

Supplementary Materials

Tables

Table E1. Summary of the results for within-group ROI/Seed-based analysis using three other brain parcellations

	Control group			mTBI group			Pearson Correlation	
Brain parcellation	Positively connected*	Negatively connected*	Total	Positively connected*	Negatively connected*	Total	Coefficient	<i>p</i>
Seven functional networks ¹	9	5	14	10	5	15	0.97	< 2.5e-13
264 functional seeds ²	5502	1629	7131	6753	2624	9377	0.88	0
Standard anatomical atlas ³	3041	900	3941	3517	1200	4717	0.96	0

¹In the manuscript, this parcellation is introduced as one of the “standard functional networks”. This parcellation consists of 7 ROIs relating to 7 functional networks, including default mode, dorsal attention, frontoparietal, limbic, somatomotor, ventral attention, and visual. The location of these ROIs is depicted in Figure E2.b. Please refer to³⁰ for more details.

²A seed-based atlas is mentioned as the third parcellation in the main body. It includes 264 MNI locations which have been categorized into 14 functional networks, including Visual, Ventral attention, Uncertain, Subcortical, Sensory/somatomotor Mouth, Sensory/somatomotor Hand, Salience, Memory retrieval, Frontoparietal Task Control, Dorsal attention, Default mode, Cingulo-opercular Task Control, Cerebellar, and Auditory. The location of the seeds is depicted in Figure E2.c. Please refer to³¹ for more details.

³As explained in the manuscript, this is a standard anatomical atlas provided in CONN toolbox. This atlas consists of 132 ROIs, which have been clustered into 22 functional networks by CONN-toolbox’s clustering and ordering procedure. The networks include Visual.Secondary, Visual.Primary, Thalamus, Superior temporal gyrus, Superior lateral occipital cortex, Salience, Paracingulate gyrus, Motor, Limbic/aPaHC, Language, Inferior temporal gyrus, Frontoparietal/Language, Frontoparietal, Dorsal attention, Default mode (posterior), Default mode (lateral), Default mode (anterior), Cerebellum/pPaHC, Cerebellum, Cerebellar Crus, Auditory, and Anterior supramarginal gyrus. This parcellation is depicted in Figure E2.d. Please refer to CONN-toolbox (www.nitrc.org/projects/conn, version 21.a) for more details.

*Whether a pair of ROIs are connected or not was determined by the One-sample t-test or Wilcoxon Signed-rank test, depending on whether normality assumption (tested by Shapiro-Wilk test) holds for both ROIs or not. All numbers were extracted after correcting for multiple comparisons using the FDR method ($p_{corrected} < 0.05$, $\alpha = 5\%$).

Note: Please look at Figure E4-6 for relevant connectivity matrices.

Table E2. Summary of the results for significant connections across groups comparison according to ROI/Seed-based analysis using three other brain parcellations

<i>Brain parcellation</i> *	Connected** only in the Control group	Connected** only in the mTBI group	Connected** in both Group	Total tested*** connections
Seven functional networks	1	2	13	21
264 functional seeds	1803	4049	5328	34716
Standard anatomical atlas	495	1271	3446	8646

*Please read Table E1 caption for details of the parcellations used here.

** Whether a pair of ROIs are connected was determined by the One-sample t-test or Wilcoxon Signed-rank test, depending on whether normality assumption (tested by Shapiro-Wilk test) holds for both ROIs or not. All numbers were extracted after correcting for multiple comparisons using the FDR method ($p_{corrected} < 0.05, \alpha = 5\%$).

***This number indicates the number of hypothesis tests conducted for each parcellation. ($\frac{\#ROI \times (\#ROIs - 1)}{2}$)

Note: Please look at Figure E4-6 for relevant connectivity matrices.

Table E3. Summary of the results for group connectivity amplitude comparison according to ROI/Seed-based analysis using three other brain parcellations

	Prior to multiple comparisons**			After applying multiple comparisons**		
Brain parcellation*	Hyper. ***	Hypo. ***	Total	Hyper. ***	Hypo. ***	Total
Seven functional networks	0	0	0	0	0	0
264 functional seeds	791	814	1605	0	0	0
Standard anatomical atlas	259	193	452	0	0	0

*Please read Table E1 caption for details of the parcellations used here.

**The p -value threshold is 0.05, and FDR's α is set at 5%.

***Hyper. = Hyperconnectivity means the average connectivity amplitude (Fisher's Z-transformed of Pearson's correlation coefficient) in the mTBI group is higher than in the control group (mTBI - Control > 0), and Hypo. = hypoconnectivity is the inverse (mTBI - Control < 0). Group-level comparisons were conducted by Welch's t-test or Mann-Whitney U test, depending on whether the normality assumption (tested by the Shapiro-Wilk test) holds for tested pairs of ROIs.

Note: Please look at Figure E4-6 for relevant connectivity matrices.

Table E4. Full name of the ROIs for the standard functional parcellation (available in CONN toolbox) used in the main body

<i>Index</i>	Network	Abbreviation	Full name
1	Visual	<i>Occipital</i>	Occipital
2	Visual	<i>Medial</i>	Medial
3	Visual	<i>Lateral (R)</i>	Right lateral
4	Visual	<i>Lateral (L)</i>	Left lateral
5	Sensorimotor	<i>Superior</i>	Superior
6	Sensorimotor	<i>Lateral (R)</i>	Right lateral
7	Sensorimotor	<i>Lateral (L)</i>	Left lateral
8	Salience	<i>SMG (R)</i>	Right supramarginal gyrus
9	Salience	<i>SMG (L)</i>	Left supramarginal gyrus
10	Salience	<i>RPFC (R)</i>	Right rostral prefrontal cortex
11	Salience	<i>RPFC (L)</i>	Left rostral prefrontal cortex
12	Salience	<i>AInsula (R)</i>	Right anterior insula
13	Salience	<i>AInsula (L)</i>	Left anterior insula
14	Salience	<i>ACC</i>	Anterior cingulate cortex
15	Language	<i>pSTG (R)</i>	Right posterior superior temporal gyrus
16	Language	<i>pSTG (L)</i>	Left posterior superior temporal gyrus
17	Language	<i>IFG (R)</i>	Right inferior frontal gyrus
18	Language	<i>IFG (L)</i>	Left inferior frontal gyrus
19	Frontoparietal	<i>PPC (R)</i>	Right posterior parietal cortex
20	Frontoparietal	<i>PPC (L)</i>	Left posterior parietal cortex
21	Frontoparietal	<i>LPFC (R)</i>	Right lateral prefrontal cortex
22	Frontoparietal	<i>LPFC (L)</i>	Left lateral prefrontal cortex
23	Dorsal attention	<i>IPS (R)</i>	Right intraparietal sulcus
24	Dorsal attention	<i>IPS (L)</i>	Left intraparietal sulcus
25	Dorsal attention	<i>FEF (R)</i>	Right frontal eye fields
26	Dorsal attention	<i>FEF (L)</i>	Left frontal eye fields
27	Default mode	<i>PCC</i>	Posterior cingulate cortex
28	Default mode	<i>MPFC</i>	Medial prefrontal cortex
29	Default mode	<i>LP (R)</i>	Right lateral parietal
30	Default mode	<i>LP (L)</i>	Left lateral parietal
31	Cerebellar	<i>Posterior</i>	Posterior
32	Cerebellar	<i>Anterior</i>	Anterior

Note: The results of this parcellation are presented in the main manuscript. This table spells out the full name of the ROIs for that parcellation. Please refer to Figure E2 for the location of the ROIs in the MNI space, and check CONN toolbox (www.nitrc.org/projects/conn, version 21.a) for more details.

Figures

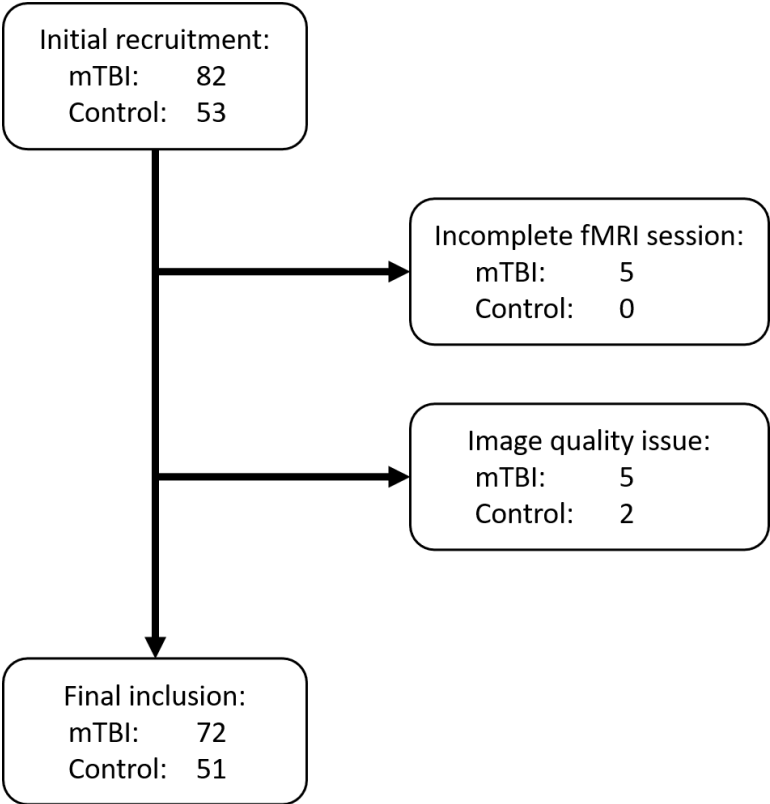


Figure E1. Flowchart of participant selection.

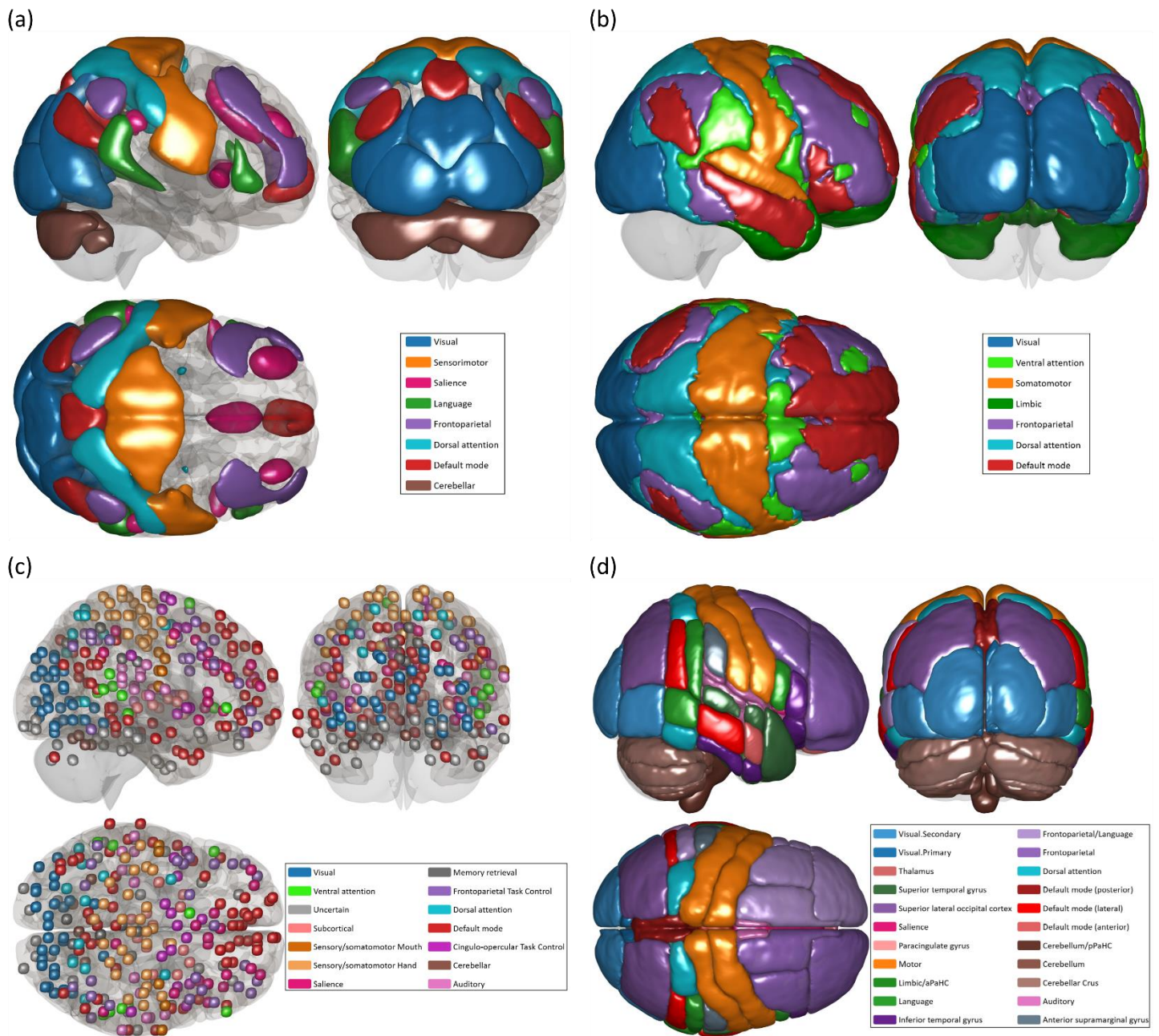


Figure E2. Four brain parcellations used in ROI/Seed-based analysis; **(a)** First standard functional parcellation, which is available in CONN toolbox (www.nitrc.org/projects/conn, version 21.a); **(b)** Seven functional networks (Second standard functional parcellation)³⁰; **(c)** 264 functional seeds³¹; **(d)** Standard anatomical atlas, which is available in CONN toolbox (www.nitrc.org/projects/conn, version 21.a).

Note: Please refer to Table E1 caption for more details of the (b), (c), and (d). The manuscript and Table E1's caption mentioned details and references for all parcellations. ROIs of parcellation (a) are listed in Table E4.

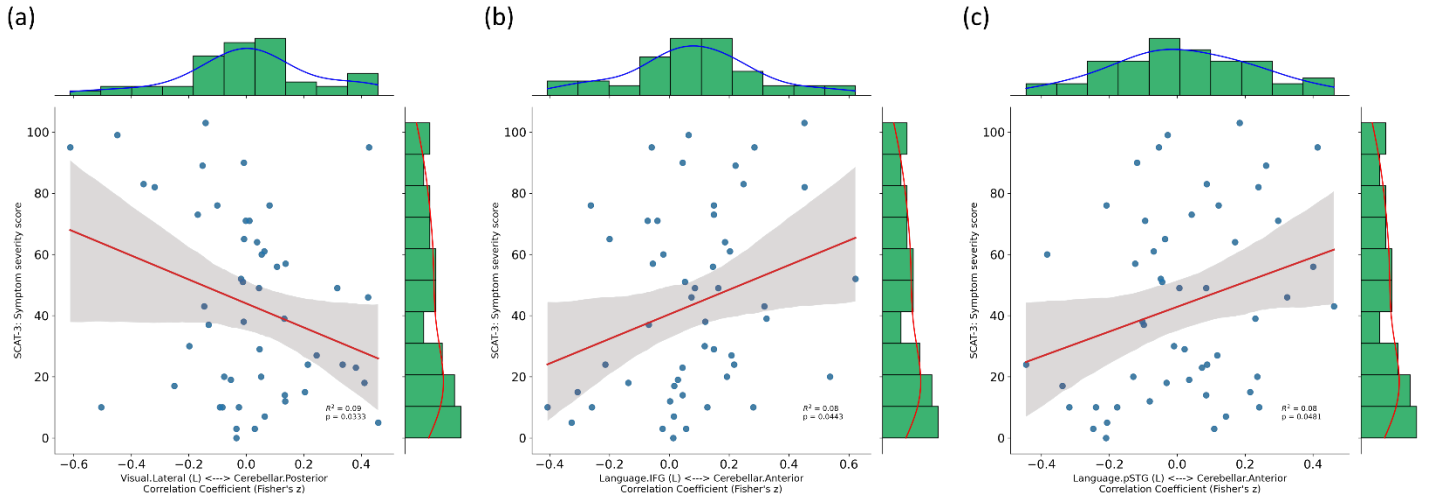


Figure E3. Regression analysis between significantly different connections prior to multiple comparison ($p_{\text{uncorrected}} < 0.05$) and SCAT-3 symptom severity score. These three connections are the only ones which revealed significant association to symptom severity scores of the 39 discovered connections ($p < 0.05$). The y-axis shows symptom severity and x-axis is Fisher's z transformed of correlation coefficient for **(a)** Visual left lateral and Cerebellar posterior, **(b)** Cerebellar anterior and Language left inferior frontal gyrus, and **(c)** Language posterior superior temporal gyrus connections among the 51 mTBI subjects who completed the SCAT-3 questionnaire.

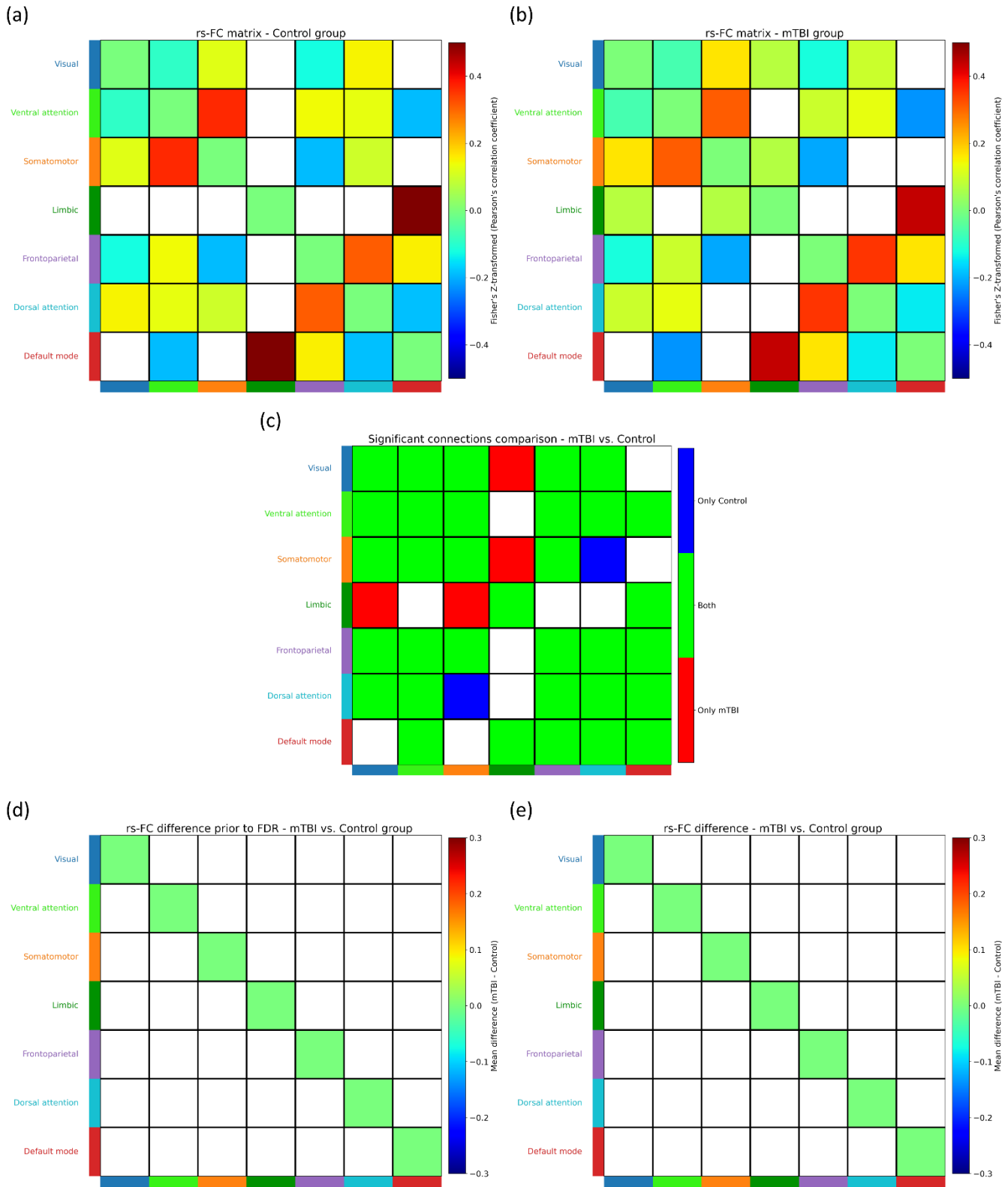


Figure E4. ROI-based analysis results using second standard functional parcellation (Please refer to Table E1 caption for details and Figure E2.b for the spatial map of this parcellation in MNI space). **(a)** and **(b)** show the connectivity matrix for control and mTBI groups. The color for each pair of ROIs reflects statistically significant connectivity after FDR correction ($p_{corrected} < 0.05$) measured by average Fisher's Z-transformed of Pearson's correlation coefficient. **(c)** Matrix of significant connections, comparing (a) and (b): red=significant connections unique to the mTBI group, blue=significant connections unique to the control group, green=significant in both mTBI and control groups. **(d)** Matrix of mean difference (mTBI - Control) for the connections that satisfy $p_{uncorrected} < 0.05$ using Welch's t-test comparing mTBI to controls. **(e)** After multiple comparisons correction (FDR) to account for the number of connections examined, no difference remains significant. Note: Diagonal values (self-connection) are set to zero.

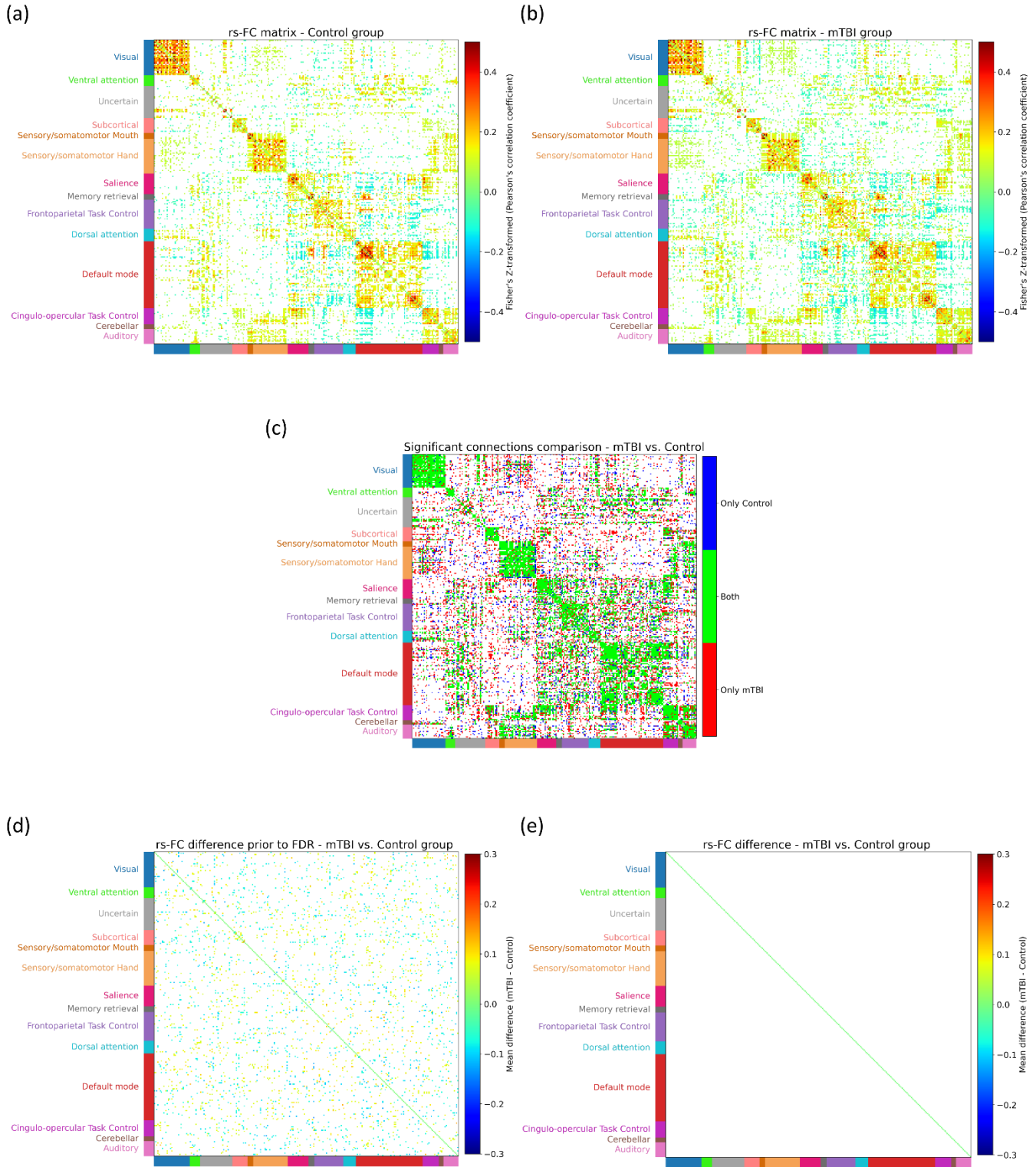


Figure E5. Seed-based analysis results using 264 functional seeds parcellation (Please refer to Table E1 caption for details and Figure E2.c for the spatial map of this parcellation in MNI space). (a) and (b) show the connectivity matrix for control and mTBI groups. The color for each pair of ROIs reflects statistically significant connectivity after FDR correction ($p_{corrected} < 0.05$) measured by average Fisher's Z-transformed of Pearson's correlation coefficient. (c) Matrix of significant connections, comparing (a) and (b): red=significant connections unique to the mTBI group, blue=significant connections unique to the control group, green=significant in both mTBI and control groups. (d) Matrix of mean difference (mTBI - Control) for the connections that satisfy $p_{uncorrected} < 0.05$ using Welch's t-test comparing mTBI to controls. (e) After multiple comparisons correction (FDR) to account for the number of connections examined, no difference remains significant. Note: Diagonal values (self-connection) are set to zero.

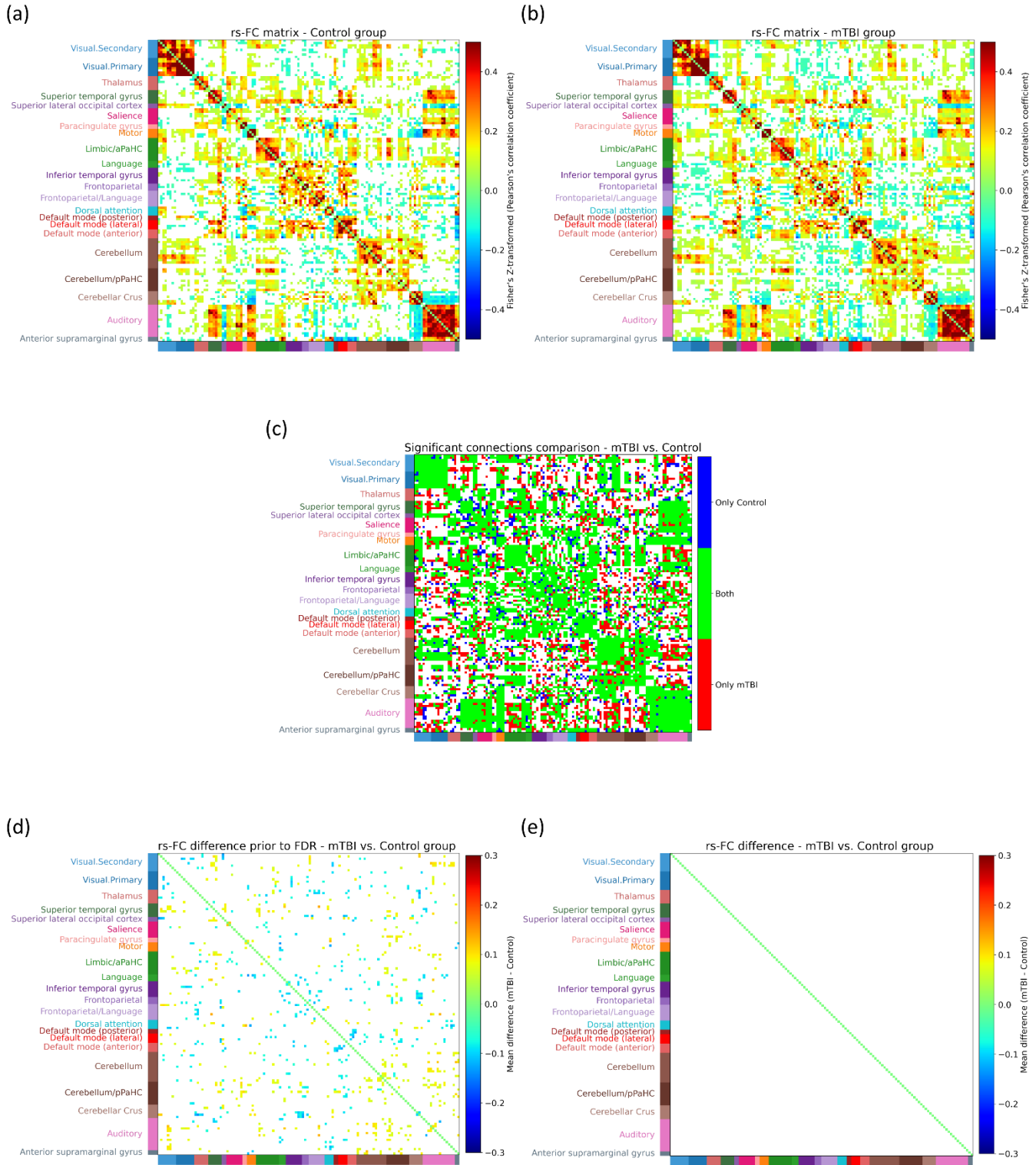


Figure E6. ROI-based analysis results using standard anatomical parcellation (Please refer to Table E1 caption for details and Figure E2.d for the spatial map of this parcellation in MNI space). **(a)** and **(b)** show the connectivity matrix for control and mTBI groups. The color for each pair of ROIs reflects statistically significant connectivity after FDR correction ($p_{corrected} < 0.05$) measured by average Fisher's Z-transformed of Pearson's correlation coefficient. **(c)** Matrix of significant connections, comparing (a) and (b): red=significant connections unique to the mTBI group, blue=significant connections unique to the control group, green=significant in both mTBI and control groups. **(d)** Matrix of mean difference (mTBI - Control) for the connections that satisfy $p_{uncorrected} < 0.05$ using Welch's t-test comparing mTBI to controls. **(e)** After multiple comparisons correction (FDR) to account for the number of connections examined, no difference remains significant. Note: Diagonal values (self-connection) are set to zero.

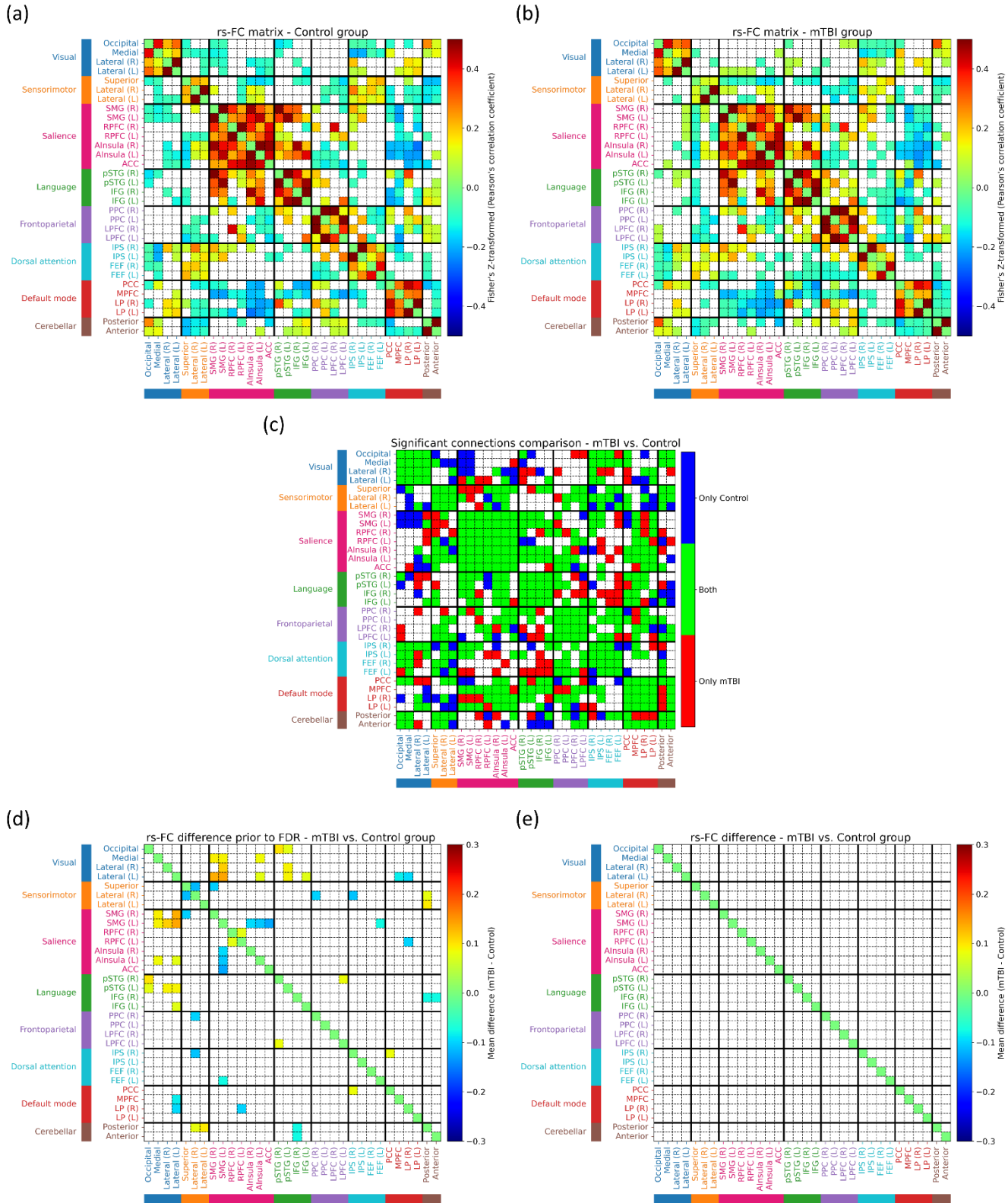


Figure E7. ROI-based analysis results using unsmoothed data and CONN toolbox standard functional parcellation. **(a)** and **(b)** show the connectivity matrix for control and mTBI groups. The color for each pair of ROIs reflects statistically significant connectivity after FDR correction ($p_{\text{corrected}} < 0.05$) measured by average Fisher's Z-transformed of Pearson's correlation coefficient. **(c)** Matrix of significant connections, comparing **(a)** and **(b)**: red=significant connections unique to the mTBI group, blue=significant connections unique to the control group, green=significant in both mTBI and control groups. **(d)** Matrix of mean difference (mTBI - Control) for the connections that satisfy $p_{\text{uncorrected}} < 0.05$ using Welch's t-test comparing mTBI to controls. Highlighted connections involve all networks and nearly all ROIs, and the magnitude of differences is small. **(e)** After multiple comparisons correction (FDR) to account for the number of connections examined, no difference remains significant. Note: Diagonal values (self-connection) are set to zero.

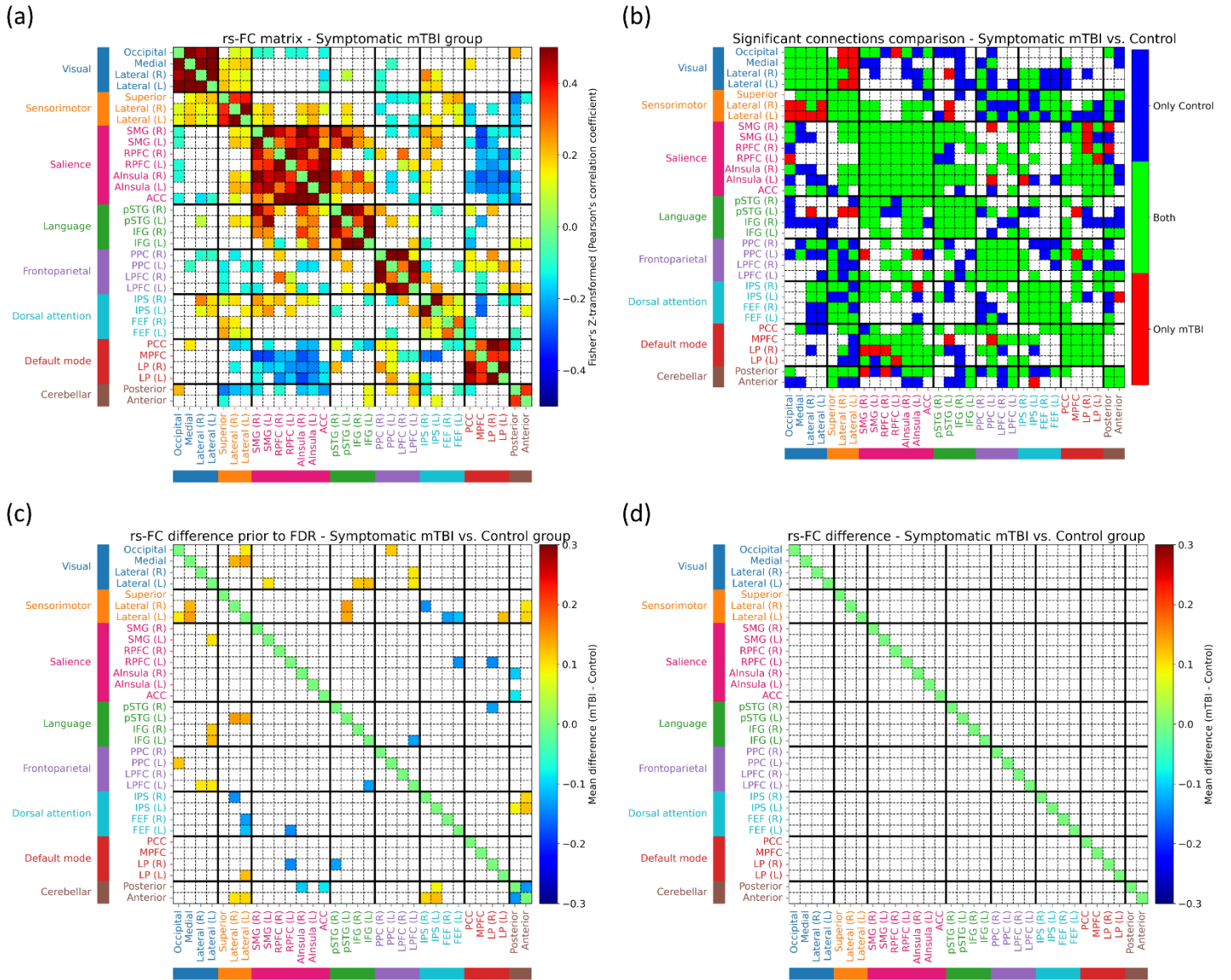


Figure E8. ROI-based analysis results using CONN toolbox standard functional parcellation using only 26 symptomatic mTBI participants. **(a)** shows the connectivity matrix for the symptomatic mTBI subset. There are 142 positively and 74 negatively connected ROIs. Although the total number of connected ROIs decreases, mainly in anti-correlated ROIs, in comparison to the connectivity matrix for all mTBI participants, it is not clear that this reduction is due to more disconnected ROIs in more severe mTBI cases or lower statistical power as a consequence of lower number of participating subjects. **(b)** Matrix of significant connections, comparing Figure 1.a (control group's connectivity matrix) and (a): red=significant connections unique to the symptomatic mTBI sub-group, blue=significant connections unique to the control group, green=significant in both symptomatic mTBI and control groups. **(c)** Matrix of mean difference (symptomatic mTBI - Control) for the connections that satisfy $p_{\text{uncorrected}} < 0.05$ using Welch's t-test comparing symptomatic mTBI to controls. Clearly, the highlighted connections differ from what has been illustrated in Figure 1.d with 17 hyper-connectivity and 10 hypo-connectivity. As an unexpected observation, total number of different connections is less than different connections while comparing total mTBI participants and control group. **(d)** Similar to the comparison between all mTBI participants and control group, none of the different connections survived whole-brain multiple comparison (FDR).

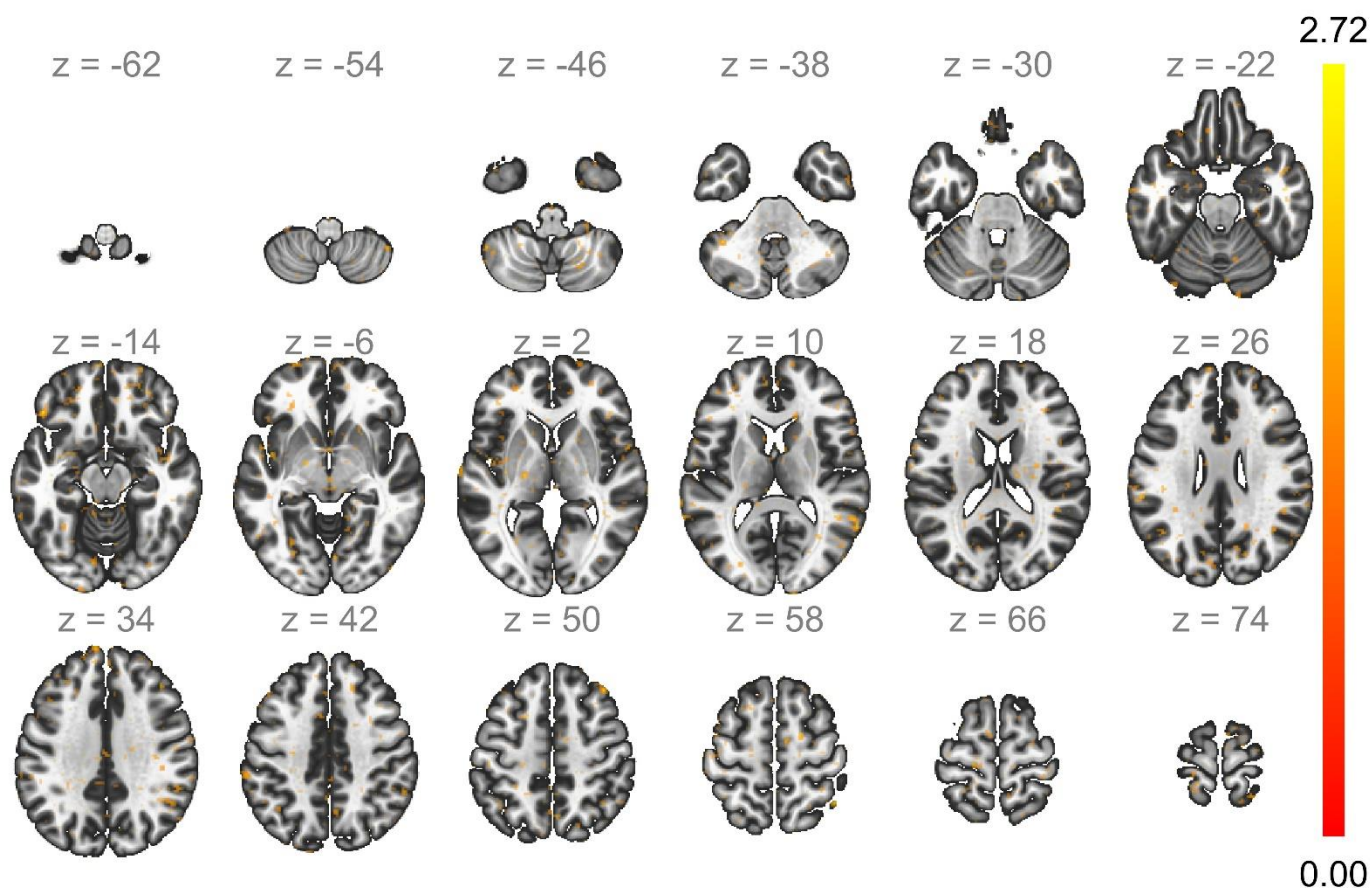


Figure E9. ROI-to-voxel result using unsmoothed data. Highlighted voxels are the ones with $p_{\text{uncorrected}} < 0.05$ based on Any effect F-test statistics. All 32 ROIs from CONN's standard functional parcellation are included and both source (the ROI average BOLD signal) and the voxel's BOLD signal were extracted from preprocessed fMRIs without spatial smoothing step. As expected, due to lower signal-to-noise ratio, differences are even more scattered and sparse which did not survive FDR and TFCE.

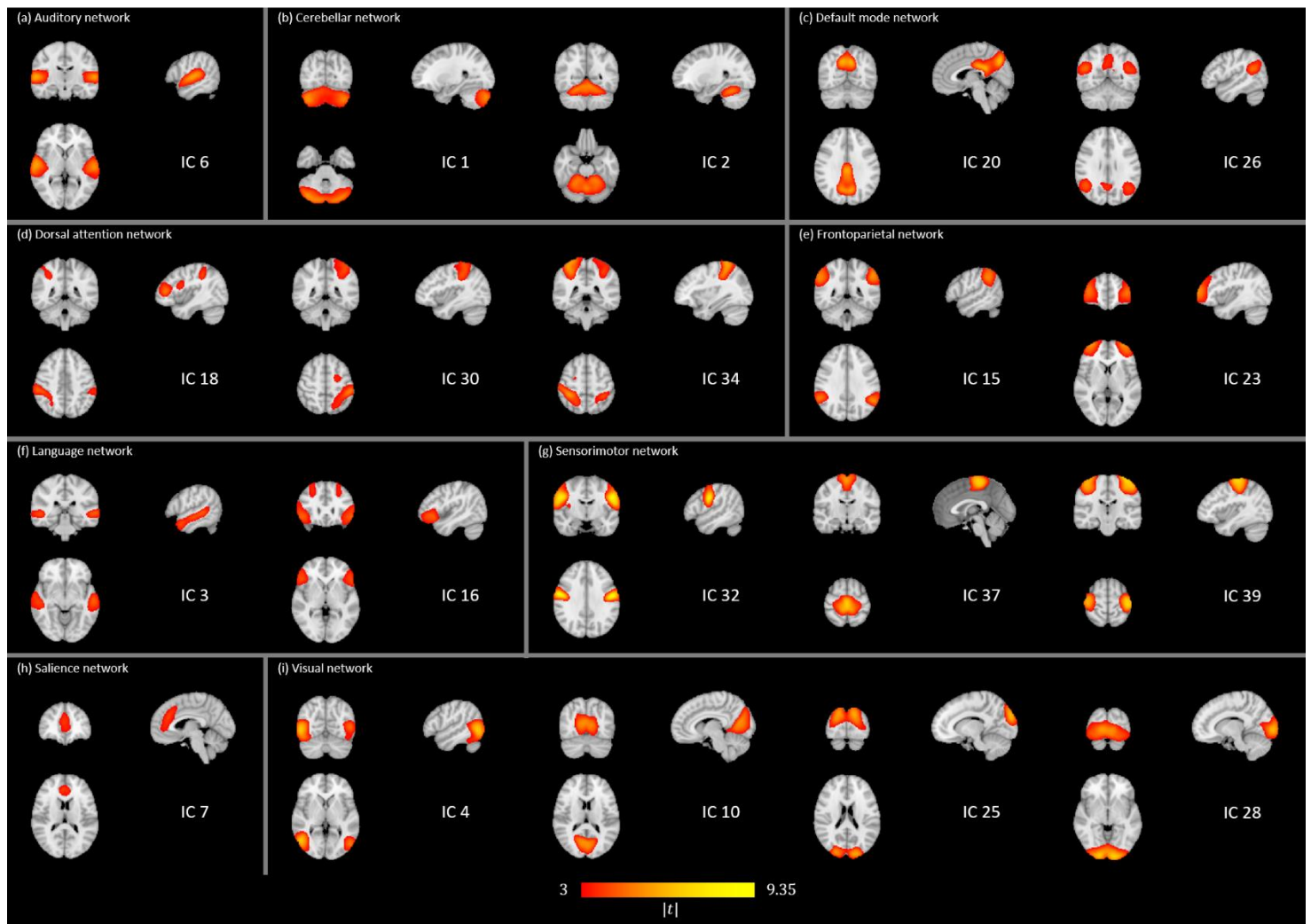


Figure E10. The spatial location of 20 identified Spatial-GICs. A threshold of $3 < |t| < 9.35$ is applied on contrasts for better visualization. (a) to (i) illustrates the 9 IFCNs identified using the maximum dice coefficient technique available in the CONN toolbox. The reference was set as the standard functional parcellation used in the main manuscript (Figure E1.a).