

Hearing loss meta-analysis

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Methods

Eligibility Criteria

We included peer-review publications in English, involving patients with bilateral congenital and mixed hearing loss and controls with structural Magnetic Resonance Imaging.

Study design was using cross-sectional including control groups, investigating the structural relation between MRI changes and the Hearing loss. ROI were selected among the included studies Analysis method, the most common outcome measures were **volume, FA, VBM and thickness**. A total of 41 studies were included, with a total of 851 patients and 964 patients.

Notes:

1. I excluded Xia et al. Chin J Rad, 2008 because I don't understand chinese and it appears to be the same data as Xia et al. Chin J Med Img Tech, 2008
2. Kim et al. Hear Res 2014 used two groups prelingual deaf and post lingual deaf, I used the average for the main table.
3. Xia et al. Chin J Med Img Tech, 2008 had a total of 40 patients, two groups 9-12 years and 19-22 years, no controls
4. Zheng et al. Sci Rep, 2017 this variables change; Con rangeLow Con rangeHigh. Why? I didn't find them on the original paper

Effect size direction was directly include in the Cohen's D value by mutiplied by -1 if the effect was decrease and by 1 if it was none of increased. Forests plots were calculated the meta-regression for left and right. We measure a global meta regression for white and gray mater by side (Left and righth). We include those ROI with most frequency of apearing.

Effects were summarized across studies using the generic inverse-variance weighting method with DerSimonian and Laird random effects, meaning studies were weighted by $1/SE^2$ (where SE is the standard error)

$$Hedges'G = \frac{X_1 - X_2}{\sqrt{\frac{(n_1-1)s_1^2 + (n_2-1)s_2^2}{n_1 + n_2 - 2}}}$$

Assumptions:

1. We assume that the calculation of the cohen's D is correct.
2. We assume that the direction of the effect is correct.
3. Variance was estimated using the cohen's D and sample size of each study. Our estimated variance was used for all meta-regressions, therefore we could have and additional in the between studies variance and eterogeneity calculations. We should have done the mean and standart deviation from each study. Variance was estimated using the following formula:

$$Variance = \frac{n1 + n2}{n1 \times n2} + \frac{Hedges'G^2}{2 \times (n1 + n2 - 2)}$$

Estimate of heterogeneity per model

“We estimated heterogeneity in results using the τ statistic, which represents the standard deviation” such as overall.hetstat or a heterogeneity test x^2 and I^2 index

We performed a multi-level meta-analytic model, over our multiple effect size estimates nested withing variables: Big brain area, ROI, etc. We expect that the underlying true effects are more similar for the same level of the grouping variable than threue effects arising from different levels

“We can account for the correlation in the true effects by adding a random effect to the model at the level corresponding to the grouping variable.” The dataset contains the result from N studies, each comparing different measurements between patients and controls. The diference of between groups was quantified in terms of Cohen’s D.

Notes from Francis

Remember I created the effect size because are the variables and metric were different. This take mean and SD out of the equation. But you can represent the mean and SD as another variable if you want to calculate what effect sizes would create a cohen’s d and cc r for specific variables. That way we would standardize it across our different means and SD. 2.1.16. CC which is the correlation coefficient

2.3. Calculate Hedges’ g which takes into consideration sample size

> I used Cohen’s D instead of these last two because ai calculated the variace from the cohen’s D, but I can do it for the Hedges’G as well

Table 1: Total included studies: 41

	Hearing Loss	Healthy
Total number of patients	2778	4214
Number mean	47.08	71.42
Number sd	128.5	250.6
Age mean	33.07	30.96
Age SD	22.66	20.5
%Female mean	50.02	55.71
%Female sd	12.05	12.78

Table of included studies

Table 2: Studies with incomplete information (NA)

	Source	MRI Tesla	all.techniques	all.measures
5	2006, Kara et al. J Neuroradiol	1.5	VBM	length, Thickness, volume
9	2008, Xia et al. Chin J Med Img Tech	1.5	VBM	volume
12	2010, Husain et al. Brain Res	3	DTI, VBM	FA, volume
26	2014, Lyness et al. Neuroimage	1.5	DTI	FA, MD, RD
41	2017, Karns et al. Hear Res	3	DTI	AD, FA, RD, volume
48	2018, Kumar U, Mishra M. Brain Res	3	VBM	Thickness, VBM

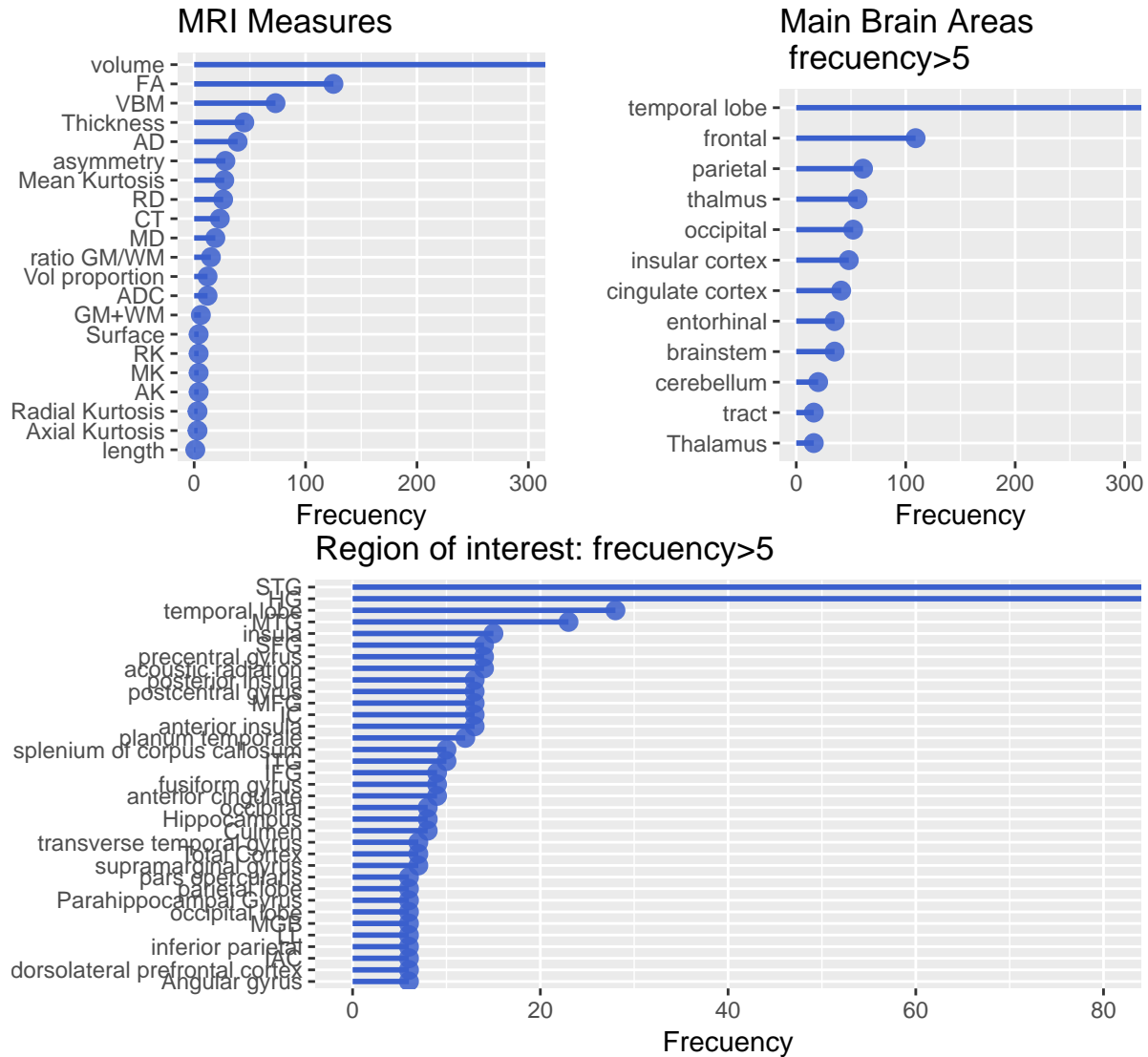
Table 3: Included studies

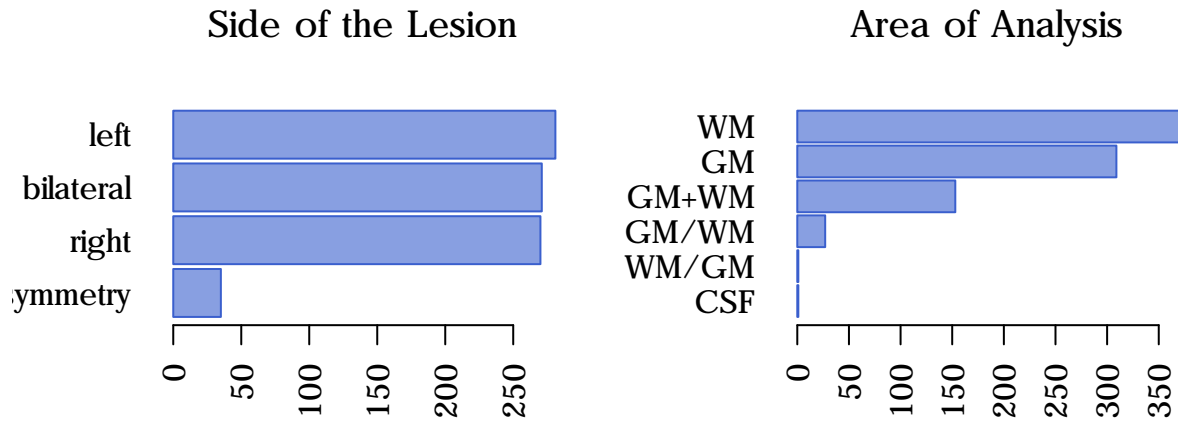
	Source	MRI Tesla	all.techniques	all.measures
1	2000, Bavelier et al. J Neurosci	1.5	VBM	volume
2	2003, Emmorey et al. PNAS	1.5	VBM	asymmetry, GM+WM, ratio GM/WM, volume
3	2003, Penhune et al. Neuroimage	1.5	VBM	asymmetry, ratio GM/WM, volume
4	2004, Chang et al. Neuroreport	3	DTI	asymmetry, FA

	Source	MRI Tesla	all.techniques	all.measures
6	2007, Meyer et al. Restor Neurol Neurosci	3	VBM	volume
7	2007, Shibata DK. Am J Neuroradiol	1.5	VBM	volume
8	2008, Allen et al. J Neurosci	1.5	VBM	asymmetry, ratio GM/WM, Vol proportion, volume
10	2009, Kim et al. Neuroreport	3	DTI, VBM	FA, volume
11	2009, Wang et al. Chin J Med Img Tech	3	DTI	FA
13	2010, Leporé et al. Hum Brain Mapp	1.5	VBM	VBM
14	2010, Li, et al. J Clin Rad	1.5	VBM	volume
15	2010, Liu et al. Chin J Med Img Tech	3	CT	FA
16	2011, Smith et al. Cereb Cortex	3	VBM	asymmetry, ratio GM/WM, volume
17	2012, Li et al. Brain Res	3	CT	Thickness
18	2012, Li et al. Hum Brain Mapp	3	DTI	AD, FA, RD
19	2013, Allen et al. Front Neuroanat	1.5	VBM	asymmetry, volume
20	2013, Boyen et al. Hear Res	3	VBM	volume
21	2013, Miao et al. Am J Neuroradiol	3	DTI	FA, RD
22	2013, Pénicaud et al. Neuroimage	1.5	VBM	volume
23	2014, Hribar et al. Hear Res	3	DTI, VBM	AD, FA, Thickness
24	2014, Kim et al. Hear Res	3	VBM	volume
25	2014, Lin et al. Neuroimage	1.5	VBM	volume
27	2014, Olulade et al. J Neurosci	3	VBM	volume
28	2014, Profant et al. Neuroscience	3	DTI, VBM	AD, CT, FA, MD, RD, Surface, volume
29	2014, Profant et al. Neuroscience	3	DTI, VBM	AD, CT, FA, MD, RD, Surface, volume
30	2015, Huang et al. PLoS One	1.5	DTI	FA, MD
31	2015, Tae Investig Magn Reson Imaging	1.5	VBM	VBM
32	2016, Amaral et al. Eur J Neurosci	3	VBM	asymmetry, Thickness
33	2016, Chinnadurai et al. Magn Reson Imaging	1.5	DTI	AD, Axial Kurtosis, FA, Mean Kurtosis, Radial Kurtosis, RD
34	2016, Ma et al. AJNR Am J Neuroradiol	3	DTI	AD, FA, MD, RD
35	2016, Shiell et al. Neural Plasticity	3	CT	Thickness
36	2016, Shi et al. Neuroreport	3	VBM	volume
37	2016, Smittenaar et al. Open Neuroimag J	1.5	CT	CT
38	2016, Wu et al. Brain Res	1.5	VBM	ADC, FA
39	2016, Wu et al. Brain Res	1.5	VBM	ADC, FA
40	2016, Wu et al. Brain Res	1.5	VBM	ADC, FA
42	2017, Kim et al. Neuroreport	3	DTI	FA
43	2017, Shiell & Zatorre. Hear Res	3	DTI	AD, MD, RD, volume
44	2017, Zheng et al. Sci Rep	3	DTI	FA, Mean Kurtosis
45	2018, Benetti et al. Neuroimage	4	DTI	AD, FA, RD
46	2018, Chen et al. Behav Neurosci	3	VBM	volume
47	2018, Feng et al. PNAS	3	VBM	VBM
49	2018, Park et al. Biomed Res Int	3	DTI	FA
50	2018, Pereira-Jorge et al. Neural Plast	1.5	VBM	volume
51	2018, Ren et al. Front Neurosci	3	CT, VBM	Thickness, volume
52	2018, Uchida et al. Front Aging Neurosci	3	VBM	volume
53	2018, Uchida et al. Front Aging Neurosci	3	VBM	volume
54	2018, Zou et al. Otol Neurotol	3	DTI	AK, FA, MK, RK
55	2019, Belkhiria et al. Front. Aging Neurosci	3	VBM	CT, volume
56	2019, Belkhiria et al. Front. Aging Neurosci	3	VBM	CT, volume
57	2019, Luan et al. Front Neurosci	3	DTI, VBM	FA, MD, volume
58	2019, Ponticorvo et al. Hum Brain Mapp	3	VBM	volume

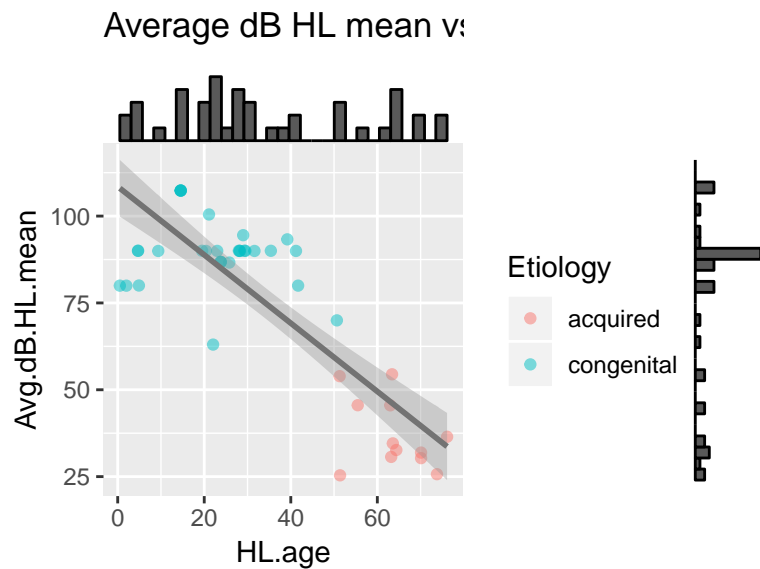
	Source	MRI Tesla	all.techniques	all.measures
59	2019, Xu et al. J Magn Reson Imaging	3	VBM	volume

Overall view of the studies





Relation of Average dB and Age



Frequency and contingency tables

- Most of the studies that measured Gray matter focus on cortical changes (volume, thickness and VBM).
- White matter studies are more heterogeneous in their measurements.
- Diffusion tensor (DT) derived measurements are the most frequent in white matter, followed by volume.
 - It is harder to interpret a meta-analysis of multiple white matter measurements because their effect varies widely and in different directions. The measurements derived from DT have the most differences.

WE conduct our meta-analysis using the **TWO** most frequent measurements for gray and white matter. We use *volume* for GM and *fractional anisotropy* for WM.

Further meta regressions can be found in the supplementary material.

Gray Matter

- thickness
- VBM

White Matter integrity

- mean diffusivity MD
- radial diffusivity RD
- axial diffusivity AD
- mean kurtosis

White Matter volume

- thickness (I am unsure how they did this)
- VBM
- volume

Frequency tables: measures of WM & GM

Table 4: Matter vs Side

	asymmetry	bilateral	left	right	total
GM	9	59	130	109	2
WM	15	164	93	97	1

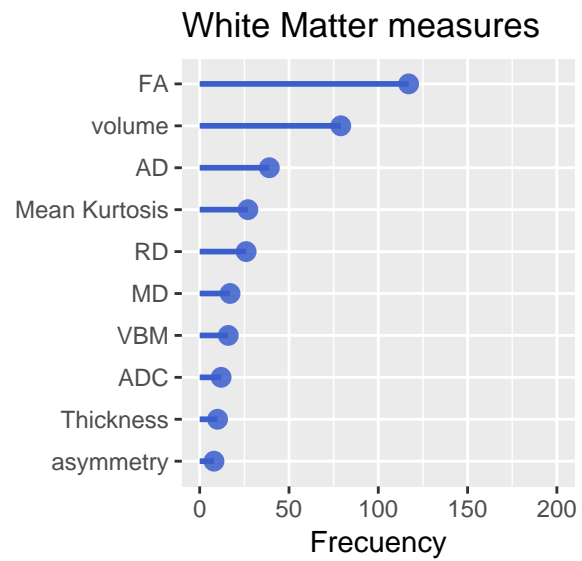
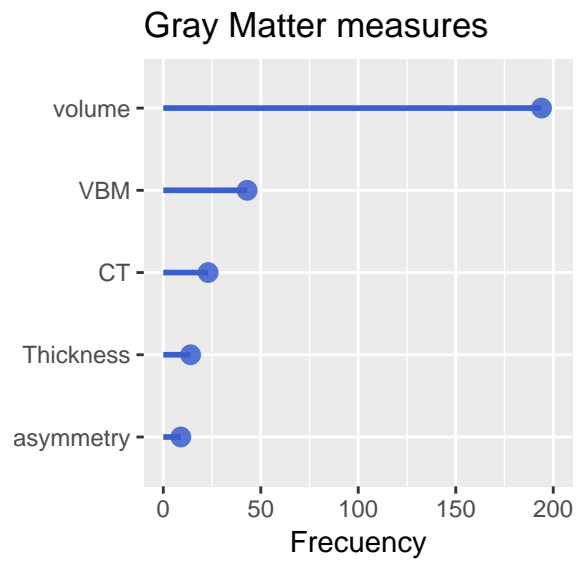
Table 5: Matter vs measure (continued below)

	AD	ADC	AK	asymmetry	Axial Kurtosis	CT	FA	GM+WM
GM	0	0	2	9	0	23	8	0
WM	39	12	2	8	3	0	117	0

Table 6: Table continues below

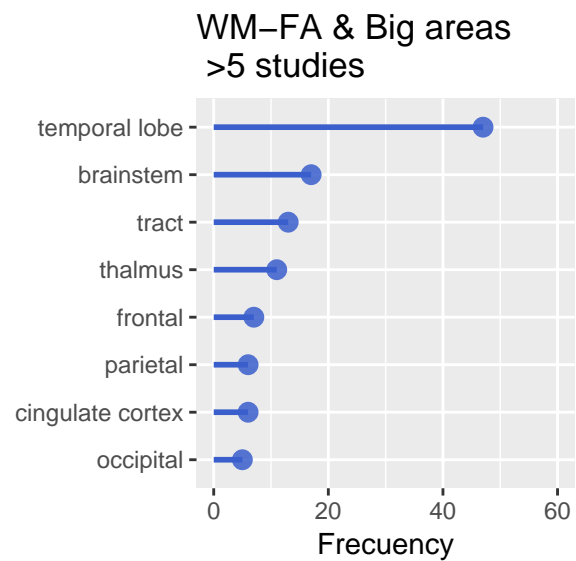
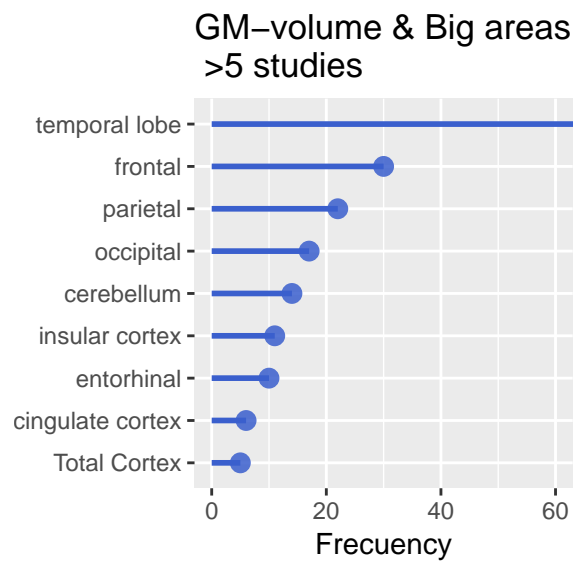
	length	MD	Mean Kurtosis	MK	Radial Kurtosis	ratio GM/WM	RD
GM	0	2	0	2	0	0	0
WM	1	17	27	2	3	0	26

	RK	Surface	Thickness	VBM	Vol proportion	volume
GM	2	4	14	43	6	194
WM	2	0	10	16	6	79



Contingency tables: Main areas and sub-areas

Sub-analys were carried out in those areas that had measures from at least five studies. Those areas were selected from the contingency tables.



Most common ROI for WM-FA and GM-volume

White matter FA ROIs: >5 studies Gray Matter volume ROIs: >5 studi

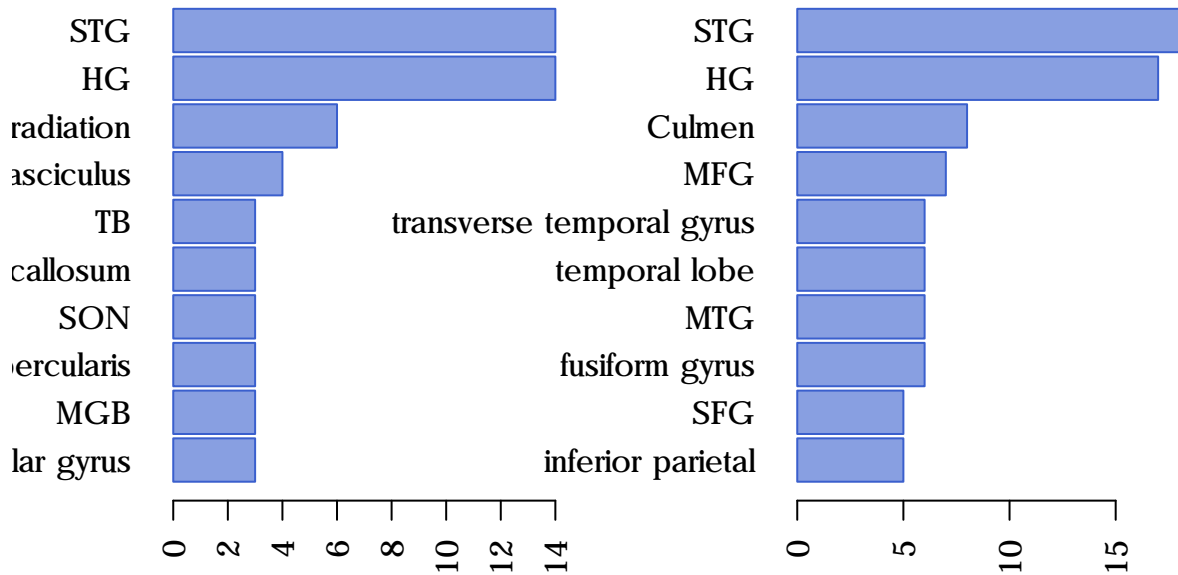
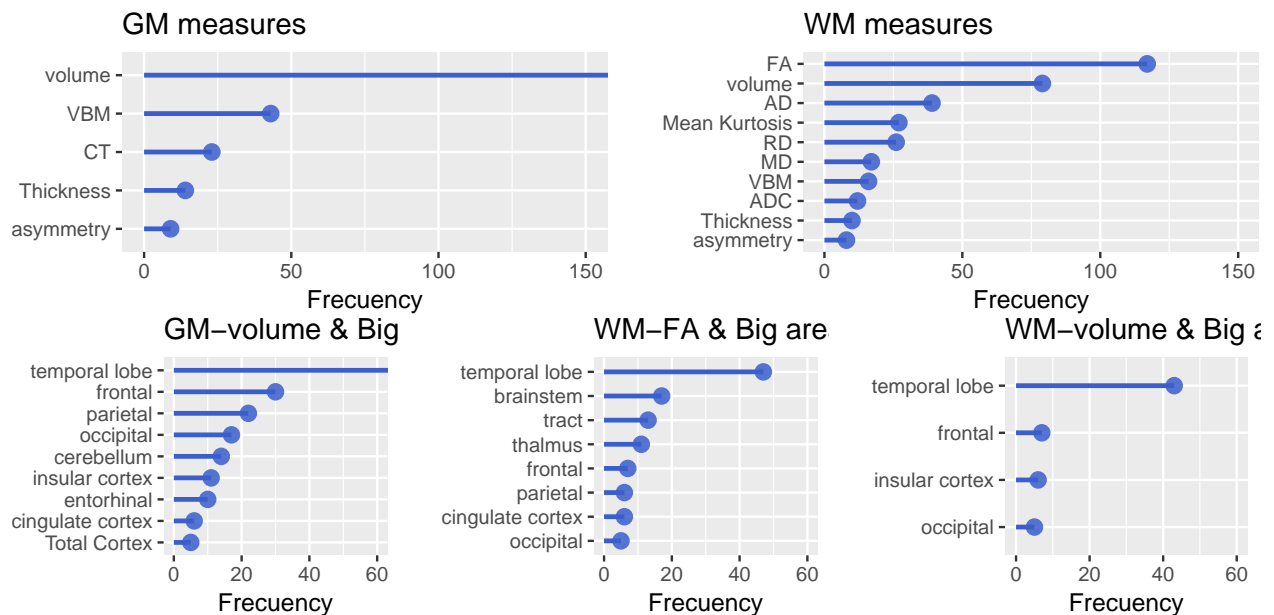
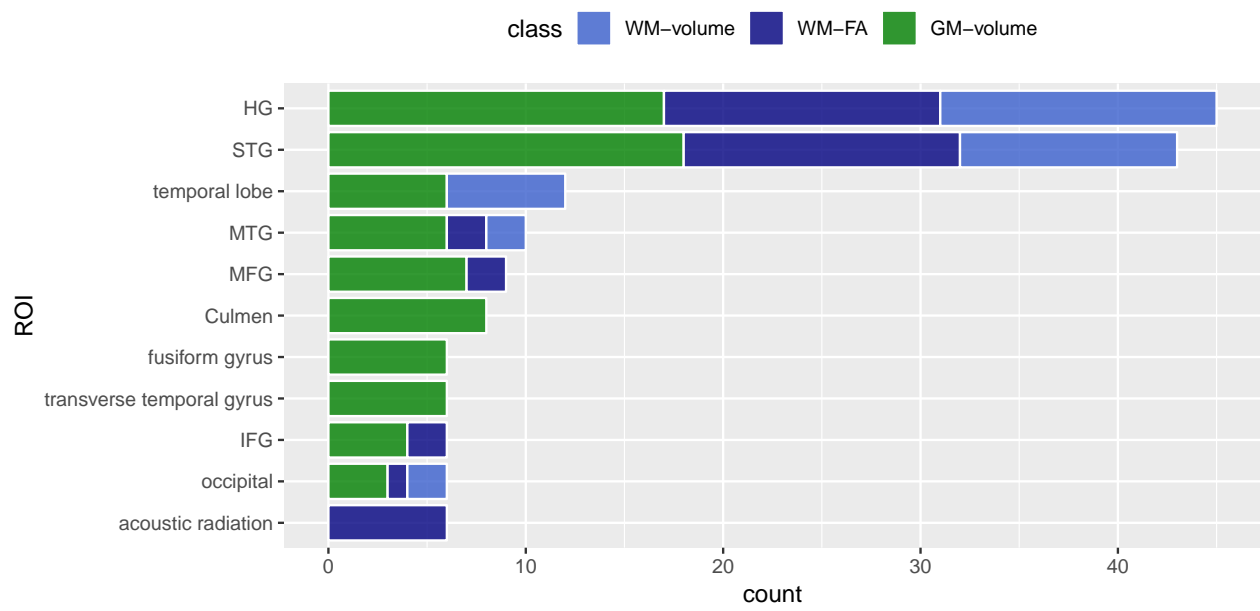
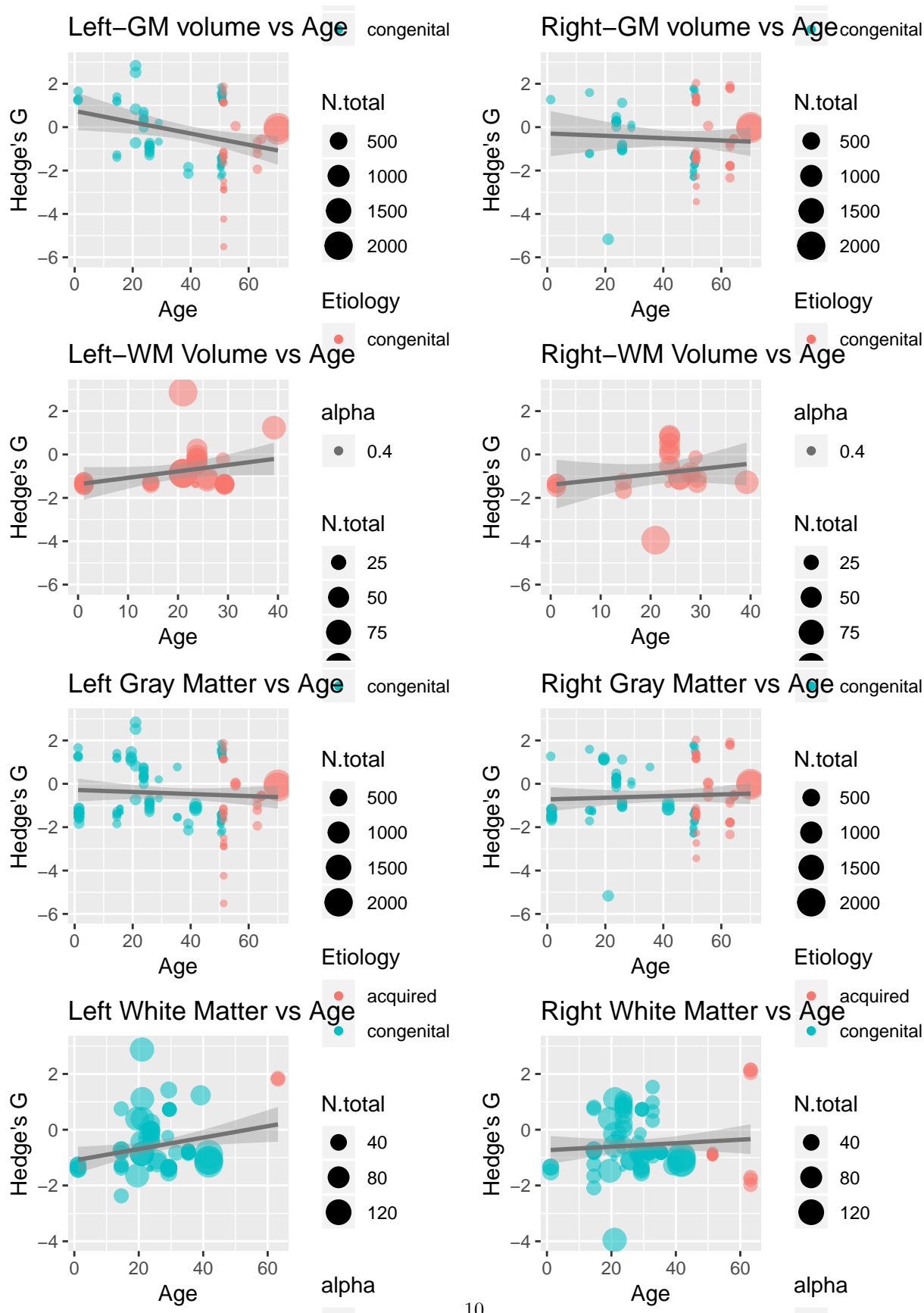


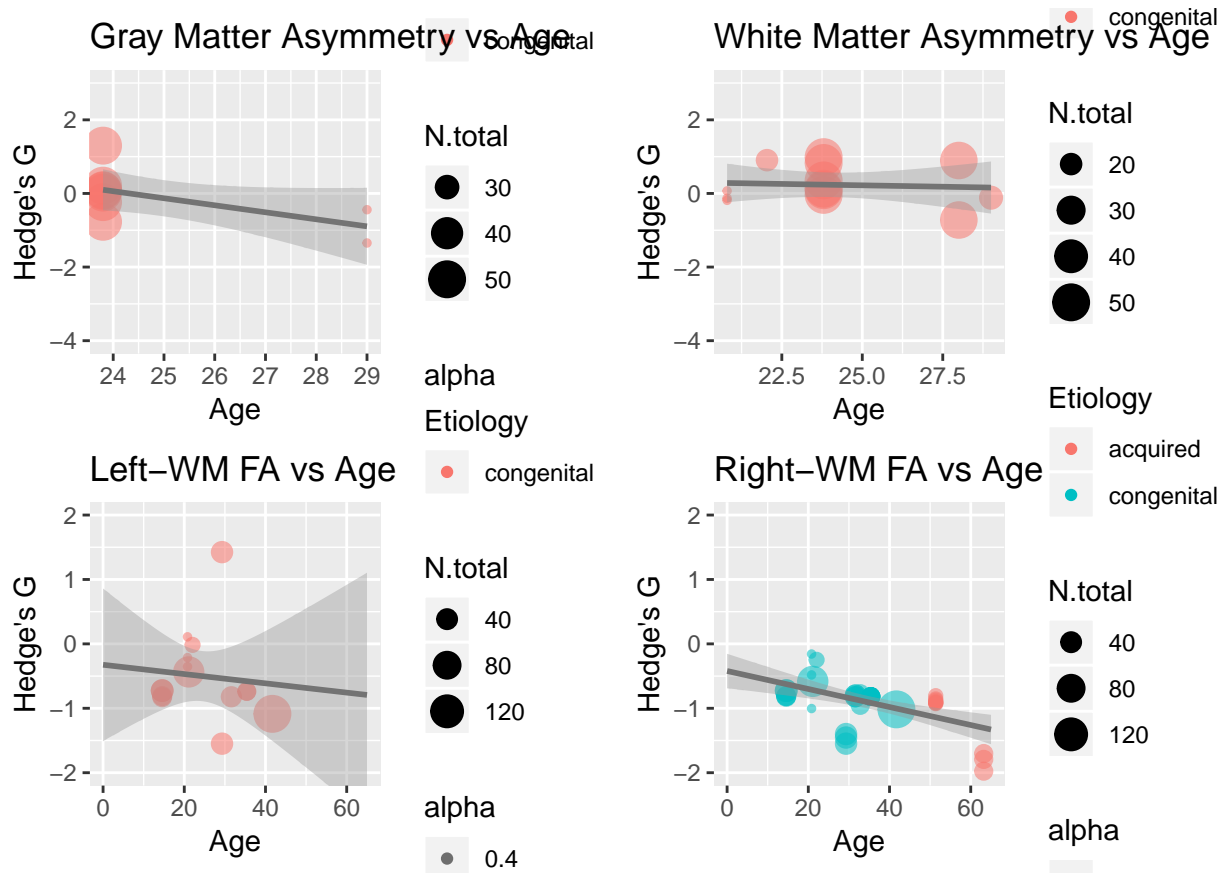
Figure 1 - Methods: Distribution of data by Gray/white matter and measure





Gray and White matter relation with Age





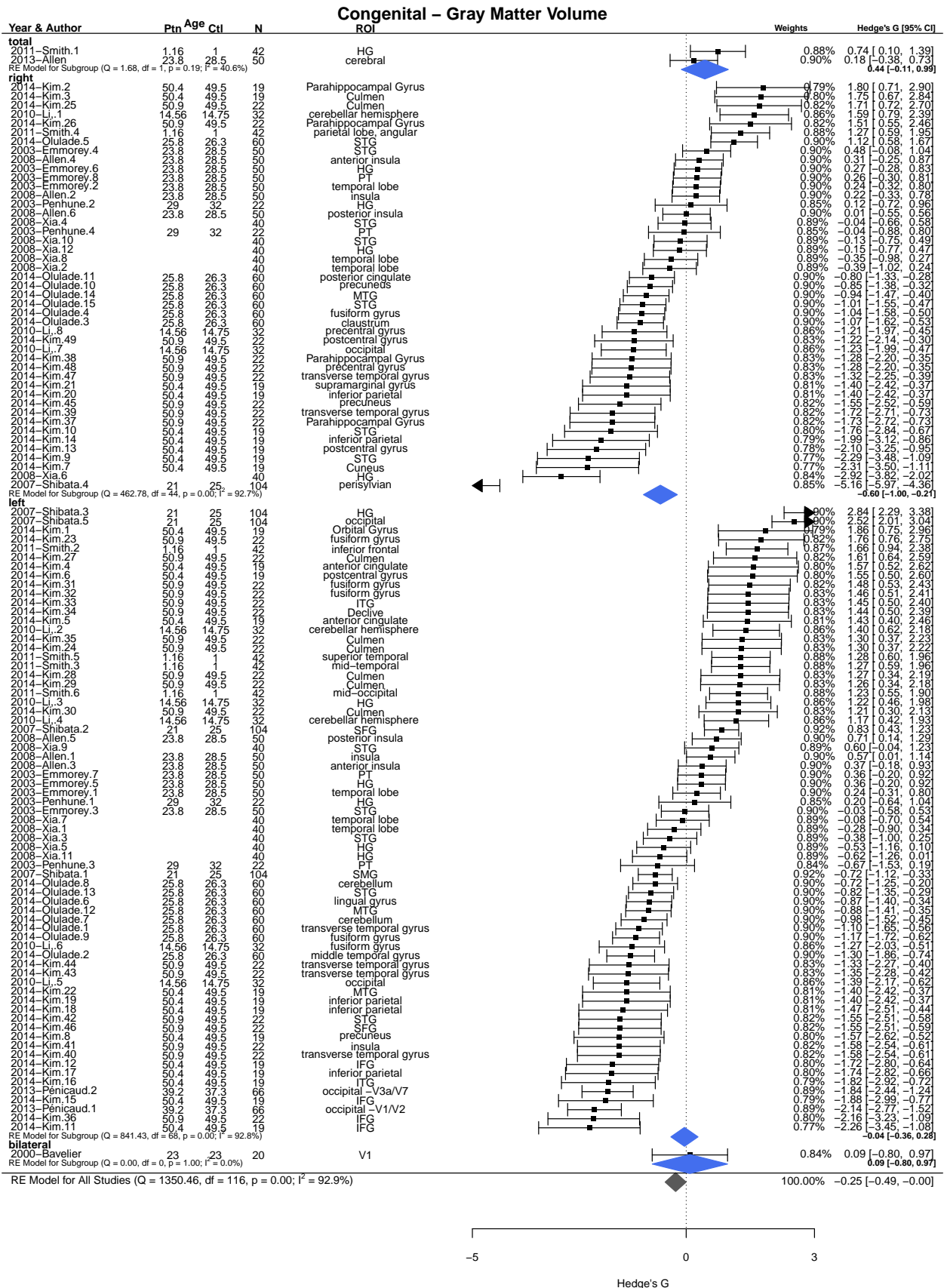
CONGENITAL - Meta-regressions of Gray Matter by Volume

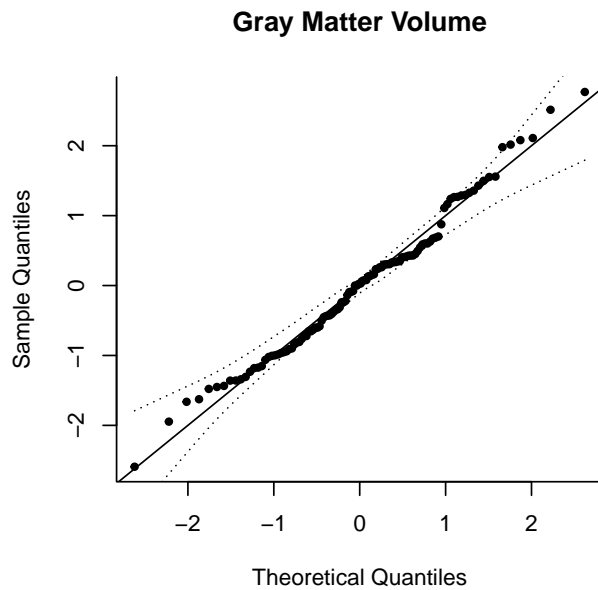
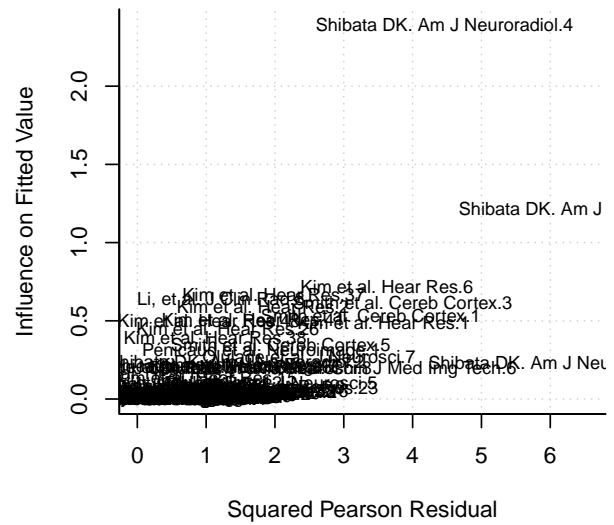
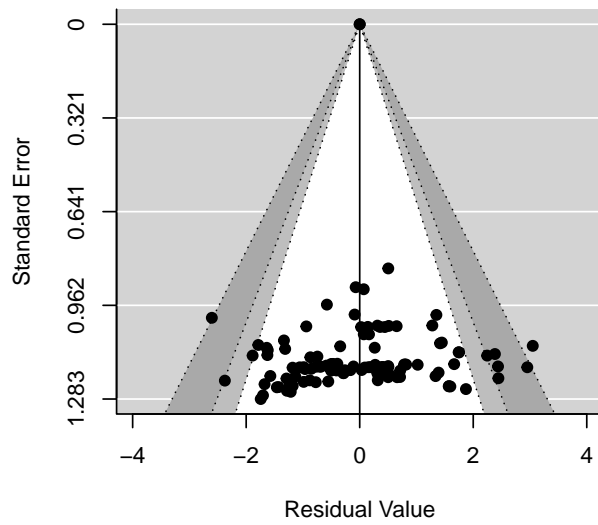
Gray Matter Volume: Random effects model no intercept covariated by Big area

Table 8: Table continues below

	HedgeG	se	zval	ci.lo	ci.up
left cerebellum	0.9013	0.3735	2.413	0.1693	1.633
left cingulate	1.5	0.9037	1.66	-0.2712	3.271
left frontal	-0.588	0.4468	-1.316	-1.464	0.2877
left insular cortex	0.0628	0.6065	0.1035	-1.126	1.252
left occipital	-0.5252	0.4567	-1.15	-1.42	0.3699
left parietal	-0.8875	0.5149	-1.724	-1.897	0.1217
left temporal lobe	-0.116	0.2235	-0.5189	-0.554	0.3221
left thalamus	1.282	1.213	1.056	-1.097	3.66
right cerebellum	1.682	0.7284	2.309	0.254	3.109
right cingulate cortex	-0.8018	1.193	-0.6721	-3.14	1.536
right entorhinal	0.05865	0.6339	0.09251	-1.184	1.301
right frontal	-2.559	0.7143	-3.583	-3.959	-1.159
right insular cortex	-0.1339	0.598	-0.2239	-1.306	1.038
right occipital	-1.73	0.8957	-1.932	-3.486	0.02545
right parietal	-1.113	0.4445	-2.503	-1.984	-0.2413
right temporal lobe	-0.5427	0.2729	-1.989	-1.078	-0.007815

	pval
left cerebellum	0.01581
left cingulate	0.09694
left frontal	0.1882
left insular cortex	0.9175
left occipital	0.2502
left parietal	0.08478
left temporal lobe	0.6039
left thalamus	0.2909
right cerebellum	0.02096
right cingulate cortex	0.5015
right entorhinal	0.9263
right frontal	0.0003399
right insular cortex	0.8228
right occipital	0.05341
right parietal	0.01233
right temporal lobe	0.04675





ACQUIRED - Meta-regressions of Gray Matter by Volume

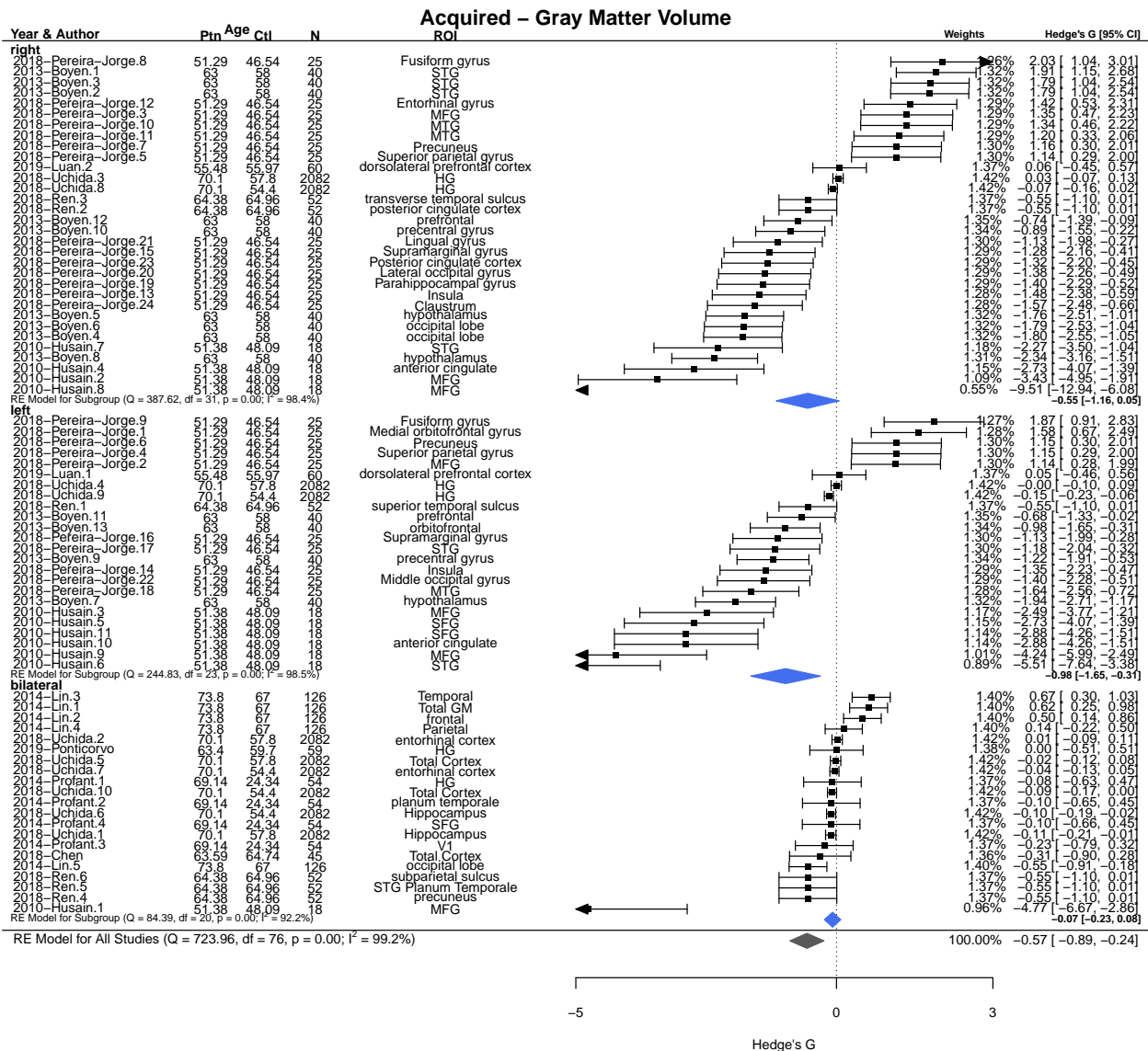
Random effects model no intercept covariated by Big area

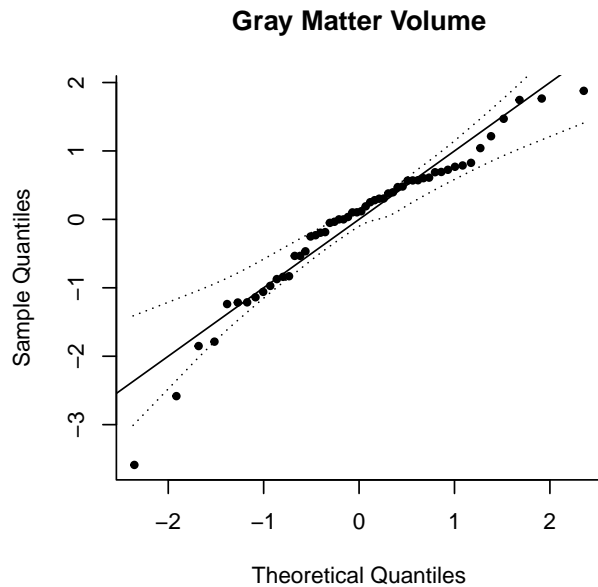
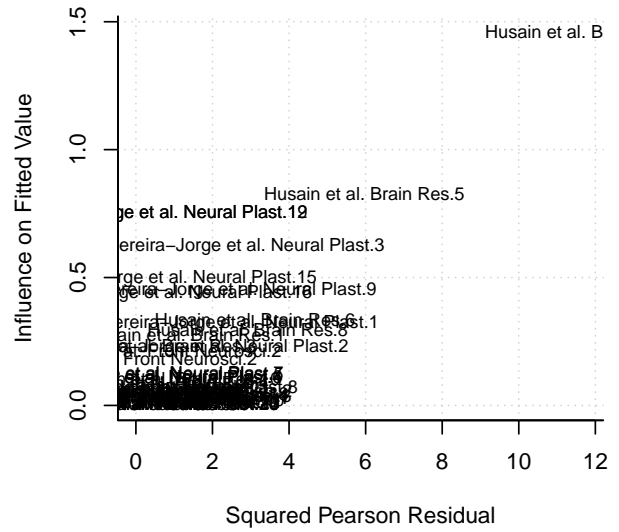
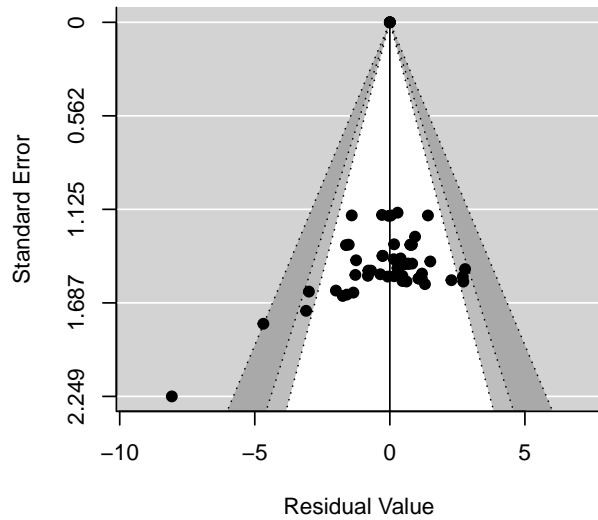
Table 10: Table continues below

	HedgeG	se	zval	ci.lo	ci.up
left cingulate cortex	-2.883	1.728	-1.669	-6.269	0.5024
left frontal	-1.14	0.5268	-2.164	-2.173	-0.1076
left hypothalamus	-1.937	1.626	-1.191	-5.124	1.25
left insular cortex	-1.353	1.641	-0.8248	-4.57	1.863
left occipital	-1.398	1.642	-0.8514	-4.616	1.82
left parietal	0.3896	0.9454	0.4121	-1.463	2.243
left temporal lobe	-0.8302	0.6236	-1.331	-2.052	0.3921
right cingulate cortex	-1.483	0.954	-1.554	-3.352	0.3872

	HedgeG	se	zval	ci.lo	ci.up
right entorhinal	0.007072	1.161	0.006091	-2.269	2.283
right frontal	-1.438	0.7012	-2.05	-2.812	-0.06331
right hypothalamus	-2.047	1.151	-1.778	-4.304	0.2095
right insular cortex	-1.525	1.163	-1.311	-3.803	0.7542
right occipital	-1.524	0.8158	-1.868	-3.123	0.07522
right parietal	0.3405	0.9459	0.36	-1.513	2.194
right temporal lobe	0.727	0.5141	1.414	-0.2806	1.735

	pval
left cingulate cortex	0.09509
left frontal	0.03045
left hypothalamus	0.2335
left insular cortex	0.4095
left occipital	0.3945
left parietal	0.6803
left temporal lobe	0.1831
right cingulate cortex	0.1202
right entorhinal	0.9951
right frontal	0.04034
right hypothalamus	0.0754
right insular cortex	0.1898
right occipital	0.0618
right parietal	0.7189
right temporal lobe	0.1573





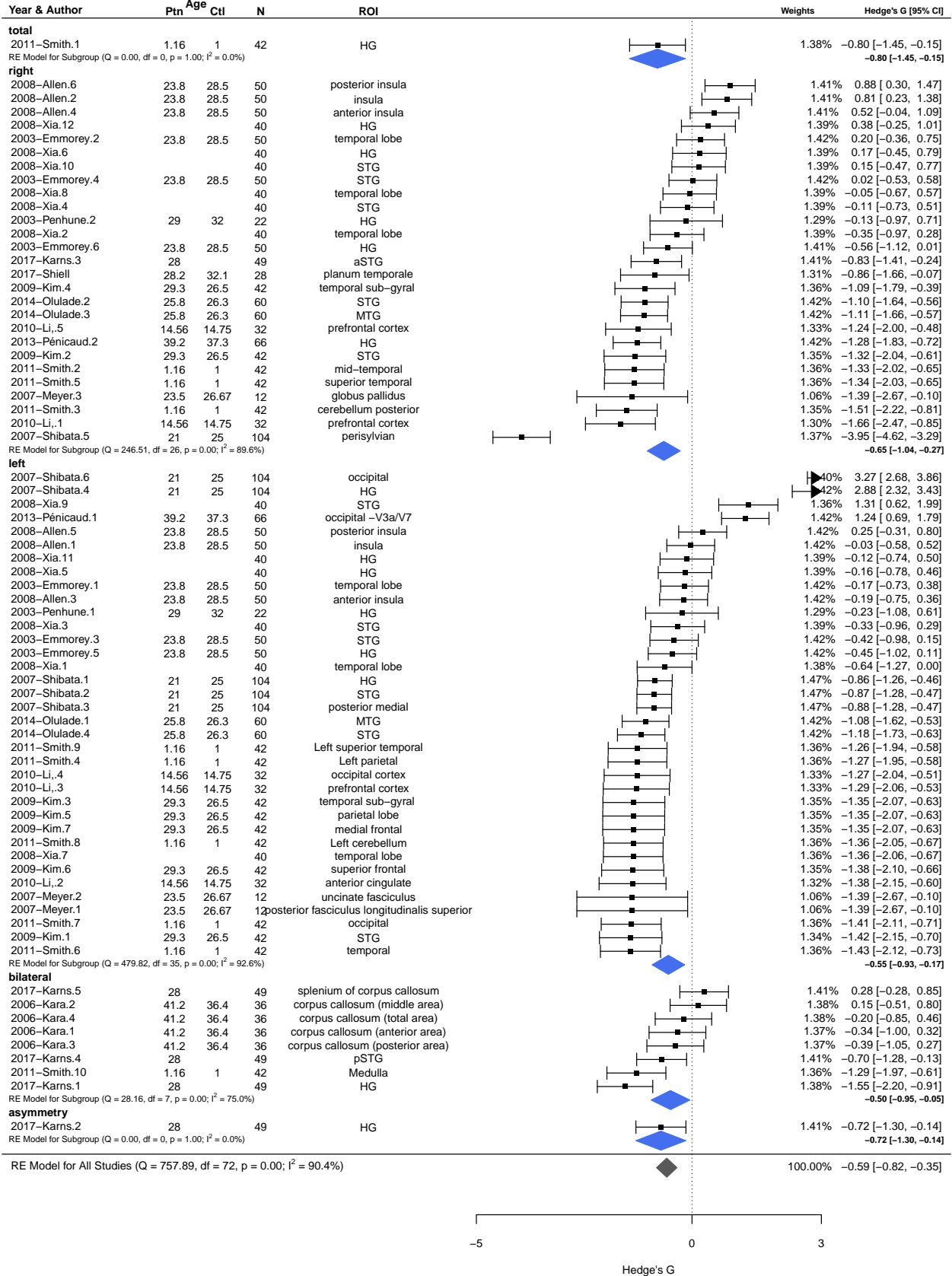
CONGENITAL - White Matter by VOLUME

Random effects model no intercept covariated by Big area

	HedgeG	se	zval	ci.lo	ci.up	N
left cerebellum	-1.107	0.6745	-1.641	-2.429	0.2149	2
left cingulate cortex	-1.379	0.9926	-1.389	-3.324	0.5668	1
left frontal	-1.34	0.5684	-2.358	-2.454	-0.2262	3
left insular cortex	0.007913	0.5504	0.01438	-1.071	1.087	3
left occipital	0.5024	0.4846	1.037	-0.4475	1.452	4
left parietal	-1.308	0.6914	-1.892	-2.663	0.04705	2
left temporal lobe	-0.478	0.2211	-2.163	-0.9113	-0.04478	19
left tract	-1.386	0.7931	-1.747	-2.94	0.1688	2
right cerebellum	-1.513	0.9789	-1.546	-3.432	0.4051	1
right forebrain	-1.386	1.122	-1.235	-3.584	0.8126	1

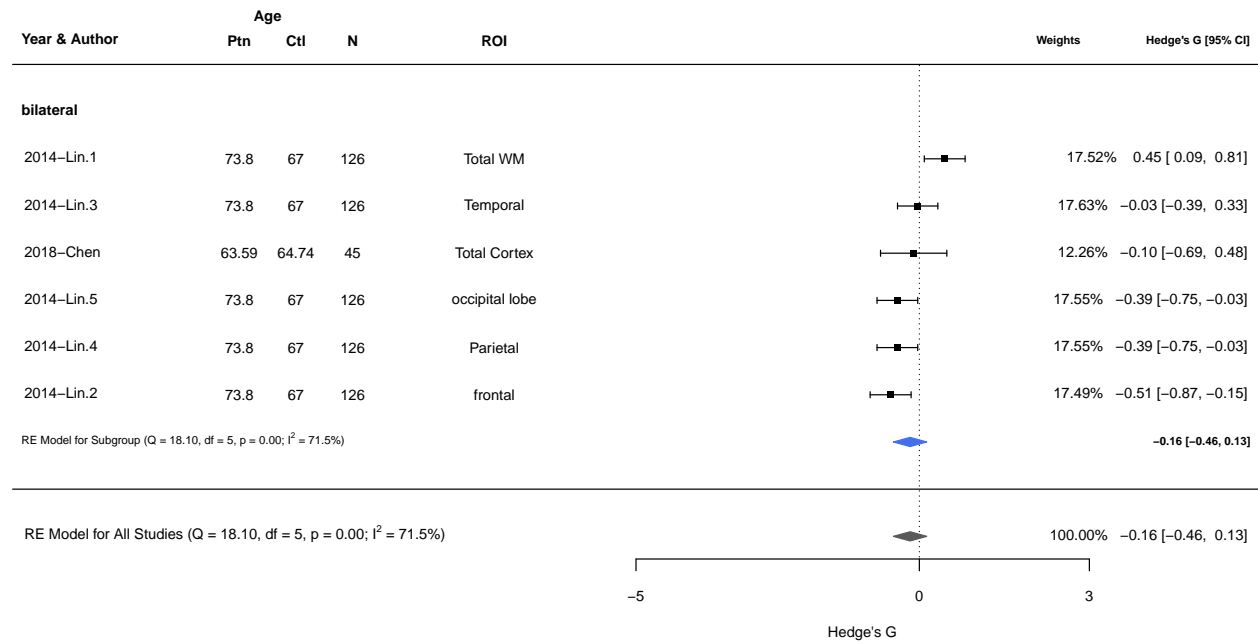
	HedgeG	se	zval	ci.lo	ci.up	N
right frontal	-2.31	0.5697	-4.055	-3.426	-1.193	3
right insular cortex	0.737	0.5521	1.335	-0.3451	1.819	3
right temporal lobe	-0.5529	0.2218	-2.493	-0.9875	-0.1183	19

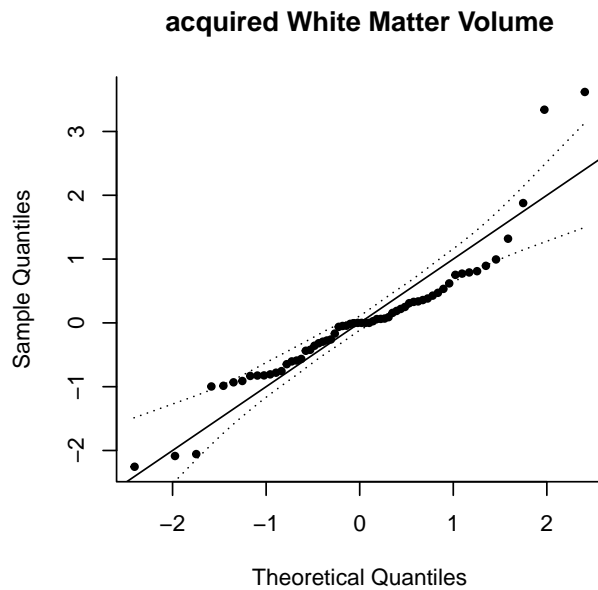
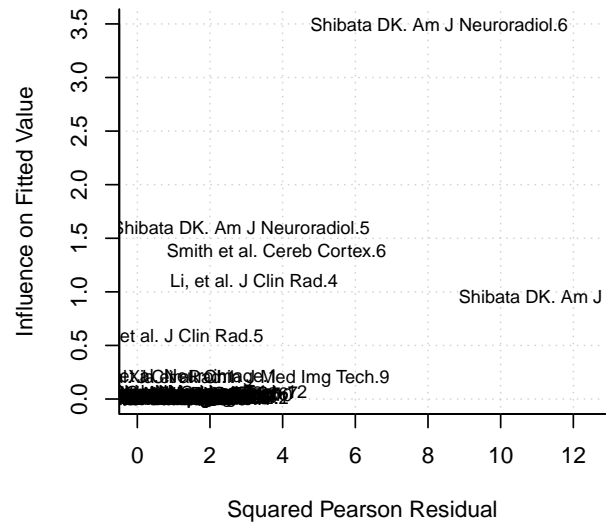
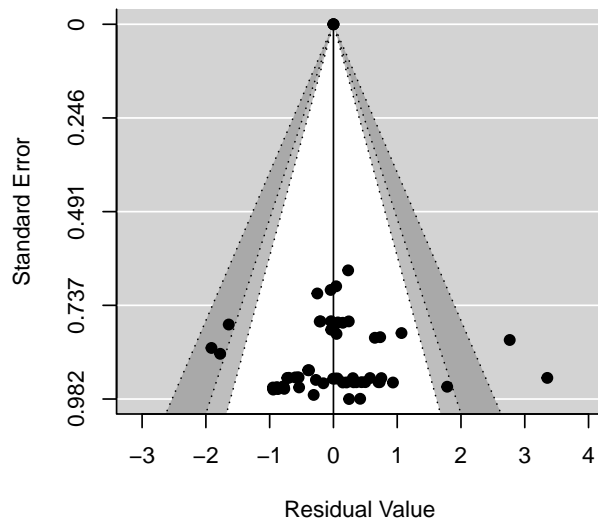
Congenital White Matter Volume



ACQUIRED - White Matter by VOLUME

Random effects model no intercept covariated by Big area and Side (left or right)
acquired White Matter Volume





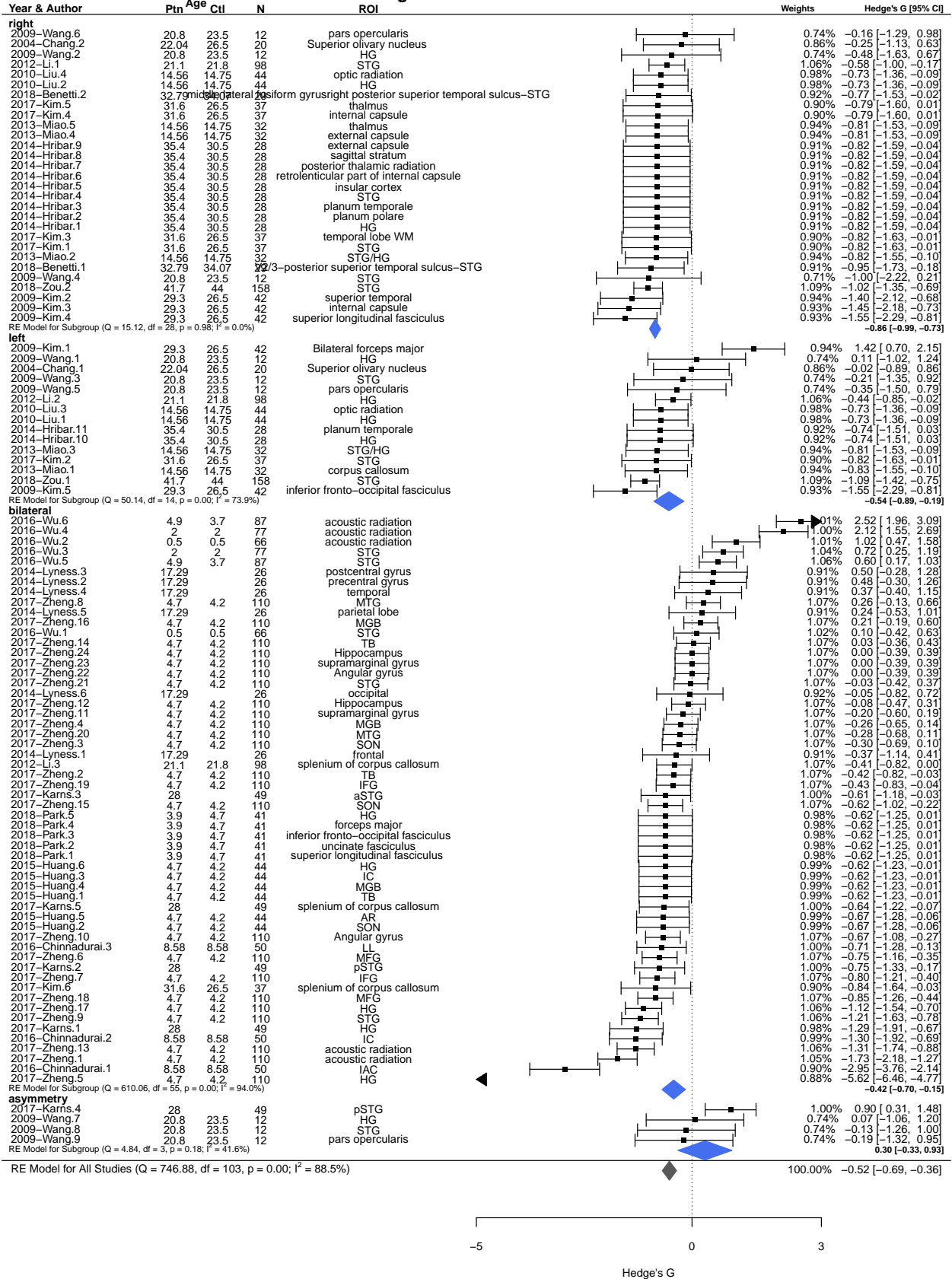
CONGENITAL - White Matter by FA fractional anisotropy

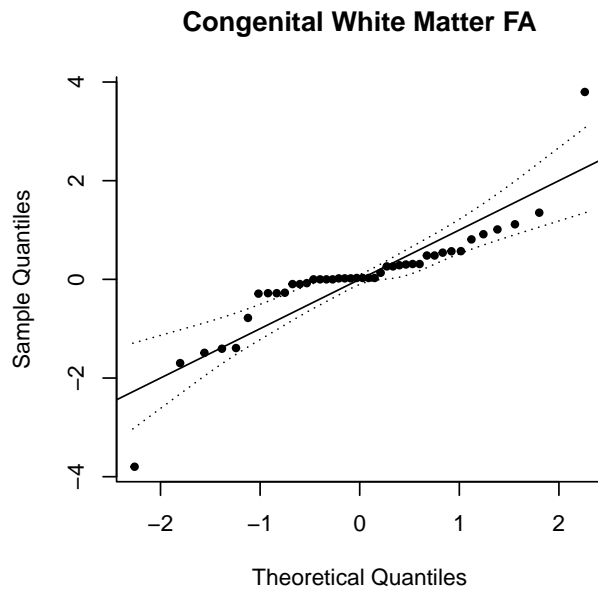
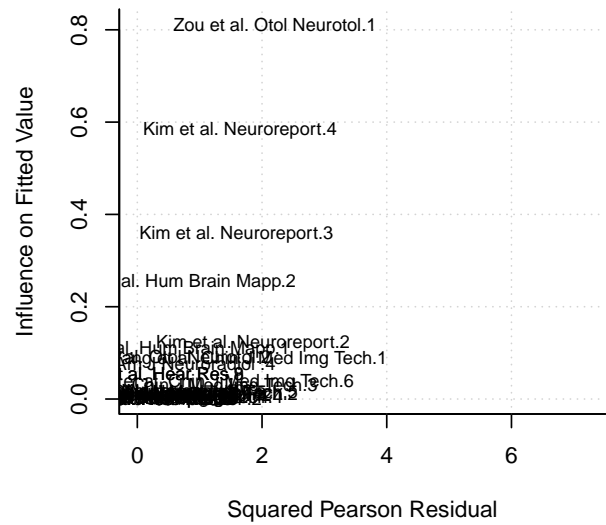
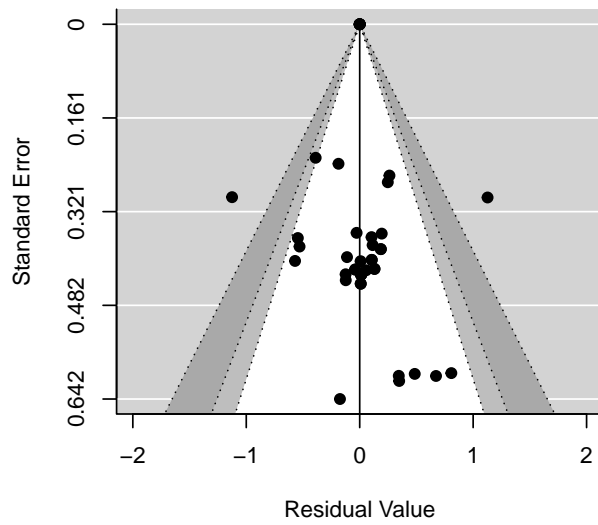
Random effects model no intercept covariated by Big area

	HedgeG	se	zval	ci.lo	ci.up	N
left brainstem	-0.01557	0.4891	-0.03183	-0.9742	0.9431	1
left cingulate cortex	0.297	0.2965	1.002	-0.2841	0.8781	2
left occipital	-0.7254	0.3791	-1.914	-1.468	0.01755	1
left temporal lobe	-0.698	0.1265	-5.518	-0.946	-0.4501	10
left tract	-1.549	0.425	-3.645	-2.382	-0.7163	1
right brainstem	-0.2476	0.4908	-0.5044	-1.21	0.7145	1
right insular cortex	-0.8178	0.4415	-1.852	-1.683	0.04759	1
right occipital	-0.7254	0.3791	-1.914	-1.468	0.01755	1
right temporal lobe	-0.8298	0.1036	-8.013	-1.033	-0.6269	16
right thalamus	-0.9238	0.1789	-5.164	-1.274	-0.5732	6

	HedgeG	se	zval	ci.lo	ci.up	N
right tract	-1.004	0.2156	-4.656	-1.427	-0.5813	4

Congenital White Matter FA



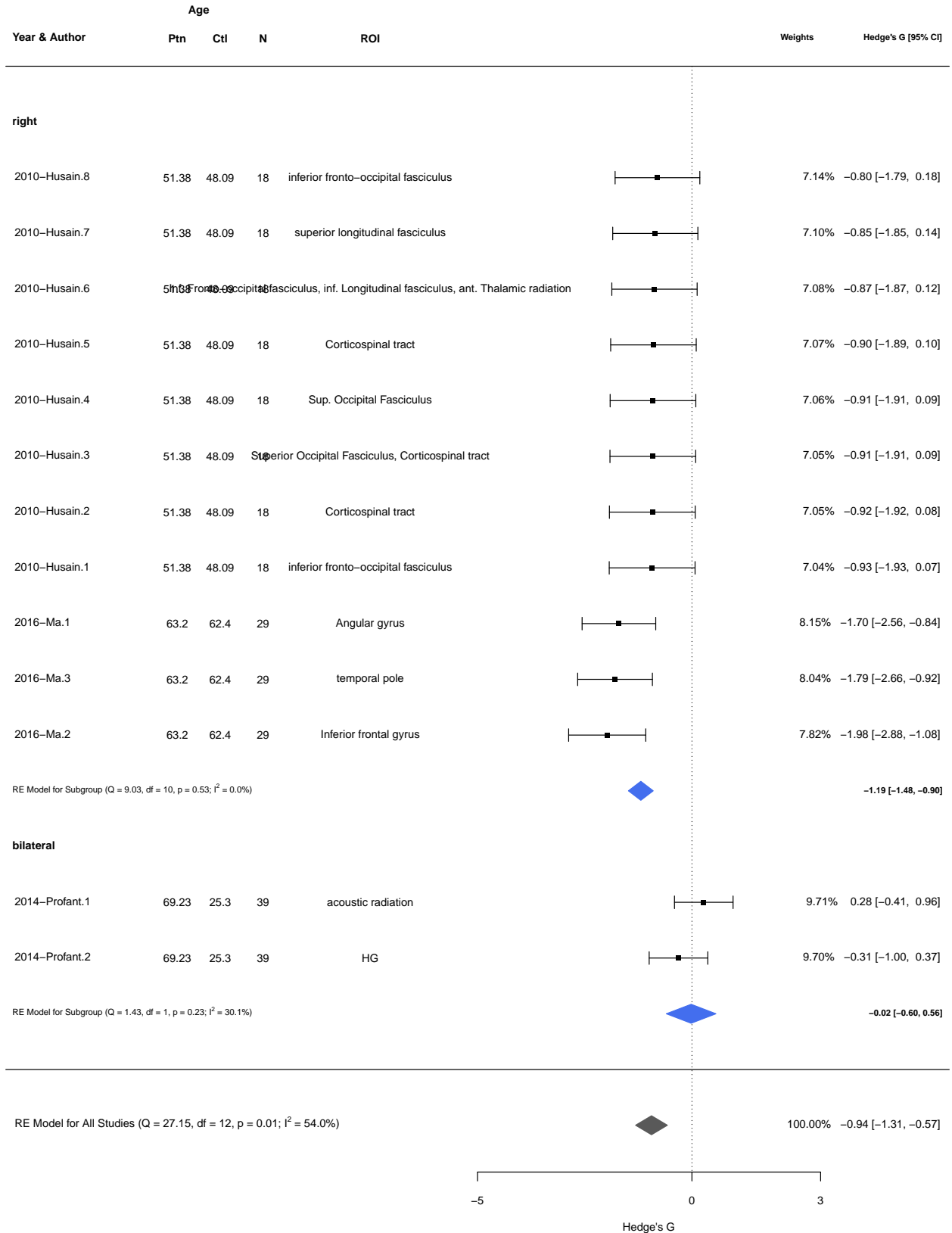


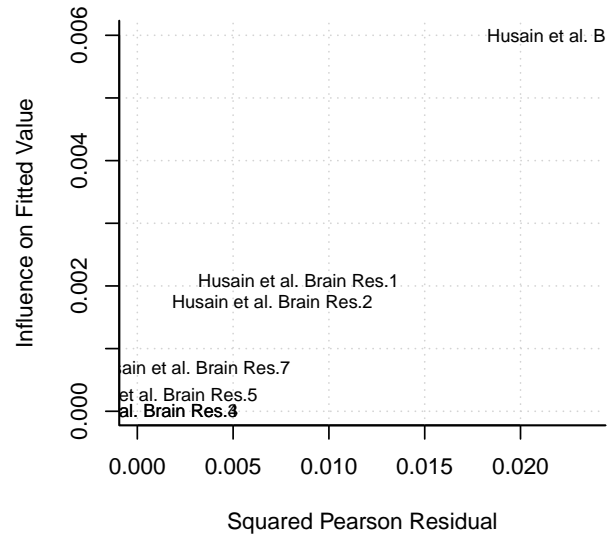
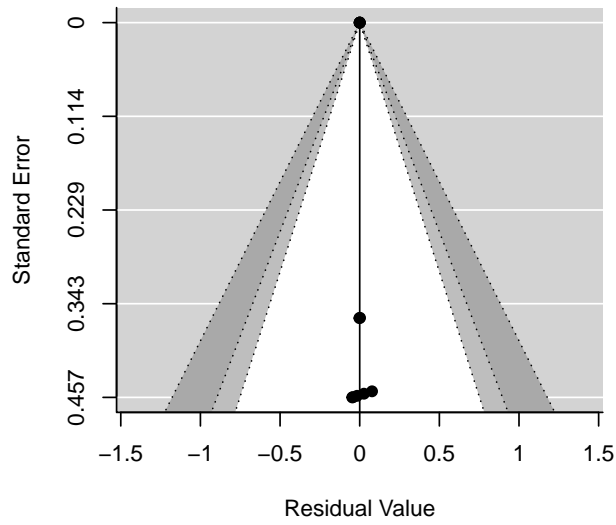
ACQUIRED - White Matter by FA fractional anisotropy

Random effects model no intercept covariated by Big area

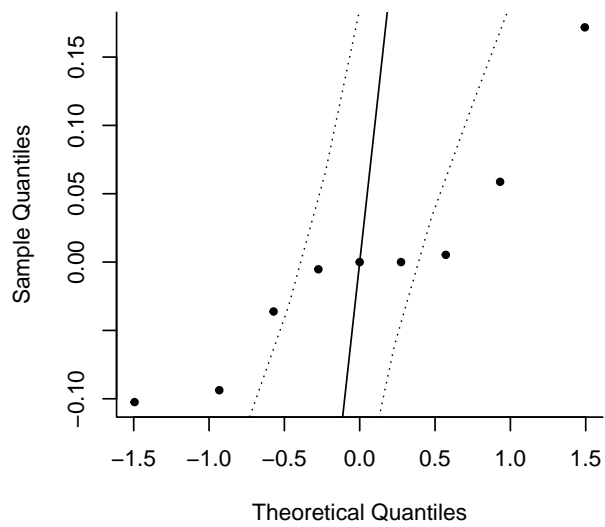
	HedgeG	se	zval	ci.lo	ci.up	N
right frontal	-0.8736	0.5076	-1.721	-1.868	0.1212	1
right frontal lobe	-1.976	0.4587	-4.308	-2.875	-1.077	1
right occipital	-0.9105	0.3603	-2.527	-1.617	-0.2042	2
right parietal lobe	-1.703	0.4379	-3.888	-2.561	-0.8443	1
right temporal lobe	-1.793	0.4446	-4.034	-2.665	-0.922	1
right tract	-0.8812	0.2272	-3.878	-1.326	-0.4359	5

acquired White Matter FA



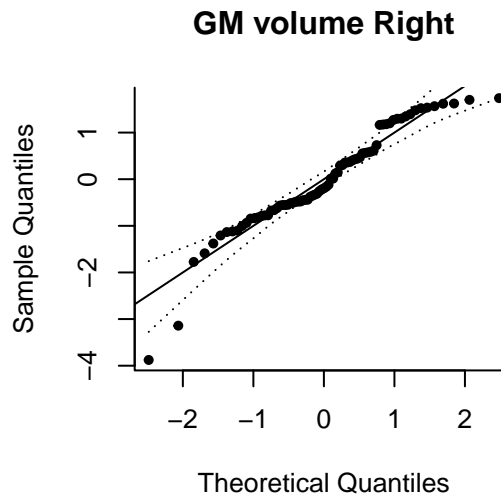
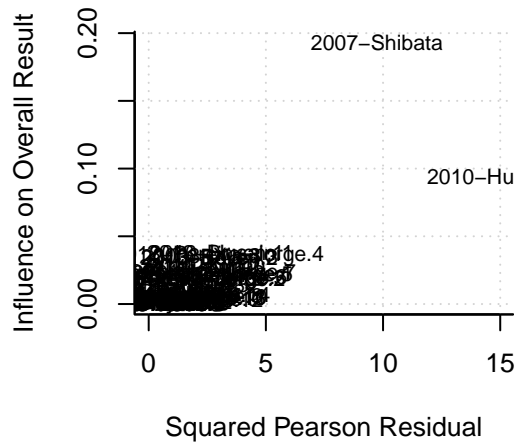
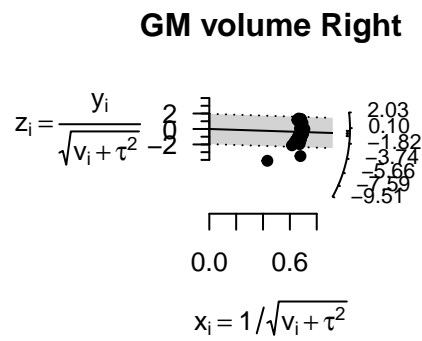
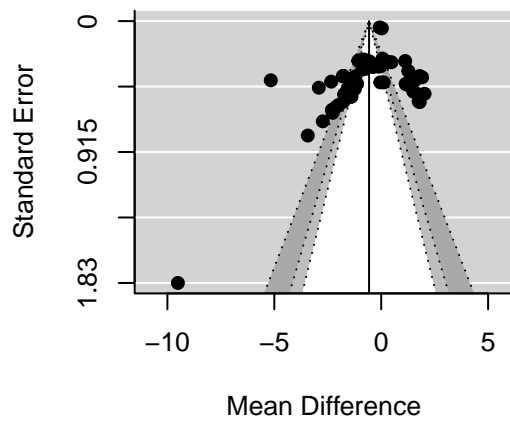


acquired White Matter FA

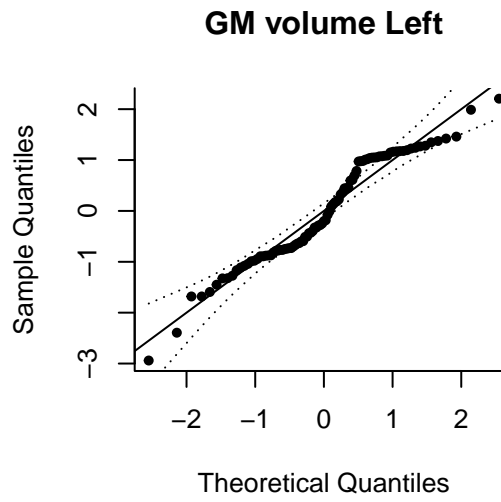
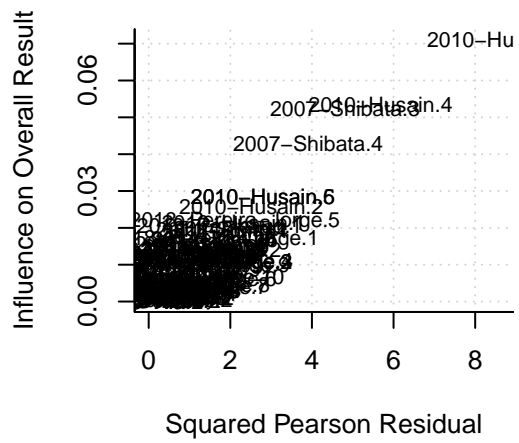
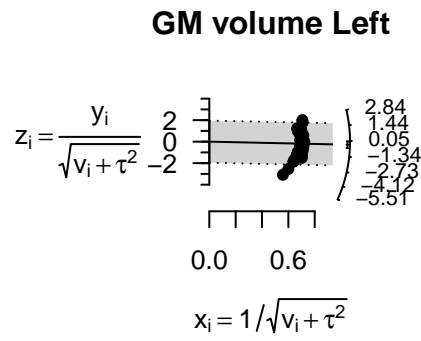
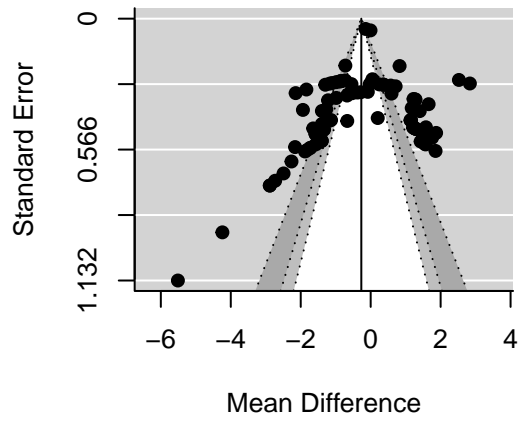


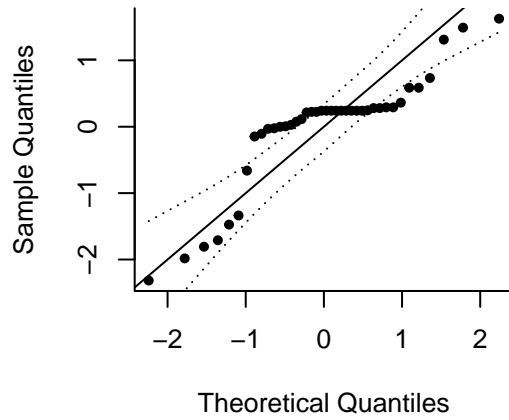
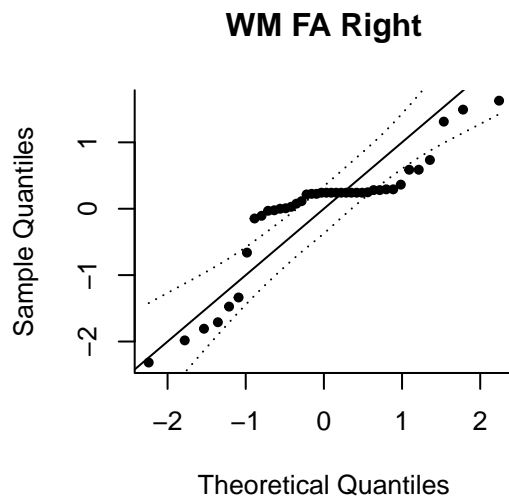
Supplementary material: heterogeneity per model

Heterogeneity: GM volume Right

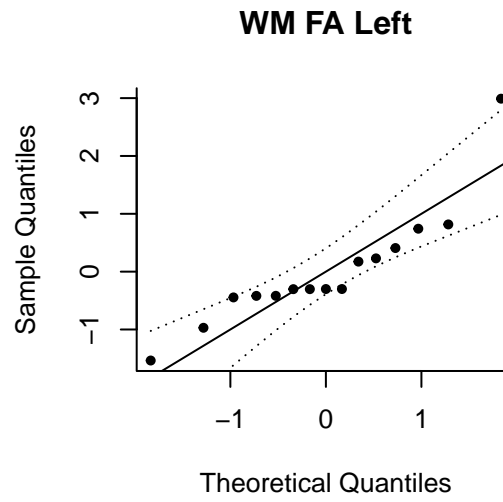
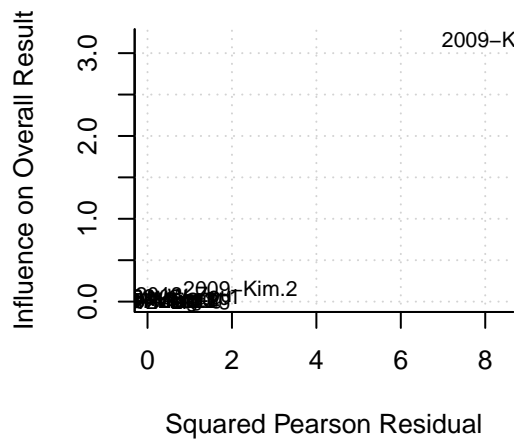
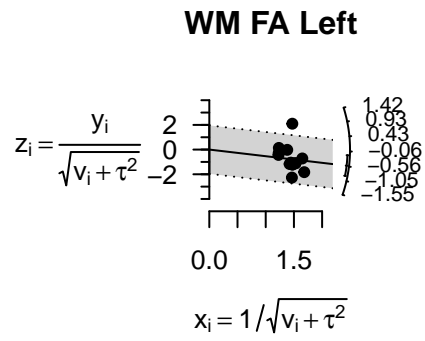
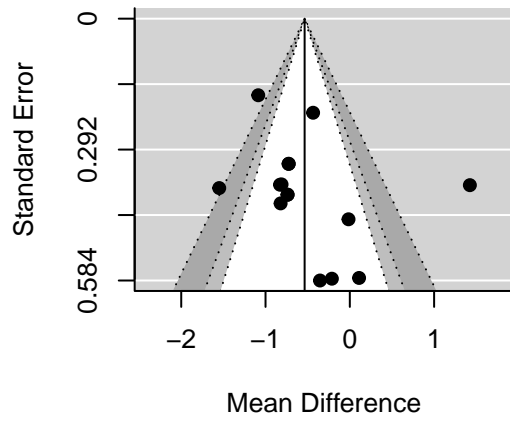


Heterogeneity: GM volume Left

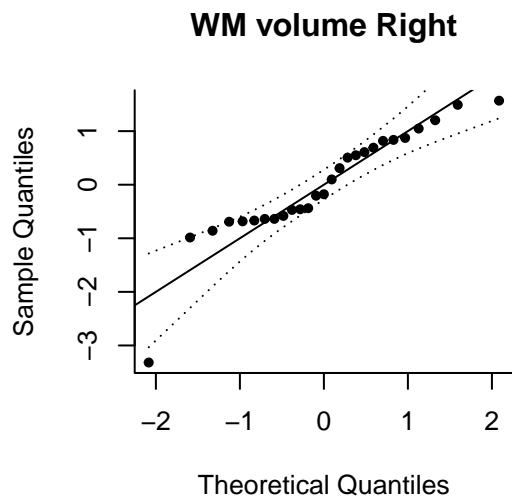
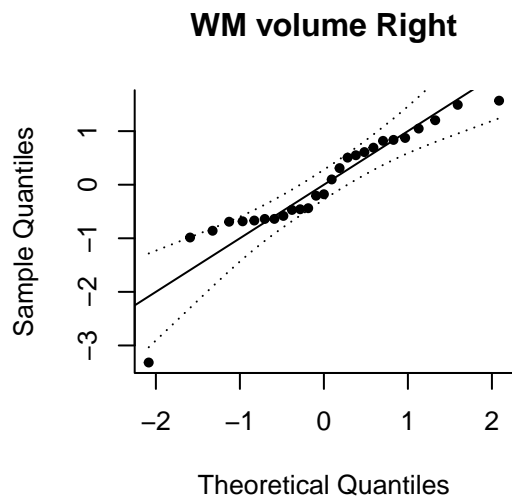




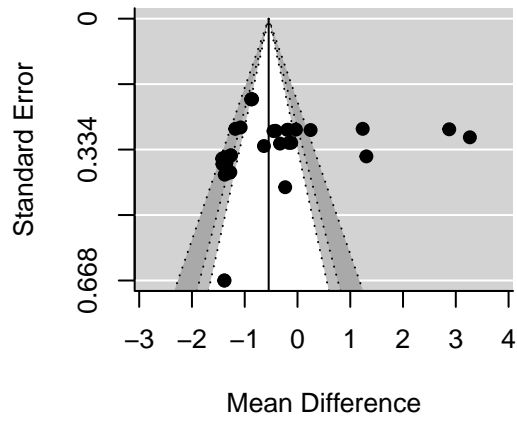
Heterogeneity: WM FA Left



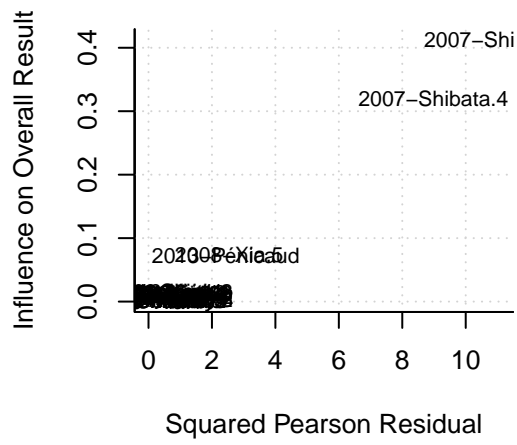
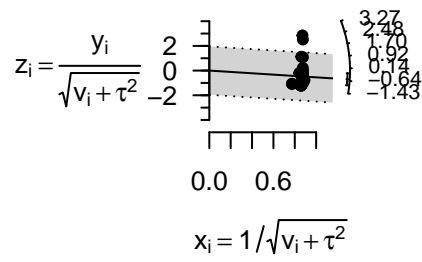
A density scatter plot showing the relationship between Mean Difference (x-axis) and Standard Error (y-axis). The x-axis ranges from -4 to 1, and the y-axis ranges from 0 to 0.668. A vertical line is drawn at Mean Difference = -0.5. The plot features a shaded gray region representing a density, with a peak around Mean Difference = -0.5 and Standard Error = 0.334. A cluster of black dots is visible in the upper right quadrant, indicating a higher density of observations in that region.



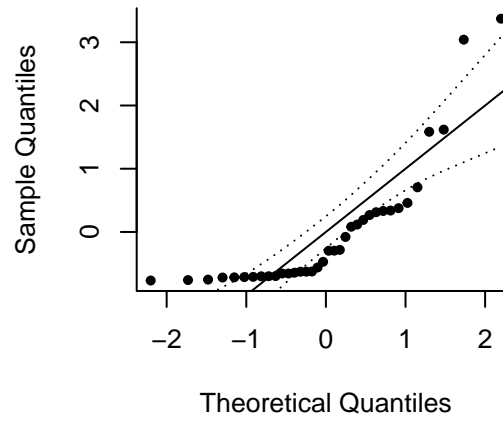
Heterogeneity: WM volume Left

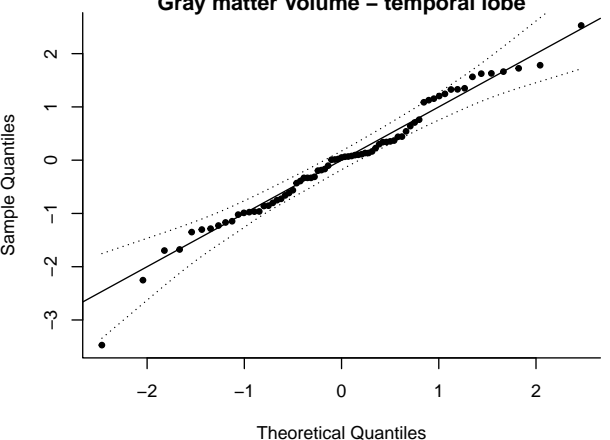
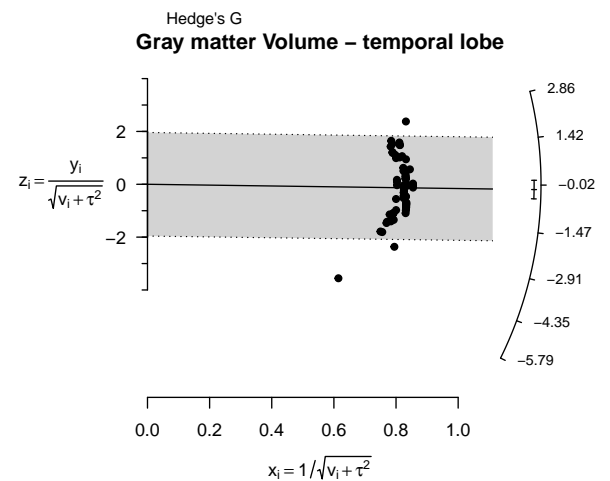


WM volume Left

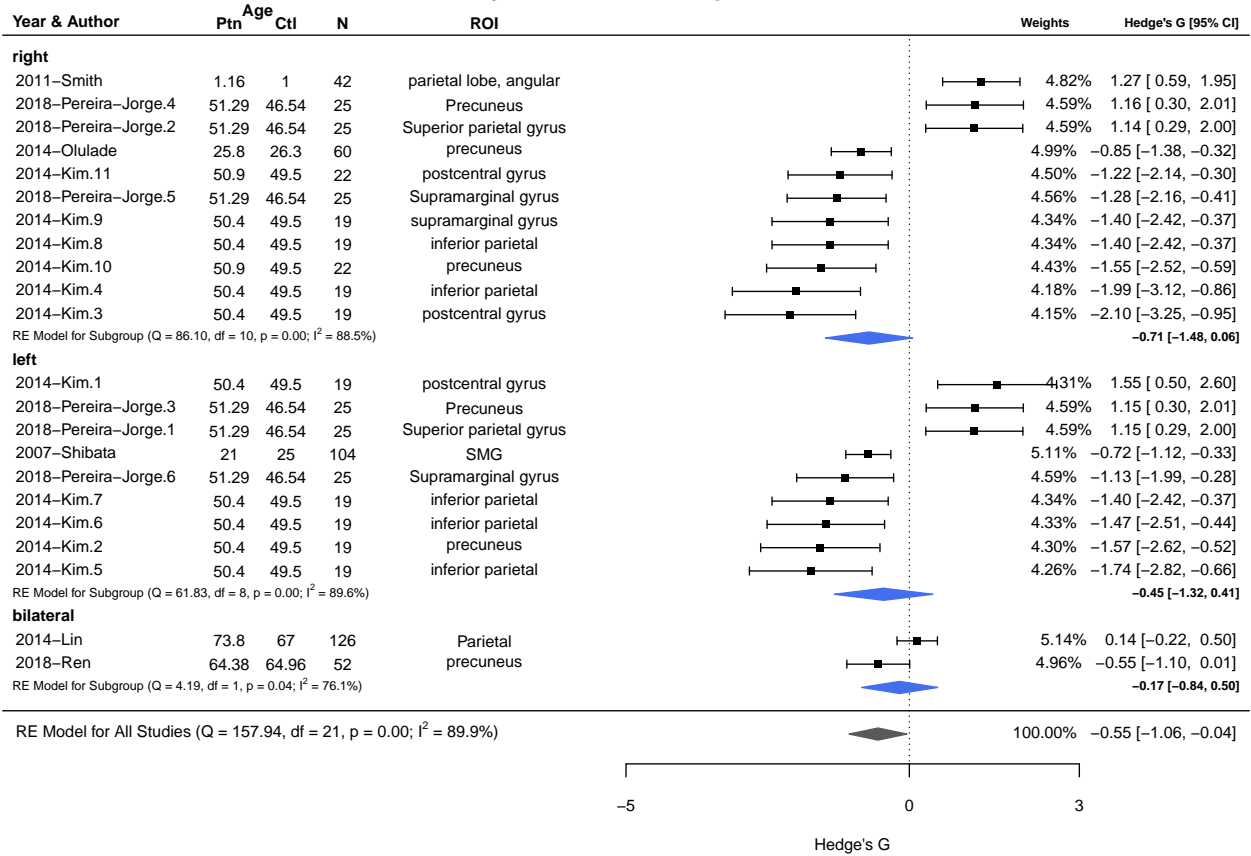


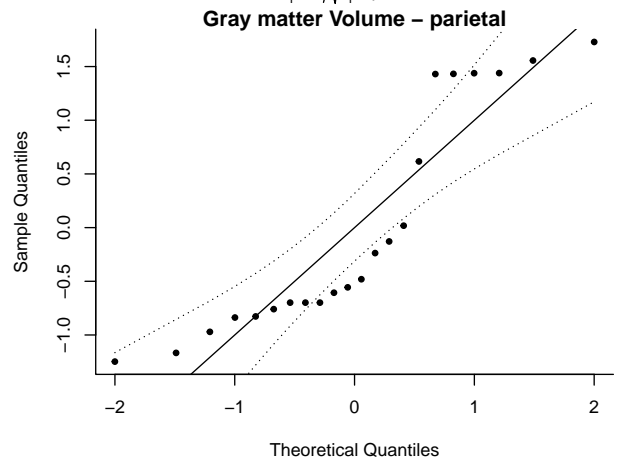
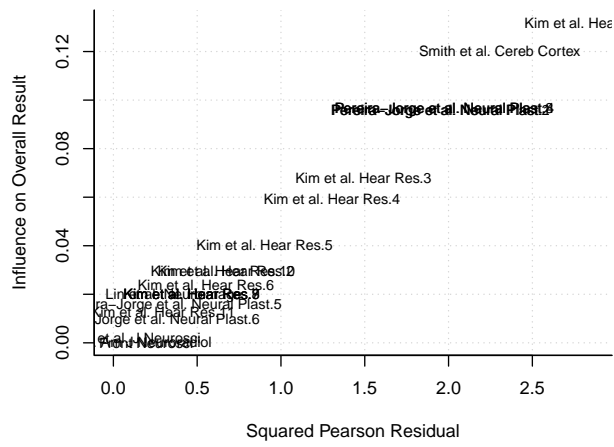
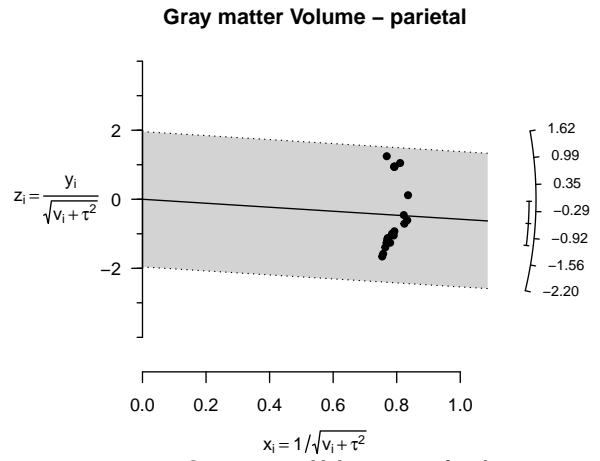
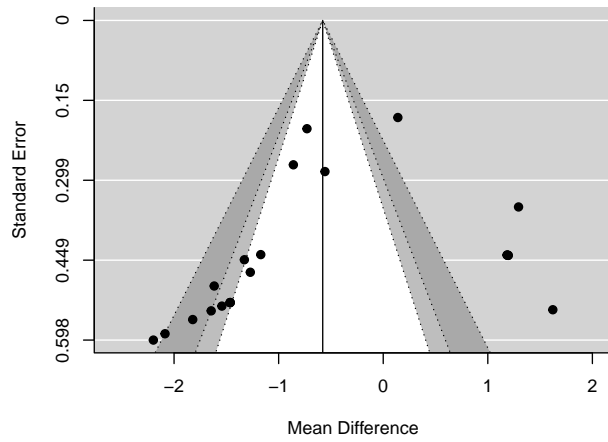
WM volume Left



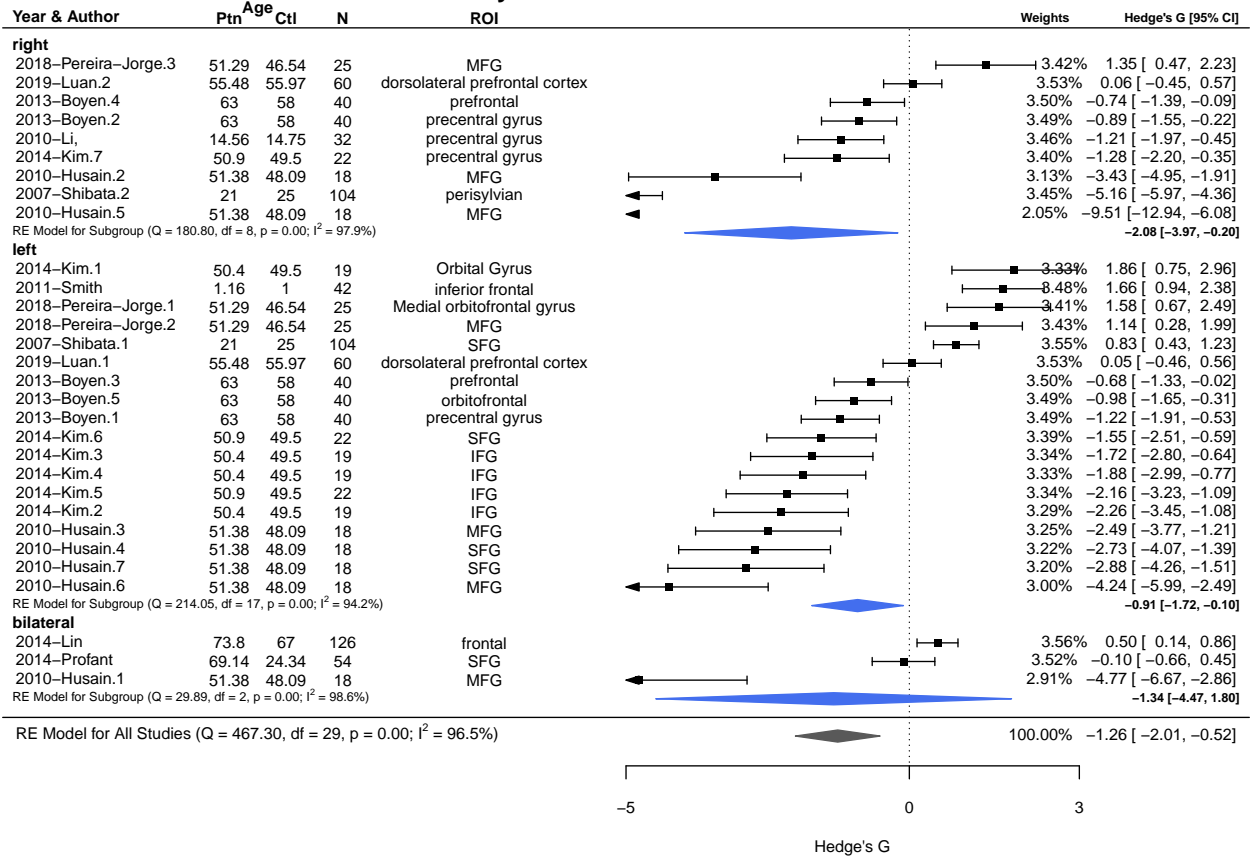
[illegible]

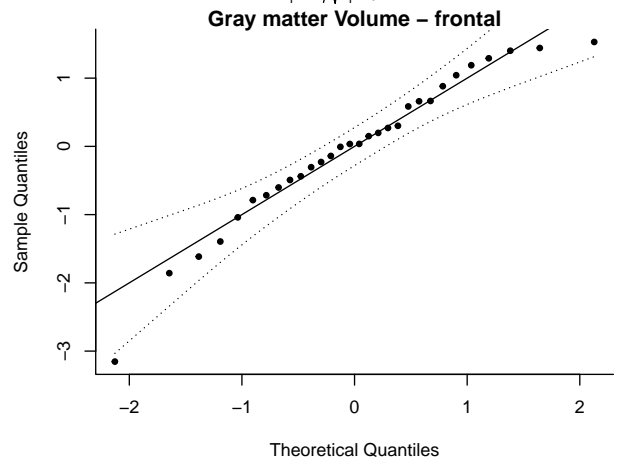
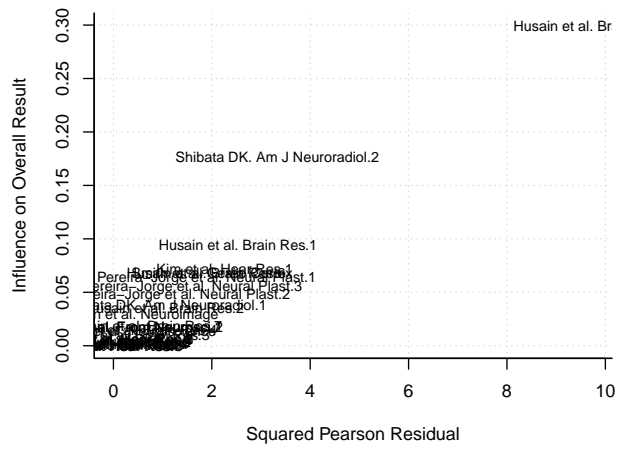
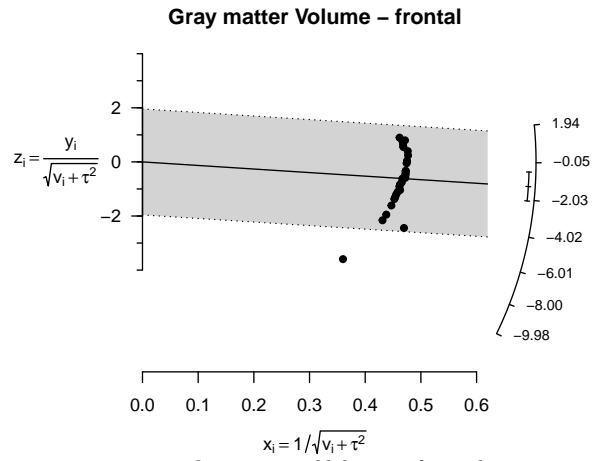
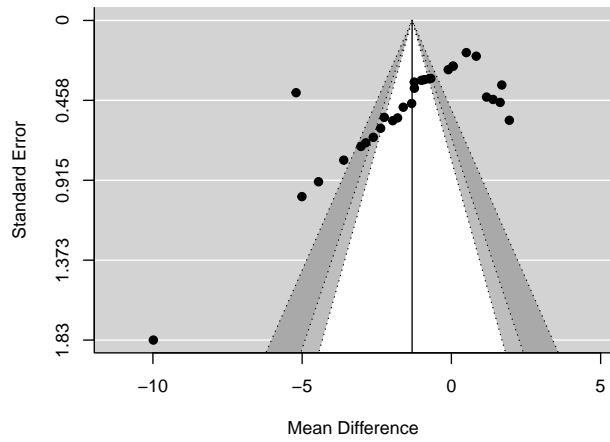
Gray matter Volume – parietal



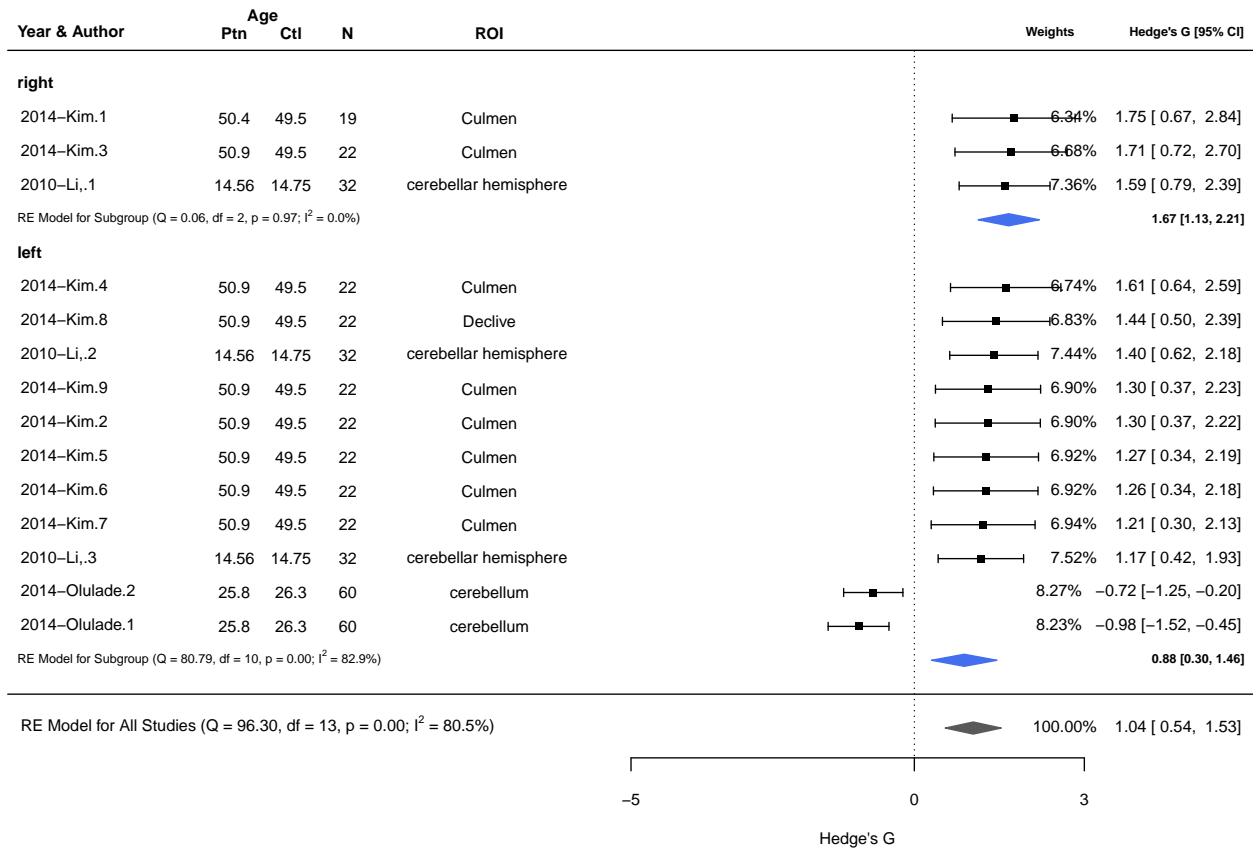


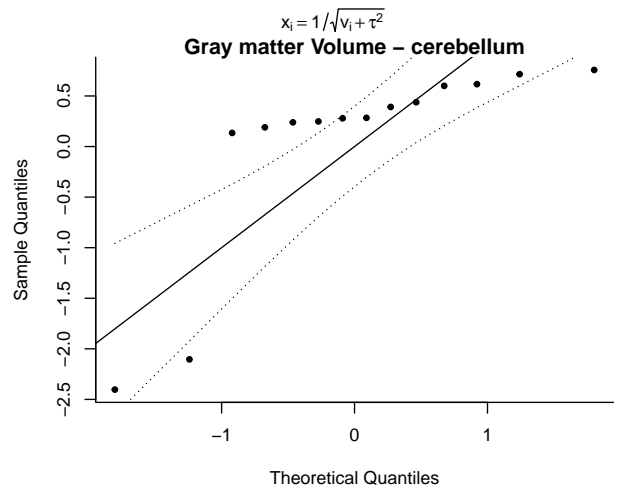
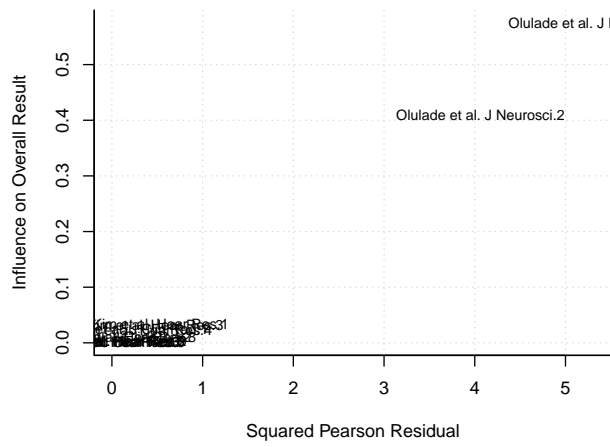
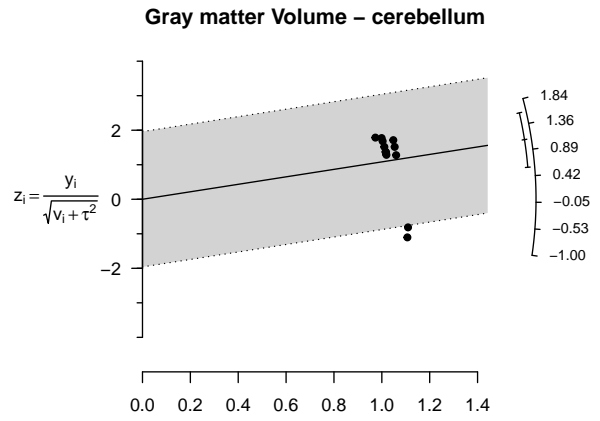
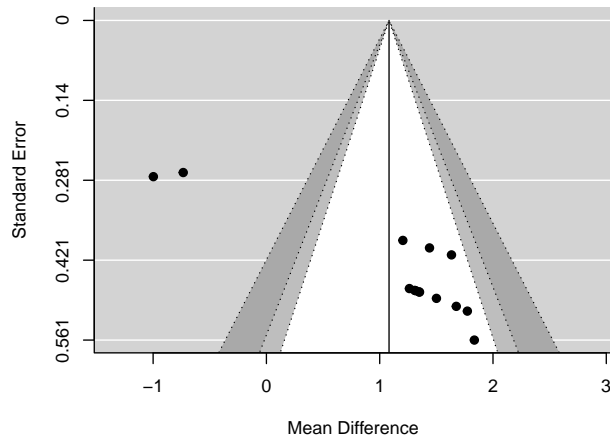
Gray matter Volume – frontal



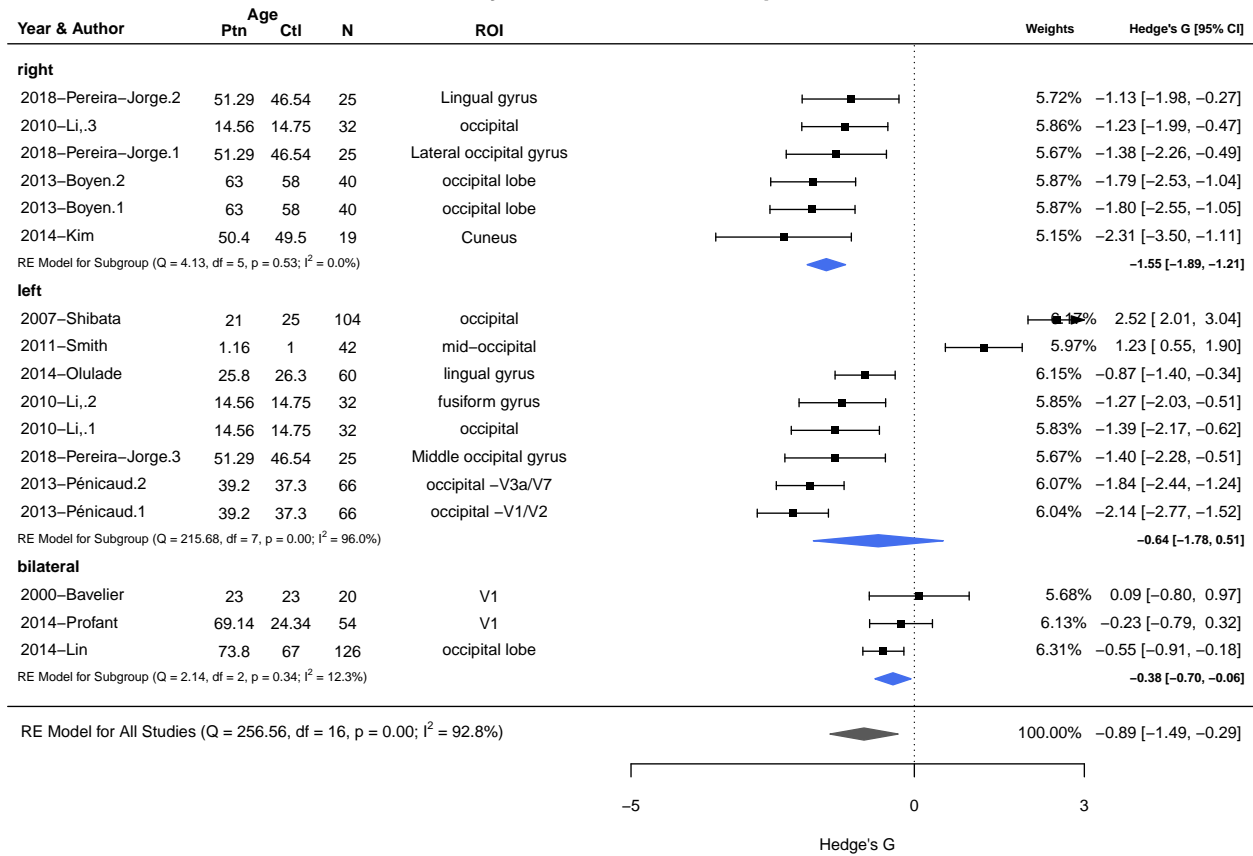


Gray matter Volume – cerebellum

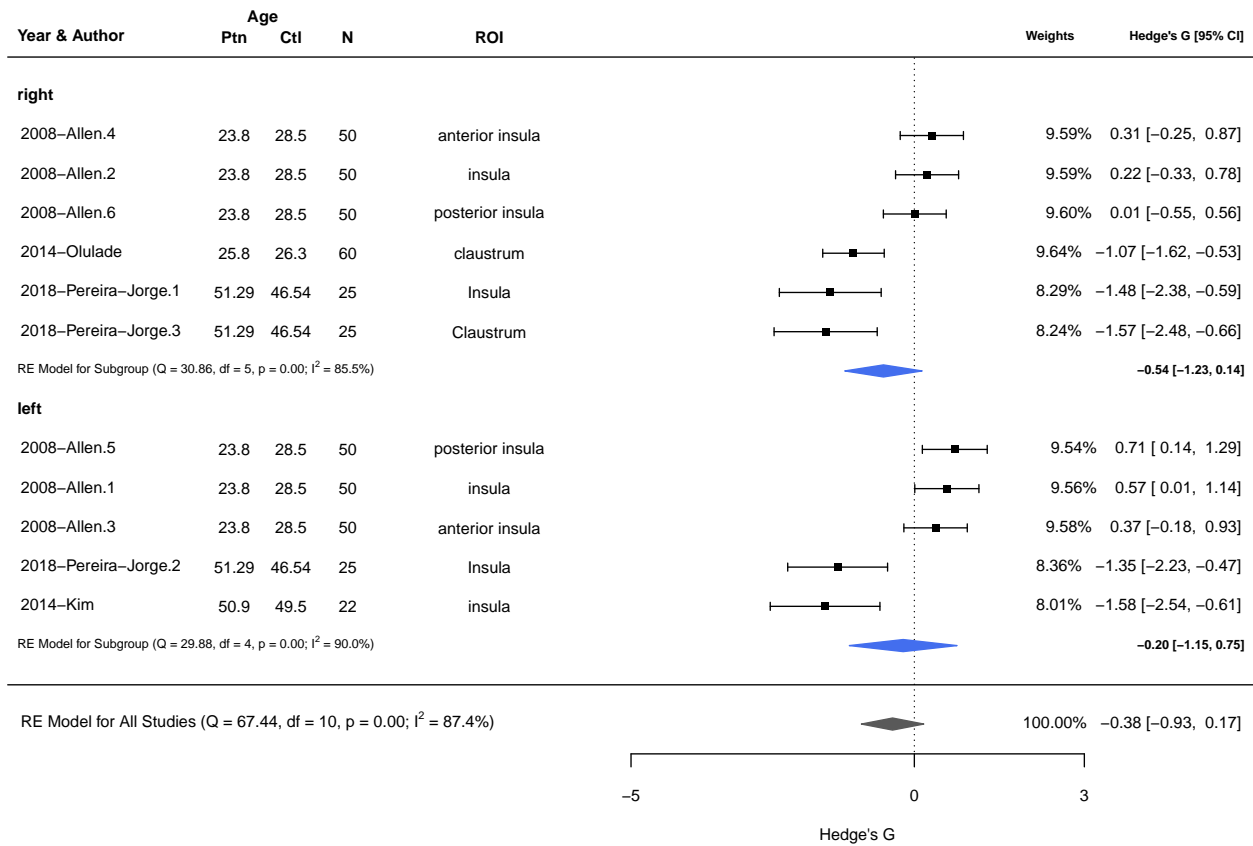


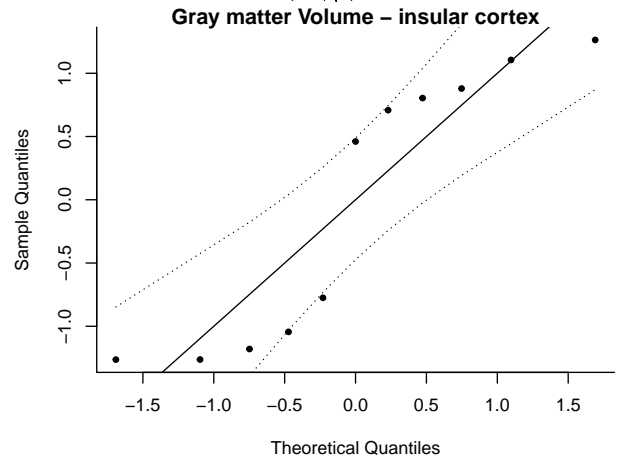
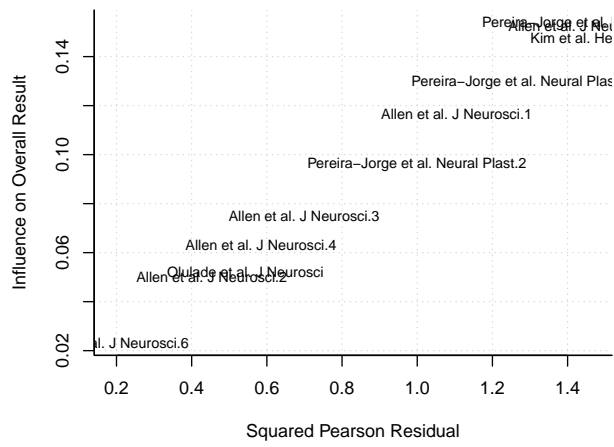
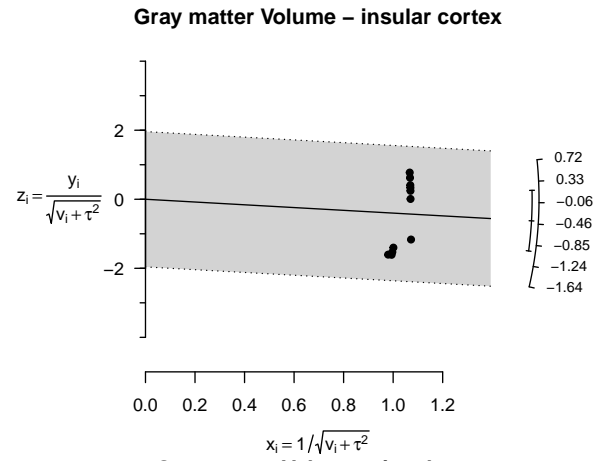
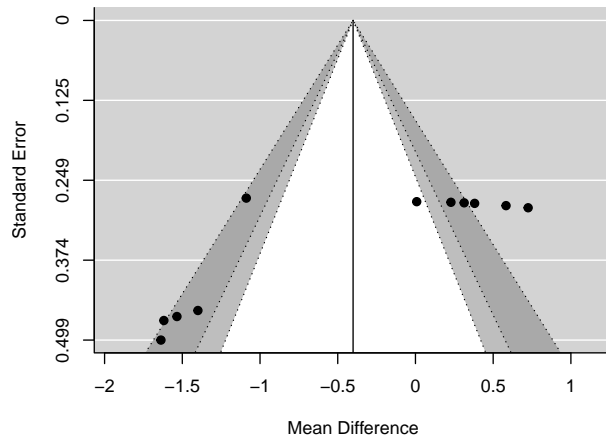


Gray matter Volume – occipital

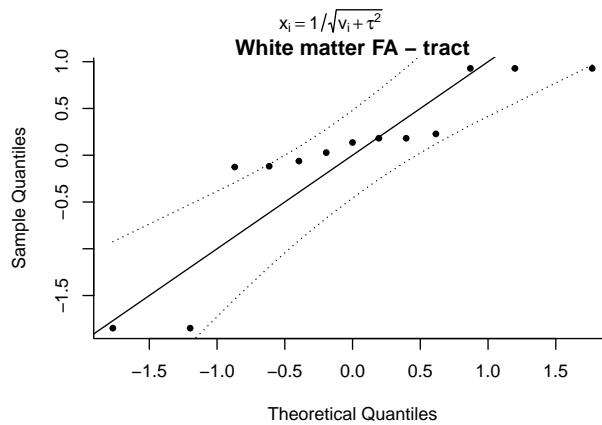
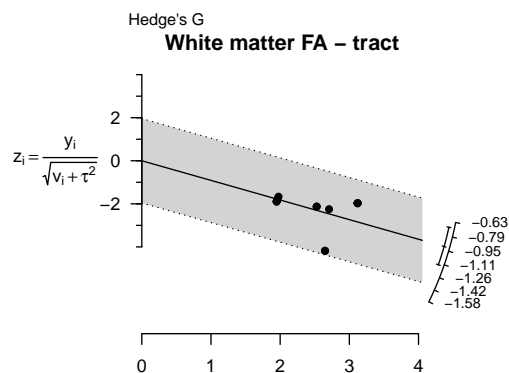


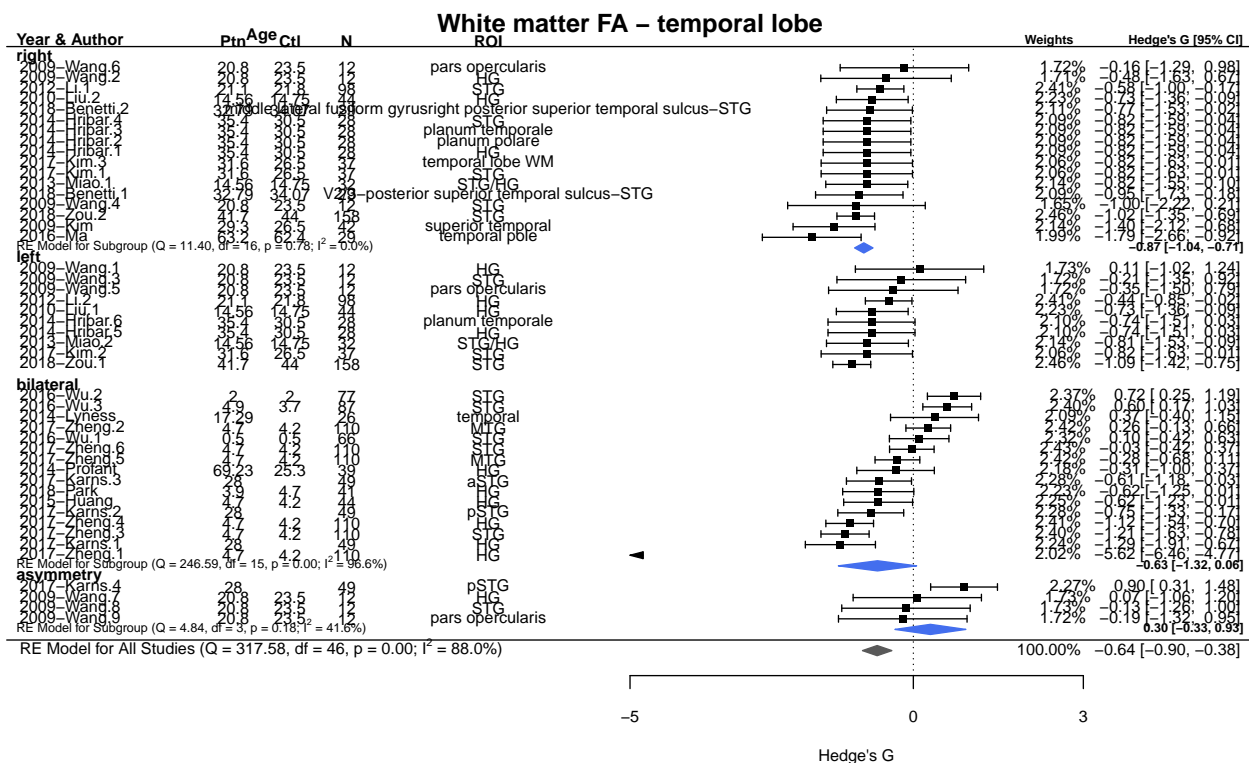
Gray matter Volume – insular cortex



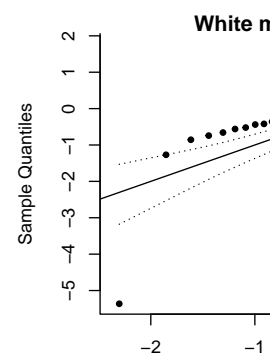
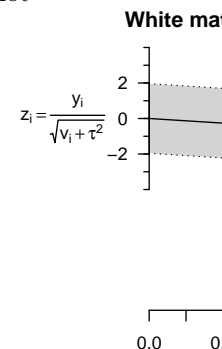
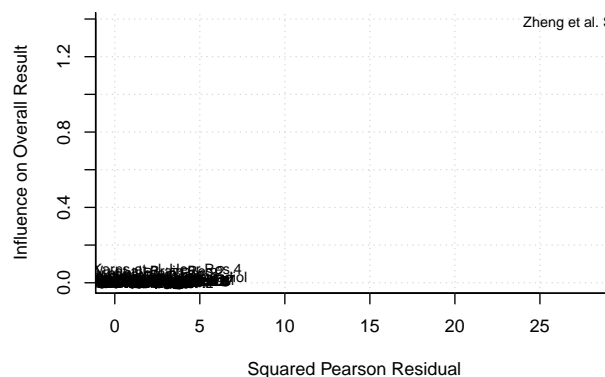
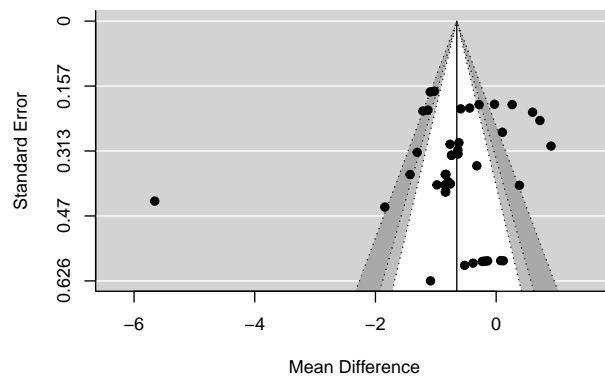


White matter FA – tract									
Year & Author	Age		N	ROI		Weights	Hedge's G [95% CI]		
	Ptn	Ctl							
right									
2010–Husain.5	51.38	48.09	18	inferior fronto–occipital fasciculus		4.75%	−0.80 [−1.79, 0.18]		
2013–Miao	14.56	14.75	32	external capsule		8.87%	−0.81 [−1.53, −0.09]		
2014–Hribar.2	35.4	30.5	28	external capsule		7.74%	−0.82 [−1.59, −0.04]		
2014–Hribar.1	35.4	30.5	28	sagittal stratum		7.74%	−0.82 [−1.59, −0.04]		
2010–Husain.4	51.38	48.09	18	superior longitudinal fasciculus		4.70%	−0.85 [−1.85, 0.14]		
2010–Husain.3	51.38	48.09	18	Corticospinal tract		4.65%	−0.90 [−1.89, 0.10]		
2010–Husain.2	51.38	48.09	18	Corticospinal tract		4.63%	−0.92 [−1.92, 0.08]		
2010–Husain.1	51.38	48.09	18	inferior fronto–occipital fasciculus		4.62%	−0.93 [−1.93, 0.07]		
2009–Kim.1	29.3	26.5	42	superior longitudinal fasciculus		8.52%	−1.55 [−2.29, −0.81]		
RE Model for Subgroup (Q = 3.04, df = 8, p = 0.93; I ² = 0.0%)							−0.95 [−1.24, −0.67]		
left									
2009–Kim.2	29.3	26.5	42	inferior fronto–occipital fasciculus		8.52%	−1.55 [−2.29, −0.81]		
RE Model for Subgroup (Q = 0.00, df = 0, p = 1.00; I ² = 0.0%)							−1.55 [−2.29, −0.81]		
bilateral									
2018–Park.3	3.9	4.7	41	inferior fronto–occipital fasciculus		11.75%	−0.62 [−1.25, 0.01]		
2018–Park.2	3.9	4.7	41	uncinate fasciculus		11.75%	−0.62 [−1.25, 0.01]		
2018–Park.1	3.9	4.7	41	superior longitudinal fasciculus		11.75%	−0.62 [−1.25, 0.01]		
RE Model for Subgroup (Q = 0.00, df = 2, p = 1.00; I ² = 0.0%)							−0.62 [−0.98, −0.26]		
RE Model for All Studies (Q = 8.45, df = 12, p = 0.75; I ² = 0.0%)						100.00%	−0.89 [−1.10, −0.67]		



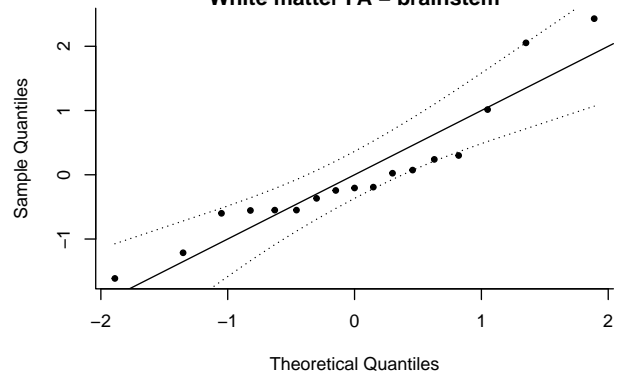
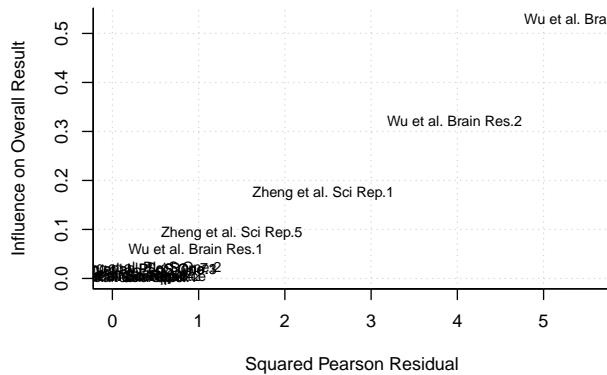
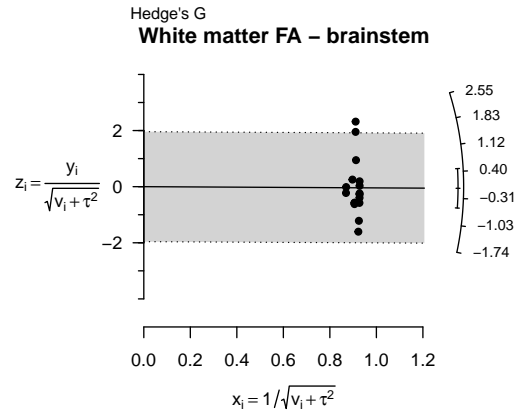
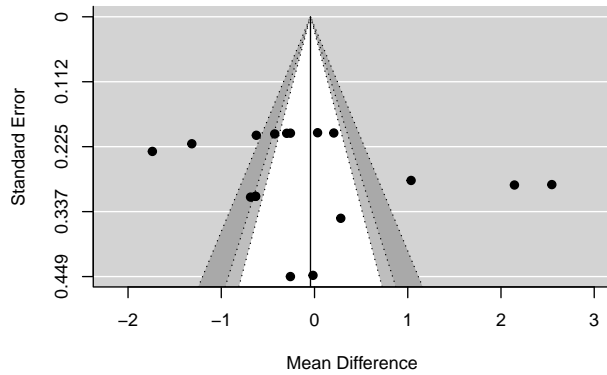
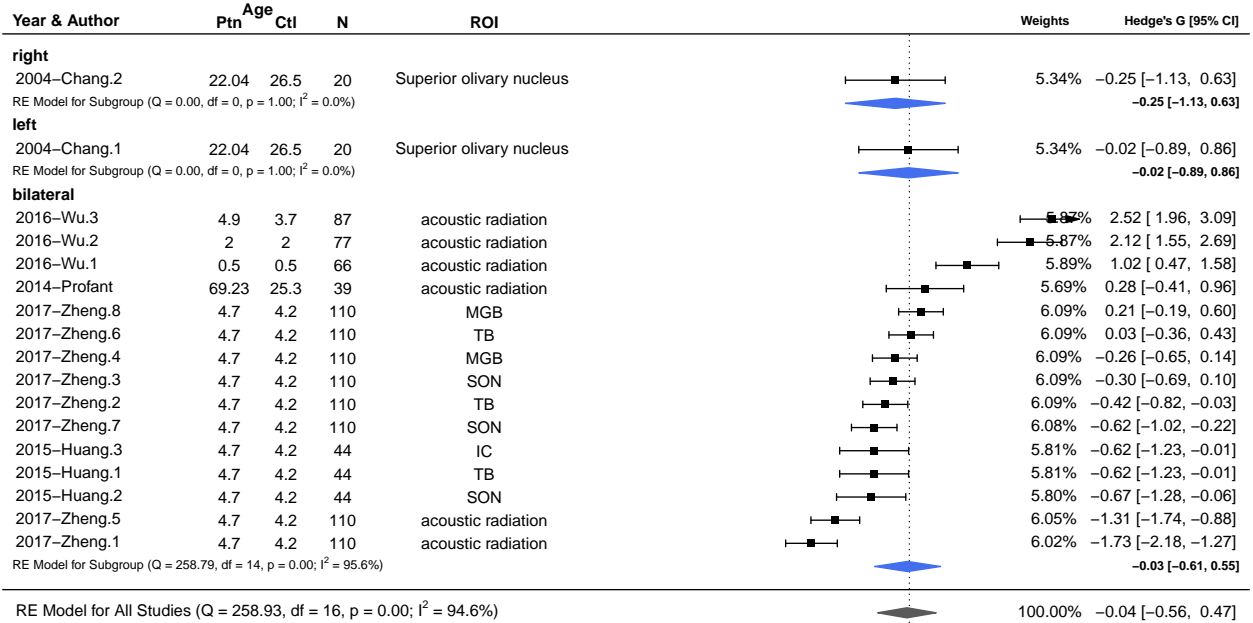


Error in rma(yi = hedgesG, vi = varG, data = meta.mod, measure = "MD", : Fisher scoring algorithm did not

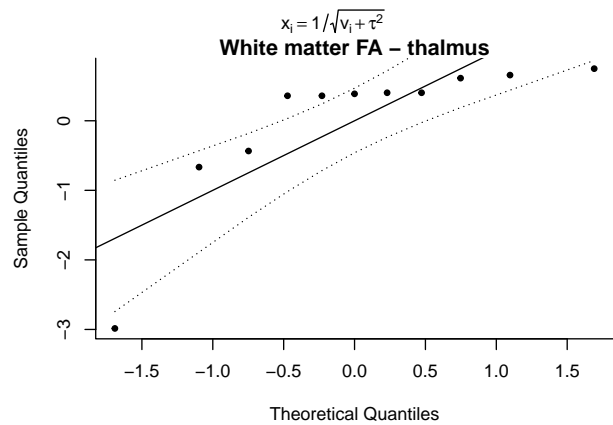
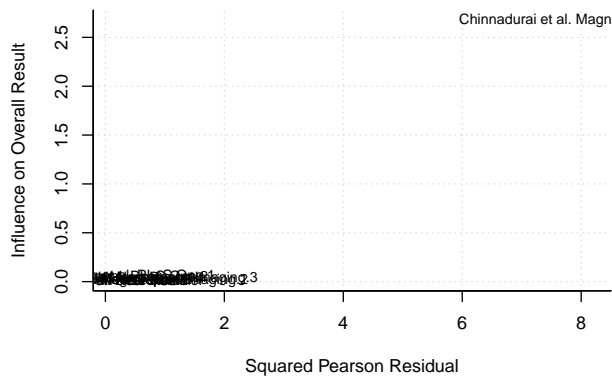
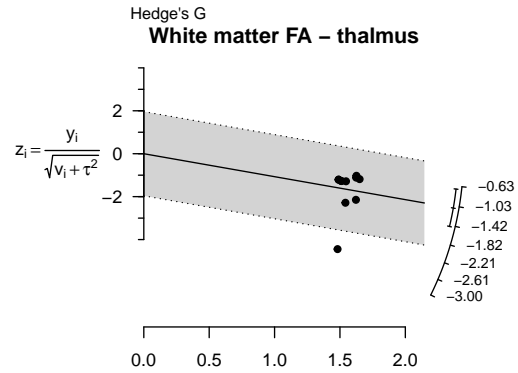
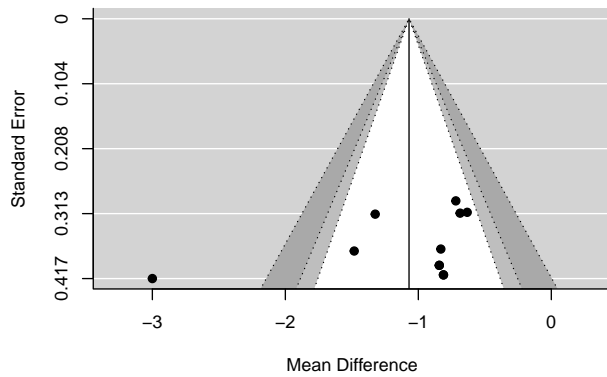
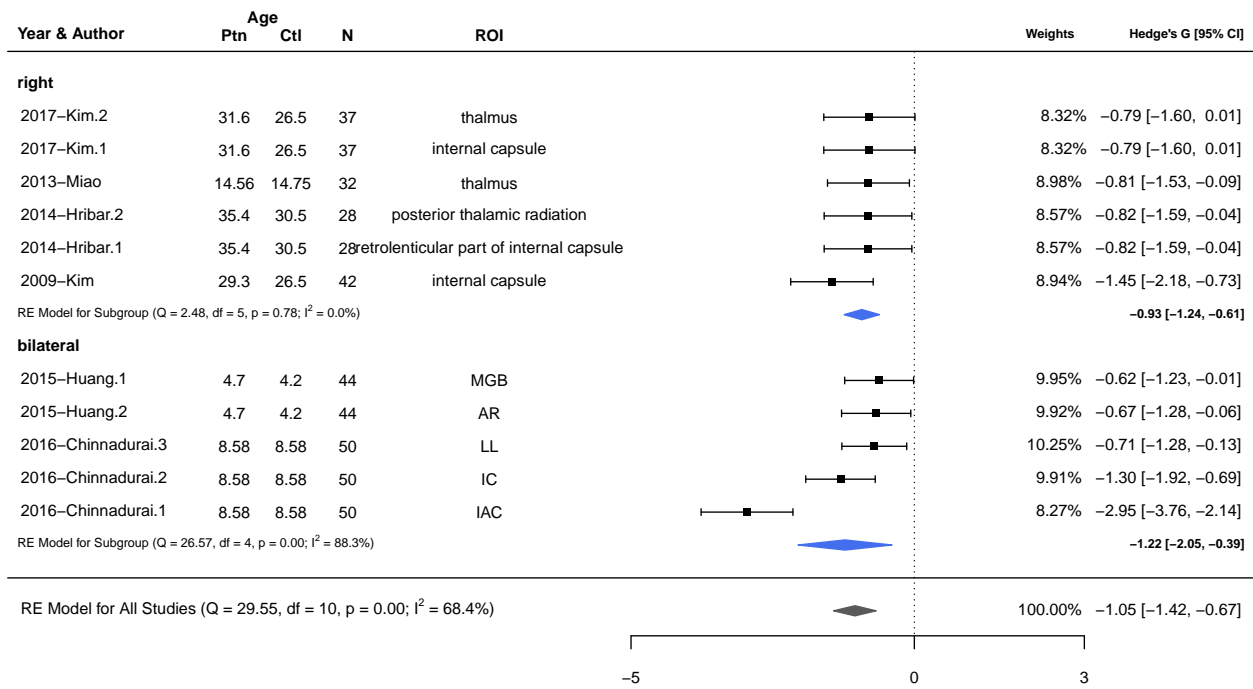


converge. See 'help(rma)' for possible remedies.

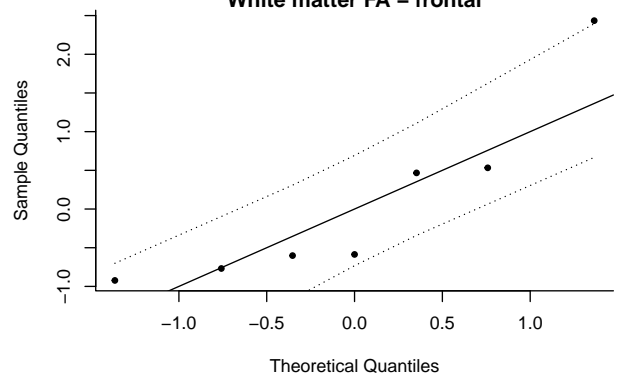
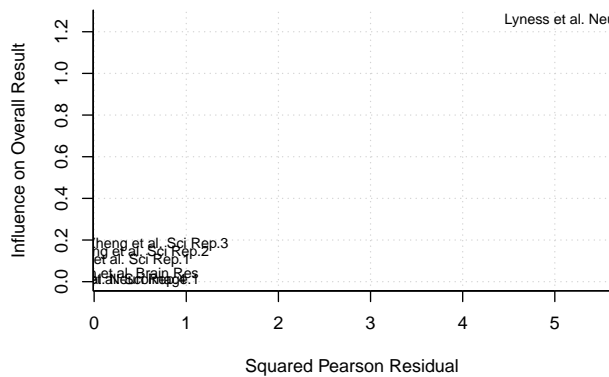
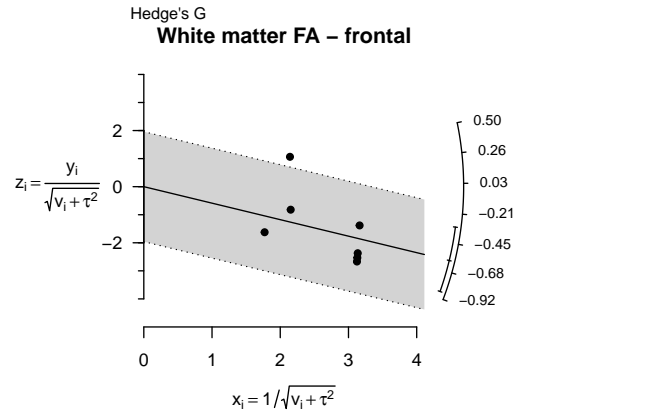
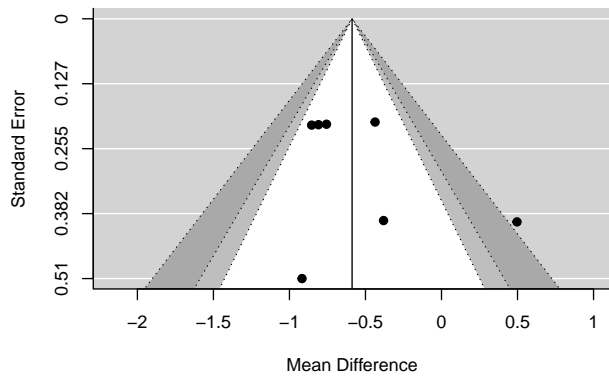
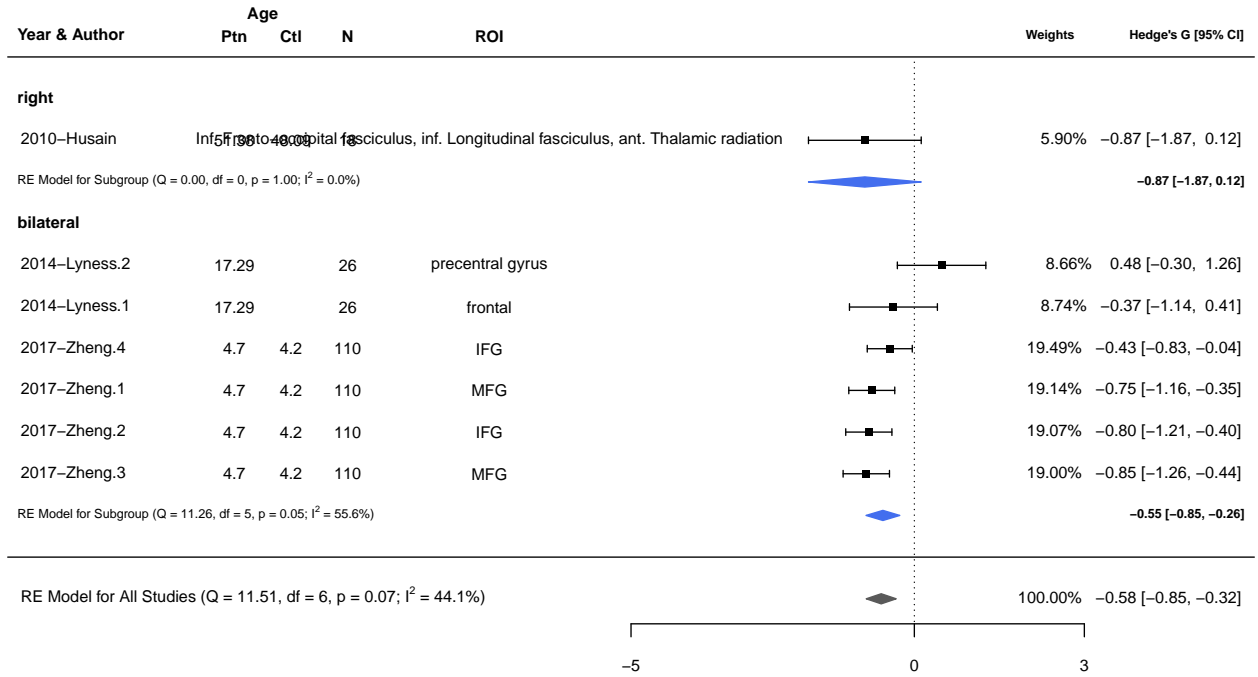
White matter FA – brainstem











White matter FA – thalamus



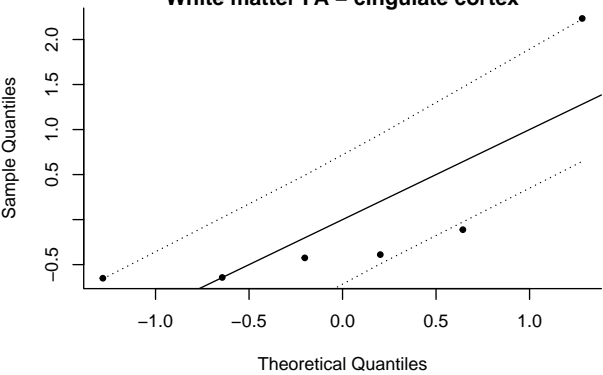
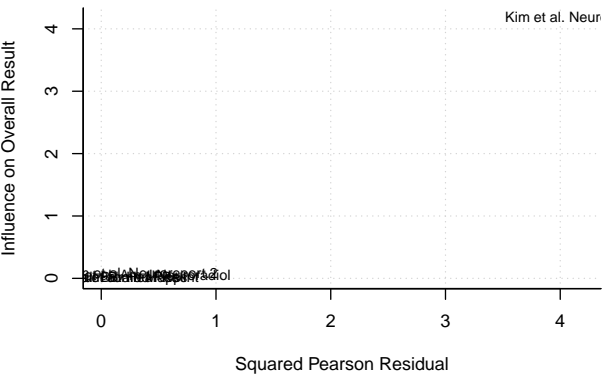
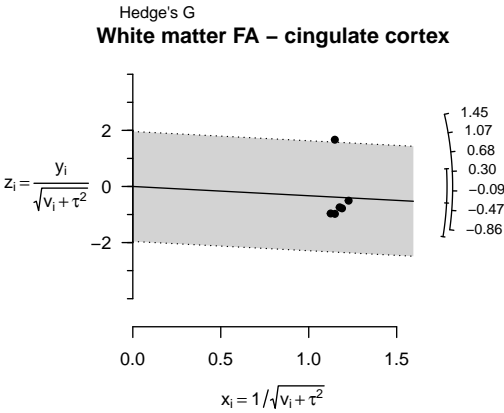
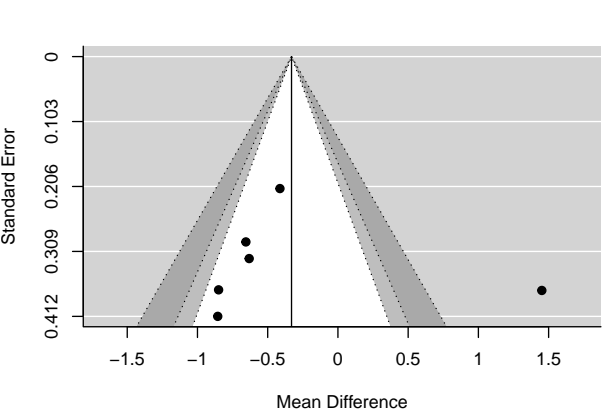
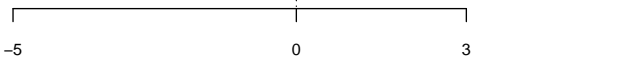
White matter FA – frontal



White matter FA – cingulate cortex

Year & Author	Age		N	ROI		Weights	Hedge's G [95% CI]
	Ptn	Ctl					
left							
2009–Kim	29.3	26.5	42	Bilateral forceps major		16.06%	1.42 [0.70, 2.15]
2013–Miao	14.56	14.75	32	corpus callosum		16.07%	-0.83 [-1.55, -0.10]
RE Model for Subgroup (Q = 18.57, df = 1, p = 0.00; I ² = 94.6%)							0.30 [-1.91, 2.51]
bilateral							
2012–Li	21.1	21.8	98	splenium of corpus callosum		18.41%	-0.41 [-0.82, 0.00]
2018–Park	3.9	4.7	41	forceps major		16.85%	-0.62 [-1.25, 0.01]
2017–Karns	28		49	splenium of corpus callosum		17.25%	-0.64 [-1.22, -0.07]
2017–Kim	31.6	26.5	37	splenium of corpus callosum		15.37%	-0.84 [-1.64, -0.03]
RE Model for Subgroup (Q = 1.09, df = 3, p = 0.78; I ² = 0.0%)							-0.56 [-0.83, -0.28]

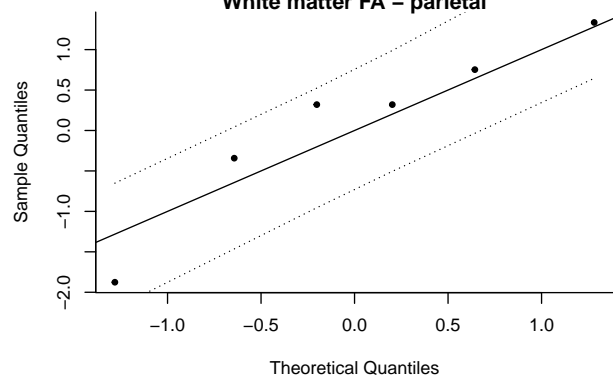
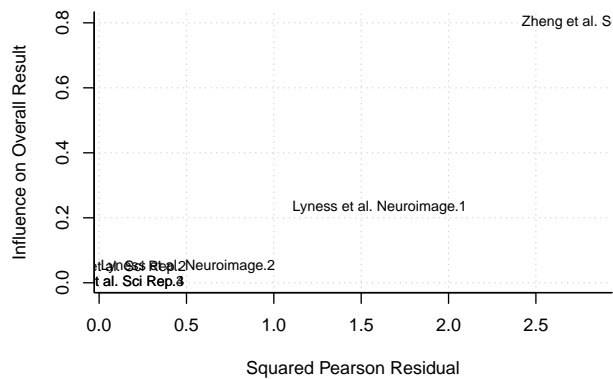
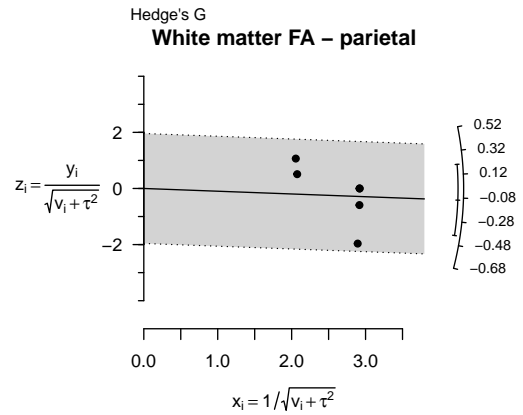
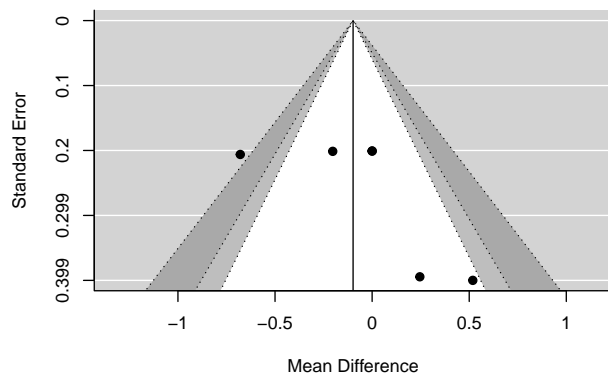
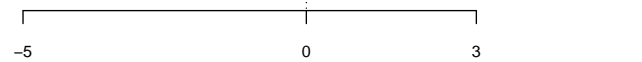
RE Model for All Studies (Q = 27.88, df = 5, p = 0.00; I² = 85.8%)



White matter FA – parietal

Year & Author	Age		N	ROI		Weights	Hedge's G [95% CI]
	Ptn	Ctl					
bilateral							
2014–Lyness.1	17.29		26	postcentral gyrus		9.84%	0.50 [–0.28, 1.28]
2014–Lyness.2	17.29		26	parietal lobe		10.02%	0.24 [–0.53, 1.01]
2017–Zheng.4	4.7	4.2	110	supramarginal gyrus		20.14%	0.00 [–0.39, 0.39]
2017–Zheng.3	4.7	4.2	110	Angular gyrus		20.14%	0.00 [–0.39, 0.39]
2017–Zheng.2	4.7	4.2	110	supramarginal gyrus		20.10%	–0.20 [–0.60, 0.19]
2017–Zheng.1	4.7	4.2	110	Angular gyrus		19.77%	–0.67 [–1.08, –0.27]
RE Model for Subgroup (Q = 11.32, df = 5, p = 0.05; I ² = 56.5%)							–0.10 [–0.40, 0.20]

RE Model for All Studies (Q = 11.32, df = 5, p = 0.05; I² = 56.5%)



White matter FA – occipital

Year & Author	Age		N	ROI		Weights	Hedge's G [95% CI]
	Ptn	Ctl					
right							
2010–Liu.2	14.56	14.75	44	optic radiation		28.71%	-0.73 [-1.36, -0.09]
2010–Husain.2	51.38	48.09	18	Sup. Occipital Fasciculus		11.55%	-0.91 [-1.91, 0.09]
2010–Husain.1	51.38	48.09	18	Superior Occipital Fasciculus, Corticospinal tract		11.55%	-0.91 [-1.91, 0.09]
RE Model for Subgroup (Q = 0.15, df = 2, p = 0.93; I ² = 0.0%)							-0.81 [-1.28, -0.34]
left							
2010–Liu.1	14.56	14.75	44	optic radiation		28.71%	-0.73 [-1.36, -0.09]
RE Model for Subgroup (Q = 0.00, df = 0, p = 1.00; I ² = 0.0%)							-0.73 [-1.36, -0.09]
bilateral							
2014–Lyness	17.29		26	occipital		19.49%	-0.05 [-0.82, 0.72]
RE Model for Subgroup (Q = 0.00, df = 0, p = 1.00; I ² = 0.0%)							-0.05 [-0.82, 0.72]
RE Model for All Studies (Q = 2.96, df = 4, p = 0.56; I ² = 0.0%)						100.00%	-0.64 [-0.98, -0.30]

-5 0 3

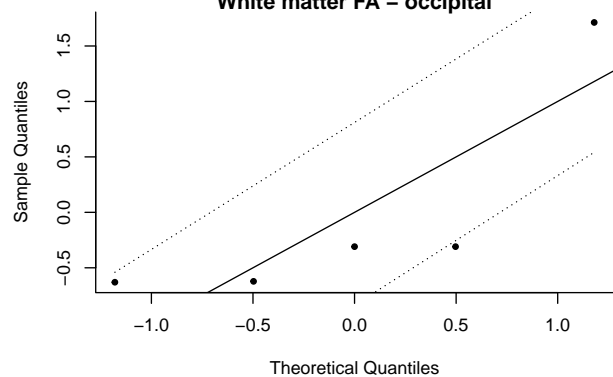
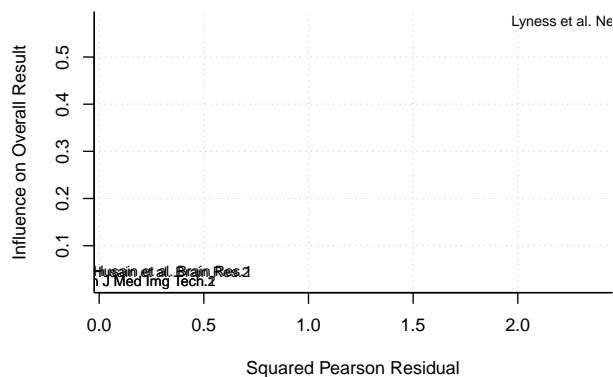
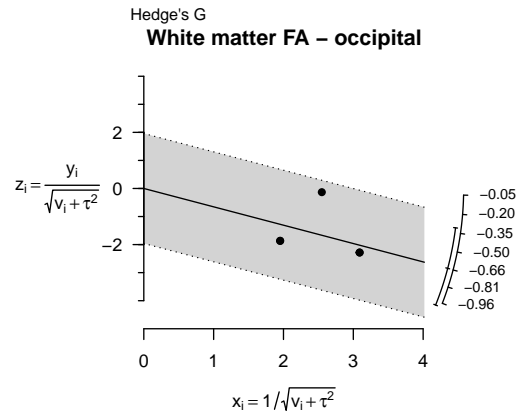
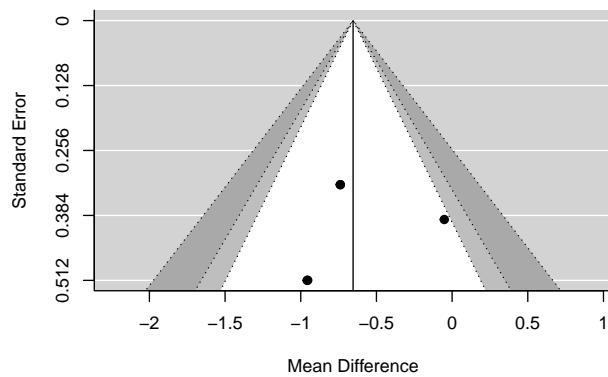
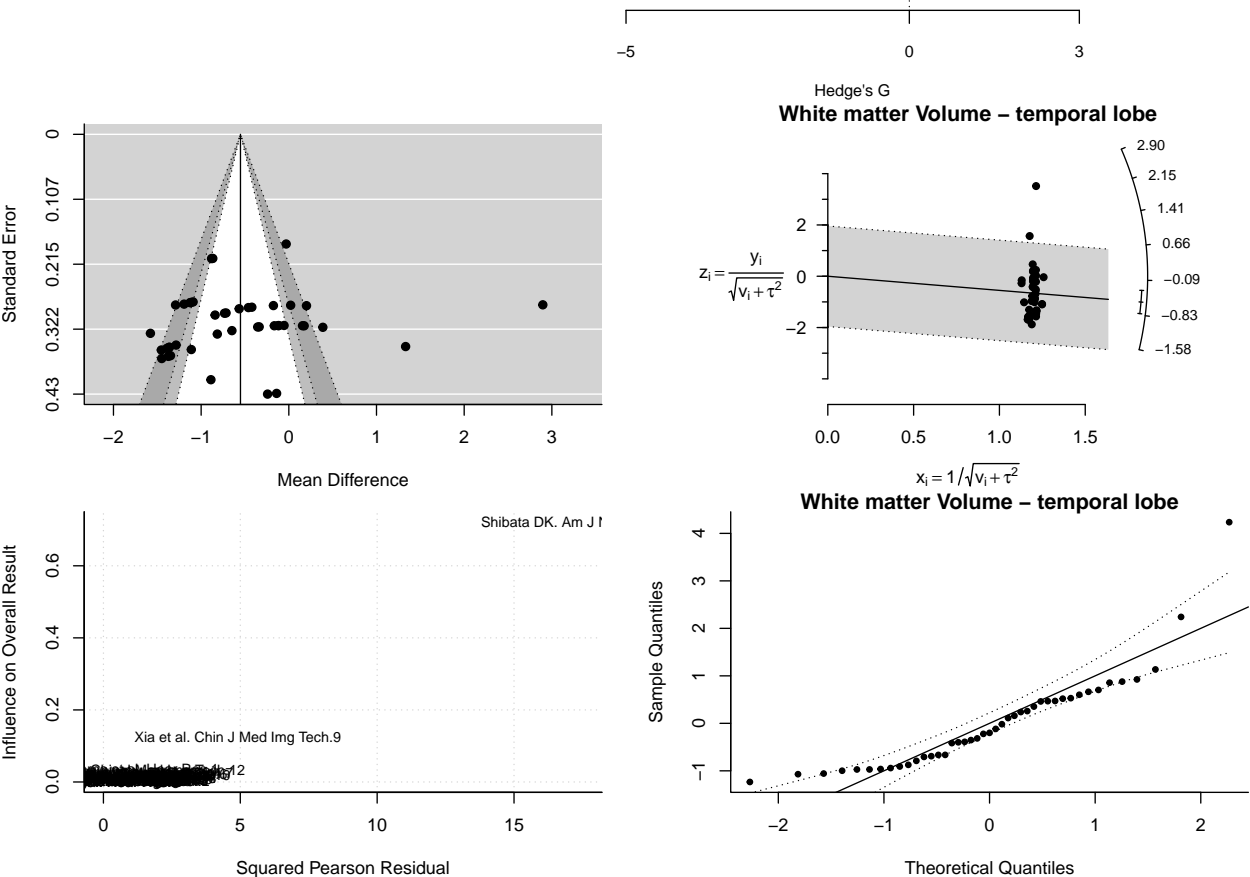
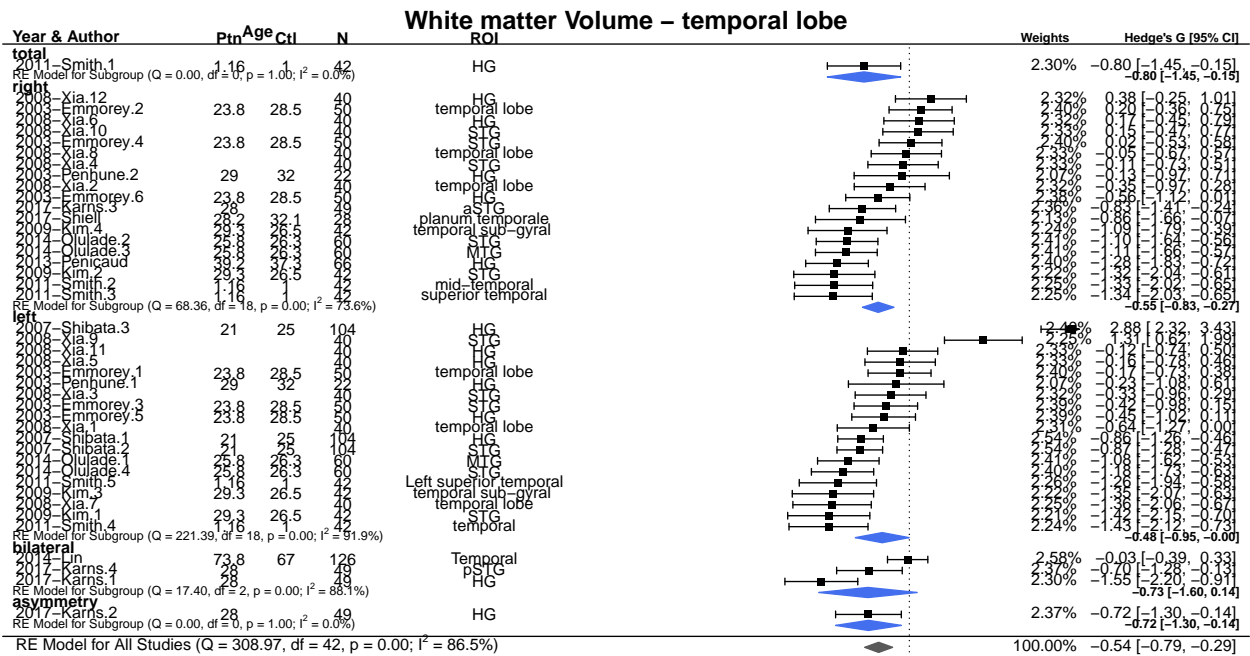











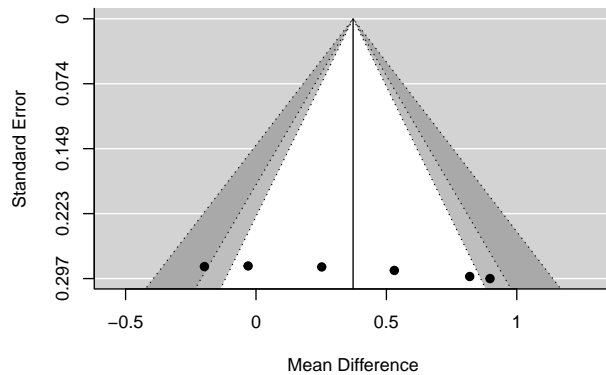
Figure 6 - Meta-regressions of White Matter Volume & Brain Areas: Random effects model no intercept covariated by Side



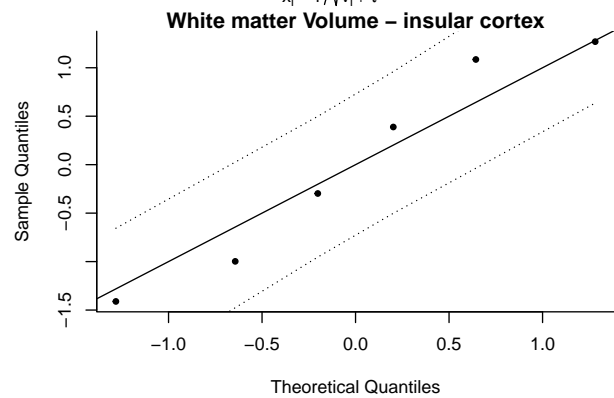
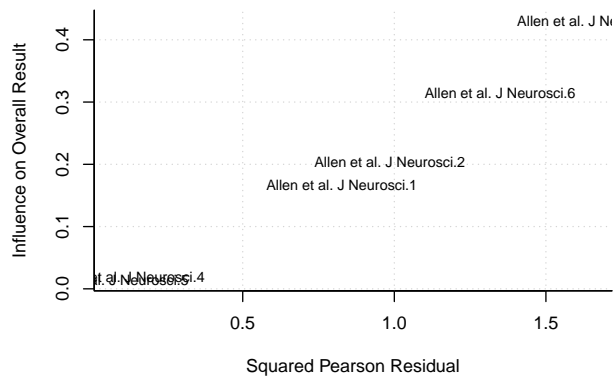
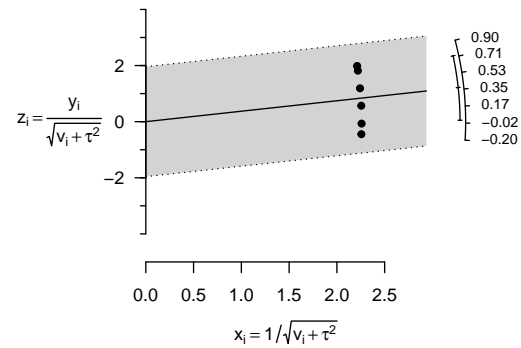
White matter Volume – insular cortex

Year & Author	Age		N	ROI		Weights	Hedge's G [95% CI]
	Ptn	Ctl					
right							
2008--Allen.6	23.8	28.5	50	posterior insula		16.24%	0.88 [0.30, 1.47]
2008--Allen.2	23.8	28.5	50	insula		16.35%	0.81 [0.23, 1.38]
2008--Allen.4	23.8	28.5	50	anterior insula		16.69%	0.52 [-0.04, 1.09]
RE Model for Subgroup (Q = 0.86, df = 2, p = 0.65; I ² = 0.0%)							0.73 [0.40, 1.06]
left							
2008--Allen.5	23.8	28.5	50	posterior insula		16.88%	0.25 [-0.31, 0.80]
2008--Allen.1	23.8	28.5	50	insula		16.94%	-0.03 [-0.58, 0.52]
2008--Allen.3	23.8	28.5	50	anterior insula		16.90%	-0.19 [-0.75, 0.36]
RE Model for Subgroup (Q = 1.24, df = 2, p = 0.54; I ² = 0.0%)							0.01 [-0.31, 0.33]
RE Model for All Studies (Q = 11.60, df = 5, p = 0.04; I ² = 57.0%)						100.00%	0.37 [0.01, 0.72]

−5 0 3

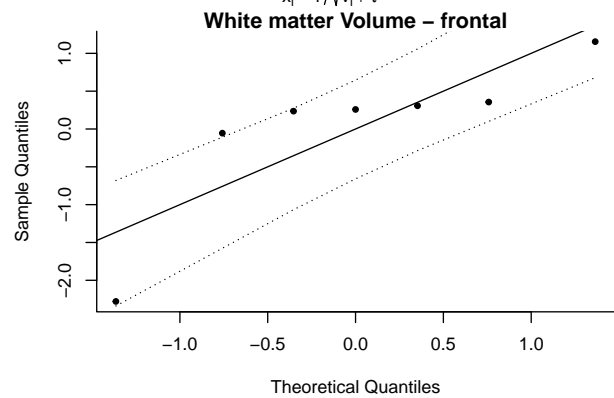
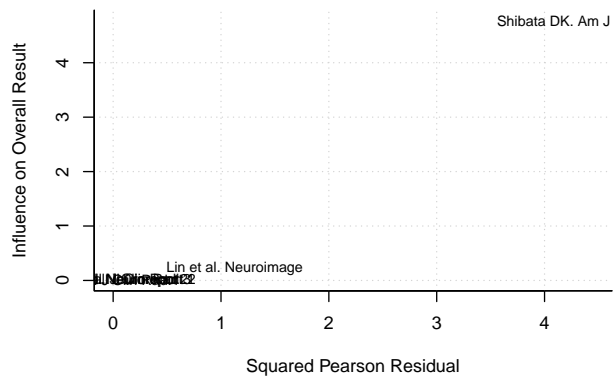
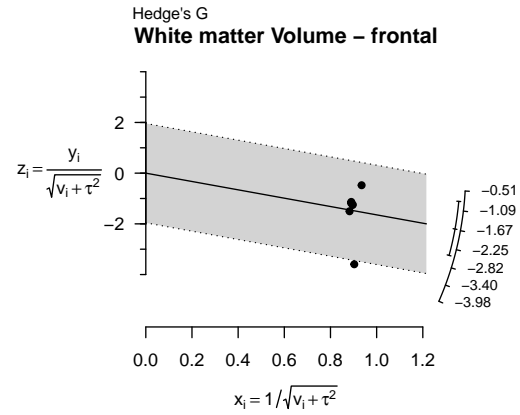
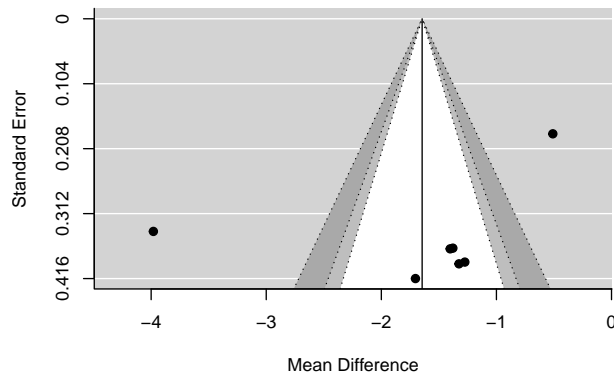


White matter Volume – insular cortex

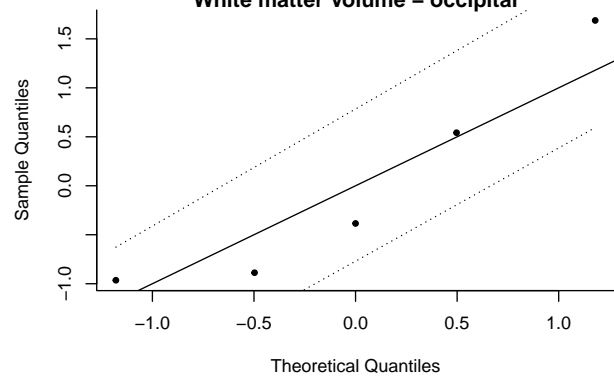
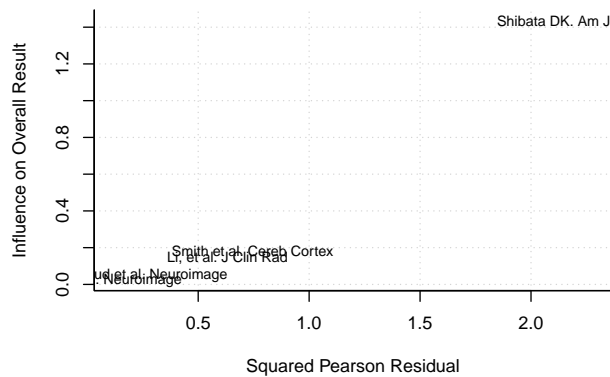
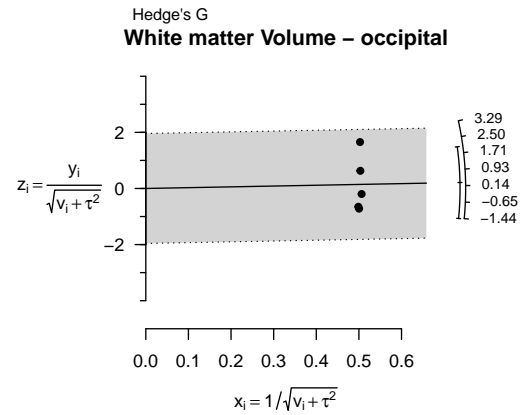
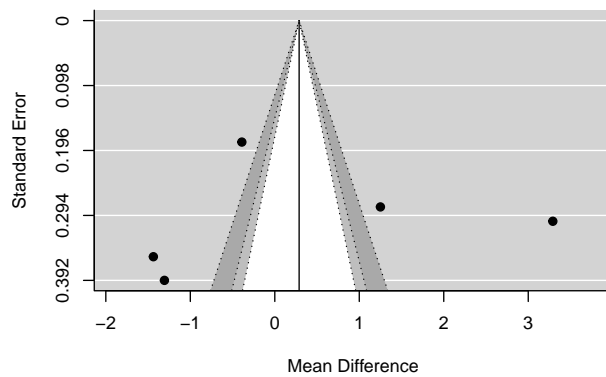
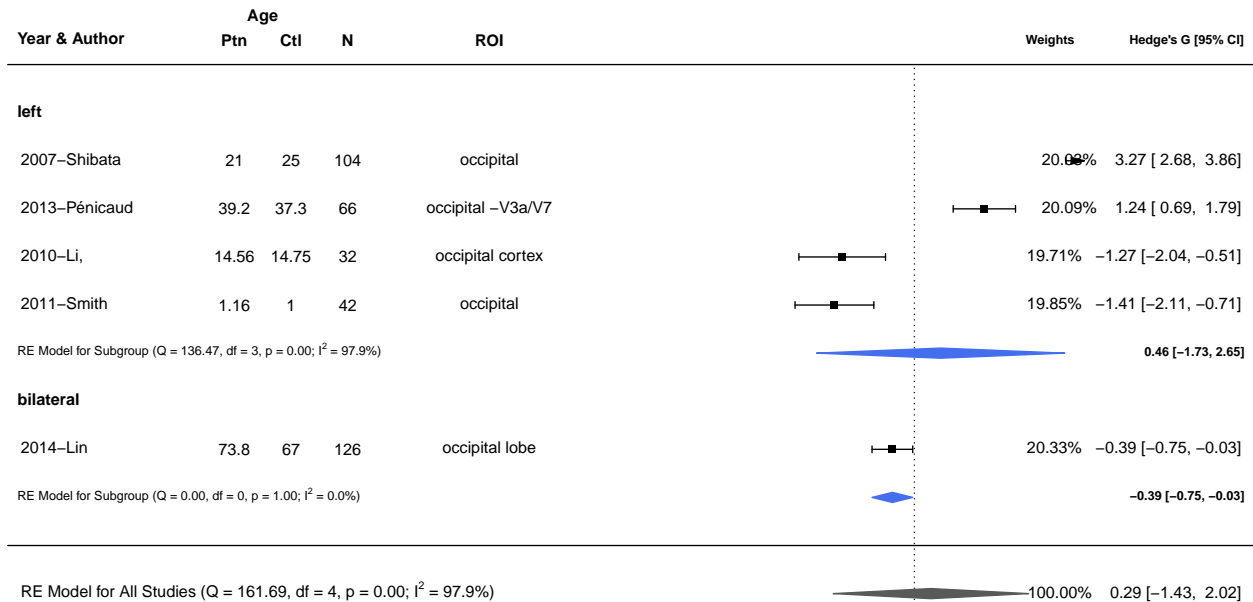


White matter Volume – frontal

Year & Author	Age		N	ROI		Weights	Hedge's G [95% CI]
	Ptn	Ctl					
right							
2010–Li,3	14.56	14.75	32	prefrontal cortex		14.00%	-1.24 [-2.00, -0.48]
2010–Li,1	14.56	14.75	32	prefrontal cortex		13.78%	-1.66 [-2.47, -0.85]
2007–Shibata	21	25	104	perisylvian		14.42%	-3.95 [-4.62, -3.29]
RE Model for Subgroup (Q = 32.91, df = 2, p = 0.00; I ² = 93.3%)							-2.30 [-3.96, -0.63]
left							
2010–Li,2	14.56	14.75	32	prefrontal cortex		13.98%	-1.29 [-2.06, -0.53]
2009–Kim,2	29.3	26.5	42	medial frontal		14.19%	-1.35 [-2.07, -0.63]
2009–Kim,1	29.3	26.5	42	superior frontal		14.18%	-1.38 [-2.10, -0.66]
RE Model for Subgroup (Q = 0.03, df = 2, p = 0.99; I ² = 0.0%)							-1.34 [-1.77, -0.92]
bilateral							
2014–Lin	73.8	67	126	frontal		15.45%	-0.51 [-0.87, -0.15]
RE Model for Subgroup (Q = 0.00, df = 0, p = 1.00; I ² = 0.0%)							-0.51 [-0.87, -0.15]
RE Model for All Studies (Q = 80.40, df = 6, p = 0.00; I ² = 91.1%)						100.00%	-1.62 [-2.44, -0.80]



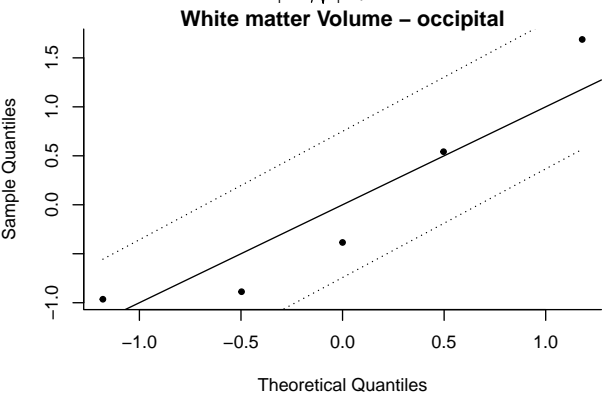
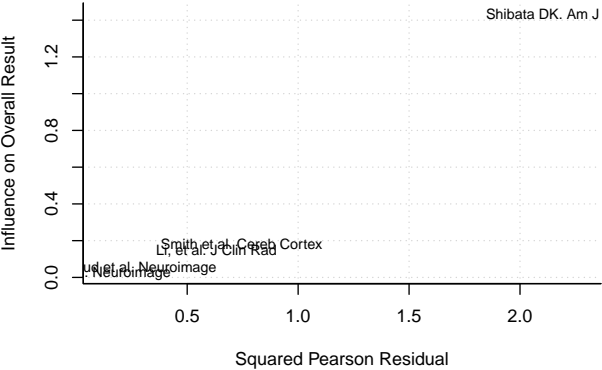
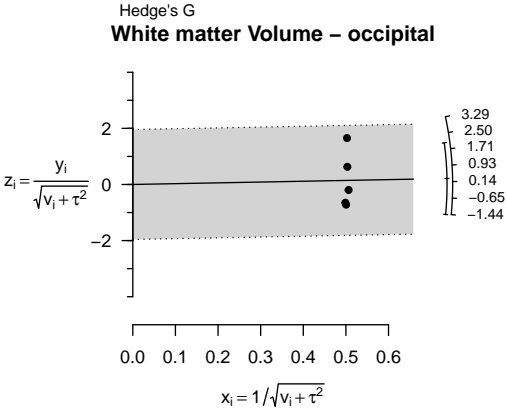
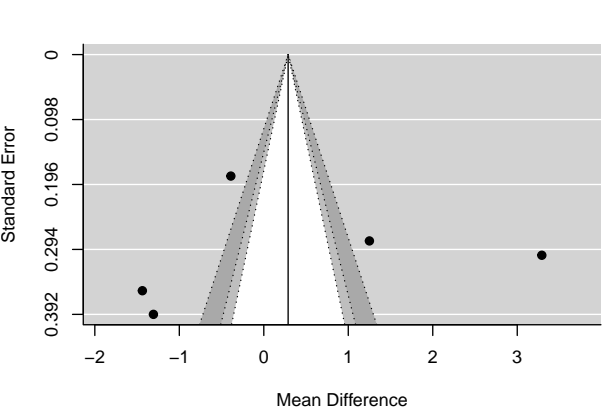
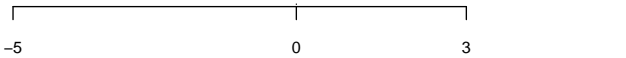
White matter Volume – occipital



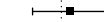




White matter Volume – occipital

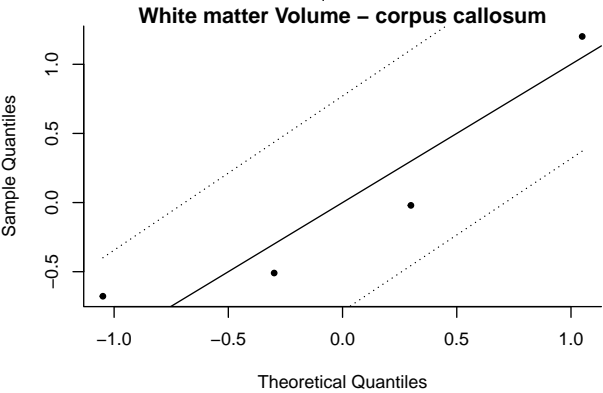
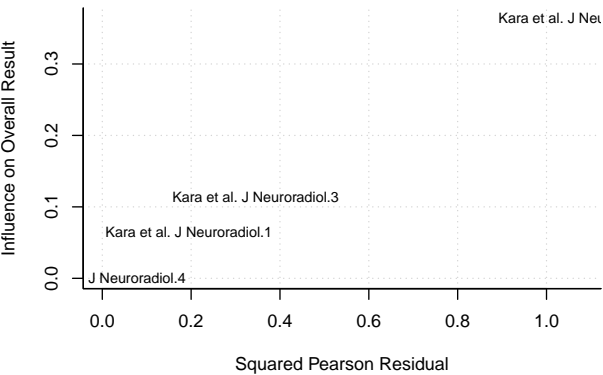
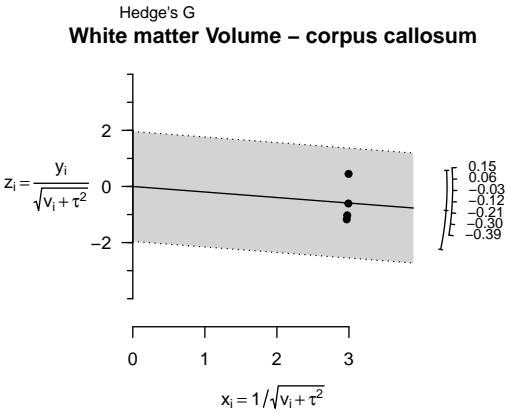
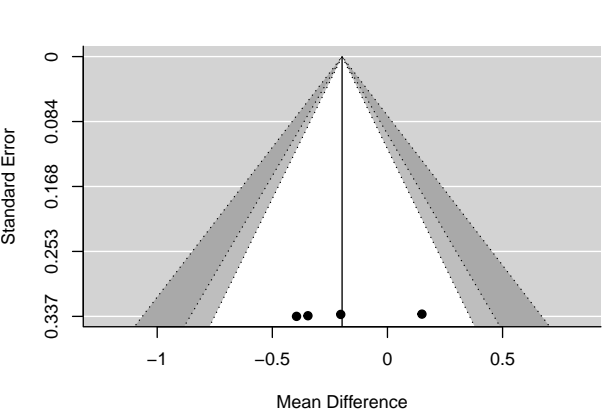
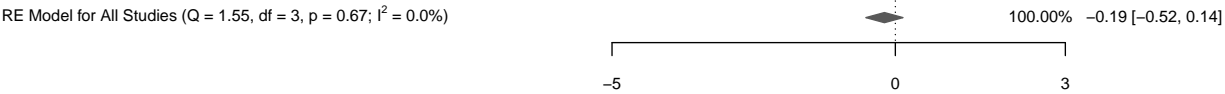
Year & Author	Age			ROI		Weights	Hedge's G [95% CI]
	Ptn	Ctl	N				
left							
2007–Shibata	21	25	104	occipital		20.09%	3.27 [2.68, 3.86]
2013–Pénicaud	39.2	37.3	66	occipital –V3a/V7		20.09%	1.24 [0.69, 1.79]
2010–Li,	14.56	14.75	32	occipital cortex		19.71%	-1.27 [–2.04, –0.51]
2011–Smith	1.16	1	42	occipital		19.85%	-1.41 [–2.11, –0.71]
RE Model for Subgroup (Q = 136.47, df = 3, p = 0.00; I ² = 97.9%)							0.46 [–1.73, 2.65]
bilateral							
2014–Lin	73.8	67	126	occipital lobe		20.33%	-0.39 [–0.75, –0.03]
RE Model for Subgroup (Q = 0.00, df = 0, p = 1.00; I ² = 0.0%)							-0.39 [–0.75, –0.03]

RE Model for All Studies (Q = 161.69, df = 4, p = 0.00; I² = 97.9%)



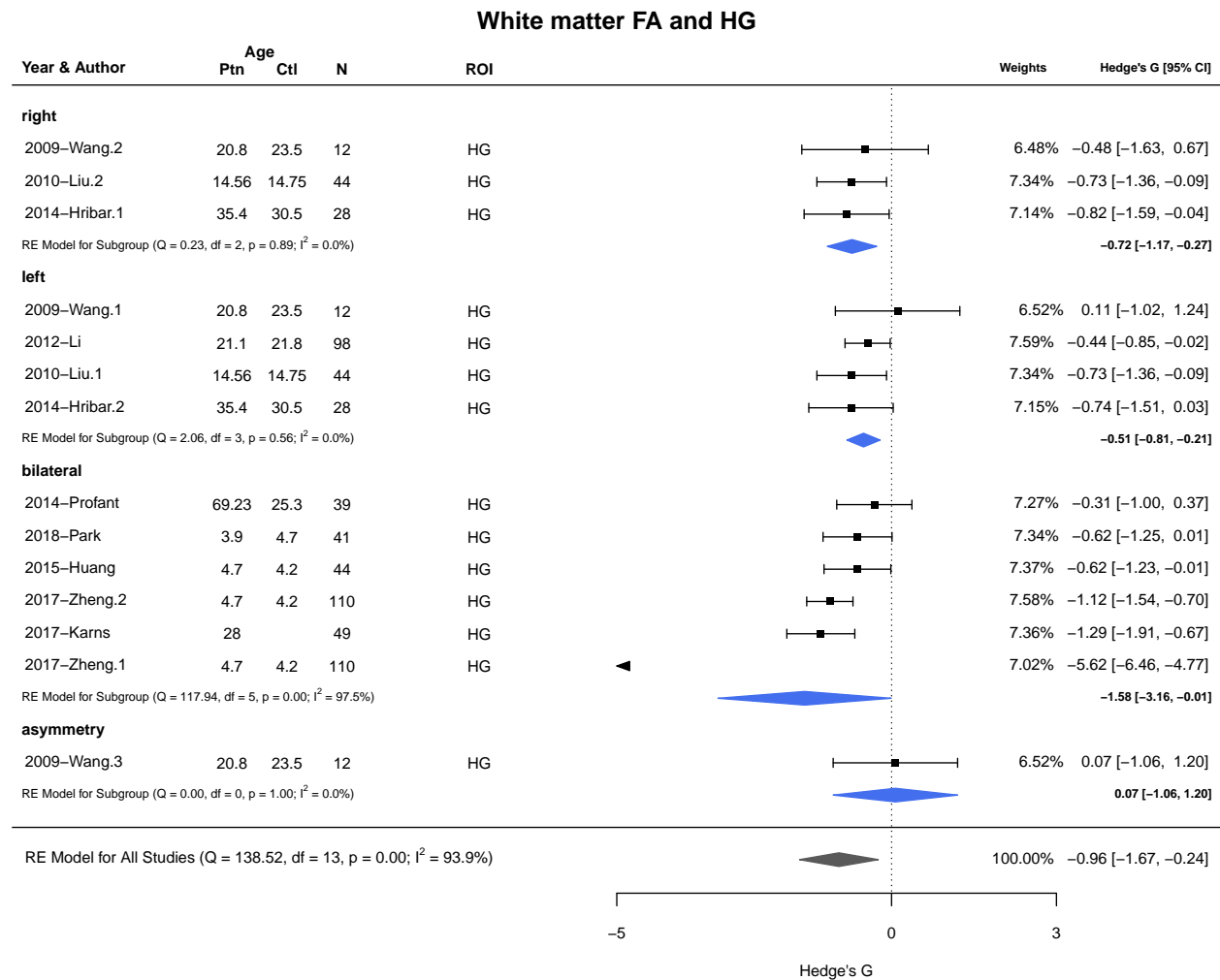
White matter Volume – corpus callosum

Year & Author	Age			ROI		Weights	Hedge's G [95% CI]
	Ptn	Ctl	N				
bilateral							
2006–Kara.2	41.2	36.4	36	corpus callosum (middle area)		25.20%	0.15 [–0.51, 0.80]
2006–Kara.4	41.2	36.4	36	corpus callosum (total area)		25.14%	–0.20 [–0.85, 0.46]
2006–Kara.1	41.2	36.4	36	corpus callosum (anterior area)		24.89%	–0.34 [–1.00, 0.32]
2006–Kara.3	41.2	36.4	36	corpus callosum (posterior area)		24.78%	–0.39 [–1.05, 0.27]
RE Model for Subgroup (Q = 1.55, df = 3, p = 0.67; I ² = 0.0%)							–0.19 [–0.52, 0.14]

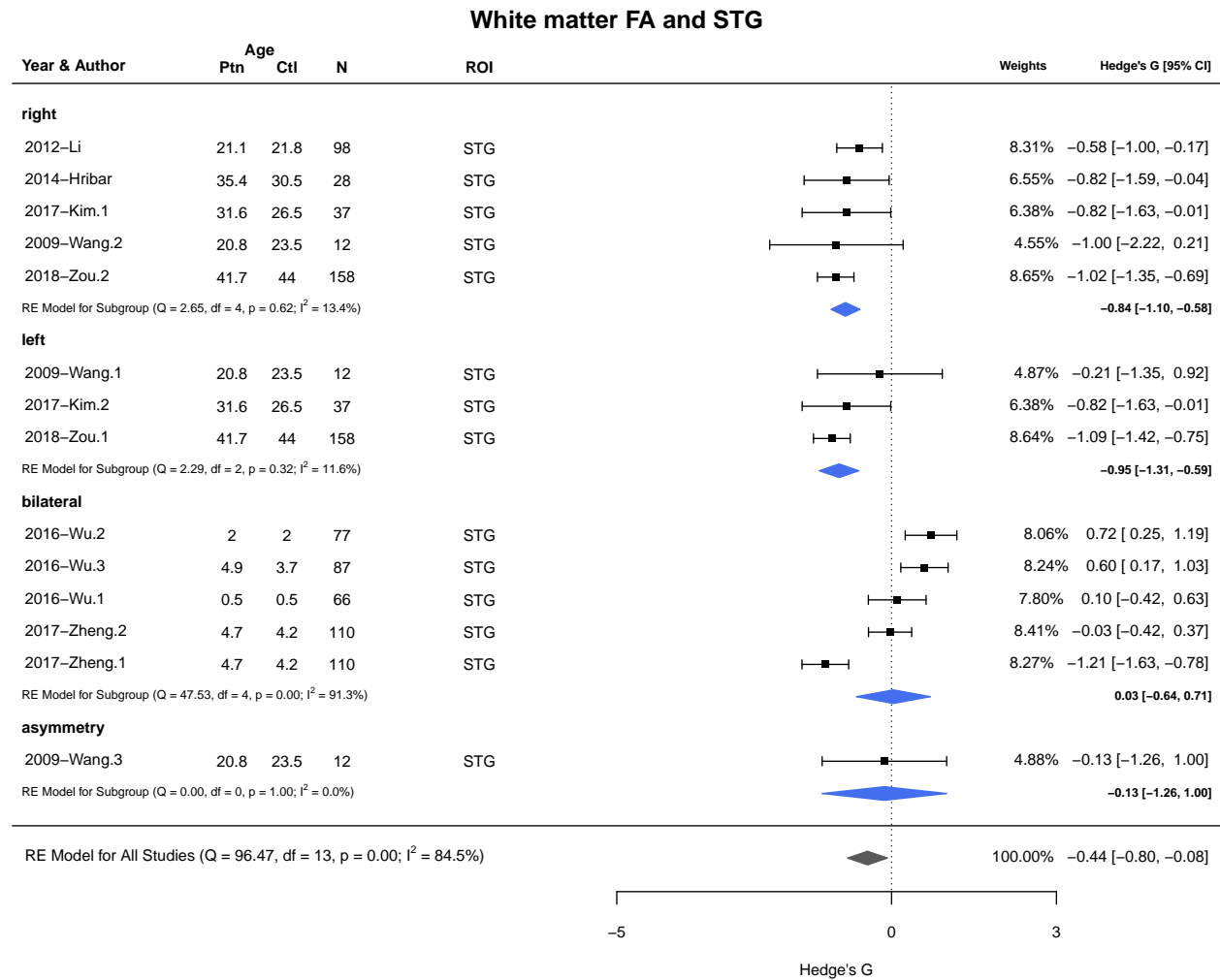


Supplementary material: Forest-plots of other Measures

Hesch gyrus FA white matter

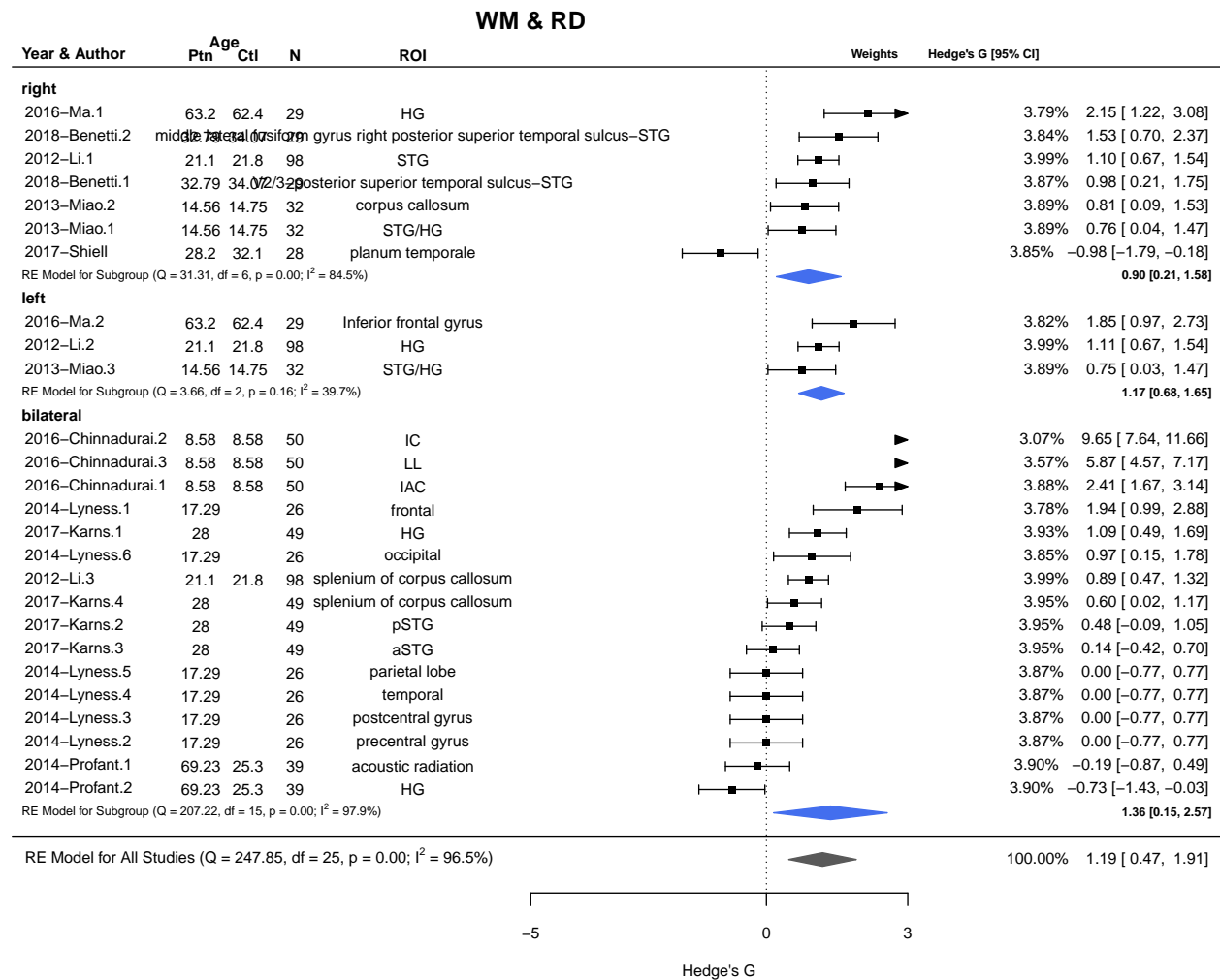


STG Volume White matter

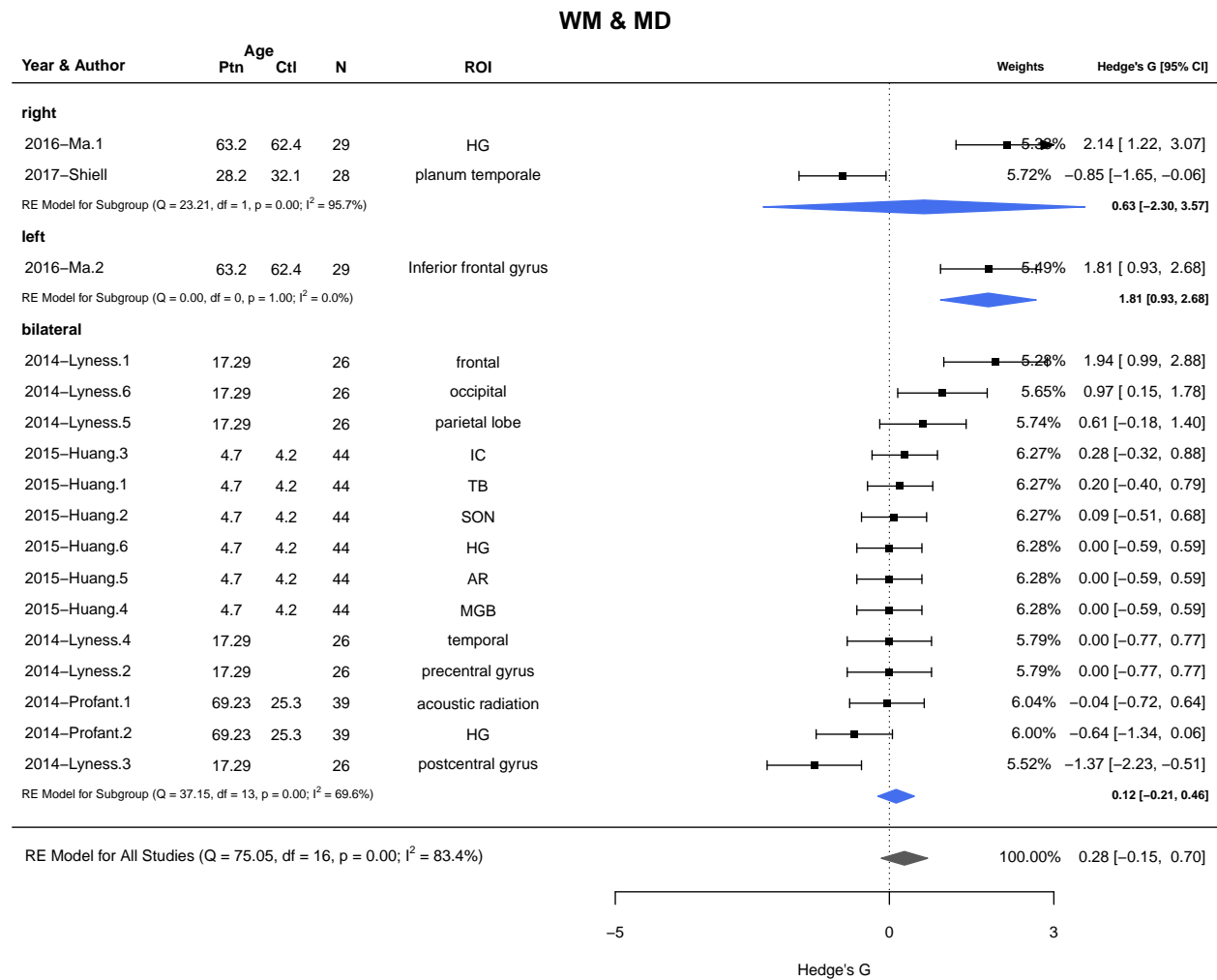


Measures of White matter Integrity

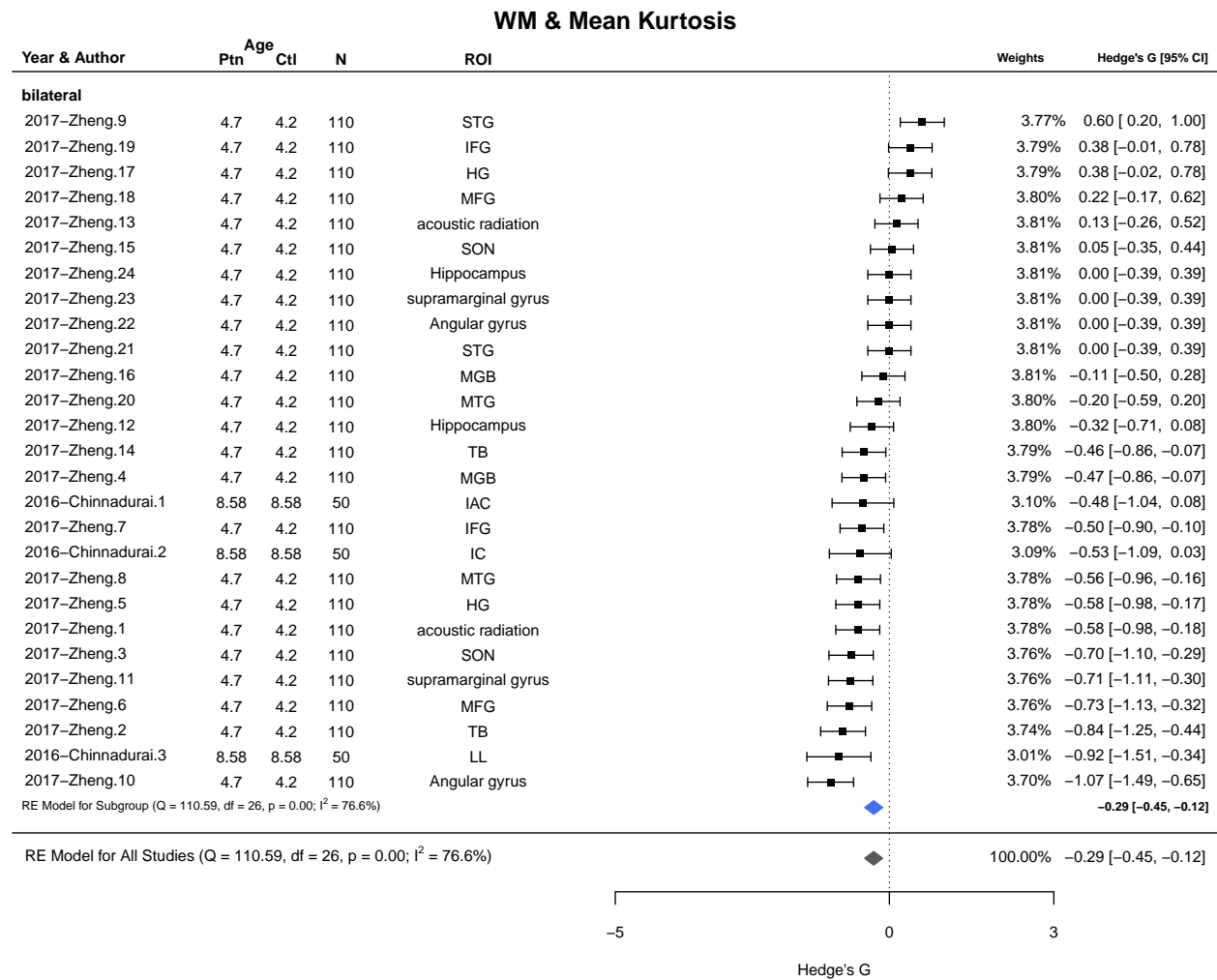
White matter: RD



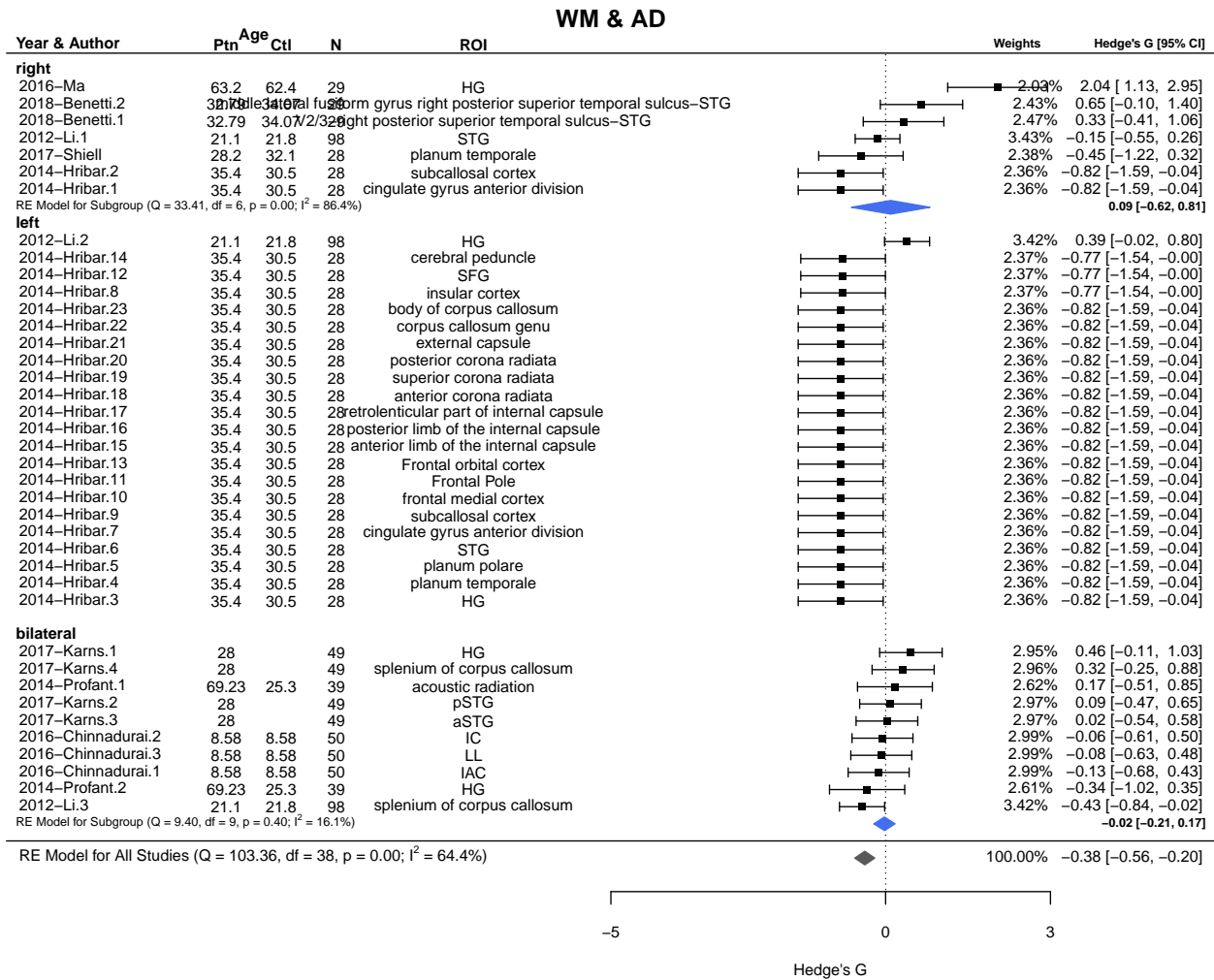
White matter: MD



White matter: Mean Kurtosis



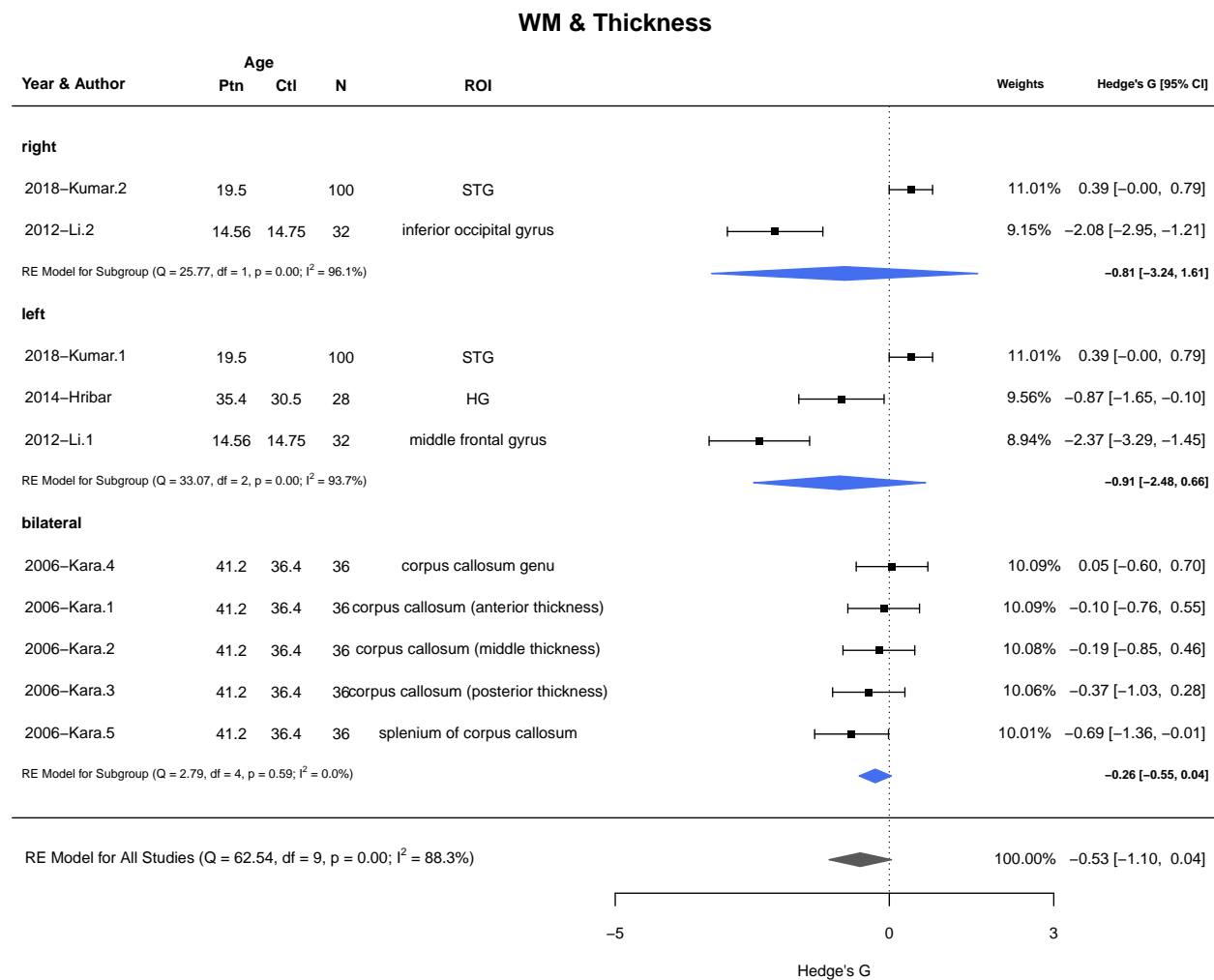
White matter: AD



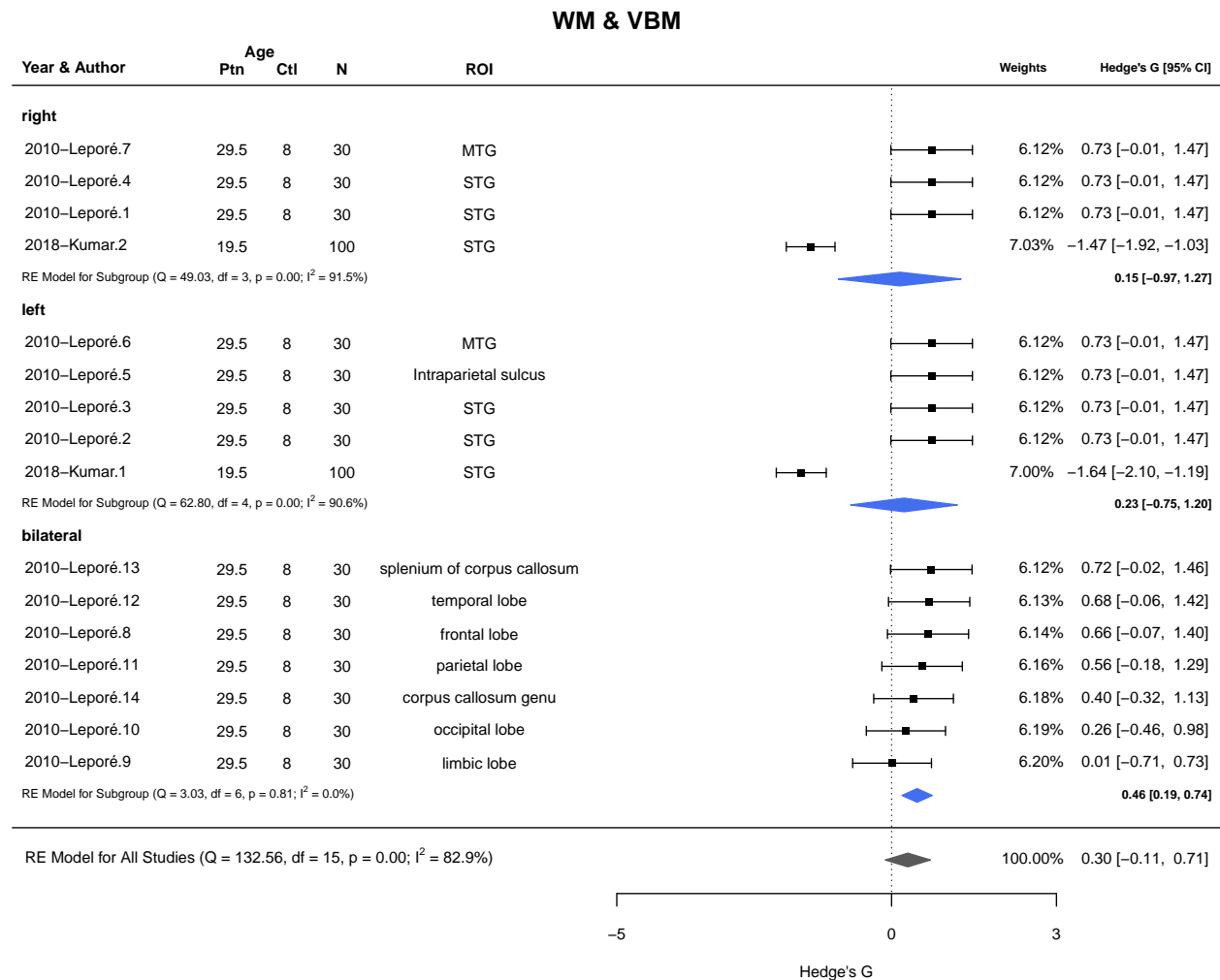
Error in rma(yi = hedgesG, vi = varG, data = meta.mod, measure = "MD", : Fisher scoring algorithm did not converge. See 'help(rma)' for possible remedies.

Other Measures of White Matter

White matter: Thickness



White matter: VBM



Meta Plots

The L'Abbé plot

In a L'Abbé plot (based on L'Abbé, Detsky, & O'Rourke, 1987), the arm-level outcomes for two experimental groups (e.g., treatment and control group) are plotted against each other. is treatment versus effect, since you have the cohen's d this should be relatively simple.

> WE DON'T HAVE TWO EXPERIMENTAL GROUPS

Baujat plot to identify studies contributing to heterogeneity

The plot shows the contribution of each study to the overall Q-test statistic for heterogeneity on the horizontal axis versus the influence of each study (defined as the standardized squared difference between the overall estimate based on a fixed-effects model with and without the ith study included in the model) on the vertical axis 2.17. Funnel plot to illustrate publication bias

Galbraith plot

Radial plot (radial) of variables and cohen's d - Galbraith, Rex (1988). "Graphical display of estimates having differing standard errors". *Technometrics*. *Technometrics*, Vol. 30, No. 3. 30 (3): 271–281.

2.18.2. We want to see this type of error plot over time for our patient cohorts by age. we want this for each measure WM and GM versus age on the x-axis so we can see GM and WM over time! Do a monte carlo simulation to connect different age population and create the error.

For a fixed-effects model, the plot shows the inverse of the standard errors on the horizontal axis against the individual observed effect sizes or outcomes standardized by their corresponding standard errors on the vertical axis. On the right hand side of the plot, an arc is drawn corresponding to the individual observed effect sizes or outcomes. A line projected from (0,0) through a particular point within the plot onto this arc indicates the value of the individual observed effect size or outcome for that point.

Resources

We are following Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines: Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., and Prisma Group. (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* 6:e1000097. doi: 10.1371/journal.pmed.1000097 AND <https://www.bmj.com/content/339/bmj.b2535>

- <https://stackoverflow.com/questions/14426637/how-to-do-bubble-plot>
- https://www.researchgate.net/publication/296680807_Menstrual_hygiene_management_among_adolescent_girls_in_India_A_Systematic_review_and_meta-analysis/figures?lo=1

Good explanation of some of the plots:

- https://ora.ox.ac.uk/objects/uuid:ff78831d-6f82-4187-97cc-349058e9abde/download_file?file_format=pdf&safe_filename=Rahimi%2Bet%2Bal%252C%2BData%2Bvisualisation%2Bfor%2Bmeta-analysis.pdf&type_of_work=Journal+article