<u>Supplementary Material 1.</u> Details of acquisition of T1-weighted, T2-weighted and FLAIR sequences.

- Axial, coronal and sagittal fast spin echo T1-weighted imaging: TR = 250ms, TE = 5ms, 90° flip angle, 35 joined slices, 6-mm section thickness; 256×256 matrix; voxel size =0.5×0.5×6mm^3.
- Axial, coronal and sagittal fast spin echo T2-weighted imaging: TR = 4800ms, TE = 90ms, 150° flip angle, 35 joined slices, 6-mm section thickness; 256×256 matrix; voxel size =0.5×0.5×6mm^3.
- Axial, coronal and sagittal FLAIR imaging: TR = 8900ms, TE = 90 ms, inversion time = 2200ms, 150° flip angle, 35 joined slices, 6-mm section thickness; 256×256 matrix; voxel size =0.5×0.5×6mm^3

<u>Supplementary Material 2.</u> List of ROI studied for quantitative DTI

- **ROI in white matter:**

Right anterior limb of internal capsule (ALIC)

Left anterior limb of internal capsule (ALIC)

Right posterior limb of internal capsule (PLIC)

Left posterior limb of internal capsule (PLIC)

Genu of corpus callosum (CC)

Splenium of corpus callosum (CC)

Middle cerebellar peduncle (Mid Cereb Ped)

Right superior cerebellar peduncle (Sup Cereb Ped)

Left superior cerebellar peduncle (Sup Cereb Ped)

Right cerebral peduncle

Left cerebral peduncle

Right anterior corona radiata

Left anterior corona radiata

Right posterior corona radiata

Left posterior corona radiata

Right superior corona radiata

Left superior corona radiata

- **ROI in grey matter:**

Frontal pole

Postcentral gyrus

Middle temporal gyrus

Occipital pole

Right caudate nucleus

Left caudate nucleus

Right thalamus

Left thalamus

<u>Supplementary Table 1.</u> Results of statistical analyses for quantitative DTI parameters in white and grey matter.

	FA				MD				AD				RD			
	PMD0-1	**PMD2**	**PMD3-4**	***p***	**PMD0-1**	**PMD2**	**PMD3-4**	***p***	**PMD0-1**	**PMD2**	**PMD3-4**	***p***	**PMD0-1**	**PMD2**	**PMD3-4**	***p***
Number of patients	8	14	10		8	14	10		8	14	10		8	14	10	
ALIC R[a]	0.33 (0.11)	0.34 (0.06)	0.37 (0.06)	0.58	1.04 (0.23)	0.90 (0.08)	0.93 (0.20)	0.18	1.37 (0.20)	1.25 (0.06)	1.31 (0.16)	0.50	0.89 (0.26)	0.73 (0.10)	0.74 (0.23)	0.12
vs. PMD0-1 (*p*-value)		0.68	0.26			0.08	0.14			0.09	0.22			0;09	0.13	
vs. PMD2 (*p*-value)			0.40				0.95				0.76				0.96	
ALIC L[a]	0.33 (0.10)	0.32 (0.07)	0.38 (0.06)	0.26	1.01 (0.16)	1.01 (0.30)	0.99 (0.28)	0.53	1.34 (0.11)	1.35 (0.30)	1.38 (0.26)	0.33	0.84 (0.20)	0.84 (0.30)	0.79 (0.29)	0.44
vs. PMD0-1 (*p*-value)		0.66	0.21			0.99	0.94			0.92	0.73			0.98	0.79	
vs. PMD2 (*p*-value)			0.08				0.93				0.78				0.79	
PLIC R[a]	0.44 (0.13)	0.42 (0.12)	0.44 (0.11)	0.81	1.01 (0.20)	1.00 (0.24)	0.93 (0.22)	0.13	1.50 (0.10)	1.47 (0.19)	1.38 (0.17)	0.18	0.76 (0.25)	0.77 (0.27)	0.70 (0.27)	0.54
vs. PMD0-1 (*p*-value)		0.64	0.85			0.87	0.67			0.56	0.48			0.99	0.76	
vs. PMD2 (*p*-value)			0.52				0.76				0.82				0.75	
PLIC L[a]	0.45 (0.09)	0.41 (0.13)	0.46 (0.07)	0.68	0.99 (0.22)	1.00 (0.23)	0.95 (0.29)	0.30	1.51 (0.19)	1.46 (0.17)	1.42 (0.28)	0.28	0.73 (0.24)	0.77 (0.28)	0.71 (0.31)	0.81
vs. PMD0-1 (*p*-value)		0.41	0.98			0.99	0.98			0.52	0.74			0.82	0.92	
vs. PMD2 (*p*-value)			0.46				0.98				0.81				0.92	
CC genu[a]	0.32 (0.06)	0.36 (0.07)	0.34 (0.09)	0.41	1.32 (0.25)	1.14 (0.18)	1.34 (0.59)	0.07	1.76 (0.29)	1.60 (0.22)	1.80 (0.54)	0.43	1.10 (0.24)	0.92 (0.18)	1.12 (0.62)	0.09
vs. PMD0-1 (*p*-value)		0.29	0.38			0.28	0.79			0.31	0.71			0.29	0.82	
vs. PMD2 (*p*-value)			0.97				0.20				0.19				0.22	
CC splenium[a]	0.31 (0.07)	0.33 (0.06)	0.30 (0.07)	0.68	1.41 (0.23)	1.27 (0.13)	1.33 (0.22)	0.36	1.82 (0.22)	1.72 (0.18)	1.73 (0.31)	0.40	1.22 (0.25)	1.04 (0.14)	1.12 (0.20)	0.16
vs. PMD0-1 (*p*-value)		0.70	0.99			0.11	0.14			0.41	0.27			0.06	0.12	
vs. PMD2 (*p*-value)			0.70				0.90				0.67				0.92	
Mid cereb ped[a]	0.30 (0.06)	0.26 (0.04)	0.29 (0.05)	0.11	1.37 (0.49)	1.60 (0.50)	1.49 (0.34)	0.55	1.74 (0.51)	1.95 (0.56)	1.83 (0.40)	0.77	1.18 (0.48)	1.42 (0.48)	1.33 (0.33)	0.38
vs. PMD0-1 (*p*-value)		0.06	0.67			0.23	0.90			0.30	0.86			0.20	0.76	
vs. PMD2 (*p*-value)			**0.03**				0.32				0.25				0.39	
Sup cereb ped R[a]	0.31 (0.08)	0.28 (0.06)	0.33 (0.04)	0.19	1.74 (0.43)	1.40 (0.33)	1.61 (0.23)	0.06	2.26 (0.48)	1.79 (0.45)	2.11 (0.39)	0.05	1.50 (0.44)	1.20 (0.28)	1.36 (0.17)	0.10
vs. PMD0-1 (*p*-value)		0.41	0.44			**0.02**	**0.04**			**0.02**	0.07			**0.04**	**0.04**	
vs. PMD2 (*p*-value)			0.12				0.93				0.80				0.76	
Sup cereb ped L[a]	0.30 (0.09)	0.29 (0.07)	0.32 (0.04)	0.53	1.81 (0.52)	1.40 (0.34)	1.60 (0.21)	0.10	2.33 (0.54)	1.80 (0.44)	2.05 (0.37)	0.09	1.55 (0.53)	1.12 (0.30)	1,37 (0.14)	0.17
vs. PMD0-1 (*p*-value)		0.72	0.54			**0.02**	**0.05**			**0.01**	**0.03**			**0.03**	0.09	
vs. PMD2 (*p*-value)			0.32				0.86				0.99				0.83	
Cerebral ped R[a]	0.40 (0.13)	0.37 (0.10)	0.45 (0.09)	0.06	1.55 (1.09)	1.16 (0.16)	1.10 (0.12)	0.44	2.08 (0.11)	1.63 (0.25)	1.64 (0.25)	0.62	1.27 (0.11)	0.92 (0.15)	0.84 (0.14)	0.25
vs. PMD0-1 (*p*-value)		0.62	0.26			0.15	0.08			0.12	0.10			0.18	0.08	
vs. PMD2 (*p*-value)			0.10				0.57				0.75				0.50	
Cerebral ped L[a]	0.40 (0.13)	0.37 (0.12)	0.45 (0.10)	0.13	1.46 (0.92)	1.18 (0.14)	1.11 (0.16)	0.54	2.00 (0.95)	1.64 (0.21)	1.63 (0.22)	0.64	1.19 (0.92)	0.94 (0.16)	0.85 (0.19)	0.19
vs. PMD0-1 (*p*-value)		0.44	0.45			0.20	0.11			0.13	0.12			0.27	0.12	
vs. PMD2 (*p*-value)			0.12				0.56				0.76				0.49	
Ant corona radiata R[a]	0.28 (0.07)	0.31 (0.08)	0.31 (0.03)	0.69	1.07 (0.09)	1.05 (0.16)	1.10 (0.24)	0.65	1.39 (0.09)	1.40 (0.16)	1.43 (0.29)	0.94	0.90 (0.11)	0.88 (0.17)	0.93 (0.22)	0.87
vs. PMD0-1 (*p*-value)		0.37	0.80			0.86	0.60			0.96	0.73			0.77	0.55	
vs. PMD2 (*p*-value)			0.57				0.45				0.73				0.35	
Ant corona radiata L[a]	0.027 (0.05)	0.32 (0.09)	0.32 (0.03)	0.20	1.12 (0.12)	1.08 (0.18)	1.00 (0.05)	0.15	1.43 (0.11)	1.44 (0.23)	1.32 (0.09)	0.11	0.96 (0.13)	0.90 (0.17)	0.84 (0.05)	0.17
vs. PMD0-1 (*p*-value)		0.11	0.28			0.54	0.18			0.95	0.26			0.32	0.17	
vs. PMD2 (*p*-value)			0.75				0.37				0.21				0.57	

Supplementary Table 1. **Results of statistical analyses for quantitative DTI parameters in white and grey matter.**

	FA				MD				AD				RD			
	PMD0-1	**PMD2**	**PMD3-4**	***p***	**PMD0-1**	**PMD2**	**PMD3-4**	***p***	**PMD0-1**	**PMD2**	**PMD3-4**	***p***	**PMD0-1**	**PMD2**	**PMD3-4**	***p***
Post corona radiata R[a]	0.29 (0.06)	0.27 (0.05)	0.30 (0.05)	0.27	1.18 (0.20)	1.11 (0.09)	1.13 (0.19)	0.64	1.54 (0.22)	1.42 (0.09)	1.44 (0.17)	0.39	1.00 (0.20)	0.95 (0.10)	0.97 (0.21)	0.85
vs. PMD0-1 (*p*-value)		0.36	0.86			0.33	0.44			0.12	0.12			0.53	0.69	
vs. PMD2 (*p*-value)			0.31				0.93				0.80				0.87	
Post corona radiata L[a]	0.28 (0.04)	0.26 (0.05)	0.30 (0.02)	0.12	1.08 (0.10)	1.04 (0.06)	1.11 (0.11)	0.22	1.42 (0.12)	1.32 (0.08)	1.42 (0.11)	**0.05**	0.91 (0.09)	0.89 (0.07)	0.095 (0.12)	0.37
vs. PMD0-1 (*p*-value)		0.22	0.95			0.24	0.59			**0.04**	0.69			0.60	0.34	
vs. PMD2 (*p*-value)			0.23				0.10				0.13				0.13	
Sup corona radiata R[a]	0.30 (0.07)	0.26 (0.05)	0.29 (0.04)	0.20	1.14 (0.20)	1.01 (0.09)	1.01 (0.16)	0.06	1.46 (0.19)	1.28 (0.08)	1.29 (0.14)	**0.03**	0.98 (0.22)	0.88 (0.10)	0.87 (0.18)	0.20
vs. PMD0-1 (*p*-value)		0.19	0.60			0.06	0.11			**<0.01**	**0.02**			0.16	0.28	
vs. PMD2 (*p*-value)			0.51				0.96				0.92				0.88	
Sup corona radiata L[a]	0.28 (0.06)	0.27 (0.05)	0.31 (0.04)	0.11	1.12 (0.26)	1.02 (0.13)	1.07 (0.24)	0.24	1.42 (0.25)	1.30 (0.15)	1.39 (0.28)	0.14	0.97 (0.27)	0.87 (0.13)	0.92 (0.23)	0.58
vs. PMD0-1 (*p*-value)		0.46	0.54			0.27	0.70			0.25	0.65			0.30	0.76	
vs. PMD2 (*p*-value)			0.19				0.54				0.55				0.53	
Frontal pole[a]	0.26 (0.03)	0.29 (0.05)	0.29 (0.04)	0.13	1.29 (0.20)	1.14 (0.09)	1.17 (0.17)	0.09	1.56 (0.24)	1.45 (0.13)	1.46 (0.20)	0.47	1.16 (0.19)	0.99 (0.08)	1.02 (0.15)	**0.03**
vs. PMD0-1 (*p*-value)		0.08	0.11			**0.03**	0.10			**0.21**	0.21			**0.01**	0.08	
vs. PMD2 (*p*-value)			0.90				0.78				0.84				0.55	
Postcentral gyrus[a]	0.23 (0.06)	0.27 (0.03)	0.30 (0.05)	0.31	1.11 (0.13)	1.14 (0.15)	1.11 (0.18)	0.78	1.32 (0.16)	1.43 (0.19)	1.38 (0.20)	0.40	1.01 (0.13)	0.99 (0.14)	0.98 (0.18)	0.60
vs. PMD0-1 (*p*-value)		0.06	**0.01**			0.79	0.92			0.23	0.48			0.81	0.82	
vs. PMD2 (*p*-value)			0.31				0.88				0.72				0.98	
Mid temporal gyrus[a]	0.21 (0.03)	0.25 (0.05)	0.23 (0.03)	0.09	1.26 (0.32)	1.09 (0.22)	1.02 (0.18)	0.10	1.46 (0.39)	1.36 (0.29)	1.23 (0.20)	0.37	1.16 (0.30)	0.96 (0.18)	0.92 (0.18)	0.10
vs. PMD0-1 (*p*-value)		**0.02**	0.18			0.10	0.18			0.41	0.33			**0.04**	0.11	
vs. PMD2 (*p*-value)			0.48				0.95				0.77				0.76	
Occipital pole[a]	0.20 (0.05)	0.25 (0.06)	0.24 (0.03)	0.15	1.31 (0.31)	1.22 (0.41)	1.14 (0.11)	0.15	1.56 (0.28)	1.52 (0.49)	1.37 (0.12)	0.13	1.18 (0.33)	1.08 (0.38)	1.02 (0.10)	0.19
vs. PMD0-1 (*p*-value)		0.05	0.26			0.60	0.23			0.84	0.24			0.47	0.23	
vs. PMD2 (*p*-value)			0.52				0.41				0.28				0.52	
Caudate nucleus R[a]	0.17 (0.05)	0.22 (0.04)	0.18 (0.04)	**0.04**	1.69 (0.36)	1.34 (0.37)	1.16 (0.44)	0.10	1.94 (0;50)	1.62 (0;47)	1.90 (0.55)	0.19	1.54 (0.42)	1.09 (0.22)	1.42 (0.36)	**0.05**
vs. PMD0-1 (*p*-value)		**0.01**	0.15			0.06	0.28			0.19	0.34			**0.03**	0.27	
vs. PMD2 (*p*-value)			0.38				0.54				0.85				0.40	
Caudate nucleus L[a]	0.18 (0.04)	0.20 (0.03)	0.19 (0.05)	0.45	1.67 (0.38)	1.21 (0.25)	1.56 (0.40)	**0.01**	1.94 (0.40)	1.45 (0.31)	1.85 (0.54)	**0.02**	1.54 (0.42)	1.10 (0.22)	1.42 (0.36)	**<0.01**
vs. PMD0-1 (*p*-value)		0.15	0.08			**<0.01**	0.14			**0.02**	0.16			**<0.01**	0.17	
vs. PMD2 (*p*-value)			0.55				0.24				0.36				0.20	
Thalamus R[a]	0.21 (0.04)	0.25 (0.03)	0.23 (0.04)	0.07	1.83 (0.42)	1.39 (0.39)	1.53 (0.40)	0.06	2.02 (0.55)	1.73 (0.47)	1.87 (0.46)	0.40	1.73 (0.40)	1.22 (0.35)	1.37 (0.38)	**0.03**
vs. PMD0-1 (*p*-value)		**0.02**	0.09			**0.03**	0.07			0.22	0.28			**<0.01**	**0.03**	
vs. PMD2 (*p*-value)			0.74				0.89				0.97				0.81	
Thalamus L[a]	0.21 (0.03)	0.24 (0.02)	0.23 (0.05)	0.09	1.80 (0.42)	1.38 (0.39)	1.56 (0.40)	0.07	2.05 (0,44)	1.68 (0.47)	1.89 (0.52)	0.12	1.67 (0.472)	1.23 (0.35)	1.39 (0.36)	0.06
vs. PMD0-1 (*p*-value)		0.06	0.11			**0.03**	0.10			0.11	0.24			**0.02**	0.06	
vs. PMD2 (*p*-value)			0.99				0.79				0.80				0.78	

[a]Results are expressed as means (SD); boldface for *p*-value <0.05; Omnibus *p*-value (*p*) obtained without age adjustment (Kruskall-Wallis test performed, when appropriate, with log information to meet the normality assumption) whereas other *p*-values were computed using ANCOVA with age as the adjustment covariate. Effect sizes with 95% confidence intervals are given in Supplementary Table 1. FA: fractional anisotropy, MD: mean diffusivity, AD: axial diffusivity, RD: radial diffusivity, MD, AD and RD values are expressed as 10^{-3} values. NA: not applicable, ALIC: anterior limb of the internal capsule, PLIC: posterior limb of the internal capsule, R: right, L: left, CC: corpus callosum, Mid: middle, Ant: anterior, Post: posterior, Sup: superior, Ped: peduncle, Cereb: cerebellar, vs: versus

<u>Supplementary Table 2.</u> Results of statistical correlation between GMFM and quantitative DTI parameters in white and grey matter.

	Coefficient of correlation (*p*-value)			
GMFM correlation	**FA**	**MD**	**AD**	**RD**
ALIC R	0.05 (0.284)	-0.05 (0.713)	-0.42 (0.898)	-0.04 (0.601)
ALIC L	0.07 (0.372)	-0.07 (0.589)	-0.26 (0.717)	-0.06 (0.543)
PLIC R	-0.15 (0.870)	0.04 (0.189)	-0.03 (**0.037**)	0.11 (0.331)
PLIC L	-0.23 (0.371)	0.10 (0.256)	-0.12 (0.127)	0.18 (0.358)
CC genu	0.13 (0.606)	-0.32 (0.986)	-0.22 (0.794)	-0.27 (0.931)
CC splenium	-0.11 (0.783)	0.06 (0.963)	-0.08 (0.480)	0.09 (0.581)
Frontal pole	0.27 (0.498)	-0.30 (0.388)	-0.28 (0.687)	-0.34 (0.297)
Occipital Pole	0.24 (0.467)	-0.37 (0.914)	-0.27 (0.964)	-0.41 (0.849)
Post-central gyrus	0.10 (0.094)	-0.06 (0.896)	-0.18 (0.948)	-0.05 (0.878)
Mid temporal gyrus	-0.10 (0.756)	-0.35 (0.071)	-0.40 (0.078)	-0.25 (0.077)
Mid cereb ped	0.12 (0.518)	-0.15 (0.330)	-0.21 (0.269)	-0.12 (0.378)
Sup cereb ped R	0.19 (0.247)	-0.20 **(0.011)**	-0.23 (**0.029**)	-0.18 (**0.007**)
Sup cereb ped L	0.27 (0.350)	-0.43 **(0.043)**	-0.41 (**0.036**)	-0.41 (0.075)
Cerebral ped R	-0.02 (0.374)	-0.10 (0.230)	-0.26 (0.726)	-0.02 (0.152)
Cerebral ped L	-0.09 (0.402)	-0.07 (0.155)	-0.34 (0.460)	0.06 (0.191)
Ant corona radiata R	0.11 (0.182)	-0.48 (0.629)	-0.42 (0.747)	-0.37 (0.857)
Ant corona radiata L	0.00 (0.850)	-0.53 (0.122)	-0.51 (0.188)	0.46 (0.098)
Post corona radiata R	-0.05 (0.273)	0.02 (0.827)	-0.11 (0.662)	0.12 (0.907)
Post corona radiata L	-0.01 (0.110)	-0.07 (0.112)	-0.14 (**0.049**)	0.04 (0.238)
Sup corona radiata R	-0.10 (0.188)	-0.14 (0.299)	-0.25 (0.423)	0.02 (0.291)
Sup corona radiata L	0.02 (0.324)	-0.23 (0.936)	-0.31 (0.765)	0.01 (0.794)
Caudate nucleus R	-0.08 (0.087)	-0.01 (0.330)	0.00 (0.295)	-0.07 (0.367)
Caudate nucleus L	0.01 (0.062)	-0.13 (0.205)	-0.02 (0.183)	-0.15 (0.235)
Thalamus R	0.20 (0.888)	-0.12 (0.922)	-0.07 (0.743)	-0.15 (0.973)
Thalamus L	0.12 (0.529)	-0.15 (0.783)	-0.15 (0.790)	-0.14 (0.793)

[a]Results are expressed as coefficient of correlation (*p*-value). Boldface for *p*-value <0.05. GMFM: gross motor function measure, FA: fractional anisotropy, MD: mean diffusivity, AD: axial diffusivity, RD: radial diffusivity, NA: not applicable, ALIC: anterior limb of internal capsule, PLIC: posterior limb of internal capsule, R: right, L: left, CC: corpus callosum, Mid: middle, Ant: anterior, Post: posterior, Sup: superior, Ped: peduncle, Cereb: cerebellar.

<u>Supplementary Table 3.</u> Results of statistical analysis for quantitative parameters of left and right tractograms in each group of patients.

	PMD0-1	PMD2	PMD3-4	*p*
TIV[a]	1401.3 (75.4)	1472.1 (119.2)	1589.4 (212.9)	0.16
vs. PMD0-1 (*p*-value)		0.60	0.29	
vs. PMD2 (*p*-value)			0.38	
Right volume / TIV[a]	0.067 (0.013)	0.076 (0.040)	0.123 (0.054)	0.09
vs. PMD0-1 (*p*-value)		0.62	**0.02**	
vs. PMD2 (*p*-value)			**0.006**	
Left volume / TIV[a]	0.058 (0.006)	0.078 (0.041)	0.128 (0.048)	**0.048**
vs. PMD0-1 (*p*-value)		0.37	**0.008**	
vs. PMD2 (*p*-value)			**0.005**	
NOF right hemisphere / TIV[a]	0.856 (0.209)	1.007 (0.390)	1.827 (0.773)	**0.02**
vs. PMD0-1 (*p*-value)		0.55	**0.005**	
vs. PMD2 (p-value)			**<0.001**	
NOF left hemisphere / TIV [a]	0.769 (0.379)	1.030 (0.392)	1.901 (0.768)	**0.007**
vs. PMD0-1 (*p*-value)		0.41	**0.004**	
vs. PMD2 (*p*-value)			**0.001**	

[a]Results are expressed as means (SD); boldface for *p*-value <0.05; Omnibus *p*-value (*p*) obtained without age adjustment (Kruskall-Wallis test performed, when appropriate, with log information to meet the normality assumption) whereas other *p*-values were computed using ANCOVA with age as the adjustment covariate. NOF: number of fibers, Total intracranial volume (TIV) and tractogram volume are expressed in mm^3. vs: versus.

Legends to supplementary figures

<u>Supplementary Figure 1.</u> Additional results of statistical analyses for the different biomarkers: representation of effect sizes. Effect-sizes are shown and can be compared to the effect-size bounds proposed by Cohen[20], i.e. small (±0.2), medium (±0.5) and large (±0.8, "grossly perceptible and therefore large")**.** Squares correspond to PMD0-1 versus PMD2, circles to PMD0-1 versus PMD3-4 and triangles to PMD2 versus PMD3-4. FA: fractional anisotropy, MD: mean diffusivity, AD: axial diffusivity, RD: radial diffusivity. ALIC: anterior limb of internal capsule, PLIC: posterior limb of internal capsule, R: right, L: left, CC: corpus callosum, Mid: middle, Ant: anterior, Post: posterior, Sup: superior, Ped: peduncle, Cereb: cerebellar.

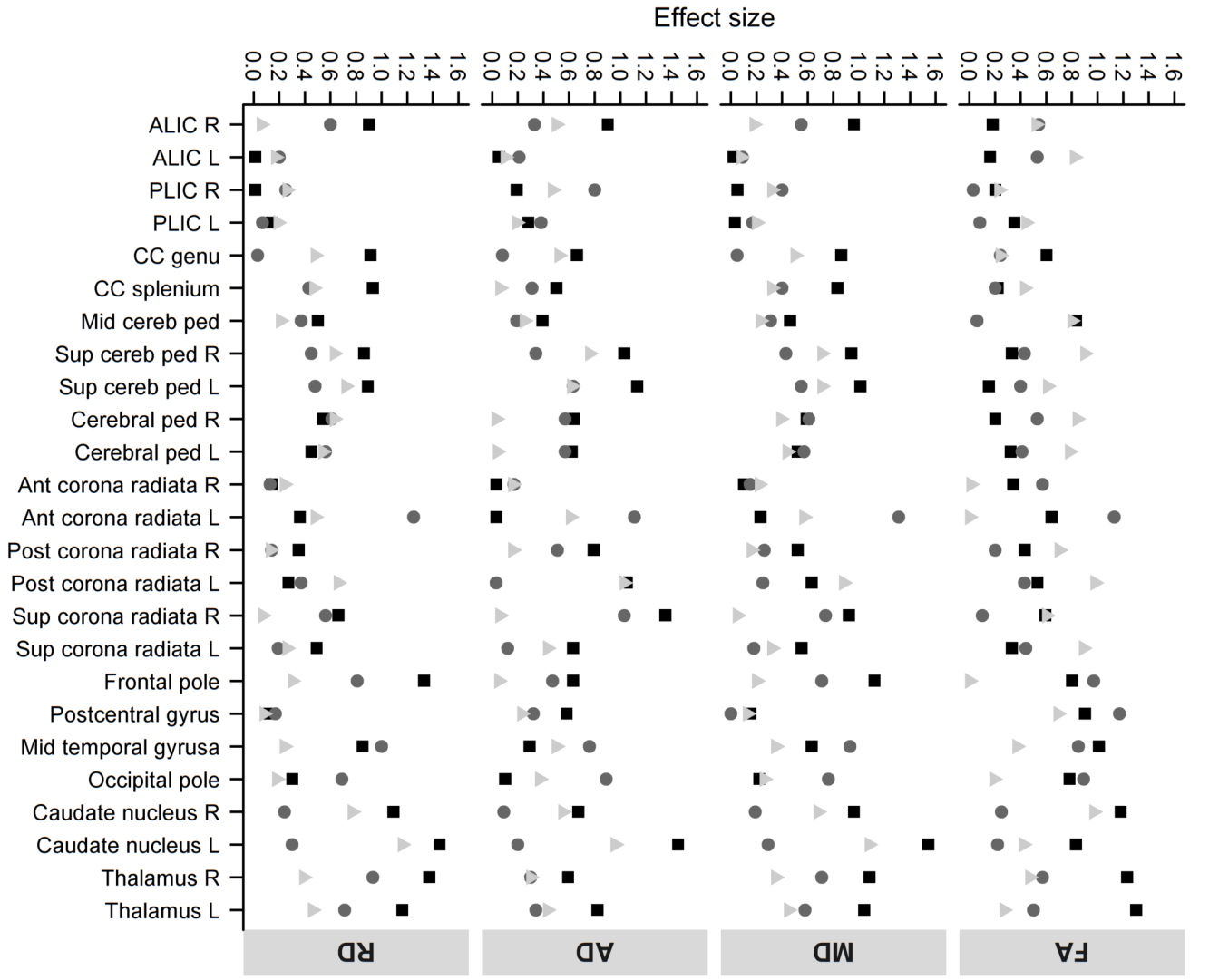
<u>Supplementary Figure 2.</u> Superior views of both hemisphere tractograms of different severity groups and ages in PMD/SPG2 patients.

Tractograms were realized for two ROI corresponding to the right/left hemispheres. Colors correspond to the DMSF: blue = vertical direction, green = longitudinal direction, red = transversal direction. For clinical comparison, Gross Motor Functional Measure (GMFM) at the time of MRI is given under each tractogram when available. **A**. Examples of tractograms in each group of severity in hypomyelinating leukodystrophies. ETP were relatively preserved in all groups whereas smaller than in controls. Compared to controls (a,e), CF and IHC were smaller or lacking in all groups: (1) the most severe PMD0-1 (b,f), (2) the classical PMD2 (c,g) and the mildest PMD3-4 patients (d,h). DMSF in IHC was marked by longitudinal (or rare transversal) over representation. **B**. Each image corresponds to tractograms of PMD2 patients of different ages. These results show that (1) the youngest patients (a,b) had less developed ETP, CF and IHC than patients at the late infancy (c,d) and adolescent patients (e,f), (2) the oldest patients (g,h) had smaller ETP, CF and IHC than adolescent patients (e,f).

<u>Supplementary Figure 3.</u> Lateral left views of right hemisphere tractogram of different severity groups and ages in PMD/SPG2 patients.

Tractogram was realized for one ROI corresponding to the right hemisphere. Colors correspond to the DMSF: blue = vertical direction, green = longitudinal direction, red = transversal direction. For clinical comparison, Gross Motor Functional Measure (GMFM) at the time of MRI is given under each tractogram when available. **A**. Examples of tractograms in each group of severity in hypomyelinating leukodystrophies. ETP were relatively preserved in all groups

whereas smaller than in controls. Compared to controls (a,e), CF and IHC were smaller or lacking in all groups: (1) the most severe PMD0-1 (b,f), (2) the classical PMD2 (c,g) and the mildest PMD3-4 patients (d,h). DMSF in IHC was marked by longitudinal (or rare transversal) over representation. **B**. Each image corresponds to tractograms of PMD2 patients of different ages. These results show that (1) the youngest patients (a,b) had less developed ETP, CF and IHC than patients at the late infancy (c,d) and adolescent patients (e,f), (2) the oldest patients (g,h) had smaller ETP, CF and IHC than adolescent patients (e,f).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CC splenium
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Sup cereb ped R
Sup cereb ped L
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Cerebral ped L
Ant corona radiata R
Ant corona radiata L
Post corona radiata R
Post corona radiata L
Sup corona radiata R
Sup corona radiata L
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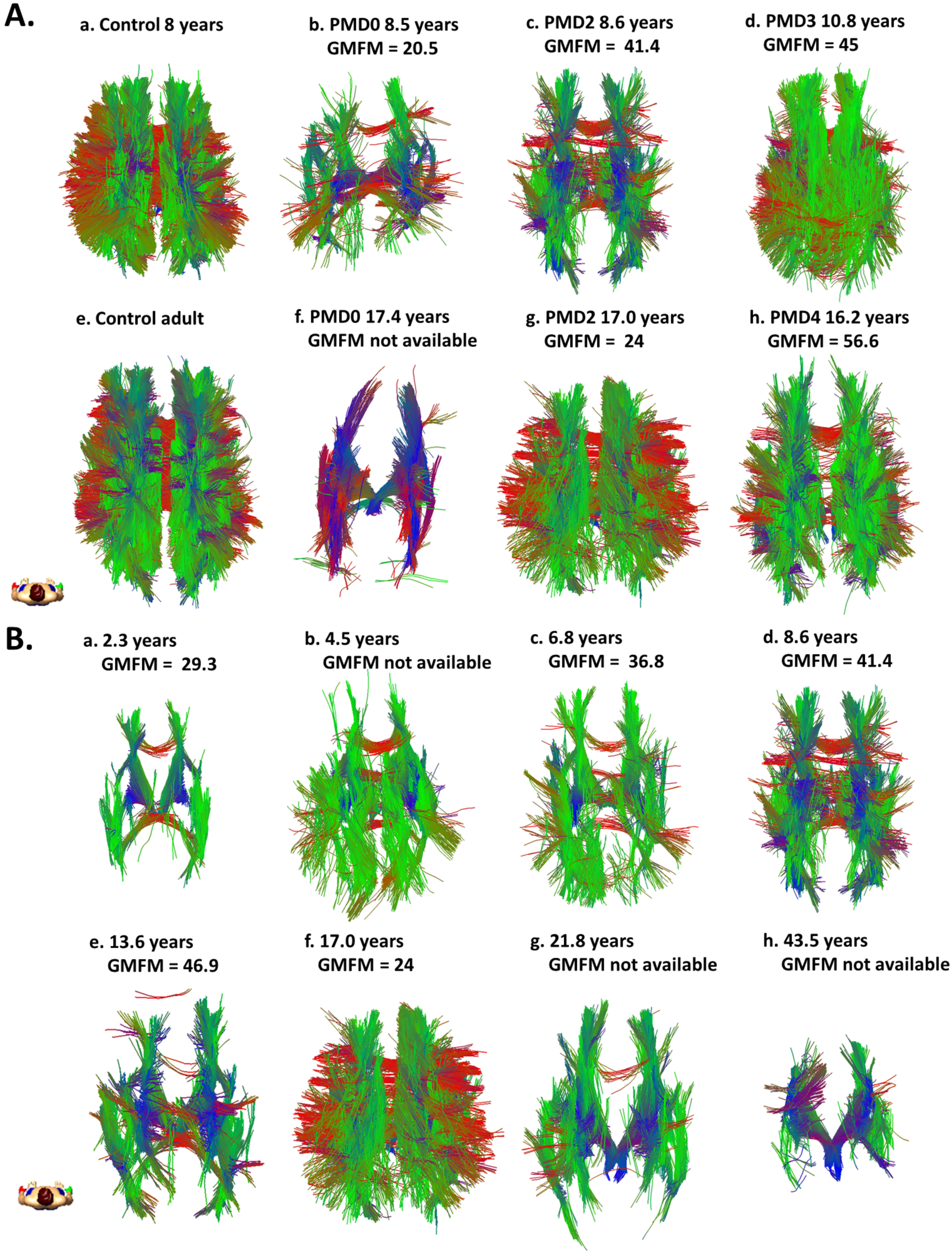
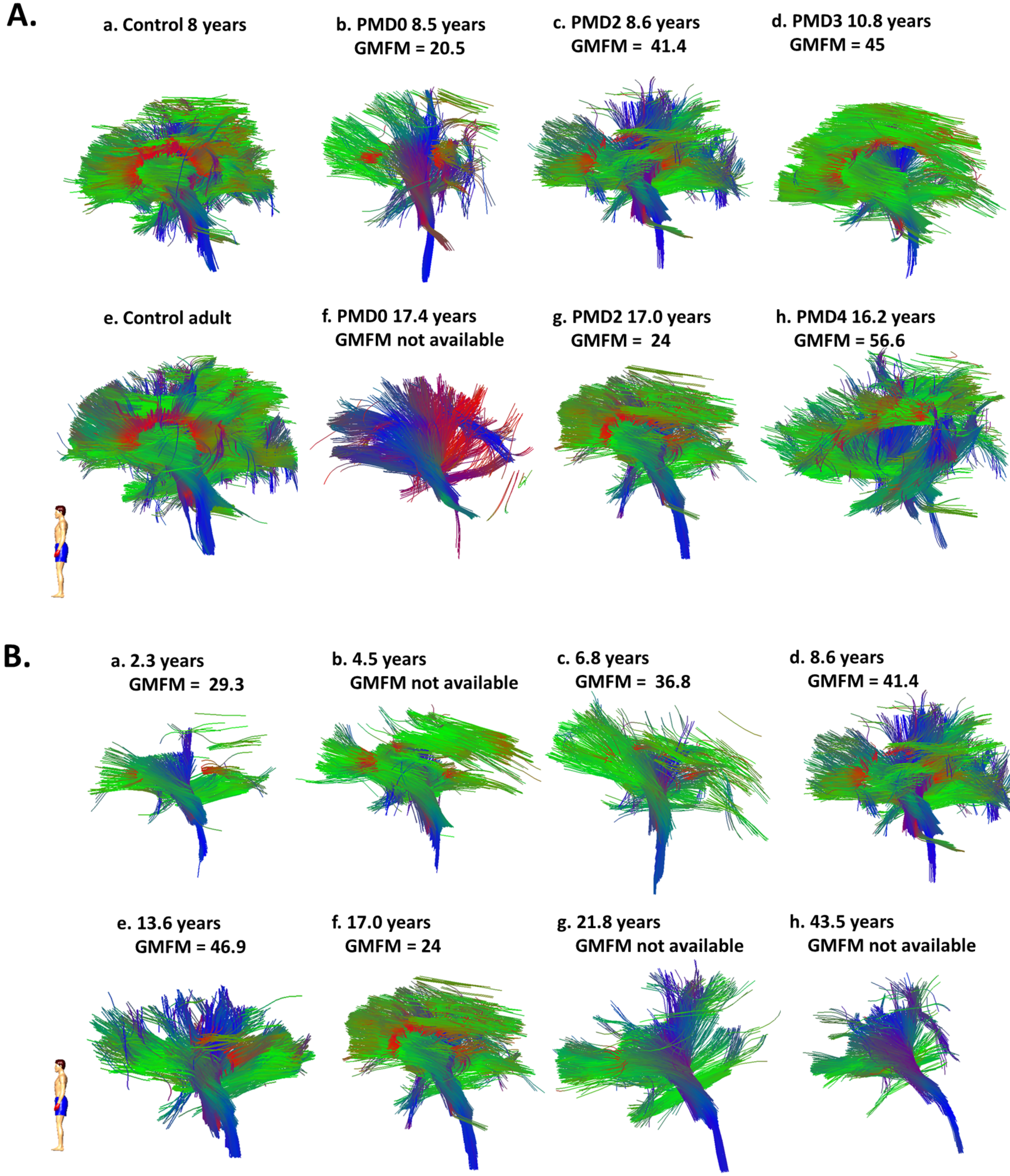


Supplementary Figure 2. Superior views of both hemisphere tractrograms of different severity groups and ages in PMD/SPG2 patients.



Supplementary Figure 3. Lateral left views of right hemisphere tractogram of different severity groups and ages in PMD/SPG2 patients.