

# 6-Thalamic\_nuclei\_and\_disability

November 24, 2025

title: ""

## 1 Choroid Plexus and Thalamic Nuclei

### Reload Modules

#### 1.1 Baseline Models of Disability

EDSS\_sqrt ~ \*predictor\* + age + Female + tiv + dzdur

predictor	coef	p_fdr	se	ci	R2
WBV	-0.3837	0.00031	0.1013	[-0.582, -0.185]	0.27
GMV	-0.2601	0.0026	0.0826	[-0.422, -0.0982]	0.26
WMV	-0.2526	0.0069	0.0903	[-0.43, -0.0756]	0.26
WTV	-0.2553	7.9e-07	0.0479	[-0.349, -0.161]	0.29
cortical_thickness	-0.195	2.5e-05	0.0432	[-0.28, -0.11]	0.27
CP	0.0535	0.22	0.0438	[-0.0322, 0.139]	0.25
T2LV_log1p	0.1762	5.5e-05	0.0414	[0.095, 0.257]	0.27
PRL	0.1024	0.015	0.0413	[0.0216, 0.183]	0.25

SDMT ~ \*predictor\* + age + Female + tiv + dzdur

predictor	coef	p_fdr	se	ci	R2
WBV	0.7144	3e-08	0.1262	[0.467, 0.962]	0.24
GMV	0.4034	0.0053	0.1426	[0.124, 0.683]	0.2
WMV	0.5467	7.6e-08	0.1001	[0.35, 0.743]	0.22
WTV	0.373	4.6e-10	0.0584	[0.258, 0.487]	0.25
cortical_thickness	0.3614	1.5e-12	0.0491	[0.265, 0.458]	0.25
CP	-0.1556	0.0056	0.0562	[-0.266, -0.0454]	0.17
T2LV_log1p	-0.3245	4.6e-10	0.0506	[-0.424, -0.225]	0.24
PRL	-0.1452	0.0053	0.0509	[-0.245, -0.0454]	0.17

##### 1.1.1 Effects of WTV and CT together

CT does not explain EDSS when WTV is included as a covariate. CT does a better job of explaining SDMT than WTV

EDSS\_sqrt ~ WTV + CT + age + Female + tiv

	coef	p_fdr	se	ci	R2
CT	-0.0679	0.46	0.0568	[-0.179, 0.0434]	0.27
WTV	-0.2496	0.00018	0.0622	[-0.371, -0.128]	0.27

SDMT ~ WTV + CT + age + Female + tiv

	coef	p_fdr	se	ci	R2
CT	0.2372	0.00063	0.0618	[0.116, 0.358]	0.27
WTV	0.2054	0.0074	0.0708	[0.0668, 0.344]	0.27

### 1.1.2 Regional Thalamic Atrophy

**Control for WBV** All the nuclei explain disability when controlling for WBV, but none better than WTV. The posterior and ventral nuclei have similar effect sizes on both EDSS and SDMT, greater than the anterior and medial nuclei.

EDSS\_sqrt ~ \*predictor\* + WBV + age + Female + tiv + dzdur

predictor	coef	p_fdr	se	ci	R2
WTV	-0.2433	0.0011	0.0671	[-0.375, -0.112]	0.28
posterior	-0.2051	0.0011	0.0584	[-0.32, -0.0906]	0.28
ventral	-0.2004	0.0023	0.0642	[-0.326, -0.0745]	0.28
anterior	-0.1676	0.0023	0.0536	[-0.273, -0.0625]	0.28
medial	-0.1447	0.019	0.0616	[-0.265, -0.024]	0.27

SDMT ~ \*predictor\* + WBV + age + Female + tiv + dzdur

predictor	coef	p_fdr	se	ci	R2
WTV	0.2455	0.0049	0.0793	[0.09, 0.401]	0.25
posterior	0.2083	0.0049	0.0673	[0.0764, 0.34]	0.25
ventral	0.2049	0.0053	0.0731	[0.0617, 0.348]	0.25
medial	0.1911	0.0053	0.0675	[0.0588, 0.323]	0.25
anterior	0.1445	0.0053	0.0519	[0.0428, 0.246]	0.25

**Control for WTV** No thalamic nucleus predicts disability after controlling for global thalamic atrophy

EDSS\_sqrt ~ \*predictor\* + WTV + age + Female + tiv + dzdur

predictor	coef	p_fdr	se	ci	R2
medial	0.1347	0.51	0.1182	[-0.0969, 0.366]	0.29
anterior	-0.1053	0.46	0.0667	[-0.236, 0.0255]	0.29

predictor	coef	p_fdr	se	ci	R2
posterior	-0.0968	0.56	0.1337	[-0.359, 0.165]	0.29
ventral	-0.0626	0.56	0.1081	[-0.275, 0.149]	0.29

SDMT ~ \*predictor\* + WTV + age + Female + tiv + dzdur

predictor	coef	p_fdr	se	ci	R2
posterior	0.0798	0.81	0.1269	[-0.169, 0.329]	0.25
anterior	0.0667	0.81	0.0596	[-0.05, 0.183]	0.25
ventral	0.0494	0.81	0.1072	[-0.161, 0.26]	0.25
medial	0.0333	0.81	0.1359	[-0.233, 0.3]	0.25

## 1.2 Moderated Mediation Models

### 1.2.1 T2LV moderates CP on WTV

T2LV moderates the effect of CP on WTV. That is, CP and T2LV have a significant interaction effect, and the effect of CP is greater at higher T2LV.

WTV ~ CP\*T2LV\_log1p + age + Female + tiv

	coef	pval	se	ci	R2
CP:T2LV_log1p	-0.1604	2.1e-08	0.0286	[-0.217, -0.104]	0.65
CP	-0.2651	8e-10	0.0431	[-0.35, -0.181]	_____
T2LV_log1p	-0.5283	2.3e-36	0.042	[-0.61, -0.446]	_____

The interaction term adds explanatory power according to an F-test and a likelihood ratio test

base model	full model	$\Delta R^2$	F-statistic	F-test pval	LR	LR pval	df
0	CP+T2LV_log1p	0.028048	38.43	1.26131e-09	37.4724	9.27136e-10	1

### 1.2.2 T2LV moderates CP on CT

T2LV moderates the effect of CP on CT too.

CT ~ CP\*T2LV\_log1p + age + Female + tiv

	coef	pval	se	ci	R2
CP:T2LV_log1p	-0.1289	0.00013	0.0337	[-0.195, -0.0627]	0.46
CP	-0.204	8.4e-06	0.0458	[-0.294, -0.114]	_____
T2LV_log1p	-0.4176	6.4e-17	0.05	[-0.516, -0.32]	_____

F-test and LLR test are significant here as well

	base model	full model	$\Delta R$	F- statistic	F-test pval	LR	LR pval	df
0	CP+T2LV_log1p	CP+T2LV_log1p+CT	0.021387	15.9236	7.6703e-05	15.8925	6.70438e-05	1

### 1.2.3 Modelling EDSS

**WTV alone mediates the effect of CP on EDSS** Although CP does not have a significant baseline association with EDSS, it does have a significant indirect effect through WTV. It does not have an effect through WBV when the WTV pathway is tested in parallel.

Direct effect of CP on EDSS\_sqrt:

Effect	SE	t	p	LLCI	ULCI
-0.0649	0.0499	-1.3016	0.1937	-0.1627	0.0328

Indirect effect of CP on EDSS\_sqrt:

	Effect	Boot SE	BootLLCI	BootULCI
WTV	0.0931	0.0314	0.0382	0.1592
CT	0.0254	0.0180	-0.0069	0.0635

**Full moderated mediation model** Does T2LV's moderation extend through the entire indirect pathway

Direct effect of CP on EDSS\_sqrt:

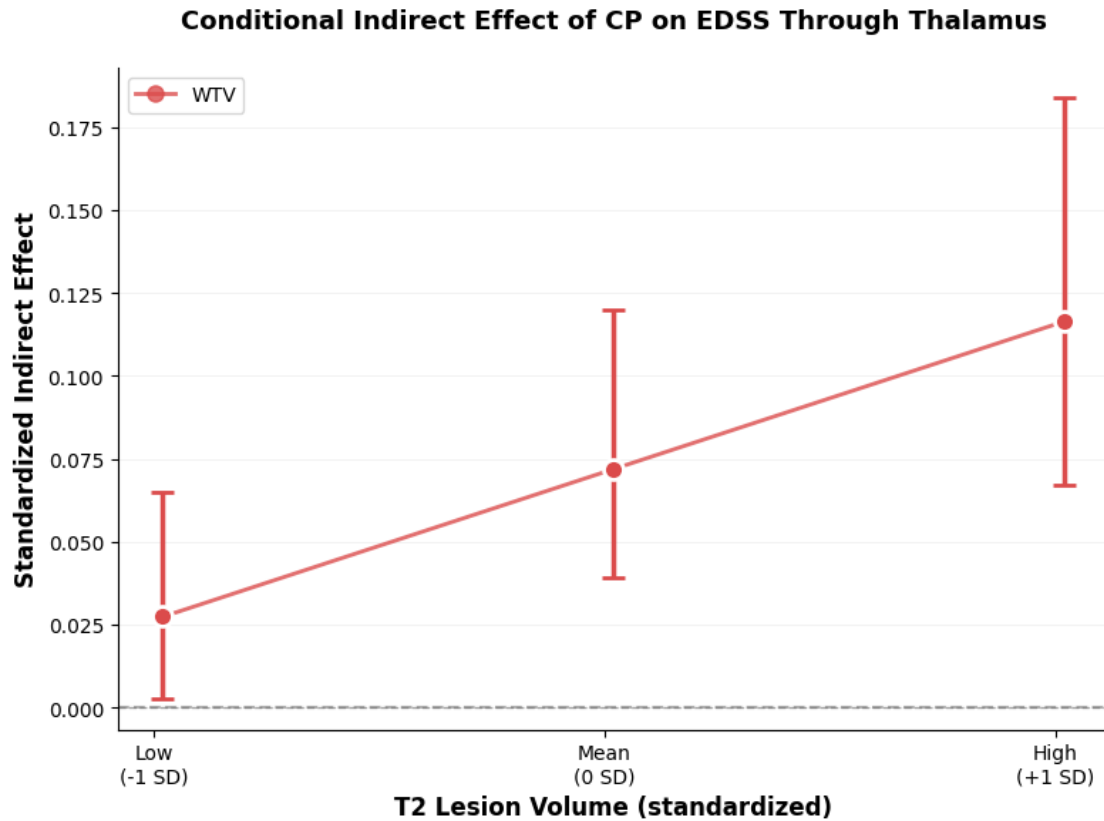
Effect	SE	t	p	LLCI	ULCI
-0.0600	0.0498	-1.2042	0.2292	-0.1575	0.0376

Conditional indirect effect(s) of CP on EDSS\_sqrt at values of the moderator(s):

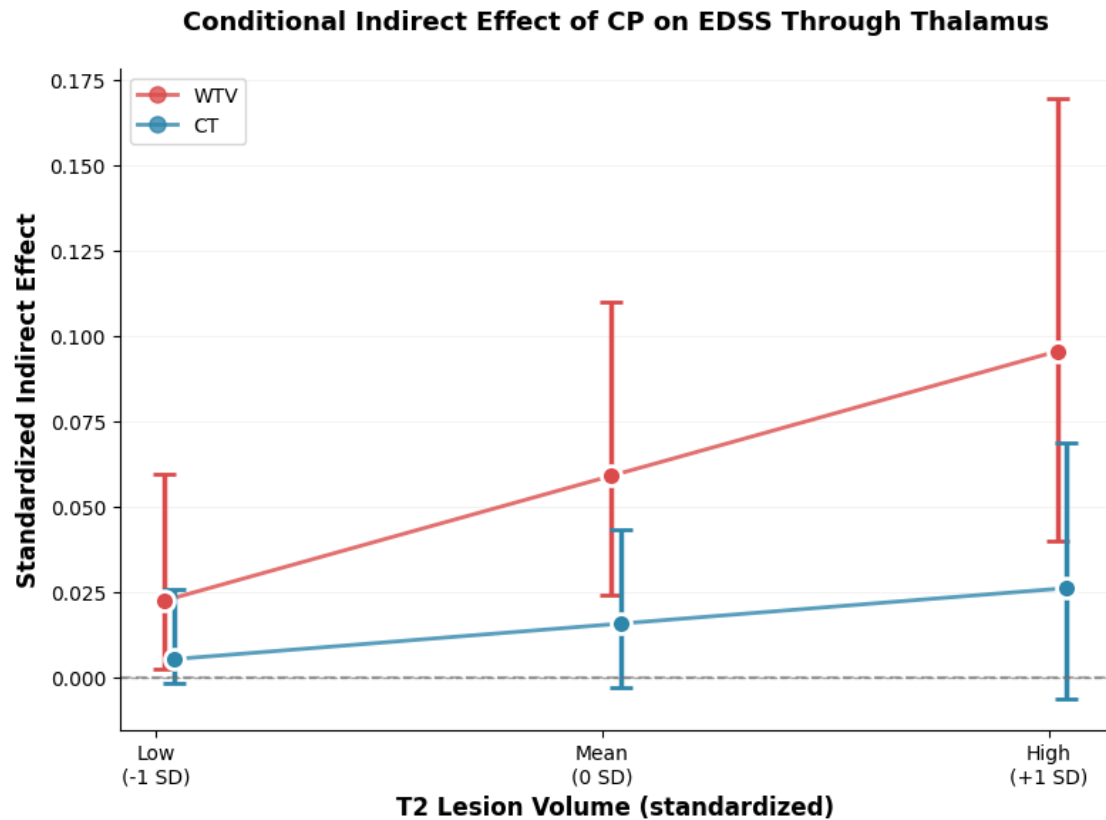
Mediator	T2LV_log1p	Effect	Boot SE	BootLLCI	BootULCI
WTV	-0.9791	0.0274	0.0155	0.0025	0.0651
WTV	0.0208	0.0719	0.0203	0.0390	0.1198
WTV	1.0207	0.1164	0.0298	0.0671	0.1839

\*\*\*\*\* INDEX OF MODERATED MEDIATION \*\*\*\*\*

Moderator	Mediator	Index	Boot SE	LLCI	ULCI
T2LV_log1p	WTV	0.0445	0.0124	0.0240	0.0732



Although we already saw that WBV does not mediate CP's effect on EDSS when the WTV pathway is accounted for, let's look at the plot with both mediators to drive home the point



### 1.2.4 Modelling SDMT

WTV and CT mediate CP on SDMT in parallel

Direct effect of CP on SDMT:

Effect	SE	t	p	LLCI	ULCI
0.0104	0.0512	0.2031	0.8392	-0.0899	0.1107

Indirect effect of CP on SDMT:

	Effect	Boot SE	BootLLCI	BootULCI
WTV	-0.0900	0.0339	-0.1607	-0.0287
CT	-0.0760	0.0228	-0.1263	-0.0357

**Full moderated mediation model** T2LV amplifies both indirect pathways

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Direct effect of CP on SDMT:

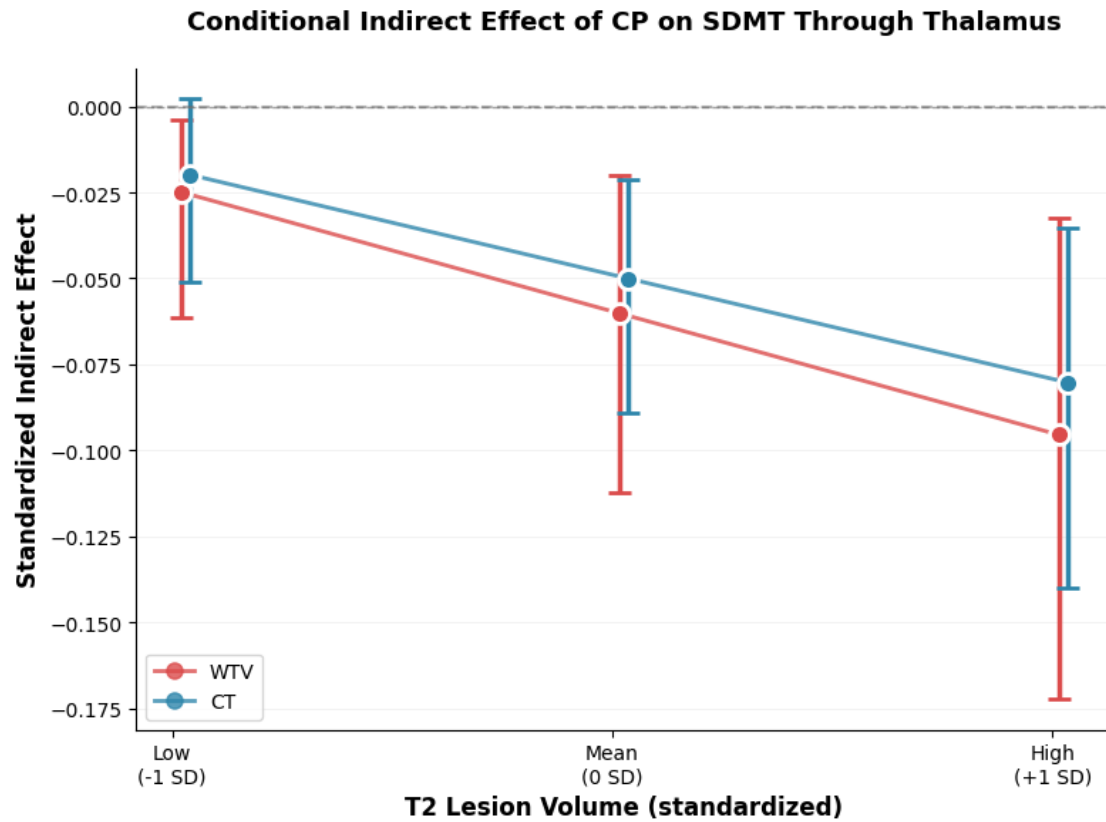
Effect	SE	t	p	LLCI	ULCI
0.0104	0.0512	0.2031	0.8392	-0.0899	0.1107

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Conditional indirect effect(s) of CP on SDMT at values of the moderator(s):

Mediator	T2LV_log1p	Effect	Boot SE	BootLLCI	BootULCI
WTV	-0.9805	-0.0249	0.0143	-0.0613	-0.0040
WTV	0.0167	-0.0602	0.0236	-0.1123	-0.0201
WTV	1.0139	-0.0955	0.0362	-0.1724	-0.0323
CT	-0.9805	-0.0198	0.0133	-0.0510	0.0024
CT	0.0167	-0.0501	0.0172	-0.0891	-0.0211
CT	1.0139	-0.0803	0.0262	-0.1400	-0.0355

\*\*\*\*\* INDEX OF MODERATED MEDIATION \*\*\*\*\*

Moderator	Mediator	Index	Boot SE	LLCI	ULCI
T2LV_log1p	WTV	-0.0354	0.0141	-0.0665	-0.0114
T2LV_log1p	CT	-0.0303	0.0118	-0.0577	-0.0112

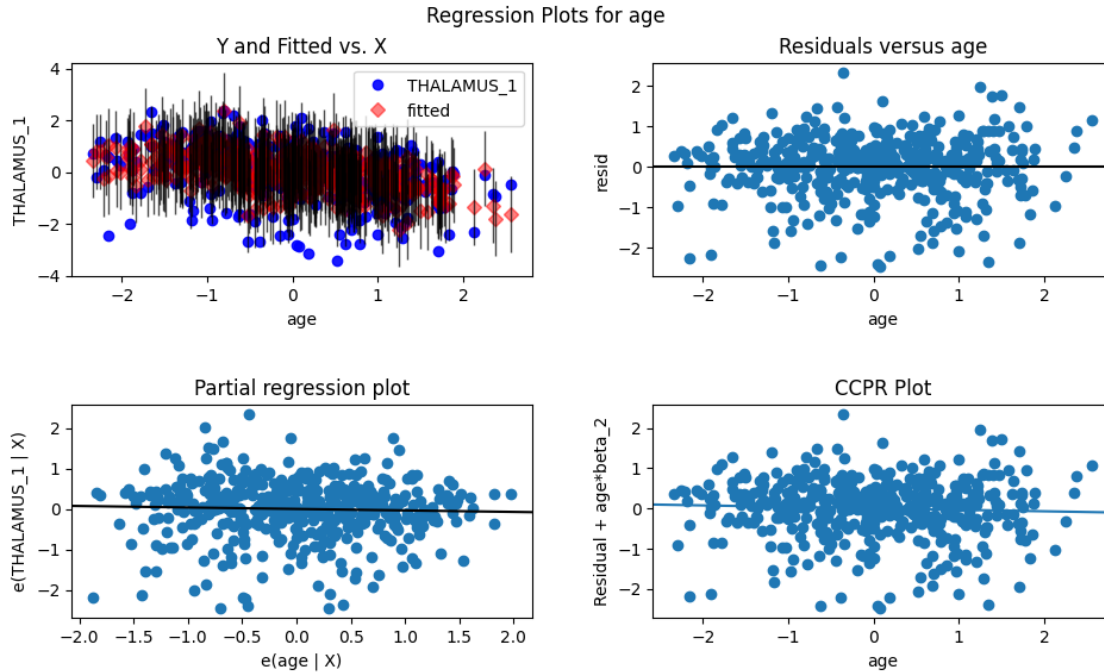


### 1.2.5 Assumption Checks

Linearity

Check: Residual plots, component-residual plots Test: Look for curved patterns in residuals vs. fitted values





Breusch-Pagan p-value: 5.506487166550046e-07

	Variable	VIF
0	CP	1.571211
1	T2LV_log1p	1.981889
2	WTV	3.373885
3	CT	2.246996
4	age	1.831986
5	Female	1.081938
6	tiv	1.680319
7	dzdur	1.716890

### 1.3 Extras

EDSS\_sqrt ~ \*predictor\* + age + Female + tiv + dzdur

predictor	coef	p_fdr	se	ci	R2
WTV	-0.2553	1.8e-06	0.0479	[-0.349, -0.161]	0.29
medial	-0.204	4.7e-05	0.046	[-0.294, -0.114]	0.27
posterior	-0.2344	1.8e-06	0.0446	[-0.322, -0.147]	0.29
ventral	-0.2496	2.1e-05	0.053	[-0.353, -0.146]	0.28
anterior	-0.2149	6.1e-05	0.0496	[-0.312, -0.118]	0.28
cortical_thickness	-0.195	4e-05	0.0432	[-0.28, -0.11]	0.27
brain	-0.3213	0.025	0.1384	[-0.593, -0.0499]	0.25

predictor	coef	p_fdr	se	ci	R2
white	-0.0655	0.64	0.1308	[-0.322, 0.191]	0.24
grey	-0.2486	0.012	0.0936	[-0.432, -0.0651]	0.26
CP	0.0535	0.25	0.0438	[-0.0322, 0.139]	0.25
t2lv_log	0.1088	0.018	0.0434	[0.0237, 0.194]	0.25
T2LV_log1p	0.1762	7.4e-05	0.0414	[0.095, 0.257]	0.27
periV_T2LV_log1p	0.15	0.0013	0.0435	[0.0648, 0.235]	0.26
juxcort_T2LV_log1p	0.149	0.0012	0.0427	[0.0653, 0.233]	0.26
subcort_T2LV_log1p	0.0292	0.59	0.0484	[-0.0656, 0.124]	0.24
infraT_T2LV_log1p	0.1335	0.0013	0.0393	[0.0564, 0.211]	0.26
PRL	0.1024	0.018	0.0413	[0.0216, 0.183]	0.25
LV_log	0.1567	0.0014	0.0467	[0.0652, 0.248]	0.26
thirdV_log	0.1715	0.00089	0.0477	[0.0781, 0.265]	0.27
fourthV_log	0.0841	0.059	0.0428	[0.000196, 0.168]	0.25
allCSF	0.1632	0.025	0.0698	[0.0263, 0.3]	0.25
periCSF	0.0264	0.7	0.0675	[-0.106, 0.159]	0.24
CCR_log	0.1496	0.0014	0.0448	[0.0618, 0.237]	0.26
CCR2_log	0.1525	0.0013	0.0449	[0.0645, 0.24]	0.26
periCSF_frac_reflect_log	0.1682	0.00062	0.0452	[0.0796, 0.257]	0.27

SDMT ~ \*predictor\* + age + Female + tiv + dzdur

predictor	coef	p_fdr	se	ci	R2
WTV	0.373	1.4e-09	0.0584	[0.258, 0.487]	0.25
medial	0.3351	2.3e-09	0.0538	[0.23, 0.441]	0.23
posterior	0.3353	4.9e-09	0.0551	[0.227, 0.443]	0.24
ventral	0.3545	6.4e-09	0.0591	[0.239, 0.47]	0.23
anterior	0.2659	9.4e-08	0.0483	[0.171, 0.361]	0.21
cortical_thickness	0.3614	4.8e-12	0.0491	[0.265, 0.458]	0.25
brain	0.7955	2.5e-07	0.1498	[0.502, 1.09]	0.21
white	0.1915	0.14	0.1306	[-0.0645, 0.448]	0.16
grey	0.5945	1.5e-09	0.0939	[0.411, 0.779]	0.22
CP	-0.1556	0.0067	0.0562	[-0.266, -0.0454]	0.17
t2lv_log	-0.3146	6.4e-09	0.0525	[-0.417, -0.212]	0.24
T2LV_log1p	-0.3245	1.4e-09	0.0506	[-0.424, -0.225]	0.24
periV_T2LV_log1p	-0.2843	9.4e-08	0.0515	[-0.385, -0.183]	0.22
juxcort_T2LV_log1p	-0.2307	3.2e-06	0.0485	[-0.326, -0.136]	0.2
subcort_T2LV_log1p	-0.1242	0.012	0.0485	[-0.219, -0.0291]	0.17
infraT_T2LV_log1p	-0.1595	0.00043	0.0444	[-0.247, -0.0724]	0.18
PRL	-0.1452	0.0054	0.0509	[-0.245, -0.0454]	0.17
LV_log	-0.2868	8.2e-07	0.0566	[-0.398, -0.176]	0.21
thirdV_log	-0.2422	1.1e-05	0.0542	[-0.348, -0.136]	0.2
fourthV_log	-0.0936	0.061	0.0495	[-0.191, 0.00338]	0.16
allCSF	-0.3353	5.4e-06	0.0723	[-0.477, -0.194]	0.2
periCSF	-0.1352	0.055	0.069	[-0.271, 0.000126]	0.16
CCR_log	-0.2647	2.3e-06	0.0546	[-0.372, -0.158]	0.21

predictor	coef	p_fdr	se	ci	R2
CCR2_log	-0.2664	2.2e-06	0.0548	[-0.374, -0.159]	0.21
periCSF_frac_reflect_log	-0.2559	1.1e-05	0.0572	[-0.368, -0.144]	0.21