

Supplementary material for:

## **White Matter Changes in Chronic and Episodic Migraine: A Diffusion Tensor Imaging Study**

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Supplementary Figure 2: White matter alterations in migraine including duration of migraine history as a covariate

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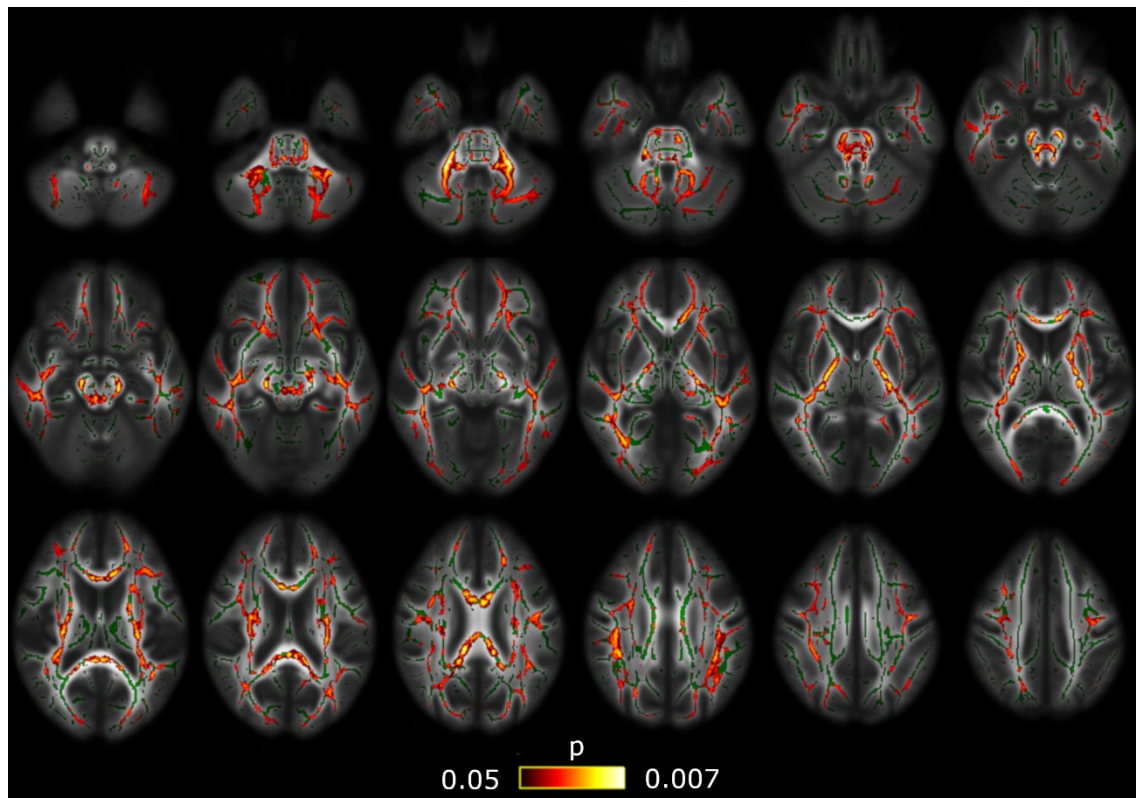
Supplementary Figure 7: Cohen's d FA bar plots (part 2)

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**Supplementary Figure 1. White matter alterations in chronic migraine compared to episodic migraine patients.** TBSS shows decreased AD values in CM compared to EM in widespread locations. White matter skeleton is shown in green, and voxels with significant differences in red-yellow. The colour bar shows the p-values (FWE-corrected).

**Supplementary Table 1.** White matter regions where decreased AD values were found in CM compared to EM (FWE-corrected).

White Matter tract	Minimum p-value (FWE-corrected)	Volume (mm <sup>3</sup> )	MNI peak coordinate (mm), (x,y,z)
Middle cerebellar peduncle	.007	2206	(-20,-50,-32)
Superior cerebellar peduncle R/L	.020/.020	142/126	(5,-28,-19) / (-4,-28,-19)
Inferior cerebellar peduncle R/L	.019/.009	75/89	(12,-43,-35) / (-13,-45,-31)
Superior longitudinal fasciculus R/L	.021/.021	971/874	(33,-4,20) / (-36,-49,15)
Genu of corpus callosum	.019	455	(-10,28,1)
Body of corpus callosum	.032	842	(-4,-30,23)
Splenium of corpus callosum	.025	873	(22,-50,25)
Anterior corona radiata R/L	.024/.018	556/805	(18,21,-11) / (-18,38,-1)
Superior corona radiata R/L	.020/.022	666/396	(28,-16,21) / (-27,-11,20)
Posterior corona radiata R/L	.022/.022	201/214	(25,-24,24) / (-30,-52,22)
External capsule R/L	.020/.018	459/695	(30,-10,14) / (-22,16,-12)
Posterior limb of internal capsule R/L	.020/.022	569/536	(26,-17,13) / (-27,-17,17)
Retrolenticular part of internal capsule R/L	.023/.023	457/344	(31,-34,15) / (-25,-22,3)
Anterior limb of internal capsule R/L	.022/.020	216/290	(15,-1,7) / (-20,18,3)
Sagittal stratum R/L	.022/.022	471/359	(37,-49,-4) / (-41,-18,-13)
Posterior thalamic radiation R/L	.022/.022	353/279	(37,-50,-2) / (-35,-52,13)

Cerebral peduncle R/L	.020/.022	234/265	(11,-23,-21) / (-9,-19,-20)
Corticospinal tract R/L	.019/.023	106/165	(10,-27,-26) / (-7,-18,-22)
Medial lemniscus R/L	.020/.015	82/103	(8,-39,-40) / (-7,-37,-40)
Pontine crossing tract	.018	82	(8,-31,-27)
Fornix (cres) R/L	.024/.024	74/45	(35,-12,-14) / (-34,-15,-13)
Cingulum (hippocampus) L	.036	56	(-17,-42,-2)

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FWE = Family-wise error; L = left; R = right.

The column Volume represents the volume from the atlas region with  $p < .05$  (FWE-corrected). No regions with volume equal or lower than  $30 \text{ mm}^3$  were included in this Table.

**Supplementary Table 2.** White matter regions where decreased AD values were found in CM compared to EM considering only patients with migraine without aura (FWE-corrected).

White Matter tract	Minimum p-value (FWE-corrected)	Volume (mm <sup>3</sup> )	MNI peak coordinate (mm), (x,y,z)
Middle cerebellar peduncle	.014	1382	(-23,-46,-36)
Superior longitudinal fasciculus R	.040	388	(33,-4,20)
Superior corona radiata R	.031	166	(28,-17,23)
External capsule R	.034	103	(29,-8,18)
Posterior limb of internal capsule R	.030	428	(26,-17,13)
Retrolenticular part of internal capsule R	.034	323	(31,-30,7)
Anterior limb of internal capsule R	.037	96	(15,-1,7)
Sagittal stratum R	.034	380	(37,-22,-7)
Posterior thalamic radiation R	.037	242	(30,-39,16)
Fornix (cres) R	.034	52	(35,-16,-12)

FWE = Family-wise error; R = right.

The column Volume represents the volume from the atlas region with  $p < .05$  (FWE-corrected). No regions with volume equal or lower than 30 mm<sup>3</sup> were included in this Table.

**Supplementary Table 3.** White matter regions from the ICBM-DTI-81 White Matter Atlas for which decreased AD values were found in CM compared to EM considering the effect of duration of migraine history (FWE-corrected).

White Matter tract	Minimum p-value (FWE-corrected)	Volume (mm <sup>3</sup> )	MNI peak coordinate (mm), (x,y,z)
Middle cerebellar peduncle	.028	1816	(-20,-50,-32)
Superior cerebellar peduncle R/L	.066/.067	138/124	(5,-28,-19) / (-4,-28,-19)
Inferior cerebellar peduncle R/L	.069/.039	44/61	(13,-42,-36) / (-13,-45,-31)
Superior longitudinal fasciculus R/L	.088/.079	254/411	(42,-43,3) / (-36,-50,15)
Body of corpus callosum	.094	233	(13,-29,28)
Splenium of corpus callosum	.090	618	(-10,-33,25)
Superior corona radiata R/L	.091/.095	261/71	(28,-15,21) / (-27,-11,20)
Posterior corona radiata L	.080	116	(-28,-51,25)
External capsule R/L	.076/.095	94/63	(35,-14,-9) / (-28,-10,17)
Posterior limb of internal capsule R/L	.087/.095	77/126	(26,-17,13) / (-23,-20,13)
Retro-lenticular part of internal capsule R/L	.078/.095	323/81	(38,-29,-1) / (-29,-38,14)
Sagittal stratum R	.066	407	(37,-49,-3)
Posterior thalamic radiation R/L	.066/.081	256/54	(37,-50,-3) / (-35,-52,13)
Cerebral peduncle R/L	.068/.092	153/127	(9,-19,-21) / (-9,-19,-20)
Corticospinal tract R/L	.067/.093	98/109	(8,-27,-26) / (-7,-18,-22)
Pontine crossing tract	.067	51	(8,-31,-27)

Fornix (cres) R	.024	37	(35,-12,-14)
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FWE = Family-wise error; L = left; R = right.

The column Volume represents the volume from the atlas region with p-values < .1 (FWE-corrected). No regions with volume equal or lower than 30 mm<sup>3</sup> were included in this Table.



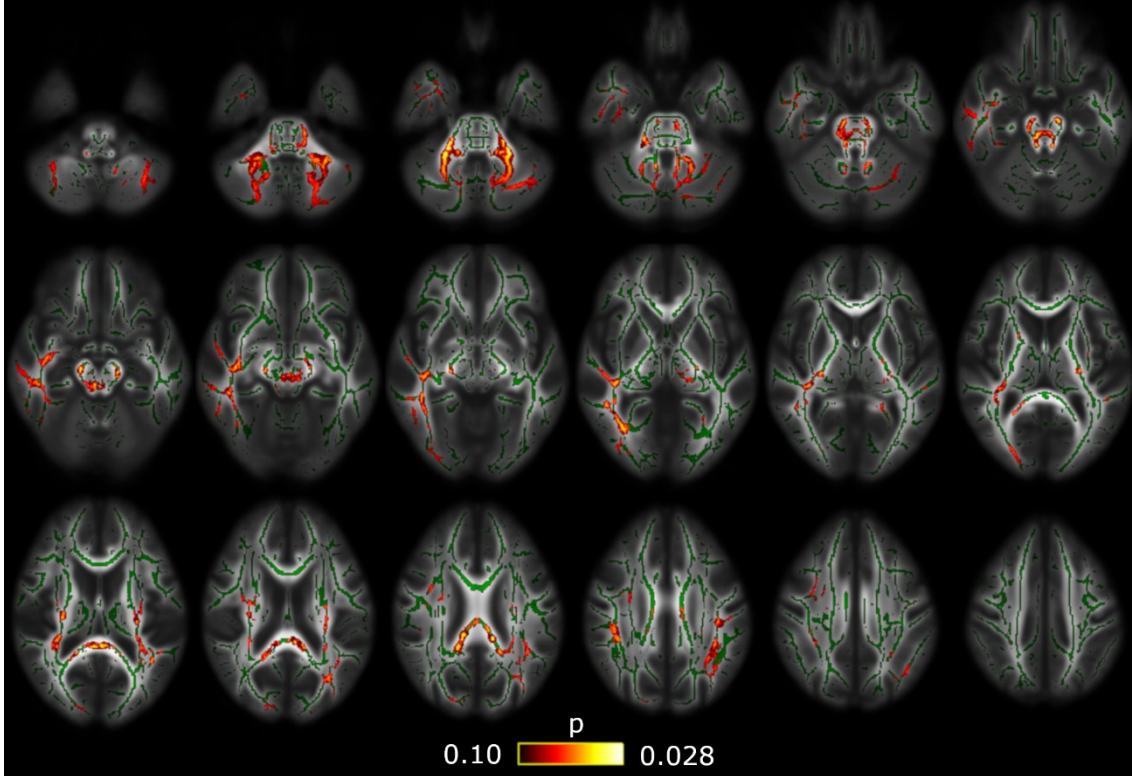
**Supplementary Table 4.** White matter regions from the ICBM-DTI-81 White Matter Atlas for which increased AD values were found in EM compared to HC considering the effect of duration of migraine history (FWE-corrected).

White Matter tract	Minimum p-value (FWE-corrected)	Volume (mm <sup>3</sup> )	MNI peak coordinate (mm), (x,y,z)
Superior corona radiata L	.026	116	(-26,-11,20)
External capsule L	.022	303	(-34,-15,-8)
Posterior limb of internal capsule L	.024	472	(-15,-10,0)
Retrolenticular part of internal capsule L	.025	347	(-33,-34,6)
Sagittal stratum L	.023	133	(-36,-17,-9)
Posterior thalamic radiation L	.025	38	(-35,-39,7)
Cerebral peduncle L	.024	105	(-15,-13,-5)

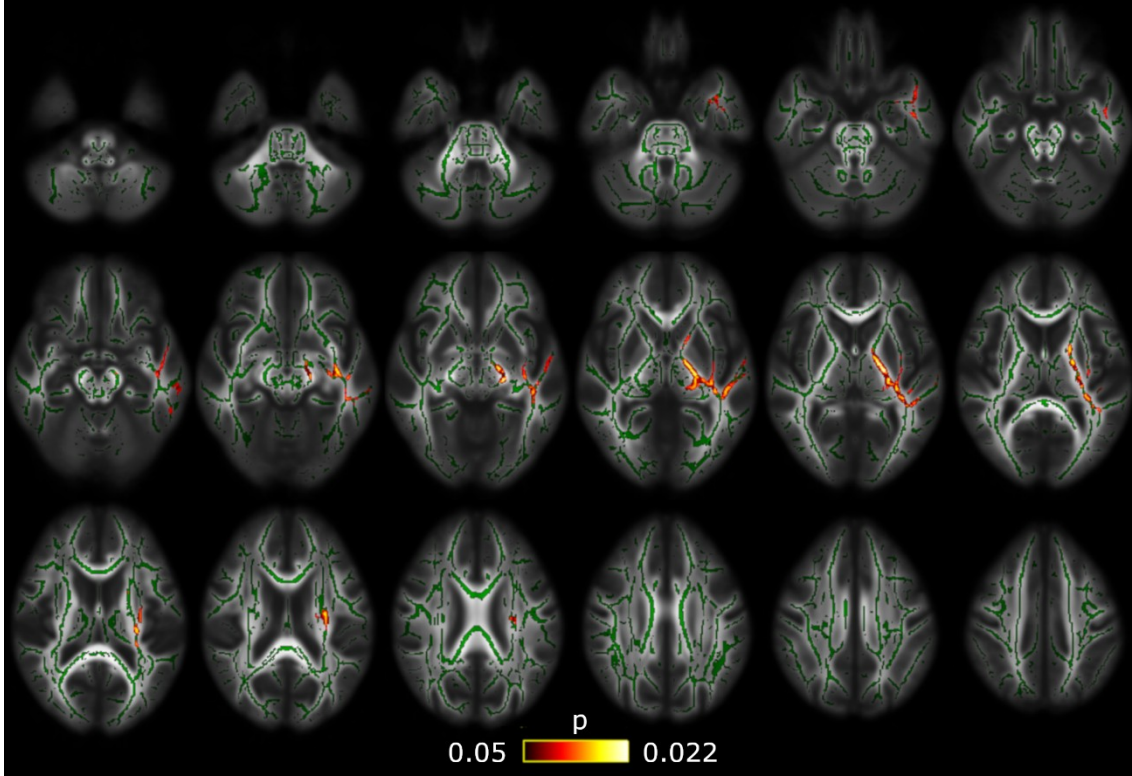
FWE = Family-wise error; L = left.

The column Volume represents the volume from the atlas region with p-values < .05 (FWE-corrected). No regions with volume equal or lower than 30 mm<sup>3</sup> were included in this Table.

AD: CM < EM



AD: EM > HC



**Supplementary Figure 2. White matter alterations in migraine including duration of migraine history as a covariate.** TBSS showed decreased AD values in CM compared to EM in widespread locations (top) and increased AD values in EM compared to healthy controls (bottom) in left hemisphere locations. White matter skeleton is shown in green, and voxels with the lowest p-values in red-yellow. The colour bar shows the p-values (FWE-corrected).

**Supplementary Table 5.** White matter regions from the ICBM-DTI-81 White Matter Atlas for which significant AD values were found in CM compared to EM considering the effect of time from onset of CM (FWE-corrected).

White Matter tract	Minimum p-value (FWE-corrected)	Volume (mm <sup>3</sup> )	MNI peak coordinate (mm), (x,y,z)
Middle cerebellar peduncle	.023	1295	(-20,-50,-32)
Superior cerebellar peduncle R/L	.028/.030	101/115	(5,-28,-19) / (-4,-28,-19)
Inferior cerebellar peduncle L	.035	46	(-10,-50,-25)
Superior longitudinal fasciculus R	.033	720	(32,-4,20)
Splenium of corpus callosum	.042	32	(18,-49,27)
Superior corona radiata R/L	.030/.032	335/136	(28,-15,19) / (-27,-11,20)
Posterior corona radiata R	.035	83	(28,-34,19)
External capsule R/L	.033/.031	127/171	(30,-10,14) / (-28,-10,18)
Posterior limb of internal capsule R/L	.029/.032	301/281	(26,-17,13) / (-27,-17,17)
Retro-lenticular part of internal capsule R/L	.031/.032	473/59	(30,-29,7) / (-25,-23,12)
Sagittal stratum R	.034	150	(38,-28,-4)
Posterior thalamic radiation R	.034	51	(30,-39,16)
Cerebral peduncle R/L	.028/.031	207/258	(10,-28,-16) / (-9,-20,-20)
Corticospinal tract R/L	.030/.031	105/125	(11,-22,-22) / (-7,-18,-22)
Pontine crossing tract	.030	56	(4,-26,-24)
Fornix (cres) R	.037	46	(35,-12,-14)

FWE = Family-wise error; L = left; R = right.

The column Volume represents the volume from the atlas region with p-values  $< .05$  (FWE-corrected). No regions with volume equal or lower than  $30 \text{ mm}^3$  were included in this Table.

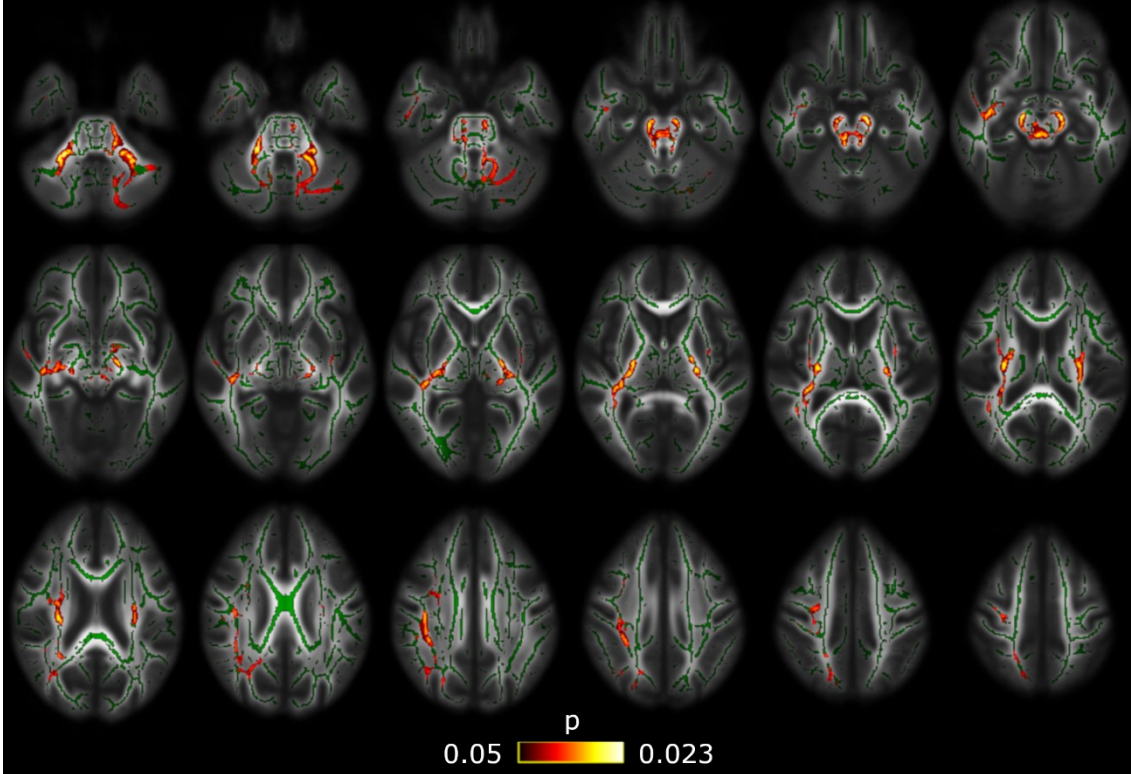
**Supplementary Table 6.** White matter regions from the ICBM-DTI-81 White Matter Atlas for which decreased FA values were found in CM compared to HC considering the effect of time from onset of CM (FWE-corrected).

White Matter tract	Minimum p-value (FWE-corrected)	Volume (mm <sup>3</sup> )	MNI peak coordinate (mm), (x,y,z)
Superior longitudinal fasciculus R	.033	271	(32,-4,19)
Body of corpus callosum	.042	47	(19,-30,31)
Splenium of corpus callosum	.042	209	(19,-31,31)
Anterior corona radiata R	.033	295	(25,17,12)
Superior corona radiata R	.038	236	(32,-6,20)
Posterior corona radiata R	.039	133	(25,-23,22)
External capsule R	.031	661	(30,1,13)
Posterior limb of internal capsule R	.039	217	(24,-19,1)
Retrolenticular part of internal capsule R	.036	425	(38,-29,0)
Anterior limb of internal capsule R	.035	83	(23,17,11)
Sagittal stratum R	.036	132	(33,-23,-4)
Fornix (cres) R	.035	36	(33,-22,-6)

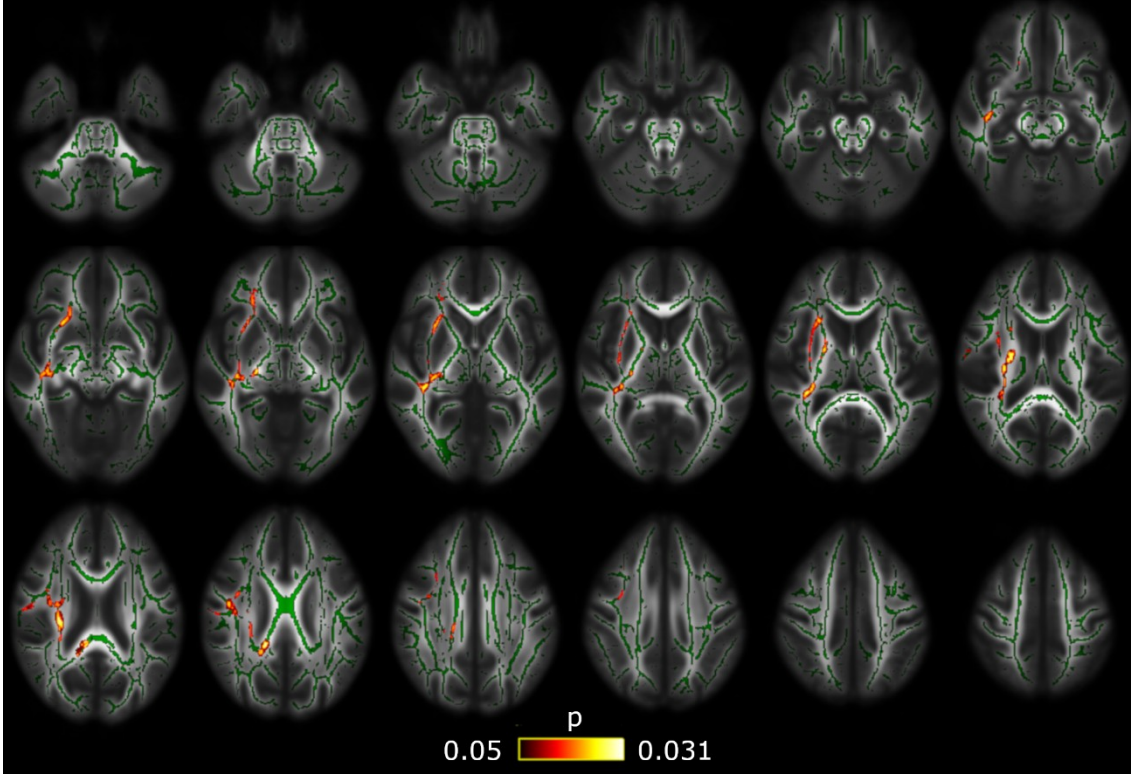
FWE = Family-wise error; L = left; R = right.

The column Volume represents the volume from the atlas region with p-values < .05 (FWE-corrected). No regions with volume equal or lower than 30 mm<sup>3</sup> were included in this Table.

AD: CM < EM



FA: CM < HC



**Supplementary Figure 3. White matter alterations in CM including time from onset of chronic migraine as a covariate.** TBSS showed decreased AD values in CM compared to EM in widespread locations (top) and decreased FA values in CM compared to healthy controls (bottom). Mean white matter skeleton is shown in green, and voxels with the lowest p-values in red-yellow. The colour bar shows the p-values (FWE-corrected).



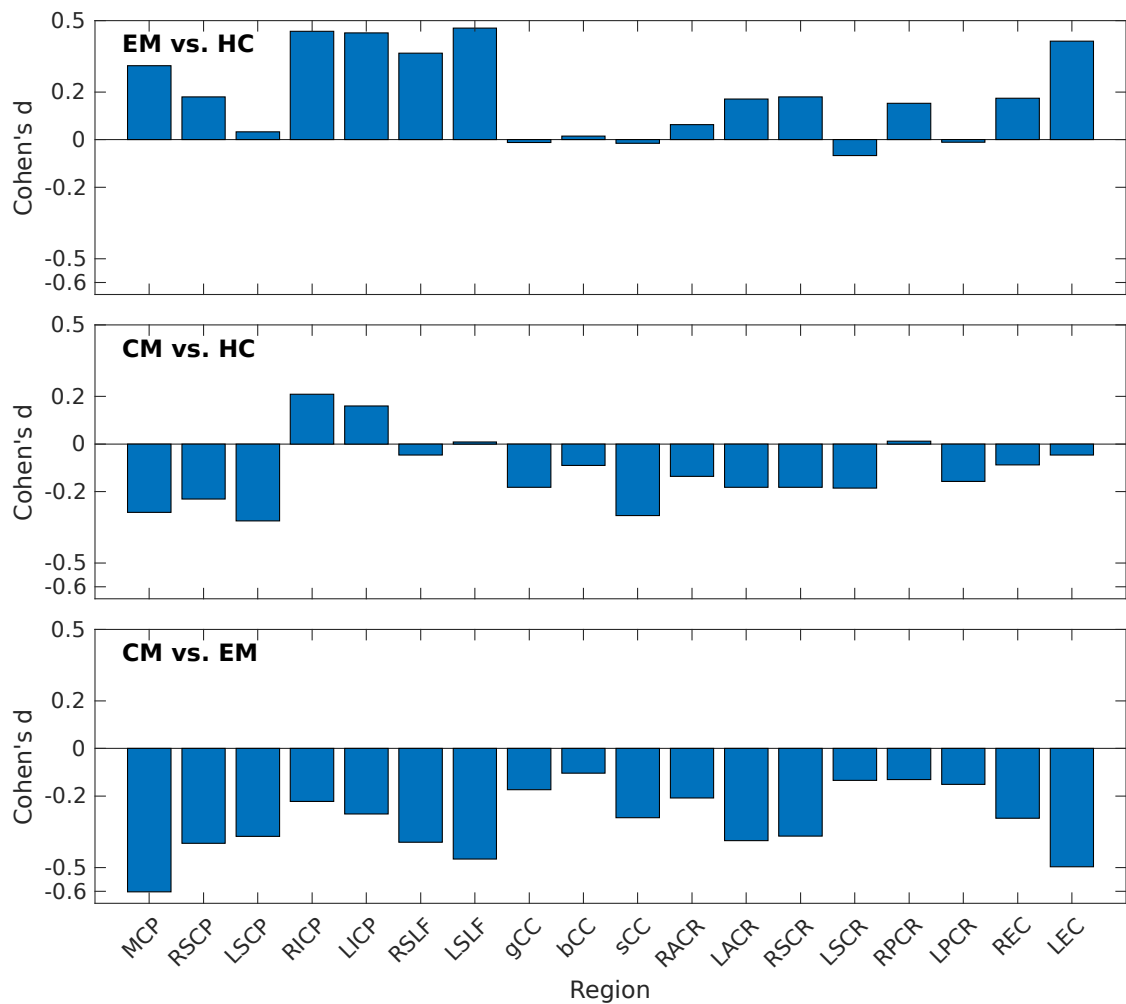
**Supplementary Table 7.** Cohen's d skeleton AD values in regions with significant differences between EM and CM.

White matter region	EM vs. HC Cohen's d	CM vs. HC Cohen's d	CM vs. EM Cohen's d
Middle cerebellar peduncle (MCP)	.31	-.29	<b>-.60</b>
Superior cerebellar peduncle R (RSCP)/L (LSCP)	.18/.03	-.23/-.32	-.40/-.37
Inferior cerebellar peduncle R (RICP)/L (LICP)	.45/.45	.21/.16	-.22/-.28
Superior longitudinal fasciculus R (RSLF)/L (LSLF)	.36/.47	-.05/.01	-.39/-.46
Genu of corpus callosum (gCC)	-.01	-.18	-.17
Body of corpus callosum (bCC)	.01	-.09	-.10
Splenium of corpus callosum (sCC)	-.02	-.30	-.29
Anterior corona radiata R (RACR)/L (LACR)	.06/.17	-.14/-.18	-.21/-.39
Superior corona radiata R (RSCR)/L (LSCR)	.18/-.07	-.18/-.19	-.37/-.13
Posterior corona radiata R (RPCR)/L (LPCR)	.15/-.01	.01/-.16	-.13/-.15
External capsule R (REC)/L (LEC)	.17/.41	-.09/-.05	-.29/ <b>-.50</b>
Posterior limb of internal capsule R (RPIC)/L (LPIC)	.07/.10	-.29/-.19	-.41/-.33
Retrolenticular part of internal capsule R (RRIC)/L (LRIC)	.28/.32	-.09/.05	-.39/-.34
Anterior limb of internal capsule R (RAIC)/L (LAIC)	-.07/.23	-.27/-.01	-.22/-.29
Sagittal stratum R (RSS)/L (LSS)	.26/.31	-.30/-.04	<b>-.57</b> /-.36
Posterior thalamic radiation R (RPTR)/L (LPTR)	.07/.06	-.18/-.12	-.24/-.18
Cerebral peduncle R (RCP)/L (LCP)	.08/.07	-.15/-.26	-.27/-.40

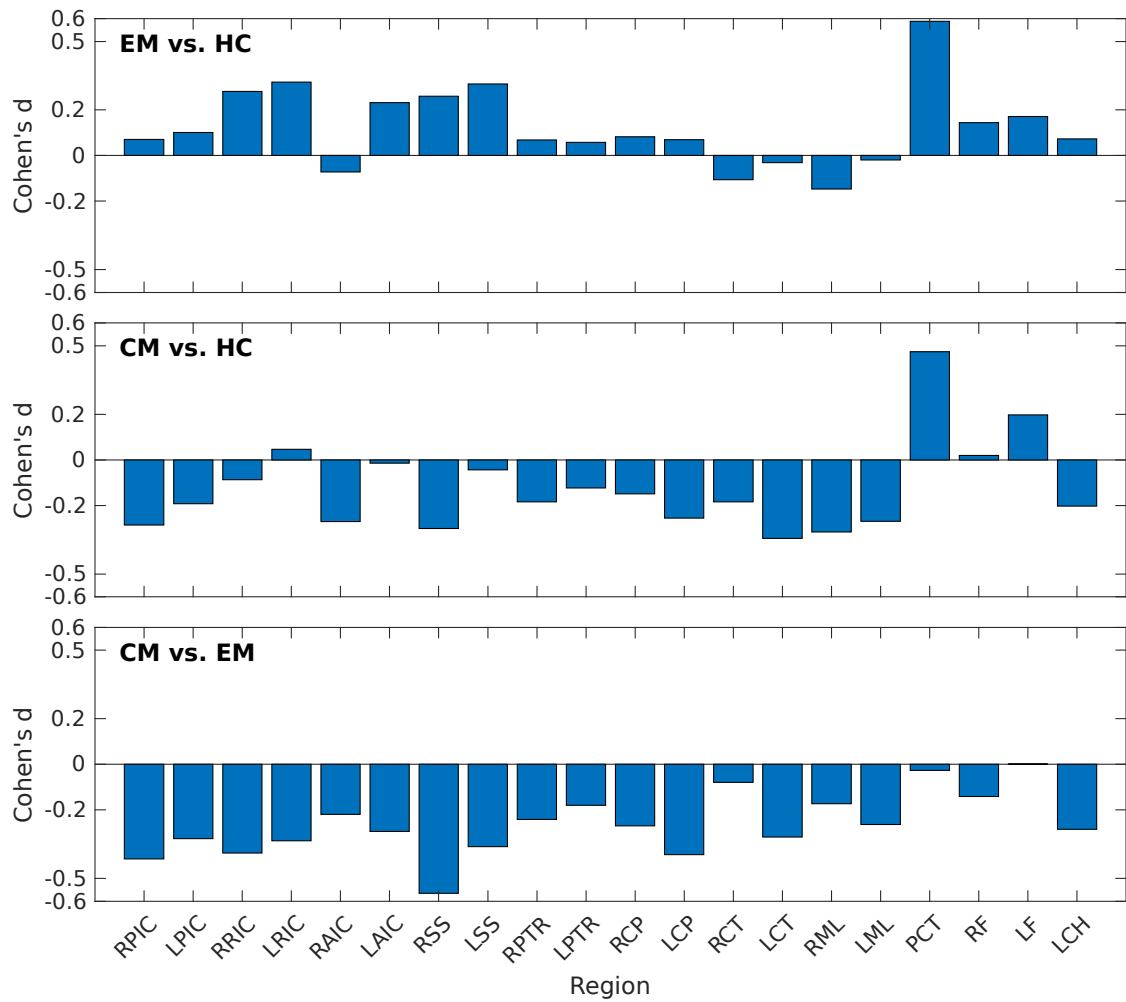
Corticospinal tract R (RCT)/L (LCT)	-.11/-.03	-.18/-.34	-.08/-.32
Medial lemniscus R (RML)/L (LML)	-.15/-.02	-.32/-.27	-.17/-.26
Pontine crossing tract (PCT)	<b>.59</b>	.47	-.03
Fornix (cres) R (RF)/L (LF)	.14/.17	.02/.20	-.14/.00
Cingulum (hippocampus) L (LCH)	.07	-.20	-.29

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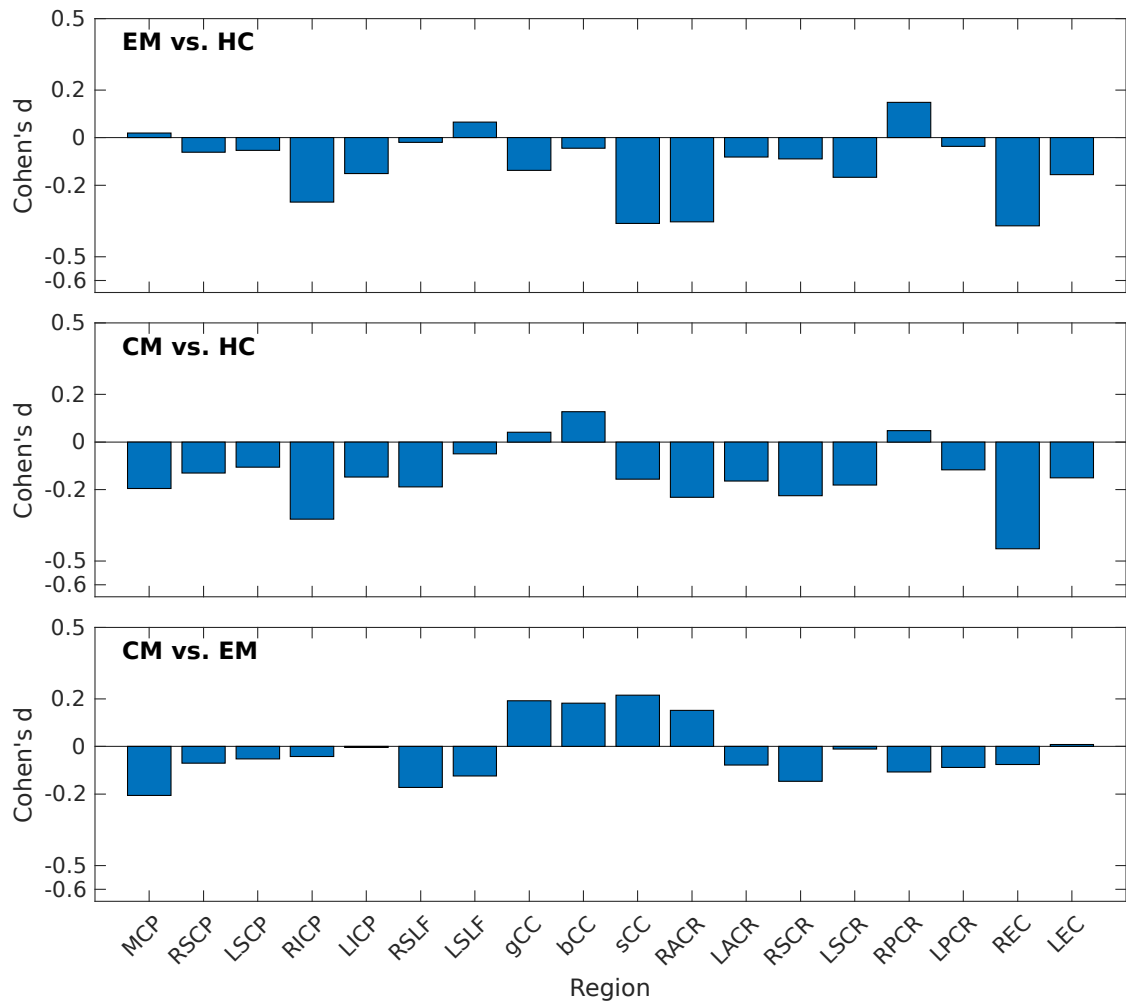
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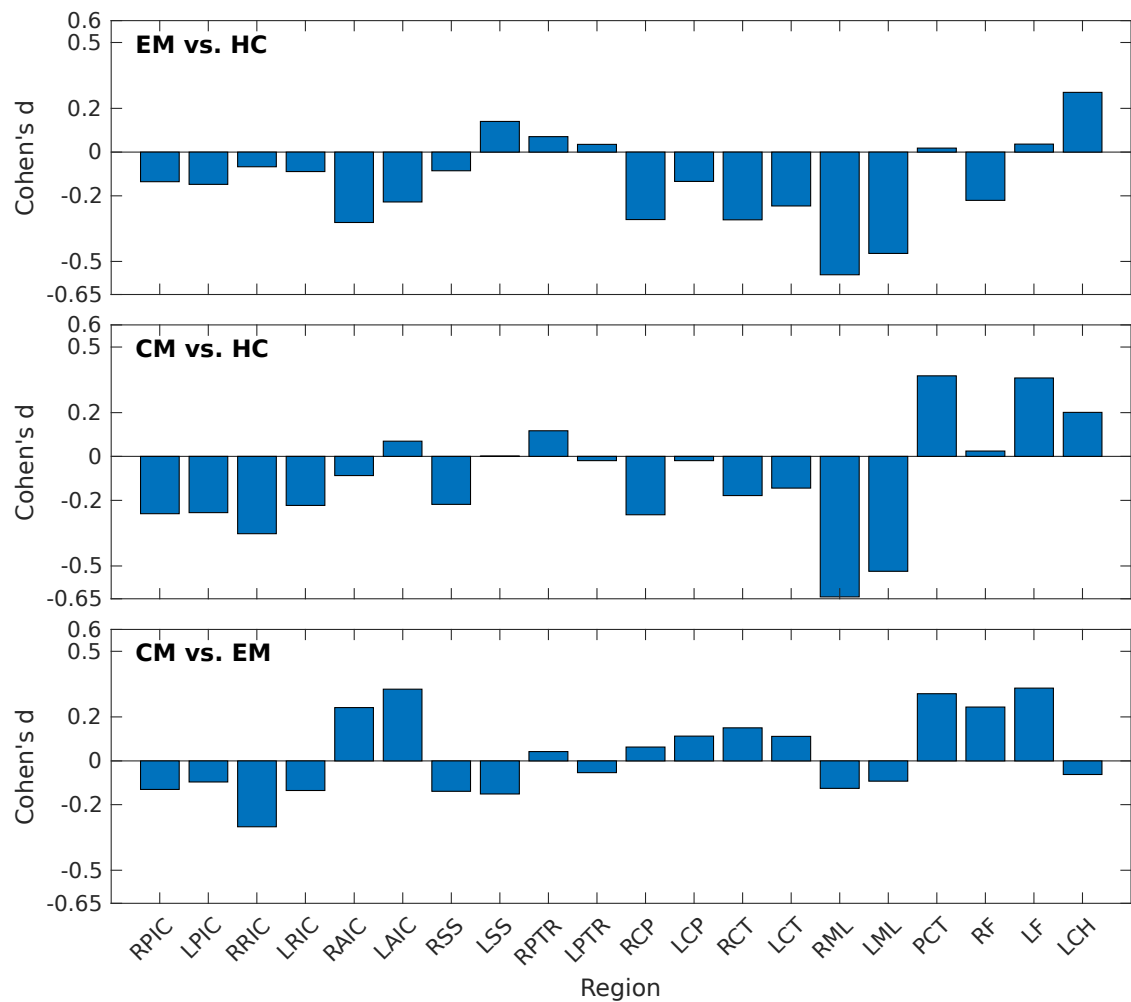
**Supplementary Figure 4 Cohen's AD bar plots of regions with FWE-corrected differences between EM and CM (part 1).** Values for all possible pairwise comparisons are shown. Region abbreviations can be seen in Supplementary Table 7.



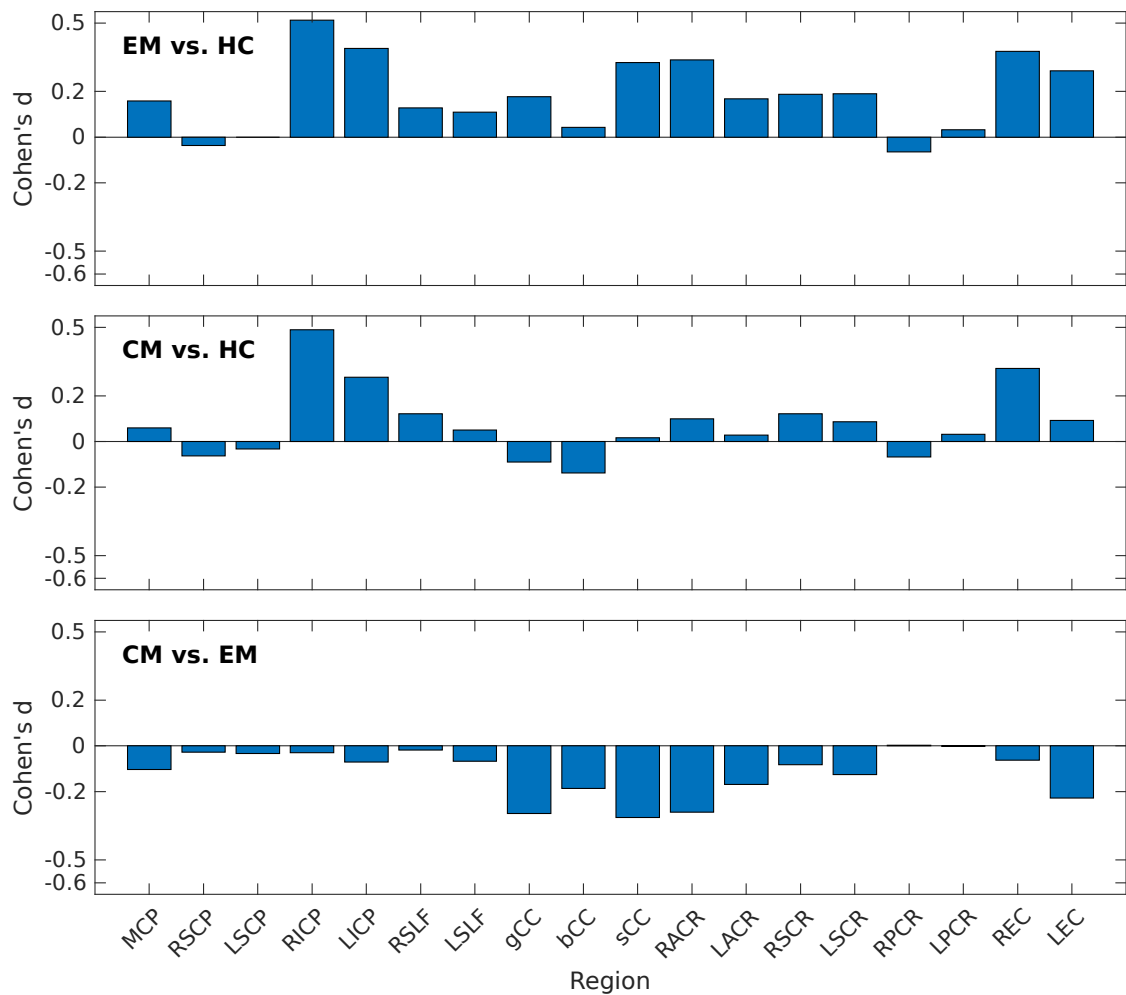
**Supplementary Figure 5 Cohen's AD bar plots of regions with FWE-corrected differences between EM and CM (part 2).** Values for all possible pairwise comparisons are shown. Region abbreviations can be seen in Supplementary Table 7.



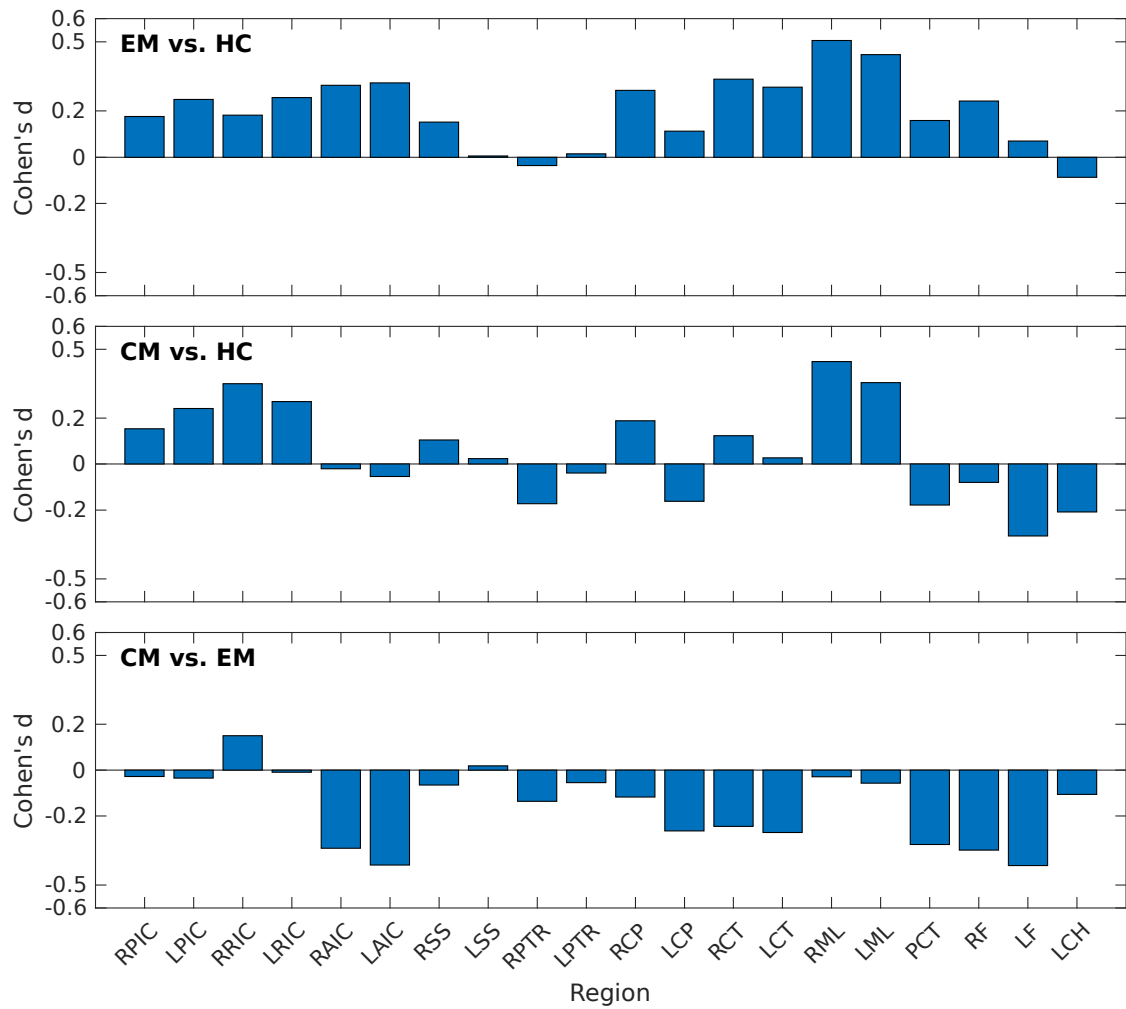
**Supplementary Figure 6 Cohen's d FA bar plots (part 1).** Values for all possible pairwise comparisons where significant differences in AD between EM and CM patients were found are shown. Region abbreviations can be seen in Supplementary Table 7.



**Supplementary Figure 7 Cohen's d FA bar plots (part 2).** Values for all possible pairwise comparisons where significant differences in AD between EM and CM patients were found are shown. Region abbreviations can be seen in Supplementary Table 7.

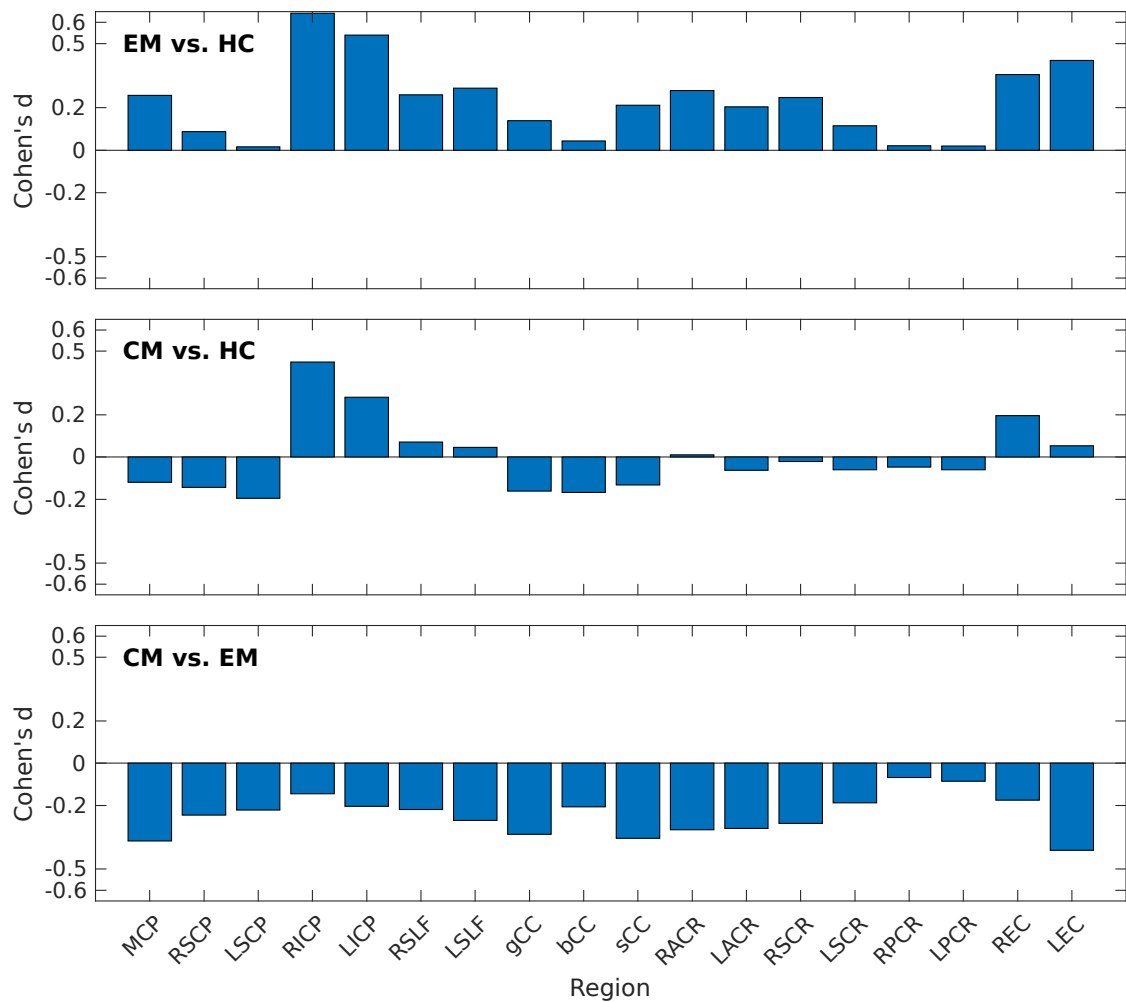


**Supplementary Figure 8 Cohen's d RD bar plots (part 1).** Values for all possible pairwise comparisons where significant differences in AD between EM and CM patients were found are shown. Region abbreviations can be seen in Supplementary Table 7.

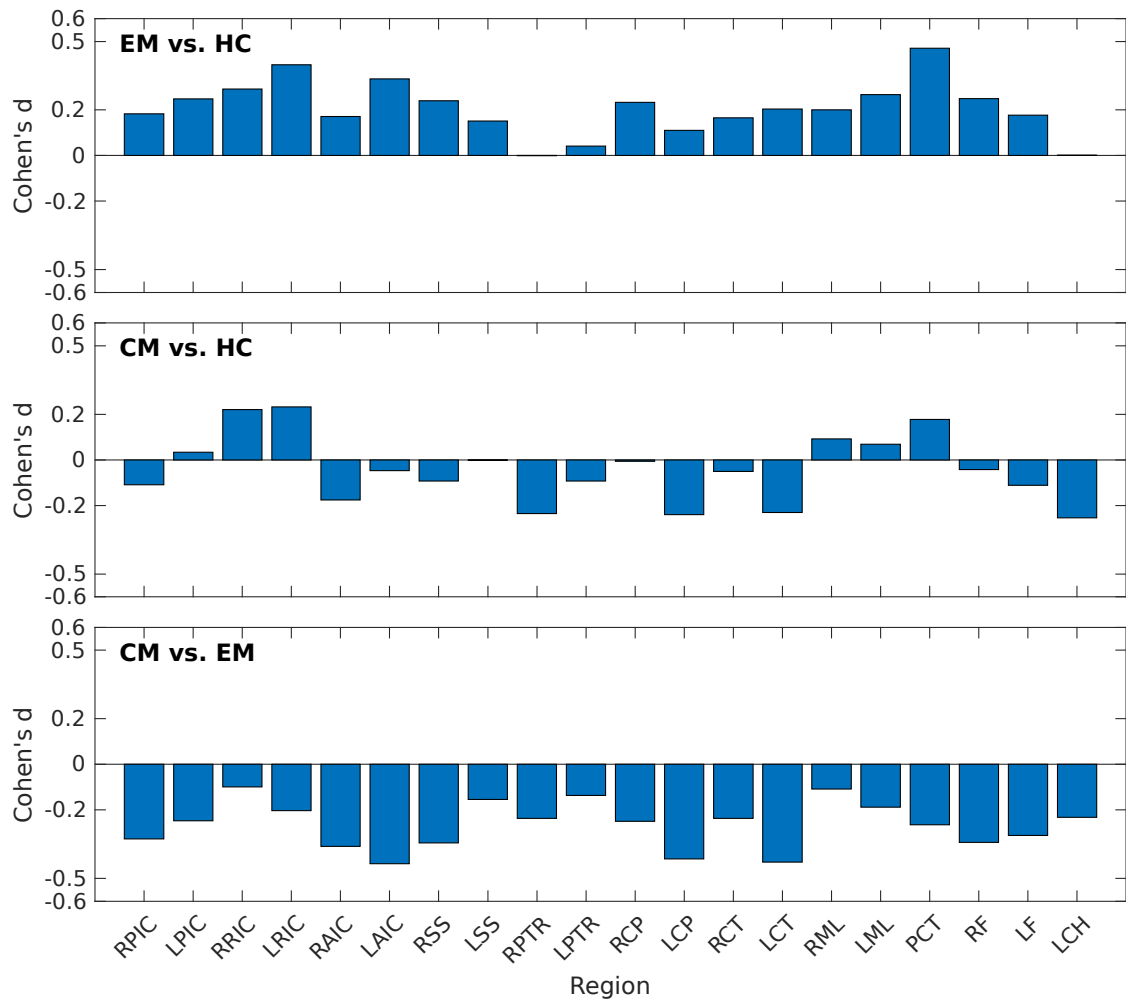


**Supplementary Figure 9 Cohen's d RD bar plots (part 2).** Values for all possible pairwise comparisons where significant differences in AD between EM and CM patients were found are shown. Region abbreviations can be seen in Supplementary Table 7.





**Supplementary Figure 10 Cohen's d MD bar plots (part 1).** Values for all possible pairwise comparisons where significant differences in AD between EM and CM patients were found are shown. Region abbreviations can be seen in Supplementary Table 7.



**Supplementary Figure 11 Cohen's d MD bar plots (part 2).** Values for all possible pairwise comparisons where significant differences in AD between EM and CM patients were found are shown. Region abbreviations can be seen in Supplementary Table 7.