Supplementary material for “The effect of network thresholding and weighting on structural brain networks in the UK Biobank”

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Tables

Title	Notes	Number of participants	Number of nodes	Tractography type	Weighting	Proportional threshold level (%)
(Jung et al., 2017)	Applied a two-step threshold: absolute weight threshold and then proportional threshold at stringent (75%) and relaxed (50%) levels	24	43	probabilistic	connection probability	50, 75
(Beare et al., 2017)	The statistical analysis (network-based statistics) used connections that were present in 50% of subjects	45	162	deterministic, probabilistic	streamline count, weighted streamline count, count fraction	50
(Nomi et al., 2018)	Applied a proportional threshold at stringent (75%) and relaxed (50%) levels	199	114	deterministic	streamline count	50, 75
(Conti et al., 2017)	Applied a two-step threshold: absolute streamline count threshold and connections that were present in all participants	90	48	probabilistic	streamline count, FA	100
(Barbagallo et al., 2017)	Applied two alternative thresholds: 1) proportional threshold at 50% ; and 2) an absolute threshold over a range of connection probabilities	93	116	probabilistic	weighted streamline count	50

Supplementary Table 1. Recent network studies using proportional-thresholding were identified by examining the first 100 results since 2017 that matched the search term, "(proportional OR consensus OR group) threshold structural brain network" (search performed using Google Scholar on 13th March 2019) and then identifying those studies that used proportional-thresholding on structural networks constructed from dMRI and tractography (the great majority of search results related to functional networks). For the above studies, the median value of the proportional threshold levels used was a threshold of 50% of subjects.

Network metric	Weighting	Raw	Proportional (50%)	Consistency (68.6%)	Proportional (99.6%)	Consistency (30%)
		sparsity = 0.002	**sparsity = 0.313**	**sparsity = 0.313**	**sparsity = 0.701**	**sparsity = 0.700**
Mean edge weight	SC	0.005 (0.001)	0.008 (0.001)	0.008 (0.001)	0.017 (0.002)	0.016 (0.002)
	FA	0.327 (0.020)	0.435 (0.021)	0.428 (0.021)	0.457 (0.016)	0.460 (0.016)
	MD	0.001 (0.000)	0.001 (0.000)	0.001 (0.000)	0.001 (0.000)	0.001 (0.000)
	ICVF	0.391 (0.028)	0.522 (0.032)	0.514 (0.032)	0.567 (0.028)	0.565 (0.028)
	ISOVF	0.058 (0.008)	0.076 (0.010)	0.075 (0.010)	0.078 (0.011)	0.078 (0.011)
	OD	0.126 (0.007)	0.169 (0.007)	0.166 (0.007)	0.199 (0.007)	0.196 (0.007)
Characteristic path length	SC	80.029 (14.630)	80.035 (14.637)	80.038 (14.638)	81.079 (17.409)	80.560 (14.794)
	FA	2.604 (0.111)	2.717 (0.102)	2.752 (0.104)	3.727 (0.123)	3.682 (0.120)
	MD	1533.703 (57.460)	1599.896 (54.738)	1617.745 (55.190)	2122.544 (74.433)	2117.128 (71.464)
	ICVF	2.230 (0.126)	2.329 (0.122)	2.355 (0.124)	3.115 (0.150)	3.093 (0.149)
	ISOVF	12.715 (1.490)	13.454 (1.655)	13.747 (1.703)	21.558 (3.400)	21.381 (3.194)
	OD	6.597 (0.253)	6.805 (0.252)	6.848 (0.255)	8.626 (0.307)	8.504 (0.303)
Network efficiency	SC	0.021 (0.003)	0.021 (0.003)	0.021 (0.003)	0.021 (0.003)	0.021 (0.003)
	FA	0.413 (0.016)	0.400 (0.015)	0.397 (0.015)	0.303 (0.010)	0.306 (0.010)
	MD	0.001 (0.000)	0.001 (0.000)	0.001 (0.000)	0.001 (0.000)	0.001 (0.000)
	ICVF	0.487 (0.026)	0.471 (0.024)	0.468 (0.024)	0.364 (0.018)	0.365 (0.018)
	ISOVF	0.089 (0.010)	0.085 (0.010)	0.084 (0.010)	0.059 (0.008)	0.059 (0.008)
	OD	0.164 (0.006)	0.160 (0.006)	0.159 (0.006)	0.132 (0.005)	0.133 (0.005)
Network clustering coefficient	SC	0.002 (0.000)	0.002 (0.000)	0.002 (0.000)	0.007 (0.001)	0.007 (0.001)
	FA	0.386 (0.016)	0.377 (0.014)	0.376 (0.014)	0.327 (0.011)	0.309 (0.011)
	MD	0.001 (0.000)	0.001 (0.000)	0.001 (0.000)	0.001 (0.000)	0.001 (0.000)
	ICVF	0.464 (0.026)	0.457 (0.024)	0.455 (0.024)	0.411 (0.020)	0.385 (0.019)
	ISOVF	0.063 (0.009)	0.062 (0.009)	0.062 (0.009)	0.050 (0.008)	0.048 (0.007)
	OD	0.149 (0.006)	0.149 (0.006)	0.149 (0.006)	0.151 (0.005)	0.140 (0.005)

Supplementary Table 2. Mean (and SD) values of four global network metrics measured across six network weightings and five thresholding approaches. Note that the absolute values of network measures are dependent on network weighting and sparsity. Mean edge weight is the mean of connection weights which survive thresholding. The characteristic path length is a measure of network integration, which reflects the average weighted path length between all pairs of nodes. Network efficiency is an alternative measure of network integration. Network clustering coefficient reflects the average of the local clustering coefficients.

Network metric	Weighting	Age	Age^2	Sex	Sex*Age	R^2
Mean edge weight	SC	**-0.141 (<0.001)**	0.009 (0.579)	**0.383 (<0.001)**	-0.015 (0.376)	0.168
	FA	-0.033 (0.079)	-0.001 (0.954)	0.005 (0.840)	0.025 (0.181)	0.000
	MD	**0.285 (<0.001)**	0.044 (0.009)	0.055 (0.022)	-0.013 (0.455)	0.078
	ICVF	**-0.097 (<0.001)**	-0.031 (0.080)	-0.006 (0.809)	0.019 (0.302)	0.008
	ISOVF	**0.362 (<0.001)**	**0.068 (<0.001)**	0.045 (0.054)	0.005 (0.790)	0.124
	OD	**-0.101 (<0.001)**	**-0.085 (<0.001)**	0.005 (0.842)	-0.016 (0.376)	0.013
Characteristic path length	SC	**0.160 (<0.001)**	0.019 (0.260)	**-0.231 (<0.001)**	0.015 (0.410)	0.077
	FA	**0.089 (<0.001)**	0.007 (0.699)	-0.030 (0.221)	-0.034 (0.062)	0.008
	MD	**-0.332 (<0.001)**	**-0.056 (<0.001)**	**-0.089 (<0.001)**	0.010 (0.553)	0.109
	ICVF	**0.149 (<0.001)**	0.043 (0.014)	-0.003 (0.896)	-0.021 (0.239)	0.020
	ISOVF	**-0.339 (<0.001)**	**-0.064 (<0.001)**	**-0.087 (<0.001)**	-0.023 (0.190)	0.115
	OD	**0.217 (<0.001)**	**0.115 (<0.001)**	0.021 (0.388)	0.024 (0.182)	0.050
Network efficiency	SC	**-0.186 (<0.001)**	0.004 (0.792)	**0.381 (<0.001)**	-0.033 (0.048)	0.182
	FA	**-0.095 (<0.001)**	0.003 (0.861)	-0.005 (0.847)	0.042 (0.021)	0.010
	MD	**0.385 (<0.001)**	**0.077 (<0.001)**	0.072 (0.002)	-0.012 (0.464)	0.144
	ICVF	**-0.160 (<0.001)**	-0.037 (0.032)	-0.019 (0.435)	0.026 (0.149)	0.024
	ISOVF	**0.380 (<0.001)**	**0.089 (<0.001)**	0.070 (0.003)	0.028 (0.105)	0.142
	OD	**-0.217 (<0.001)**	**-0.118 (<0.001)**	-0.031 (0.197)	-0.020 (0.274)	0.050
Network clustering coefficient	SC	**-0.098 (<0.001)**	0.007 (0.686)	**0.385 (<0.001)**	-0.024 (0.162)	0.160
	FA	-0.056 (0.002)	0.005 (0.755)	-0.024 (0.343)	0.036 (0.048)	0.005
	MD	**0.409 (<0.001)**	**0.073 (<0.001)**	0.036 (0.119)	-0.019 (0.258)	0.156
	ICVF	**-0.127 (<0.001)**	-0.034 (0.049)	-0.031 (0.206)	0.025 (0.175)	0.016
	ISOVF	**0.345 (<0.001)**	**0.064 (<0.001)**	0.037 (0.116)	0.002 (0.930)	0.111
	OD	**-0.142 (<0.001)**	**-0.109 (<0.001)**	-0.039 (0.109)	-0.023 (0.213)	0.026

Supplementary Table 3. Standardised regression coefficients (uncorrected *p*-values) and adjusted R^2 measuring mean edge weight, characteristic path length, network efficiency and network clustering coefficient for six network weightings. Computed with unthresholded networks.

Network metric	Weighting	Age	Age^2	Sex	Sex*Age	R^2
Mean edge weight	SC	**-0.141 (<0.001)**	0.009 (0.580)	**0.383 (<0.001)**	-0.015 (0.375)	0.168
	FA	**-0.070 (<0.001)**	-0.012 (0.478)	-0.004 (0.859)	0.028 (0.126)	0.005
	MD	**0.346 (<0.001)**	0.045 (0.007)	0.054 (0.021)	-0.021 (0.224)	0.113
	ICVF	**-0.134 (<0.001)**	-0.045 (0.009)	-0.018 (0.474)	0.019 (0.292)	0.017
	ISOVF	**0.367 (<0.001)**	**0.065 (<0.001)**	0.047 (0.042)	0.004 (0.821)	0.127
	OD	**-0.146 (<0.001)**	**-0.117 (<0.001)**	-0.021 (0.402)	-0.025 (0.177)	0.028
Characteristic path length	SC	**0.160 (<0.001)**	0.019 (0.260)	**-0.231 (<0.001)**	0.015 (0.408)	0.077
	FA	**0.109 (<0.001)**	0.010 (0.577)	-0.035 (0.160)	-0.035 (0.055)	0.012
	MD	**-0.358 (<0.001)**	**-0.057 (<0.001)**	**-0.090 (<0.001)**	0.009 (0.606)	0.126
	ICVF	**0.167 (<0.001)**	0.049 (0.005)	-0.000 (0.992)	-0.022 (0.234)	0.025
	ISOVF	**-0.341 (<0.001)**	**-0.059 (<0.001)**	**-0.103 (<0.001)**	-0.029 (0.092)	0.119
	OD	**0.229 (<0.001)**	**0.121 (<0.001)**	0.033 (0.169)	0.028 (0.122)	0.056
Network efficiency	SC	**-0.186 (<0.001)**	0.004 (0.792)	**0.381 (<0.001)**	-0.033 (0.048)	0.182
	FA	**-0.117 (<0.001)**	-0.000 (0.985)	-0.004 (0.887)	0.044 (0.016)	0.014
	MD	**0.405 (<0.001)**	**0.077 (<0.001)**	0.072 (0.002)	-0.012 (0.473)	0.158
	ICVF	**-0.176 (<0.001)**	-0.043 (0.014)	-0.023 (0.359)	0.026 (0.149)	0.029
	ISOVF	**0.389 (<0.001)**	**0.087 (<0.001)**	**0.079 (<0.001)**	0.031 (0.064)	0.151
	OD	**-0.225 (<0.001)**	**-0.124 (<0.001)**	-0.044 (0.069)	-0.022 (0.210)	0.055
Network clustering coefficient	SC	**-0.087 (<0.001)**	0.012 (0.450)	**0.366 (<0.001)**	-0.020 (0.252)	0.145
	FA	**-0.107 (<0.001)**	-0.000 (0.987)	-0.016 (0.517)	0.038 (0.039)	0.013
	MD	**0.406 (<0.001)**	**0.071 (<0.001)**	0.045 (0.051)	-0.022 (0.197)	0.155
	ICVF	**-0.162 (<0.001)**	-0.042 (0.016)	-0.027 (0.268)	0.024 (0.188)	0.025
	ISOVF	**0.338 (<0.001)**	**0.061 (<0.001)**	0.046 (0.051)	0.002 (0.913)	0.108
	OD	**-0.178 (<0.001)**	**-0.121 (<0.001)**	-0.047 (0.055)	-0.025 (0.170)	0.039

Supplementary Table 4. Standardised regression coefficients (uncorrected *p*-values) and adjusted R^2 measuring mean edge weight, characteristic path length, network efficiency and network clustering coefficient for six network weightings. Computed with proportional-thresholding using connections present in 50% of subjects.

Network metric	Weighting	Age	Age^2	Sex	Sex*Age	R^2
Mean edge weight	SC	**-0.172 (<0.001)**	0.000 (0.997)	**0.379 (<0.001)**	-0.022 (0.192)	0.172
	FA	**-0.179 (<0.001)**	0.004 (0.800)	-0.012 (0.635)	0.047 (0.009)	0.033
	MD	**0.378 (<0.001)**	**0.072 (<0.001)**	0.048 (0.039)	-0.022 (0.203)	0.135
	ICVF	**-0.206 (<0.001)**	-0.044 (0.010)	-0.021 (0.400)	0.026 (0.145)	0.040
	ISOVF	**0.353 (<0.001)**	**0.062 (<0.001)**	0.057 (0.015)	0.003 (0.844)	0.119
	OD	**-0.198 (<0.001)**	**-0.126 (<0.001)**	-0.034 (0.158)	-0.024 (0.185)	0.045
Characteristic path length	SC	**0.160 (<0.001)**	0.020 (0.227)	**-0.230 (<0.001)**	0.018 (0.312)	0.076
	FA	**0.140 (<0.001)**	-0.004 (0.799)	-0.051 (0.040)	-0.031 (0.093)	0.021
	MD	**-0.364 (<0.001)**	**-0.062 (<0.001)**	**-0.081 (<0.001)**	0.010 (0.570)	0.129
	ICVF	**0.184 (<0.001)**	0.043 (0.014)	-0.007 (0.785)	-0.020 (0.282)	0.031
	ISOVF	**-0.290 (<0.001)**	-0.050 (0.003)	**-0.137 (<0.001)**	-0.022 (0.201)	0.095
	OD	**0.219 (<0.001)**	**0.121 (<0.001)**	0.020 (0.409)	0.026 (0.153)	0.052
Network efficiency	SC	**-0.192 (<0.001)**	-0.000 (0.992)	**0.378 (<0.001)**	-0.036 (0.033)	0.182
	FA	**-0.158 (<0.001)**	0.012 (0.481)	0.007 (0.765)	0.048 (0.009)	0.027
	MD	**0.409 (<0.001)**	**0.084 (<0.001)**	0.066 (0.004)	-0.010 (0.545)	0.161
	ICVF	**-0.197 (<0.001)**	-0.040 (0.022)	-0.016 (0.518)	0.026 (0.149)	0.036
	ISOVF	**0.401 (<0.001)**	**0.080 (<0.001)**	**0.088 (<0.001)**	0.024 (0.161)	0.160
	OD	**-0.215 (<0.001)**	**-0.125 (<0.001)**	-0.033 (0.181)	-0.022 (0.222)	0.050
Network clustering coefficient	SC	**-0.179 (<0.001)**	-0.011 (0.513)	**0.310 (<0.001)**	-0.036 (0.040)	0.124
	FA	**-0.192 (<0.001)**	0.011 (0.540)	-0.008 (0.755)	0.042 (0.021)	0.038
	MD	**0.368 (<0.001)**	**0.075 (<0.001)**	0.046 (0.048)	-0.019 (0.274)	0.128
	ICVF	**-0.209 (<0.001)**	-0.041 (0.016)	-0.011 (0.658)	0.025 (0.170)	0.040
	ISOVF	**0.311 (<0.001)**	0.054 (0.001)	0.070 (0.003)	0.003 (0.856)	0.094
	OD	**-0.178 (<0.001)**	**-0.122 (<0.001)**	-0.024 (0.326)	-0.017 (0.358)	0.037

Supplementary Table 5. Standardised regression coefficients (uncorrected *p*-values) and adjusted R^2 measuring mean edge weight, characteristic path length, network efficiency and network clustering coefficient for six network weightings. Computed with consistency-thresholding at 30%.

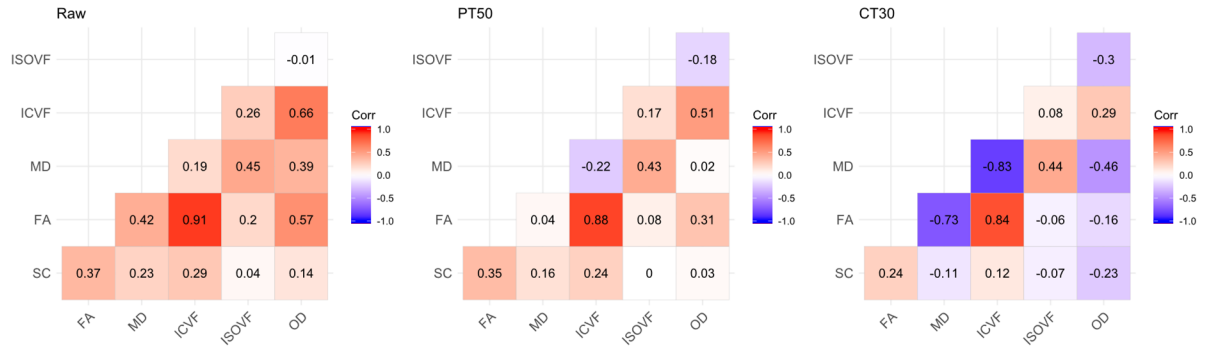
Threshold type	Weighting	Age	Age^2	Sex	Sex*Age	R^2
Raw	SC-uncorrected	**-0.141 (<0.001)**	0.009 (0.579)	**0.383 (<0.001)**	-0.015 (0.376)	0.168
	SC-WM	0.042 (0.022)	0.056 (0.001)	**-0.159 (<0.001)**	0.050 (0.006)	0.027
	SD-GMV	**0.173 (<0.001)**	0.020 (0.252)	0.045 (0.066)	0.025 (0.167)	0.033
	SD-GMA	**0.137 (<0.001)**	0.037 (0.032)	**0.082 (<0.001)**	0.023 (0.201)	0.027
Proportional (50%)	SC-uncorrected	**-0.141 (<0.001)**	0.009 (0.580)	**0.383 (<0.001)**	-0.015 (0.375)	0.168
	SC-WM	0.042 (0.022)	0.056 (0.001)	**-0.159 (<0.001)**	0.050 (0.006)	0.027
	SD-GMV	**0.173 (<0.001)**	0.020 (0.253)	0.045 (0.067)	0.025 (0.167)	0.033
	SD-GMA	**0.137 (<0.001)**	0.037 (0.032)	**0.082 (<0.001)**	0.023 (0.201)	0.027
Consistency (30%)	SC-uncorrected	**-0.172 (<0.001)**	0.000 (0.997)	**0.379 (<0.001)**	-0.022 (0.192)	0.172
	SC-WM	-0.005 (0.783)	0.042 (0.015)	**-0.173 (<0.001)**	0.042 (0.020)	0.030
	SD-GMV	**0.116 (<0.001)**	-0.004 (0.823)	0.025 (0.305)	0.011 (0.531)	0.014
	SD-GMA	**0.067 (<0.001)**	0.014 (0.427)	0.061 (0.015)	0.007 (0.691)	0.007
Proportional (99.6%)	SC-uncorrected	**-0.154 (<0.001)**	0.007 (0.640)	**0.384 (<0.001)**	-0.015 (0.358)	0.172
	SC-WM	0.023 (0.217)	0.054 (0.002)	**-0.160 (<0.001)**	0.050 (0.006)	0.027
	SD-GM	**0.146 (<0.001)**	0.014 (0.430)	0.036 (0.145)	0.025 (0.170)	0.023
	SD-GMA	**0.105 (<0.001)**	0.032 (0.067)	0.074 (0.003)	0.022 (0.226)	0.017
Consistency (68.6%)	SC-uncorrected	**-0.142 (<0.001)**	0.009 (0.587)	**0.383 (<0.001)**	-0.015 (0.372)	0.168
	SC-WM	0.041 (0.025)	0.056 (0.001)	**-0.159 (<0.001)**	0.049 (0.007)	0.027
	SD-GMV	**0.172 (<0.001)**	0.019 (0.267)	0.044 (0.076)	0.025 (0.170)	0.032
	SD-GMA	**0.136 (<0.001)**	0.037 (0.035)	0.080 (0.001)	0.023 (0.204)	0.026

Supplementary Table 6. Standardised regression coefficients (uncorrected *p*-values) and adjusted R^2 measuring mean edge weight for four streamline count network weightings: SC) Uncorrected streamline count; SC-WM) network-wise correction by number of seed points per subject (count of white matter voxels); SD-GM) streamline density with edge-wise correction by node volumes (count of voxels in node ROI); and SD-GMA) streamline density with edge-wise correction by node surface area at the white matter interface (the count of voxels which directly neighbour a white matter voxel).

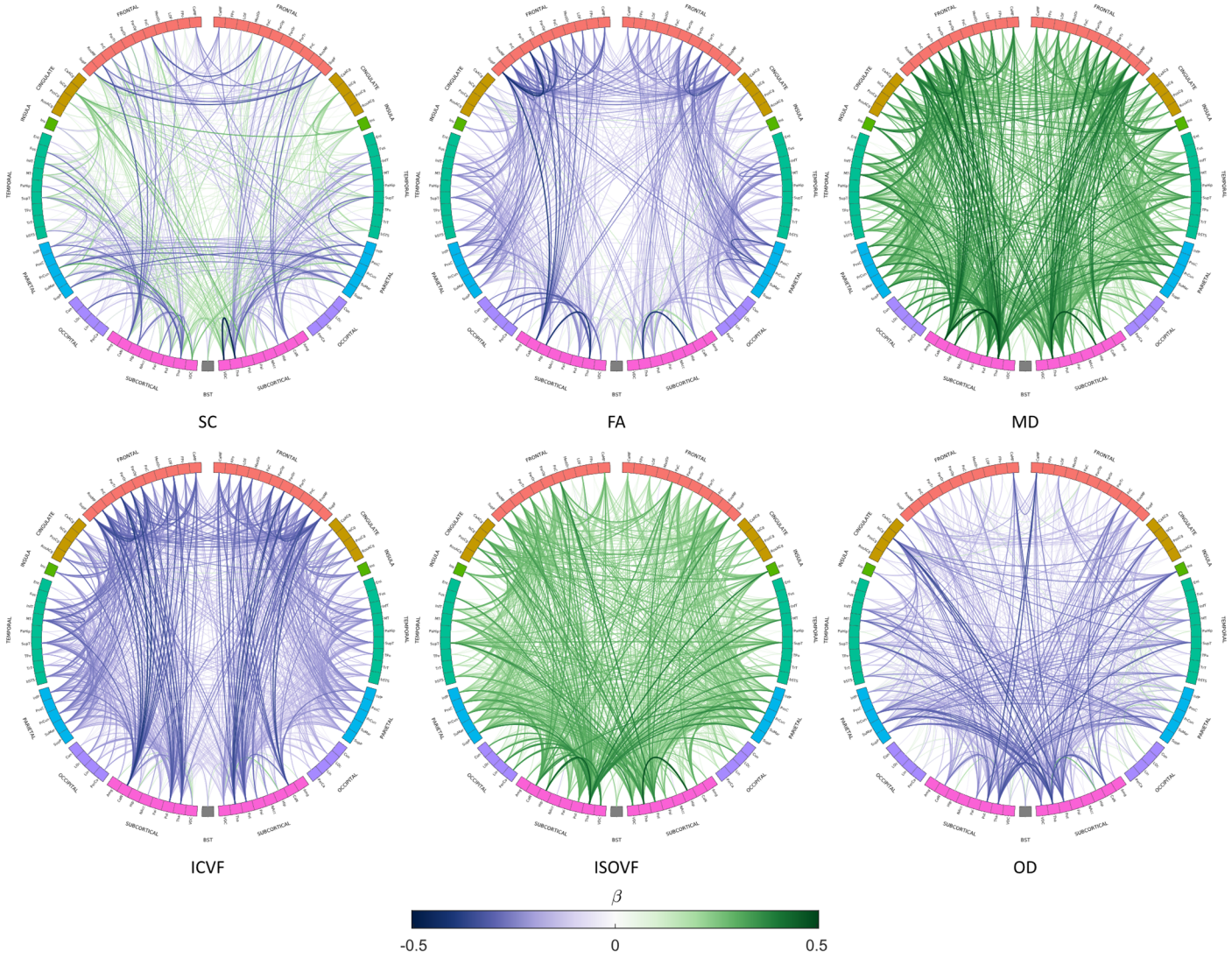
Region	Abbreviation	Lobe/Grouping
Caudal middle frontal	CaMF	Frontal
Frontal pole	FPo	Frontal
Lateral orbitofrontal	LOF	Frontal
Medial orbitofrontal	MedOr	Frontal
Paracentral	PaC	Frontal
Pars opercularis	ParOp	Frontal
Pars orbitalis	ParOr	Frontal
Pars triangularis	ParTr	Frontal
Precentral	PrC	Frontal
Rostral middle frontal	RosMF	Frontal
Superior frontal	SupF	Frontal
Caudal anterior cingulate	CaACg	Cingulate
Isthmus cingulate	IsCg	Cingulate
Posterior cingulate	PosCg	Cingulate
Rostral anterior cingulate	RosACg	Cingulate
Insula	Ins	-
Banks of superior temporal	bSTS	Temporal
Entorhinal	Ent	Temporal
Fusiform	Fus	Temporal
Inferior temporal	InfT	Temporal
Middle temporal	MT	Temporal
Parahippocampal	PaHip	Temporal
Superior temporal	SupT	Temporal
Temporal pole	TPo	Temporal
Transverse temporal	TrT	Temporal
Inferior parietal	InfP	Parietal
Postcentral	PosC	Parietal
Precuneus	PrCun	Parietal
Superior parietal	SupP	Parietal
Supramarginal	SuMar	Parietal
Cuneus	Cun	Occipital
Lateral occipital	LOc	Occipital
Lingual	Lin	Occipital
Pericalcarine	PerCa	Occipital
Nucleus accumbens	NAcc	Subcortical
Amygdala	Amg	Subcortical
Caudate nucleus	CaN	Subcortical
Hippocampus	Hip	Subcortical
Pallidum	Pal	Subcortical
Putamen	Put	Subcortical
Thalamus	Tha	Subcortical
Ventral diencephalon	VDC	Subcortical
Brainstem	BSt	-

Supplementary Table 7. List of neuroanatomical regions and abbreviations.

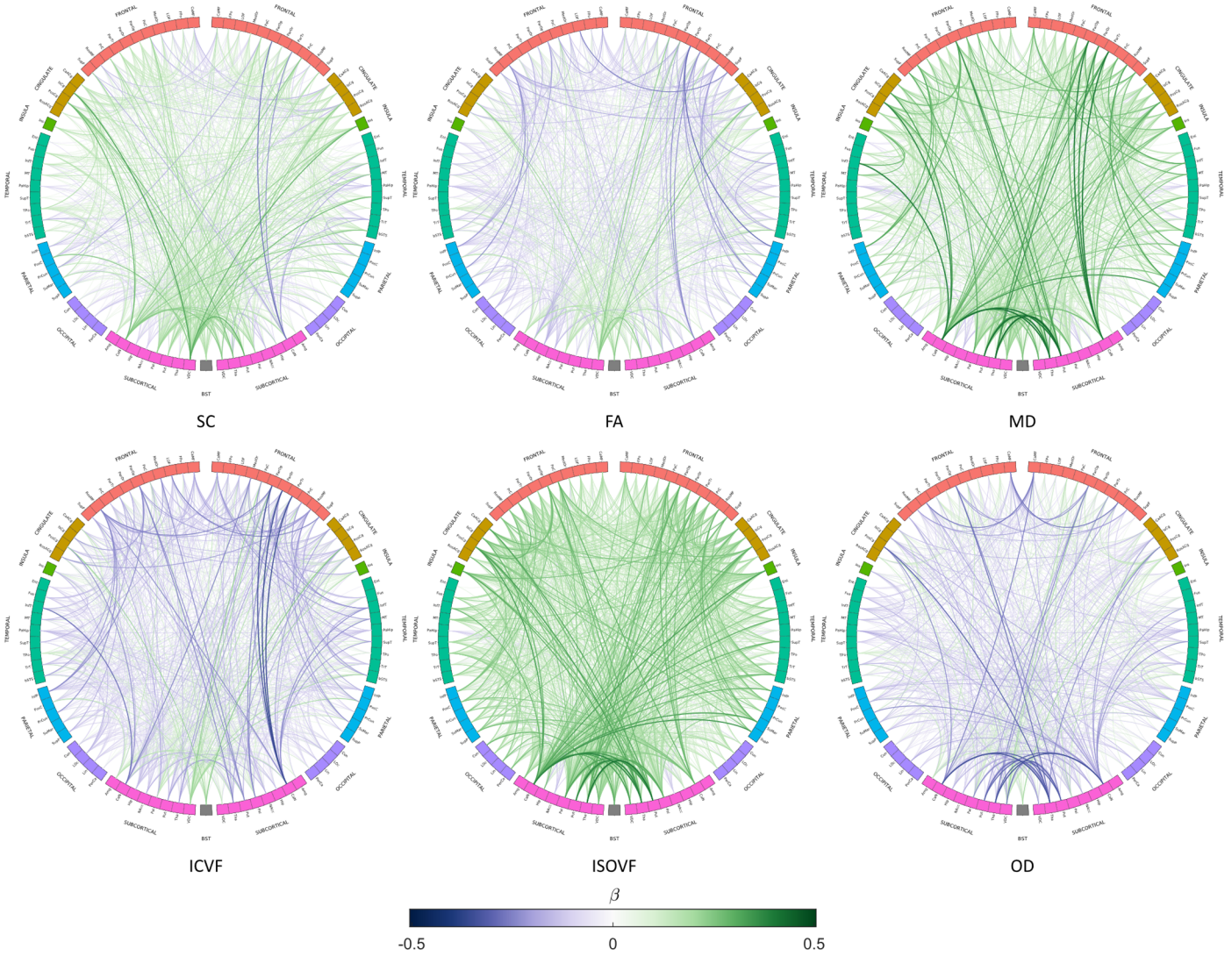
Figures



Supplementary Figure 1. Heatmap showing correlations between the mean edge weight of the six network weightings for: left) unthresholded matrices; middle) proportional-thresholding at 50% (PT50) of subjects; and consistency-thresholding at 30% (CT30).



Supplementary Figure 2. Age-associations ($p < 0.001$, uncorrected) for connections which survive consistency-thresholding at 30% for 6 network weightings (SC, FA, MD, ICVF, ISOVF and OD). Link colour and thickness represents the age-association (standardised beta) of the mean edge weight.



Supplementary Figure 3. Age-associations ($p < 0.001$, uncorrected) for connections which are discarded by consistency-thresholding at 30% for 6 network weightings (SC, FA, MD, ICVF, ISOVF and OD). Link colour and thickness represents the age-association (standardised beta) of the mean edge weight.