Table e-1: MRI acquisition parameters

Sequence	Feature	RUN DMC – InTENse sub-study	RUN DMC main study
	Scanner	Magnetom Prisma	
	Coil channels	32 (head)	
MP2RAGE	Type	Conventional	Compressed sensing
	TR [ms]	5500	5000
	TE [ms]	3.8	2.98
	TI [ms]	700, 2500[a]	732, 2500[a]
	Flip angle [˚]	7, 4[a]	4, 5[a]
	Voxel size [mm]	0.85 isotropic	
3D-FLAIR	TR [ms]	5000	
	TE [ms]	394	
	TI [ms]	1800	
	Voxel size [mm]	0.85 isotropic	
3D-GRE	TR [ms]	35	44
	TE [ms]	29.5	6.14, 10.1, 14.1, 18.1, 22.1, 26.1, 30.1, 34.1, 38.1
	Flip angle [˚]	15	20
	Voxel size [mm]	0.8 x 0.8 x 2	0.8 isotropic
MS-DWI	TR [ms]	3220	
	TE [ms]	74	
	Flip angle [˚]	90	
	In-plane resolution [mm]	1.7 x 1.7	
	Slice thickness [mm]	1.7	
	Base resolution (matrix)	130	
	Number of slices	87	
	b-values [s/mm^2]	1000, 3000	
	Directions (per b-value)	30, 60	
	b=0 [images]	10	
	Receiver bandwidth [Hz/px]	1924	
	Parallel acceleration	2	
	Multi-band acceleration	3	

[a] Double inversion

Abbreviations: FLAIR = fluid-attenuated inversion recovery; GRE = gradient echo; inTENse = Radboud University Nijmegen Diffusion tensor and Magnetic resonance imaging Cohort – Investigating The origin and EvolutioN of cerebral small vessel disease; MP2RAGE = magnetization prepared 2 rapid acquisition gradient echoes; MS-DWI = multi-shell diffusion-weighted imaging; RUN DMC = Radboud University Nijmegen Diffusion tensor and Magnetic resonance imaging Cohort; TE = echo time; TI = inversion time; TR = repetition time.

Table e-2: Simple linear regression models

		Single-shell								Multi-shell								
		Skeleton			Network					Skeleton			Network					
		FA	MD	Atlas	nSL	mLen	invLen	mFA	wFA	MK	RK	Atlas	nSL	mLen	invLen	mMK	wMK	mFA	wFA
Exploration	adj. R^2	0.066	0.080	AAL	0.109	0.073	0.079	0.077	0.111	0.176	0.151	AAL	0.125	0.059	0.027	0.117	0.025	0.011	0.134
	P	0.037	0.024		0.010	0.030	0.025	0.026	0.009	0.001	0.003		0.006	0.046	0.127	0.007	0.136	0.219	0.004
	adj. R^2	-	-	BN	0.098	0.056	0.095	0.082	0.088	-	-	BN	0.153	0.058	0.019	0.111	0.040	0.020	0.199
	P	-	-		0.014	0.050	0.015	0.023	0.019	-	-		0.002	0.046	0.167	0.009	0.084	0.158	0.001
Validation	adj. R^2	0.128	0.086	AAL	0.145	0.097	0.136	0.100	0.158	0.130	0.143	AAL	0.066	0.145	0.066	0.135	0.121	0.114	0.036
	P	0.000	0.001		0.000	0.001	0.000	0.001	0.000	0.000	0.000		0.005	0.000	0.005	0.000	0.000	0.000	0.030
	adj. R^2	-	-	BN	0.133	0.127	0.126	0.146	0.141	-	-	BN	0.003	0.125	0.084	0.136	0.102	0.124	0.001
	P	-	-		0.000	0.000	0.000	0.000	0.000	-	-		0.259	0.000	0.002	0.000	0.001	0.000	0.296

Abbreviations: adj. = adjusted; AAL = automated anatomical labelling; BN = Brainnetome; FA = fractional anisotropy; invLen = number of streamlines weighted by the inverse length of each streamline; MD = mean diffusivity; mFA = mean of fractional anisotropy of streamlines; MK = mean kurtosis; mLen= mean length of streamlines; mMK = mean of mean kurtosis of streamlines; nSL = number of streamlines; RK = radial kurtosis; wFA= number of streamlines weighted by fractional anisotropy; wMK = number of streamlines weighted by mean kurtosis.

Table e-3: Linear mixed effects models

		Single-shell								Multi-shell								
		Skeleton			Network					Skeleton			Network					
		FA	MD	Atlas	nSL	mLen	invLen	mFA	wFA	MK	RK	Atlas	nSL	mLen	invLen	mMK	wMK	mFA	wFA
Exploration	fix. ef.	0.005	0.004	AAL	0.000	0.000	0.000	0.002	0.001	0.004	0.006	AAL	0.002	0.002	0.001	0.003	0.002	0.004	0.001
	P	0.000	0.000		0.470	0.663	0.751	0.001	0.136	0.000	0.000		0.000	0.000	0.095	0.000	0.000	0.000	0.038
	m. R^2	0.219	0.140		0.002	0.000	0.000	0.031	0.007	0.107	0.248		0.022	0.035	0.009	0.087	0.037	0.108	0.008
	fix. ef.	-	-	BN	0.000	0.001	0.000	0.002	0.001	-	-	BN	0.002	0.003	0.000	0.003	0.002	0.004	0.001
	P	-	-		0.831	0.254	0.713	0.003	0.384	-	-		0.000	0.000	0.570	0.000	0.000	0.000	0.150
	m. R^2	-	-		0.000	0.003	0.000	0.019	0.002	-	-		0.033	0.056	0.001	0.091	0.043	0.149	0.004
Validation	fix. ef.	0.004	0.004	AAL	0.002	0.000	0.001	0.001	0.002	0.003	0.004	AAL	0.002	0.003	0.002	0.002	0.003	0.003	0.002
	P	0.000	0.000		0.003	0.701	0.093	0.095	0.000	0.000	0.000		0.001	0.000	0.000	0.000	0.000	0.000	0.000
	m. R^2	0.129	0.107		0.027	0.000	0.008	0.008	0.046	0.085	0.136		0.031	0.074	0.036	0.047	0.065	0.060	0.033
	fix. ef.	-	-	BN	0.001	0.000	0.000	0.001	0.001	-	-	BN	0.002	0.003	0.002	0.002	0.003	0.003	0.002
	P	-	-		0.086	0.697	0.357	0.240	0.011	-	-		0.001	0.000	0.000	0.000	0.000	0.000	0.000
	m. R^2	-	-		0.007	0.000	0.002	0.003	0.015	-	-		0.031	0.074	0.036	0.047	0.065	0.060	0.033

Abbreviations: adj. = adjusted; AAL = automated anatomical labelling; BN = Brainnetome; FA = fractional anisotropy; fix. ef. = fixed effect; invLen = number of streamlines weighted by the inverse length of each streamline; MD = mean diffusivity; mFA = mean of fractional anisotropy of streamlines; MK = mean kurtosis; mLen= mean length of streamlines; mMK = mean of mean kurtosis of streamlines; m. R^2 = marginal R^2; nSL = number of streamlines; RK = radial kurtosis; wFA= number of streamlines weighted by fractional anisotropy; wMK = number of streamlines weighted by mean kurtosis.

Table e4: Intraclass correlation coefficients

	Single-shell								Multi-shell								
	Skeleton			Network					Skeleton			Network					
	FA	MD	Atlas	nSL	mLen	invLen	mFA	wFA	MK	RK	Atlas	nSL	mLen	invLen	mMK	wMK	mFA	wFA
Exploration	0.981	0.989	**AAL**	0.958	0.883	0.951	0.958	0.963	0.973	0.988	**AAL**	0.923	0.916	0.560	0.974	0.896	0.982	0.921
	-	-	**BN**	0.949	0.944	0.939	0.965	0.953	-	-	**BN**	0.900	0.900	0.675	0.979	0.882	0.985	0.894
Validation	0.967	0.979	**AAL**	0.969	0.921	0.960	0.944	0.973	0.956	0.984	**AAL**	0.923	0.927	0.794	0.958	0.906	0.974	0.899
	-	-	**BN**	0.955	0.946	0.947	0.963	0.960	-	-	**BN**	0.849	0.886	0.767	0.971	0.835	0.977	0.791

Abbreviations: AAL = automated anatomical labelling; BN = Brainnetome; FA = fractional anisotropy; invLen = number of streamlines weighted by the inverse length of each streamline; MD = mean diffusivity; mFA = mean of fractional anisotropy of streamlines; MK = mean kurtosis; mLen= mean length of streamlines; mMK = mean of mean kurtosis of streamlines; nSL = number of streamlines; RK = radial kurtosis; wFA= number of streamlines weighted by fractional anisotropy; wMK = number of streamlines weighted by mean kurtosis.