Supplementary Materials

Methods and Materials

Participants

The following inclusion criteria applied for all participants: (i) age ≥ 18 years; (ii) right-handed; (iii) physical experience of the earthquake; (iv) personal witness of building collapse, death or serious injury; (v) no known PTSD prior to the earthquake; and (vi) no psychologic interventions or psychopharmacologic treatment before MRI. The subjects were selected through a large-scale survey, in which 4200 earthquake survivors were screened and 415 eligible patients were found. Exclusion criteria were: age < 18 years (n=24); left-handed (n=16); reported serious traumatic events before or after the earthquake, current and lifetime psychiatric comorbidities such as depression and anxiety disorders, or alcohol/drug/other substance abuse/dependence (n=134); traumatic brain injury (n=12); neurological or cardiovascular conditions (n=58); any contraindication to MRI (n=81); brain lesions identified at MRI examination (n=5); unavailable data (n=5); excessive head motion (translation > 2.0 mm, rotation > 2°) (n=9).

Modular organization of static functional networks

To construct static functional networks, the mean time course was first computed by averaging the blood oxygen level–dependent signals over all the voxels within each region in Brainnetome 246 Atlas. The resultant mean time courses were then correlated (Pearson correlation) with each other to generate a 246 × 246 static functional matrix for each participant. Negative correlations were excluded (i.e. set to zero) due to their ambiguous interpretation [1]. The modular characteristic differences (intra- and inter-modular connectivity) were calculated in Brainnetome 246 Atlas categorized into 8 networks according to Yeo's 7 networks parcellation [2] plus a subcortical network. Intra-modular connectivity of particular modules was defined as the average of all connectional weights within the module to represent the significance of the module within the brain network. Inter-modular connectivity assesses the connection between two modules, computed as the average of connectional weights between the modules.

Mediation analyses

Mediation analysis was used to evaluate the indirect effect of network switching rate in frontal areas on CAPS score via network switching rate in temporal areas as a causal mediator. The switching rate in frontal areas was considered the independent variable, switching rate in temporal areas were the mediator variable, and CAPS scores were the dependent variable. This used the SPSS macro PROCESS, incorporating a bootstrapping approach [3].

Results

Correlations between switching rate and symptom severity in each PTSD and TENP

In PTSD, there was a significant positive correlation between CAPS score and the switching rates of the fronto-parietal network (r = 0.329, P = 0.008) and default mode network (r = 0.283, P = 0.023); in TENP, there was a significant negative correlation between CAPS score and the switching rates of the limbic network (r = -0.333, P = 0.016), and left orbital gyrus (r = -0.374, P = 0.006) (**Figure S1**).

Modular organization of static functional networks

Relative to TENP controls, PTSD patients only demonstrated increased inter-modular connectivity between default mode and visual networks ($P = 0.018$, **Table S2**). We found that PTSD have stronger static functional connectivity, but reduced temporal variability of connectivity. In line with earlier work [4], the brains of PTSD are characterized by elevated static connectivity, coupled with decreased temporal variability of connectivity, leading to a situation wherein hyper-connected brain regions do not disengage effectively. Brain regions that comprise a particular network and share common functionality might show lower dynamic connectivity because they are in synchronization. Collectively, static and dynamic functional networks capture different aspects of inter-region communication and thus could provide complementary information.

Mediation analyses

The network switching rate in inferior frontal gyrus (indirect effect = 22.918, 95% CI = [-1.116, 57.521], $p > 0.05$), orbital gyrus (indirect effect = 27.044, 95% CI = [-7.482, 60.429], $p > 0.05$), or cingulate cortex (indirect effect = 9.086, 95% CI = [-17.950, 59.618], $p > 0.05$) did not affect symptom severity via the network switching rate in temporal areas.

Table S1. Network switching rate differences between PTSD and TENP with head motion parameters as covariate, with two alternate choices of γ and ω, and an alternate choice of window length and size.

Network switching rate	*P (T)* value					
	FD as covariate	γ = 0.9 ω = 0.5	γ = 0.9 ω = 0.75	Window length = 30 × TR; size = 1 × TR	FWHM 6mm	Permutation test
Global	**0.002** (3.232)	**0.006** (2.790)	**0.001** (3.350)	<**0.001** (4.086)	<**0.001** (3.387)	**0.001**
Subnetwork						
Visual network	0.068 (1.842)	**0.016** (2.432)	**0.010** (2.597)	<**0.001** (3.428)	**0.002** (3.148)	**0.035**
Somatomotor network	**0.020** (2.347)	**0.014** (2.500)	**0.010** (2.624)	**0.022** (2.314)	**0.003** (3.059)	**0.014**
Dorsal attention network	0.079 (1.769)	**0.008** (2.688)	**0.003** (3.075)	**0.005** (2.876)	**0.001** (3.406)	**0.033**
Ventral attention network	0.028 (2.215)	0.138 (1.491)	0.035 (2.125)	0.075 (1.796)	0.147 (1.460)	**0.024**
Limbic network	**0.005** (2.826)	**0.014** (2.487)	**0.002** (3.146)	**0.001** (3.310)	**0.020** (2.352)	**0.002**
Frontoparietal network	**0.002** (3.109)	**0.032** (2.164)	**0.003** (3.004)	**0.003** (3.021)	**0.010** (2.623)	**0.002**
Default mode network	**0.002** (3.082)	**0.003** (2.972)	< **0.001** (3.620)	<**0.001** (4.615)	**0.003** (3.003)	**0.001**
Subcortical network	0.252 (1.151)	0.062 (1.883)	**0.007** (2.732)	0.145 (1.467)	0.309 (1.022)	0.140
Nodal						
IFG_L (Label ID 31)	<**0.001** (3.822)	0.039 (2.081)	0.033 (2.153)	0.021 (2.321)	0.023 (2.294)	<**0.001**
OrG_L (Label ID 47)	<**0.001** (4.262)	0.034 (2.139)	**0.003** (3.005)	0.045 (2.019)	0.057 (1.922)	<**0.001**
ITG_L (Label ID 99)	<**0.001** (3.687)	0.057 (1.918)	**0.002** (3.113)	**0.002** (3.101)	0.013 (2.515)	<**0.001**
CG_R (Label ID 178)	<**0.001** (3.839)	**0.001** (3.446)	< **0.001** (4.266)	**0.002** (3.049)	0.069 (1.833)	<**0.001**

Abbreviations: PTSD, post-traumatic stress disorder; TENP, trauma-exposed non PTSD; FD, framewise-displacement; TR, repetition time; FWHM, full-width at half-maximum; IFG, inferior frontal gyrus; OrG, orbital gyrus; ITG, inferior temporal gyrus; CG, cingulate gyrus; L, left; R, right. Nodal regions were defined according to Brainnetome 246 Atlas.

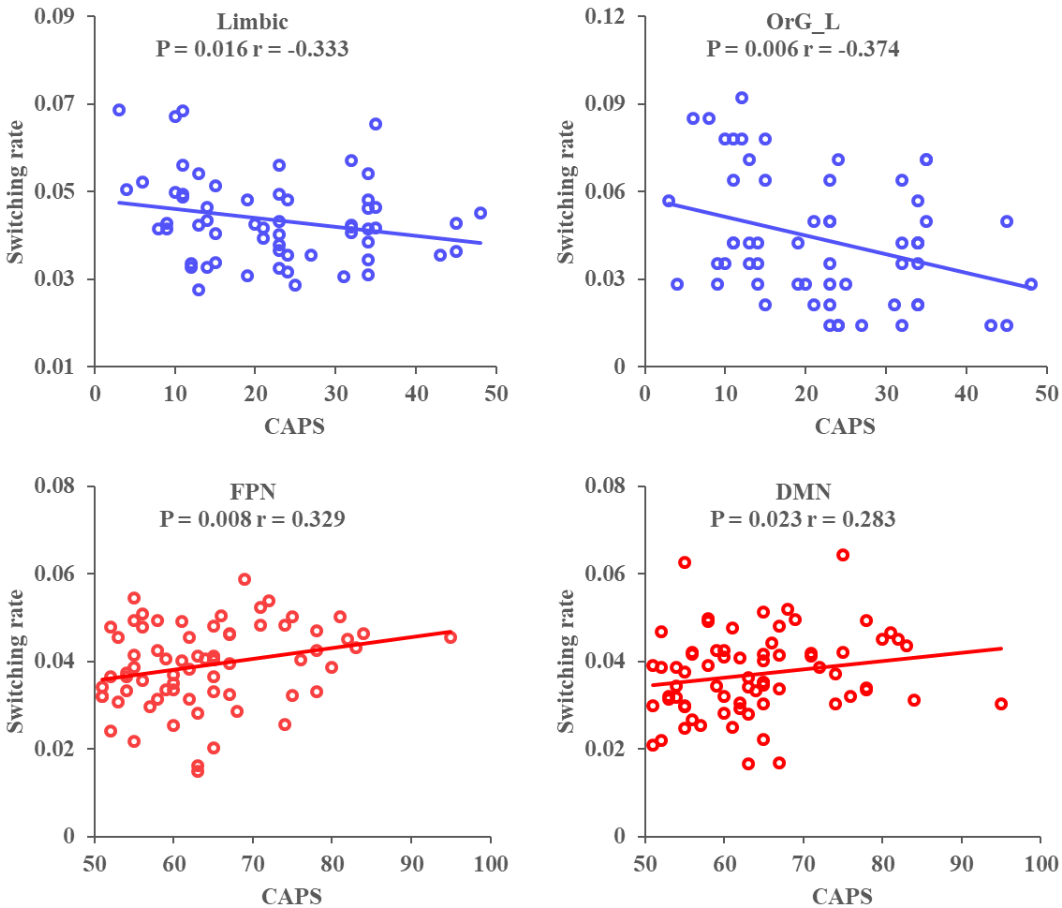
Table S2. Modular organization of static functional networks.

Modular metrics	P value
Intramodular connectivity for module I	0.553
Intramodular connectivity for module II	0.638
Intramodular connectivity for module III	0.308
Intramodular connectivity for module IV	0.253
Intramodular connectivity for module V	0.379
Intramodular connectivity for module VI	0.858
Intramodular connectivity for module VII	0.751
Intramodular connectivity for module VIII	0.734
Inter-modular connection for modules I-II	0.868
Inter-modular connection for modules I-III	0.383
Inter-modular connection for modules I-IV	0.426
Inter-modular connection for modules I-V	0.970
Inter-modular connection for modules I-VI	0.324
Inter-modular connection for modules I-VII	**0.018**
Inter-modular connection for modules I-VIII	0.249
Inter-modular connection for modules II-III	0.623
Inter-modular connection for modules II-IV	0.365
Inter-modular connection for modules II-V	0.436
Inter-modular connection for modules II-VI	0.802
Inter-modular connection for modules II-VII	0.617
Inter-modular connection for modules II-VIII	0.459
Inter-modular connection for modules III-IV	0.608
Inter-modular connection for modules III-V	0.440
Inter-modular connection for modules III-VI	0.410
Inter-modular connection for modules III-VII	0.277
Inter-modular connection for modules III-VIII	0.892
Inter-modular connection for modules IV-V	0.554
Inter-modular connection for modules IV -VI	0.942
Inter-modular connection for modules IV -VII	0.650
Inter-modular connection for modules IV -VIII	0.613
Inter-modular connection for modules V -VI	0.619
Inter-modular connection for modules V -VII	0.398
Inter-modular connection for modules V –VIII	0.312
Inter-modular connection for modules VI -VII	0.385
Inter-modular connection for modules VI -VIII	0.430
Inter-modular connection for modules VII–VIII	0.787

* $P < 0.05$, FDR corrected.

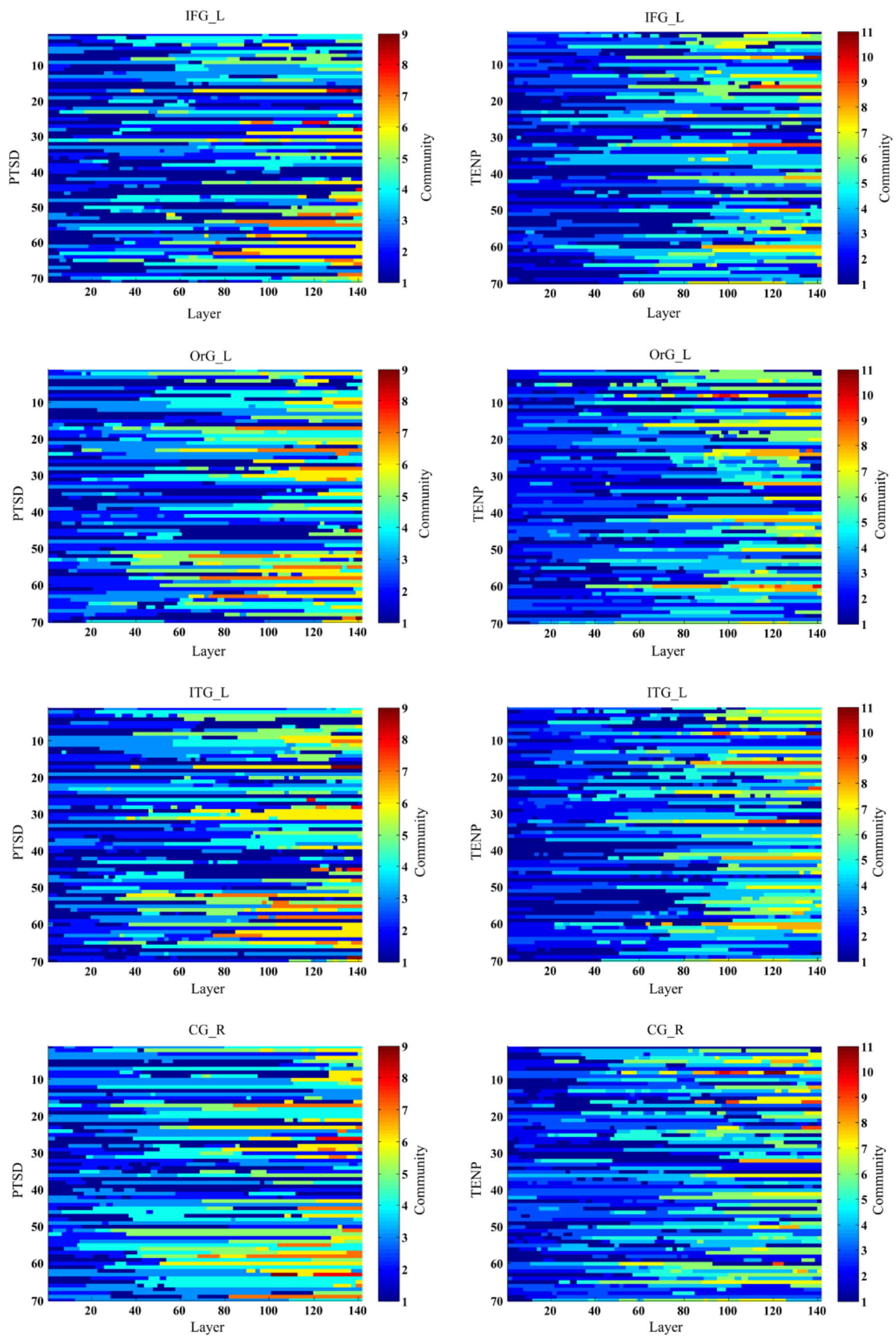
Key to Modules: I, visual network; II, somatomotor network; III, dorsal attention network; IV, ventral attention network; V, limbic network; VI, Frontoparietal network; VII, Default mode network; VIII, Subcortical network.

Figure S1. Correlation between the switching rate alterations and CAPS scores in the PTSD (red) and TENP (blue) groups.



Abbreviations: PTSD, posttraumatic stress disorder; TENP, trauma-exposed non-PTSD; CAPS, Clinician-administered PTSD scale; L, left; FPN, fronto-parietal network; DMN, default mode network; OrG, orbital gyrus. Regions were defined according to Brainnetome 246 Atlas.

Figure S2. Community assignments of IFG, OrG, ITG and CG at different network layers for each participant in the PTSD and TENP groups.



Abbreviations: PTSD, posttraumatic stress disorder; TENP, trauma-exposed non-PTSD; IFG, inferior frontal gyrus; OrG, orbital gyrus; ITG, inferior temporal gyrus; CG, cingulate gyrus; L, left; R, right. Nodal regions were defined according to Brainnetome 246 Atlas.

References

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