Traumatic Brain Injury Severity in a Network Perspective:

A Diffusion MRI Based Connectome Study

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Measure	Description	Weighted Mathematical Definition
Centrality		
Strength (degree)	Number of edges connected to a node.	$S_i = \sum_{j \in N} w_{ij}$
Betweenness centrality	Number of all shortest paths (the number of minimal 'steps' required for connecting a pair of nodes) in the network that contains a given node	$BC_z = \sum_{i \in N, j \in N} \frac{\sigma_{ij}(z)}{(\sigma_{ij})}$
Integration		
Global efficiency	Mean inverse shortest path length in the network.	$E^w_{glob} = \frac{1}{n} \sum_{i \in N} \frac{\sum_{j,h \in N, j \neq i} (d^w_{ji})^{-1}}{(n-1)}$
Segregation		
Clustering coefficient	Fraction of triangles around a node (i.e., fraction of neighbors of node i that are neighbors of each other). This measure reflects the tendency of nodes to cluster together	$C_i{}^w = \frac{1}{n} \sum_{i \in N} \frac{2t^w_i}{k_i(k_i-1)}$
Local efficiency	Efficiency of connections between (first-degree) neighbors of a node (i.e., E_{loc_i} reflects the global efficiency of the neighborhoods of node i).	$E^w_{loc} = \frac{1}{2} \sum_{i \in N} \frac{\sum_{j,h \in N, j \neq i} (w_{ij} w_{ih} [d^w_{jh}(N_i)]^{-1})^{1/3}}{k_i(k_i-1)}$

Supplementary Table S1: A description and mathematical definitions of all measures used in the current study, based on the work of Rubinov and Sporns in 2010.
Edges (i, j) are associated with connection weights w_{ij}. N is the set of all nodes in the network, and n is the number of nodes. a_{ij} is the connection status between i and j. u,v are different modules. d_{ij} is the distance between i and j. k_i is the degree of i. t_i is the number of triangles around i. σ_{ij} is the shortest path between i and j.

a:

Measure	F(2,43)	p
Strength	5.117	0.011*
Global efficiency	5.040	0.011*
Clustering coefficient	5. 575	0. 007*

b:

Regions	Control > msTBI	Control > mTBI	mTBI > msTBI
Superior Frontal L	.003*	.988	.037*
Superior Frontal R	.003*	.977	.045*
Superior Medial Frontal L	.001*	.790	.070
Supplementary motor area L	.004*	.932	.082
Anterior Cingulate L	.000*	. 993	.001*
Anterior Cingulate R	.002*	.650	.143
Medial Orbital Frontal L	.002*	.745	.001*
Medial Orbital Frontal R	.002*	1	.014*
Caudate L	.001*	.950	.018*
Olfactory R	.008*	.996	.026*

Supplementary Table S2: A: Global difference between the injury severity groups, using age as covariate and the false discovery rate (FDR) correction. B: Local strength's p-values in all significant regions: post-hoc multiple comparisons using LSD correction with age as a covariate. R, right; L, left; mTBI, mild traumatic brain injury; msTBI, moderate-severe traumatic brain injury. *FDR corrected.

Hub's Rank	Control	mTBI	msTBI
1	Putamen R	Hippocampus R	Putamen R
2	Hippocampus R	Superior Frontal Orbital L	Superior Frontal Orbital L
3	Thalamus R	Middle Occipital L	Middle Temporal L
4	Superior Parietal R	Putamen R	Putamen L
5	Superior Frontal Orbital L	Superior Parietal L	Hippocampus R
6	Putamen L	Superior Parietal R	Superior Frontal L
7	Hippocampus L	Hippocampus L	Superior Parietal R
8	Middle Occipital L	Thalamus R	Insula R
9	Superior Frontal R	Putamen L	Middle Occipital L

Supplementary Table S3: hub's rank in each group, using betweenness centrality; R, right; L, left.

Region/Network Measures	Strength		Efficiency		Cluster Coefficient	
	Groups	p	Groups	p	Groups	p
Superior Frontal L	Control > msTBI Control > mTBI mTBI > msTBI	.001* .429 .013*	Control > msTBI Control > mTBI mTBI < msTBI	.001* .000* .738	Control > msTBI Control > mTBI mTBI > msTBI	.000* .046* .078
Superior Frontal R	Control > msTBI Control > mTBI mTBI > msTBI	.001* .436 .013*	Control > msTBI Control > mTBI mTBI > msTBI	.000* .000* .714	ANOVA was not significant	
Superior Frontal medial L	Control > msTBI Control < mTBI mTBI > msTBI	.000* .488 .007*	Control > msTBI Control > mTBI mTBI > msTBI	.045* .071 .772	Control > msTBI Control > mTBI mTBI > msTBI	.006* .187 .159
Superior Occipital L	ANOVA was not significant		Control > msTBI Control > mTBI mTBI > msTBI	.000* .000* .314	ANOVA was not significant	
Middle Occipital L	ANOVA was not significant		Control > msTBI Control > mTBI mTBI < msTBI	.003* .000* .378	ANOVA was not significant	
Superior Parietal L	ANOVA was not significant		Control < msTBI Control < mTBI mTBI > msTBI	.035* .001 .329	ANOVA was not significant	
Putamen L	ANOVA was not significant		ANOVA was not significant		Control > msTBI Control > mTBI mTBI > msTBI	.015* .262 .198
Putamen R	ANOVA was not significant		Control < msTBI Control < mTBI mTBI < msTBI	.006* .005* .922	ANOVA was not significant	

Supplementary Table S4: Network measures in hubs: post-hoc multiple comparisons using LSD correction.

ANOVA tests showed significant differences between groups in some network measures within the hub regions that were tested (corrected for multiple comparisons, n=44). R, right; L, left; mTBI, mild traumatic brain injury; msTBI, moderate-severe traumatic brain injury. *FDR corrected.

Regions	Control > msTBI	Control > mTBI	mTBI > msTBI
Superior Frontal L	.001*	.429	.034*
Superior Frontal R	.001*	.436	.013*
Superior Medial Frontal L	.000*	.488	.007*
Supplementary motor area L	.001*	.800	.007*
Anterior Cingulate L	.000*	.886	.000*
Anterior Cingulate R	.001*	.165	.035*
Medial Orbital Frontal L	.000*	.936	.002*
Medial Orbital Frontal R	.000*	.391	.011*
Caudate L	.000*	.172	.012*
Olfactory R	.002*	.656	.003*

Supplementary Table S5: Local strength's p-values in all significant regions: post-hoc multiple comparisons using LSD correction. R, right; L, left; mTBI, mild traumatic brain injury; msTBI, moderate-severe traumatic brain injury. *FDR corrected.