CARDIFF UNIVERSITY
PRIFYSGOL CAERDYDD

ORCA – Online Research @ Cardiff

This is an Open Access document downloaded from ORCA, Cardiff University's institutional repository:https://orca.cardiff.ac.uk/id/eprint/120170/

This is the author's version of a work that was submitted to / accepted for publication.

Citation for final published version:

Imms, Phoebe, Clemente, Adam, Cook, Mark, D?Souza, Wendyl, Wilson, Peter H., Jones, Derek K. and Caeyenberghs, Karen 2019. The structural connectome in traumatic brain injury: A meta-analysis of graph metrics. Neuroscience and Biobehavioral Reviews 99 , pp. 128-137. 10.1016/j.neubiorev.2019.01.002

Publishers page: http://dx.doi.org/10.1016/j.neubiorev.2019.01.002

Please note:
Changes made as a result of publishing processes such as copy-editing, formatting and page numbers may not be reflected in this version. For the definitive version of this publication, please refer to the published source. You are advised to consult the publisher's version if you wish to cite this paper.

This version is being made available in accordance with publisher policies. See http://orca.cf.ac.uk/policies.html for usage policies. Copyright and moral rights for publications made available in ORCA are retained by the copyright holders.

Table 1. Demographics and Processing Methods for Graph Theoretical Studies of Traumatic Brain Injury

	PARTICIPANTS				DATA ACQUISITION			PROCESSING PIPELINE					
	Sample size *TBI (HC)*	**Age range at scan (years) *or M(SD)***	**Ave age at injury (years)**	**Severity**	**Time[a] since injury**	**Number of directions**	**b-value**	**Parcellation Scheme**	**Areas Removed**	**Number of ROIs**	**Orientation model**	**Tractography[d]**	**Weighted By[c]**
Caeyenberghs et al., 2012	12(17)	8 - 20	10.5	Moderate -severe	42 (31.2)	45	800 (1 b0)	Automated Anatomical Labelling	-	116	Principle eigenvector	DT	SD
Caeyenberghs et al., 2013	17(16)	16 - 34	21.2	Moderate -severe	51 (29)	64	1000 (1 b0)	Switching Network	-	22	Principle eigenvector	DT	NOS FA
Caeyenberghs et al., 2014	21(17)	9 - 29	21.3	Moderate -severe	51 (29)	64	1000 (1 b0)	Automated Anatomical Labelling	-	116	Principle eigenvector	DT	%
Dall'Acqua et al., 2016	51(53)	18 - 61	34.5	Mild	0.2	64	1000 (1 b0)	Automated Anatomical Labelling	Cerebellar regions	90	Principle eigenvector	DT	NOS
Hellyer et al., 2015	63(26)	37.4 (12.4)	31.9	All[b]	5.5 (3.3)	64	1000 (4 b0)	Destreux (Freesurfer)	-	164	Principle eigenvector	PT	FA
Kim et al., 2014	22(18)	17 - 57	26.0	Moderate -severe	40.9 (75.6)	30	1000 (1 b0)	Desikan (Freesurfer)	Cerebellar regions	95	Principle eigenvector	PT	SCP
Königs et al., 2017	36(27)	8 - 14	7.3	All	33.6 (13.2)	30	750 (5 b0)	Automated Anatomical Labelling and FIRST	Cerebellar regions	84	Principle eigenvector	PT	SLD FA
Solmaz et al., 2017	40(35)	18 - 64	NA	Moderate -severe	3.45 (0.6)	30	1000 (7 b0)	Desikan (Freesurfer)	-	86	Principle eigenvector	PT	NOS
van der Horn et al., 2016	53(20)	18 - 65	33.4	Mild	1 (NA)	60	1000 (7 b0)	Desikan-Killianey and subcortical	Cerebellar and ventricle regions	85	CSD	PT	NOS
Verhelst et al., 2018	17(17)	11 - 17	13.4	Moderate -severe	28.3 (13)	64	1200 (1 b0)	Individual parcellation (Freesurfer)	Not known	82	CSD	PT (ACT)	NOS
Yuan et al., 2015	23(20)	11 - 16	13.7	Mild	0.1 (NA)	61	1000 (1 b0)	Automated Anatomical Labelling	Cerebellar regions	90	Principle eigenvector	DT	NOS
Yuan, Treble-Barna et al., 2017	17(11)	9 - 18	7.8	Moderate -severe	70.9 (37.2)	61	1000 (1 b0)	Automated Anatomical Labelling	Cerebellar regions	90	Principle eigenvector	DT	NOS
Yuan, Wade et al., 2017	22(20)	15.45 (1.72)	15.3	Mild	1 - 4	61	1000 (7 b0)	Automated Anatomical Labelling	Cerebellar regions	90	Principle eigenvector	DT	NOS

[a] Time is from the injury/onset until MRI scan for TBI patients, described in months; M(SD)). NA = Not Applicable.
[b] 55 of the 63 TBI patients were moderate-severe, and as such Hellyer et al. (2015) was included in the moderate-severe subgroup analyses.
[c] NOS = number of streamlines; FA = fractional anisotropy; % = percentage of all streamlines that pass through the node; SD = streamline density (number of fibre connections per unit surface); SLD = the probability of a tract connecting two ROIs; SCP = scaled conditional probability (the number of streamlines from node i to node j, divided by the number of streamlines seeded in node i, scaled by the surface area of the ROI i.
[d] CSD = constrained spherical deconvolution; DT = deterministic tractography; PT = probabilistic tractography; ACT = anatomically constrained probabilistic tractography

Table 2. Quality Assessment Results for Graph Theoretical Studies of Traumatic Brain Injury

	SUBJECTS					METHODOLOGY							RESULTS/CONCLUSIONS				
	T1	**T2**	**T3**	**T4**	**Overall (/4)**	**T5**	**T6**	**T7**	**T8**	**T9**	**T10**	**Overall (/6)**	**T11**	**T12**	**T13**	**Overall (/3)**	**FINAL SCORE**
Verhelst et al. (2018)	1	1	1	1	**4**	1	1	1	0.5	1	1	**5.5**	1	1	1	**3**	**12.5/13**
Caeyenberghs et al. (2012)	1	1	1	0.5	**3.5**	1	1	1	1	1	0.5	**5.5**	1	1	1	**3**	**12/13**
Dall'Acqua et al. (2016)	1	1	1	1	**4**	1	0.5	0.5	1	1	1	**5**	1	1	1	**3**	**12/13**
van der Horn et al. (2017)	1	1	1	0.5	**3.5**	1	1	1	0.5	1	1	**5.5**	1	1	1	**3**	**12/13**
Yuan et al. (2015)	1	1	1	1	**4**	1	1	1	0.5	0.5	1	**5**	1	1	1	**3**	**12/13**
Caeyenberghs et al. (2013)	1	1	1	1	**4**	1	1	1	1	1	0.5	**5.5**	0	1	1	**2**	**11.5/13**
Caeyenberghs et al. (2014)	1	1	1	0.5	**3.5**	1	1	1	1	1	0.5	**5.5**	1	0.5	1	**2.5**	**11.5/13**
Konings et al. (2017)	1	1	1	1	**3.5**	1	1	1	0.5	1	1	**5.5**	0	1	1	**2**	**11.5/13**
Solmaz et al. (2017)	1	0.5	0.5	1	**3**	1	1	1	1	1	1	**6**	1	1	1	**2.5**	**11.5/13**
Yuan et al. (2017a)	1	1	1	1	**3.5**	1	1	1	0.5	1	0.5	**5**	0.5	1	1	**2.5**	**11.5/13**
Hellyer et al. (2015)	1	1	0.5	1	**3.5**	1	1	1	1	1	1	**6**	0	0.5	1	**2.5**	**11/13**
Kim et al. (2014)	1	1	0.5	1	**3.5**	1	1	1	0.5	1	1	**5.5**	0	1	1	**2**	**11/13**
Yuan et al. (2017b)	1	1	0.5	0.5	**3**	1	1	1	0.5	0.5	0.5	**4.5**	0	1	0.5	**1.5**	**9/13**

* Fagerholm et al. (2015) and Mitra et al. (2016) were excluded from the quality assessment due to incompatibility with the questionnaire (machine learning experiments).

Table 3. Graph Metrics in Patients with Traumatic Brain Injury compared to Healthy Controls.

	GRAPH METRICS													
	Segregation						Integration				Centrality/ General measures			
	Cl	γ	Q	E_{loc}	T	*a*	E_{glob}	L	λ	b	σ	k	D	s
Caeyenberghs et al., 2012	•	↑	•	↓	•	•	•	•	↓	↑	↑	•	↓	•
Caeyenberghs et al., 2014	-	-	•	•	•	•	↓	↑	-	•	-	•	•	-
Hellyer et al., 2015	↓	•	•	•	•	•	•	↑	•	•	↓	↓	•	•
Kim et al., 2014	•	•	-	•	-	•	•	↑	•	•	•	•	-	•
Königs et al., 2017	•	•	-	•	-	-	•	-	•	•	•	•	•	•
van der Horn et al., 2016	-	-	-	-	•	•	-	•	•	-	•	•	•	•
Verhelst et al., 2018	•	↑	•	•	•	•	•	•	↑	•	•	•	↓	-
Yuan et al., 2015	•	↑	↑	-	•	•	↓	•	↑	-	↑	•	•	•
Yuan, Treble-Barna et al., 2017	•	-	-	-	•	•	-	•	-	•	↑	•	•	•
Yuan, Wade et al., 2017	•	↑	-	-	•	•	↓	•	↑	•	↑	•	•	•
	3	**7**	**6**	**5**	**2**	**1**	**5**	**4**	**6**	**3**	**6**	**1**	**3**	**2**

↑/ ↓ higher/lower respectively in TBI patients than in HCs; - no significant difference between TBI and HC; • this metric wasn't measured
* the total number of times this metric was measured.

Cl Clustering coefficient	γ Normalised clustering coefficient	Q Modularity	E_{loc} Local efficiency	T Transivity	*a* Assortativity	E_{glob} Global efficiency	L Characteristic path length	λ Normalised characteristic path length	b Betweenness Centrality	σ Small-worldness	D Density	k Degree	s Strength

Table 4. Results of the Subgroup Analyses

OUTCOME	SUBGROUP	VARIABLE	N	HEDGES G	LOWER LIMIT	UPPER LIMIT	Z-VALUE	P-VALUE	I-SQUARED (%)
Global Efficiency (E_{glob})	Chronicity/Severity	Acute/mild	3	-1.610	-3.402	0.181	-1.762	0.078	95.109
		Chronic/modsev	2	-0.485	-1.408	0.437	-1.031	0.302	71.268
	Age at injury	Adult	2	-0.446	-1.368	0.475	-0.949	0.343	79.580
		Pediatric	3	-1.625	-3.298	0.047	-1.905	0.057	92.912
Local Efficiency (E_{loc})	Chronicity/Severity	Acute/mild	3	0.031	-0.292	0.354	0.188	0.851	0.000
		Chronic/modsev	2	-0.677	-2.067	0.713	-0.995	0.340	89.863
Modularity (**Q**)	Chronicity	Acute/mild	3	0.602	-0.479	1.683	1.091	0.275	89.877
		Chronic/modsev/both	3	-0.038	-0.379	0.302	-0.221	0.825	0.000
	Age at injury	Adult	2	-0.233	-0.625	0.159	-1.163	0.245	0.000
		Pediatric	4	0.532	-0.182	1.247	1.460	0.144	81.165
Normalised Clustering Coefficient (γ)	Chronicity/Severity	Acute/mild	3	0.915	-0.379	2.209	1.386	0.166	92.389
		Chronic/modsev	4	1.924	0.382	3.465	2.446	**0.014**	92.440
	Age at injury	Adult	2	0.150	-0.571	0.871	0.408	0.683	68.072
		Pediatric	5	2.000	0.857	3.143	3.430	**0.001**	89.822
Normalised Path Length (λ)	Chronicity/Severity	Acute/mild	2	0.965	0.523	1.408	4.274	***<0.001**	0.000
		Chronic/modsev	4	0.789	-0.903	2.482	0.914	0.361	94.501
Small Worldness (σ)	Chronicity	Acute	3	0.625	-0.892	2.142	0.808	0.419	94.950
		Chronic	3	0.950	0.402	1.499	3.396	***0.001**	39.536
	Severity	Mild	2	1.309	0.203	2.414	2.320	**0.020**	81.922
		Modsev	4	0.533	-0.491	1.558	1.021	0.307	89.792
	Age at injury	Adult	2	-0.087	-1.358	1.185	-0.133	0.894	90.342
		Pediatric	4	1.246	0.694	1.798	4.423	***<0.001**	56.949

significant at p<.05

***significant at p<.001**