network; SN, salience network; DAN, dorsal attention network; SMN, sensorimotor network; VN, visual network.



Supplementary Figure 2 An optimal number of k = 4 clusters were determined using the k-means clustering method.

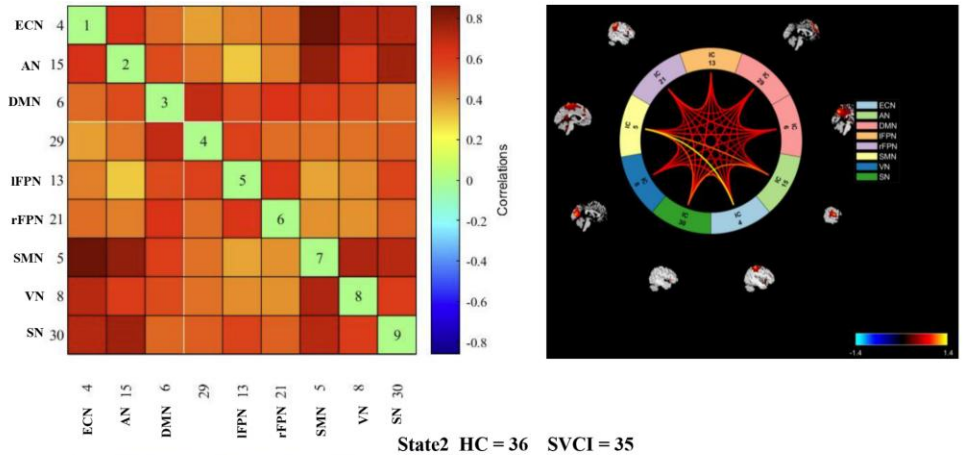


Supplementary Figure 3 The mediating role of the number of transitions between states in the relationship between CSVD summary score and MoCA score. The direct effect of the CSVD summary score on MoCA score is significant (c = -0.758, 95% CI [-1.3405, -0.1755], $p = 0.0114$). Path a (CSVD summary score → Number of transitions) is not significant (a = -0.2772, 95% CI [-1.0142, 0.5598], $p = 0.8672$), while path b (Number of transitions → MoCA score) is significant (b = 0.1854, 95% CI [0.0189, 0.3519], $p = 0.0295$). The number of transitions does not mediate the effect of CSVD summary score on MoCA score. Solid lines represent significant effects, and dashed lines represent non-significant pathways.

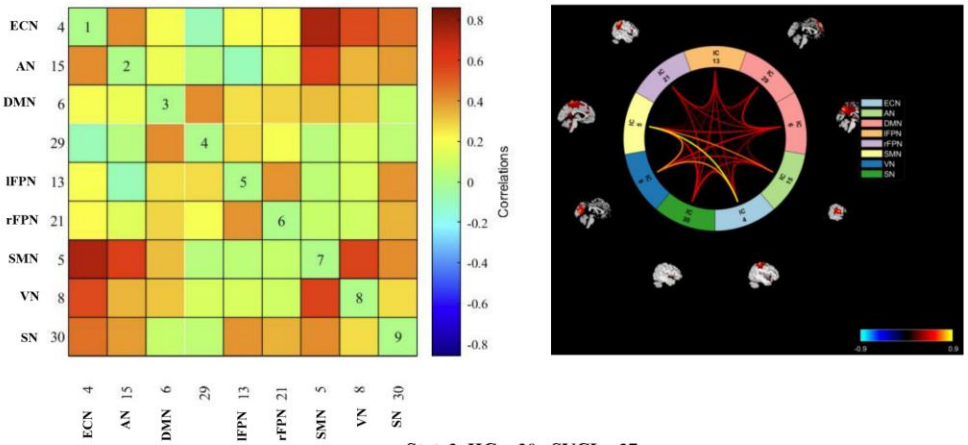


Supplementary Figure 4 Internetwork Connectivity Differences Between the SVCI Group and HC Group. Connectogram of internetwork connectivity showing reduced connectivity between the left frontoparietal network (lFPN, IC13) and the salience network (SN, IC30) in the SVCI group compared to the HC group ($P < 0.05$).

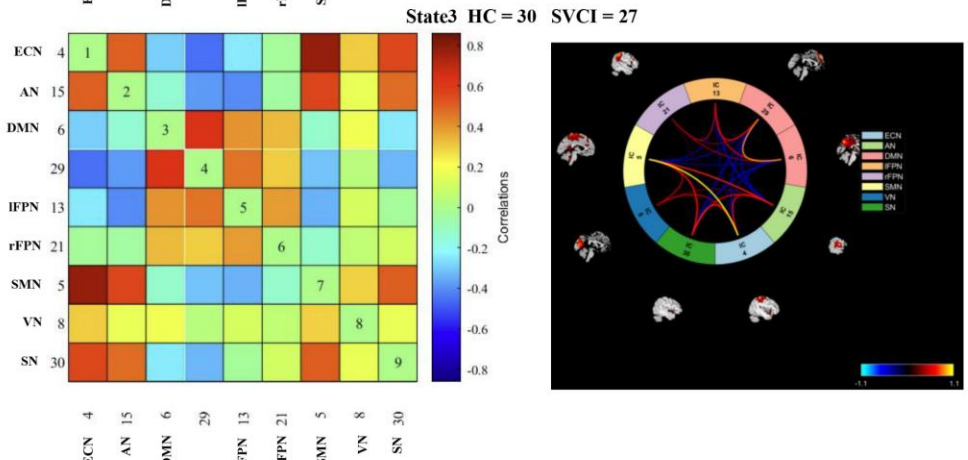
State1 HC = 22 SVCI = 16



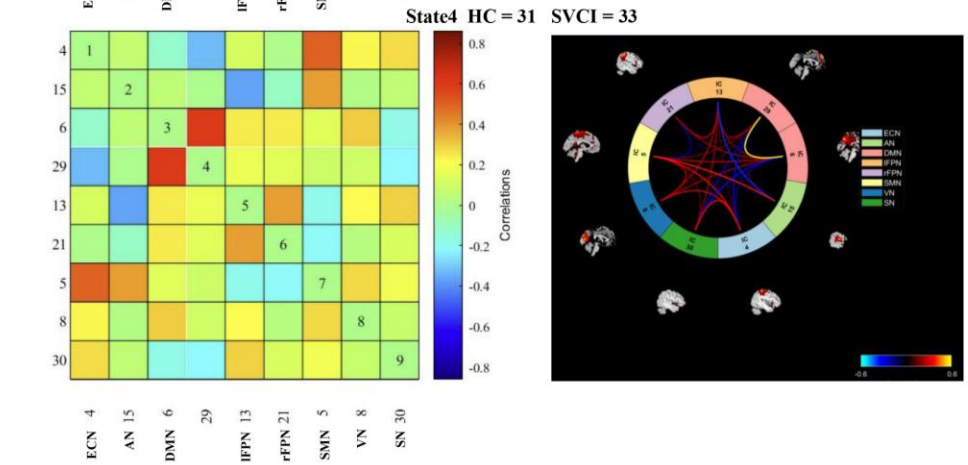
State2 HC = 36 SVCI = 35



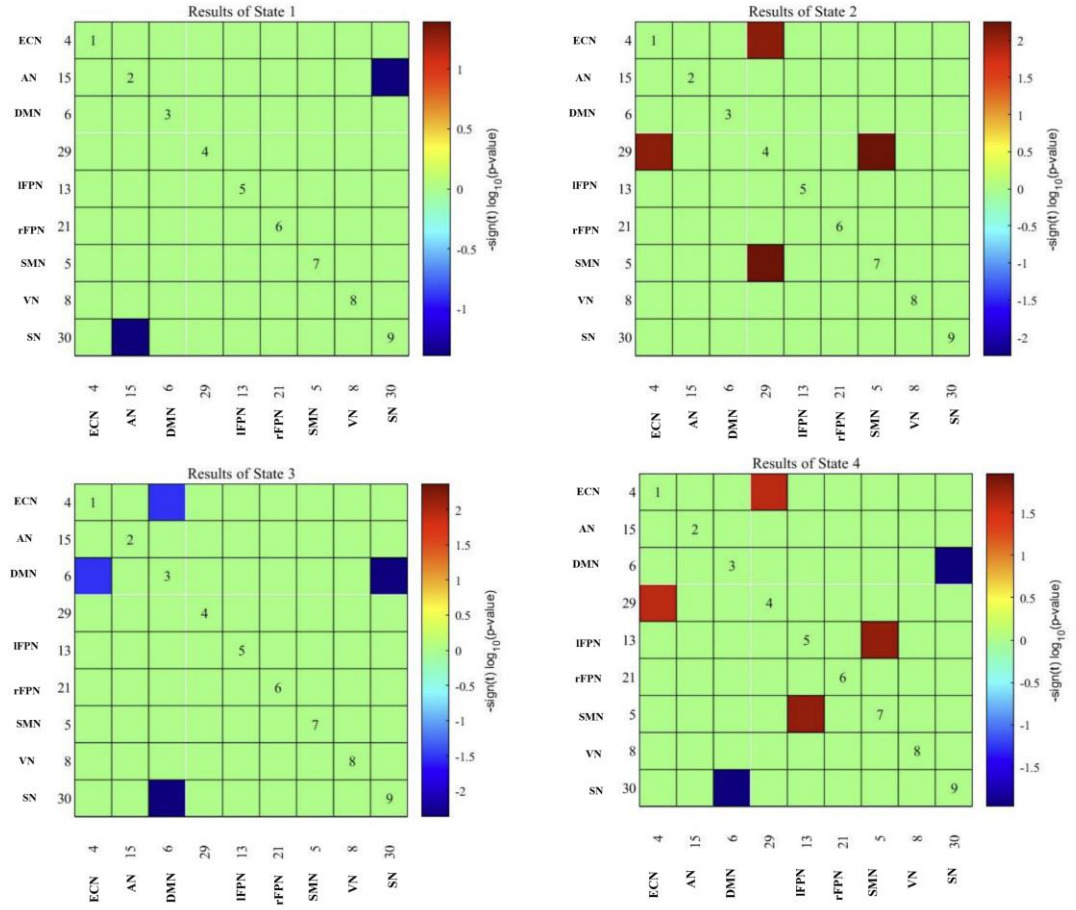
State3 HC = 30 SVCI = 27



State4 HC = 31 SVCI = 33



Supplementary Figure 5 Internetwork connectivity across four states in HC and SVCI groups. State 1 shows strong connectivity with dense network integration. State 2 displays moderate connectivity, representing a transitional state. States 3 and 4 are characterized by weak connectivity. SVCI, subcortical vascular cognitive impairment; HC, healthy control.



Supplementary Figure 6 Statistical results of network connectivity differences across four states between HC and SVCI groups. Heatmaps show significance levels (-sign(log10 *p*-value)), with red indicating SVCI > HC and blue indicating HC > SVCI. State 1 and State 3 show limited differences with localized effects. State 2 displays more widespread differences, particularly involving the DMN, lFPN, and rFPN. State 4 highlights notable differences, especially in the SN and FPN.