3-CP_CSF_analysis

November 24, 2025

title: ""

1 Choroid Plexus and CSF

Reload modules

1.1 Regressions on CSF volumes

Peripheral CSF segmentation was obtained starting from the `FAST` CSF segmentation, then subtracting the lateral, third, and fourth ventricles and also label 24 from Freesurfer's `aseg.auto_noCCseg` segmentation (technically Fastsurfer's)

1.1.1 Does CP drive central atrophy?

Previous analysis showed that CP is very strongly associated with LV; in fact, of all the variables I'm looking at, LV is the one with the strongest association with CP. Both CP and LV enlarge in MS. We know that LV enlargement can be indicative of a few different pathologic processes.

1. Overproduction of CSF
2. Atrophy
3. CSF obstruction

Also, atrophy associated with ventricular enlargement could be global or central.

CSF Subcompartments Given the relationship between CP and regional thalamic atrophy, we aimed to determine whether this reflected localized expansion of the ventricles proximal to the CP or a global ex-vacuo phenomenon affecting all periventricular structures.

Each CSF compartment was regressed on CP or other variables of interest (e.g. T2LV) with WBV as an additional covariate.

CP's association with CSF compartments The first table shows the results of using basic covariates. CP enlargement was associated with expansion of all CSF compartments, but the strength of the relationship decreased distal to the lateral ventricles.

The second table and the plot shows the results when controlling WBV. In this case, CP enlargement was associated with *smaller* peripheral CSF spaces when WBV was held constant.

Basic covariates:

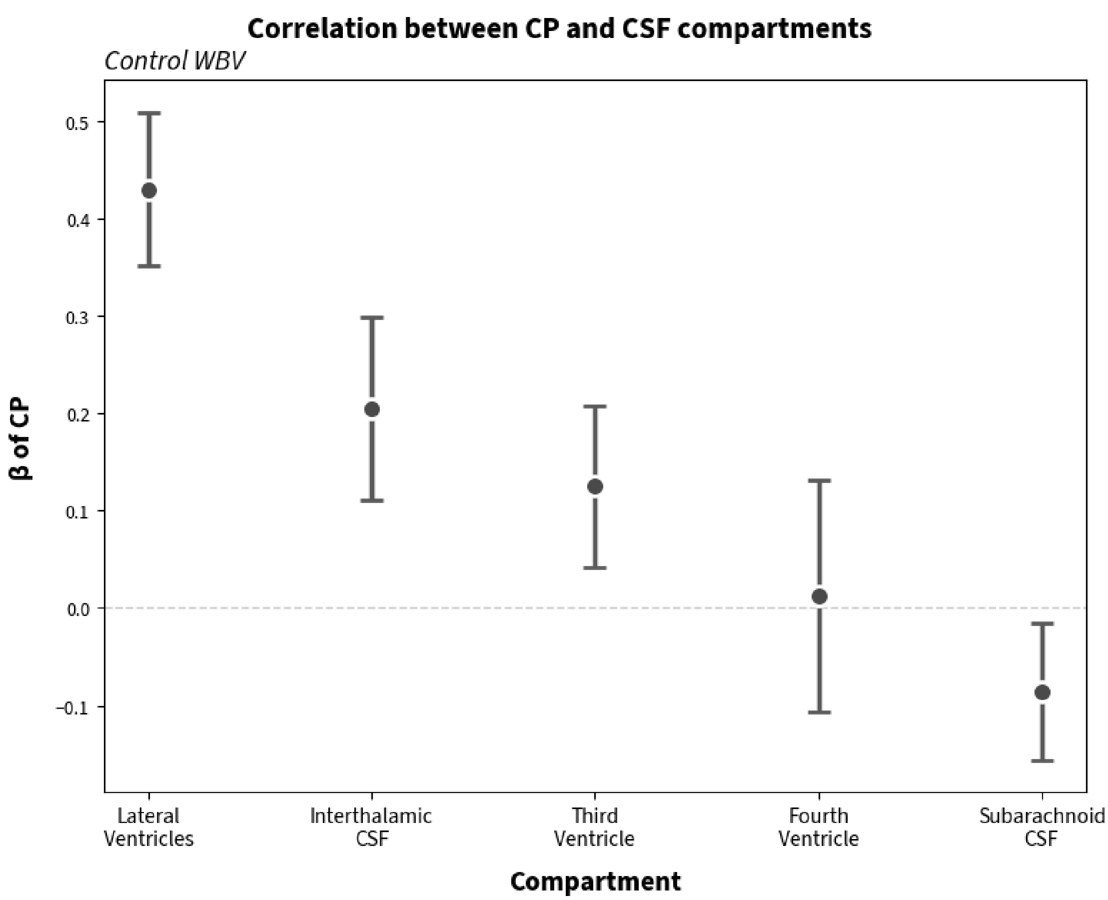
```
outcome ~ CP + age + Female + tiv
```

outcome	coef	p_fdr	se	ci	R2
LV_log	0.6444	2.9e-84	0.033	[0.58, 0.709]	0.57
interCSF_log	0.4656	2.2e-25	0.0444	[0.379, 0.553]	0.27
thirdV_log	0.4252	1.4e-23	0.0423	[0.342, 0.508]	0.35
fourthV_log	0.2281	6.9e-06	0.0502	[0.13, 0.326]	0.14
periCSF_log	0.1523	1.7e-05	0.0354	[0.0829, 0.222]	0.57

Add WBV to covariates:

```
outcome ~ CP + WBV + age + Female + tiv
```

outcome	coef	p_fdr	se	ci	R2
LV_log	0.4296	7.9e-26	0.0403	[0.351, 0.509]	0.65
interCSF_log	0.2048	4.8e-05	0.0479	[0.111, 0.299]	0.39
thirdV_log	0.1248	0.0051	0.0422	[0.0422, 0.207]	0.52
fourthV_log	0.0124	0.84	0.0603	[-0.106, 0.131]	0.23
periCSF_log	-0.0857	0.02	0.0356	[-0.156, -0.0159]	0.67



CP as the main predictor

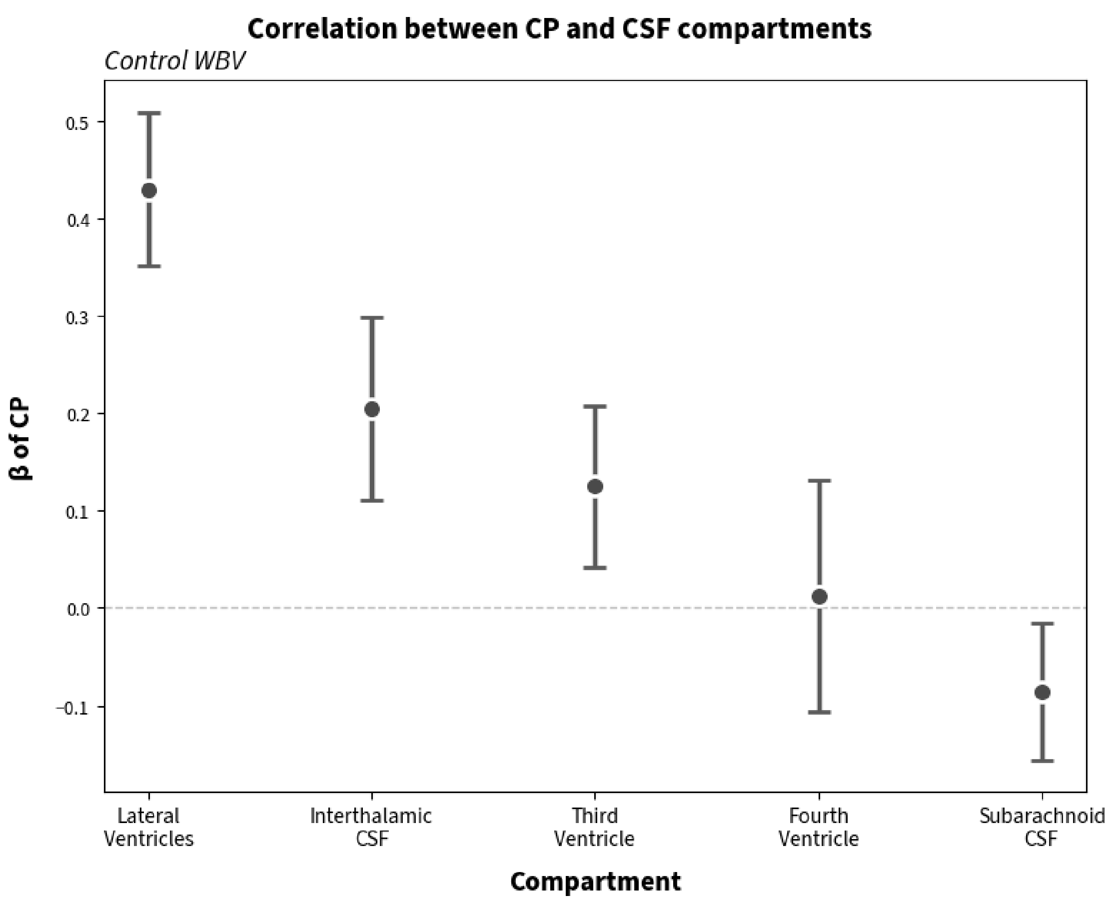
```
outcome ~ CP + age + Female + tiv
```

outcome	coef	p_fdr	se	ci	R2
LV_log	0.6444	2.9e-84	0.033	[0.58, 0.709]	0.57
interCSF_log	0.4656	2.2e-25	0.0444	[0.379, 0.553]	0.27
thirdV_log	0.4252	1.4e-23	0.0423	[0.342, 0.508]	0.35
fourthV_log	0.2281	6.9e-06	0.0502	[0.13, 0.326]	0.14
periCSF_log	0.1523	1.7e-05	0.0354	[0.0829, 0.222]	0.57

T2LV as the main predictor

```
outcome ~ T2LV_log1p + age + Female + tiv
```

outcome	coef	p_fdr	se	ci	R2
LV_log	0.4103	4.3e-22	0.0418	[0.328, 0.492]	0.39
thirdV_log	0.3838	7.8e-21	0.0406	[0.304, 0.463]	0.34
interCSF_log	0.356	4.5e-16	0.0435	[0.271, 0.441]	0.21
fourthV_log	0.1835	8e-05	0.0459	[0.0935, 0.273]	0.13
periCSF_log	0.0559	0.092	0.0332	[-0.00922, 0.121]	0.56



CP as the main predictor

```
outcome ~ CP + WBV + age + Female + tiv
```

outcome	coef	p_fdr	se	ci	R2
LV_log	0.4296	7.9e-26	0.0403	[0.351, 0.509]	0.65
interCSF_log	0.2048	4.8e-05	0.0479	[0.111, 0.299]	0.39
thirdV_log	0.1248	0.0051	0.0422	[0.0422, 0.207]	0.52
fourthV_log	0.0124	0.84	0.0603	[-0.106, 0.131]	0.23
periCSF_log	-0.0857	0.02	0.0356	[-0.156, -0.0159]	0.67

T2LV as the main predictor

```
outcome ~ T2LV_log1p + WBV + age + Female + tiv
```

outcome	coef	p_fdr	se	ci	R2
LV_log	0.1732	8.1e-05	0.0417	[0.0915, 0.255]	0.57
thirdV_log	0.1465	0.00014	0.0373	[0.0734, 0.22]	0.52
interCSF_log	0.1265	0.01	0.0478	[0.033, 0.22]	0.38
fourthV_log	0.0116	0.81	0.0488	[-0.084, 0.107]	0.23
periCSF_log	-0.1436	8.1e-05	0.0338	[-0.21, -0.0774]	0.69

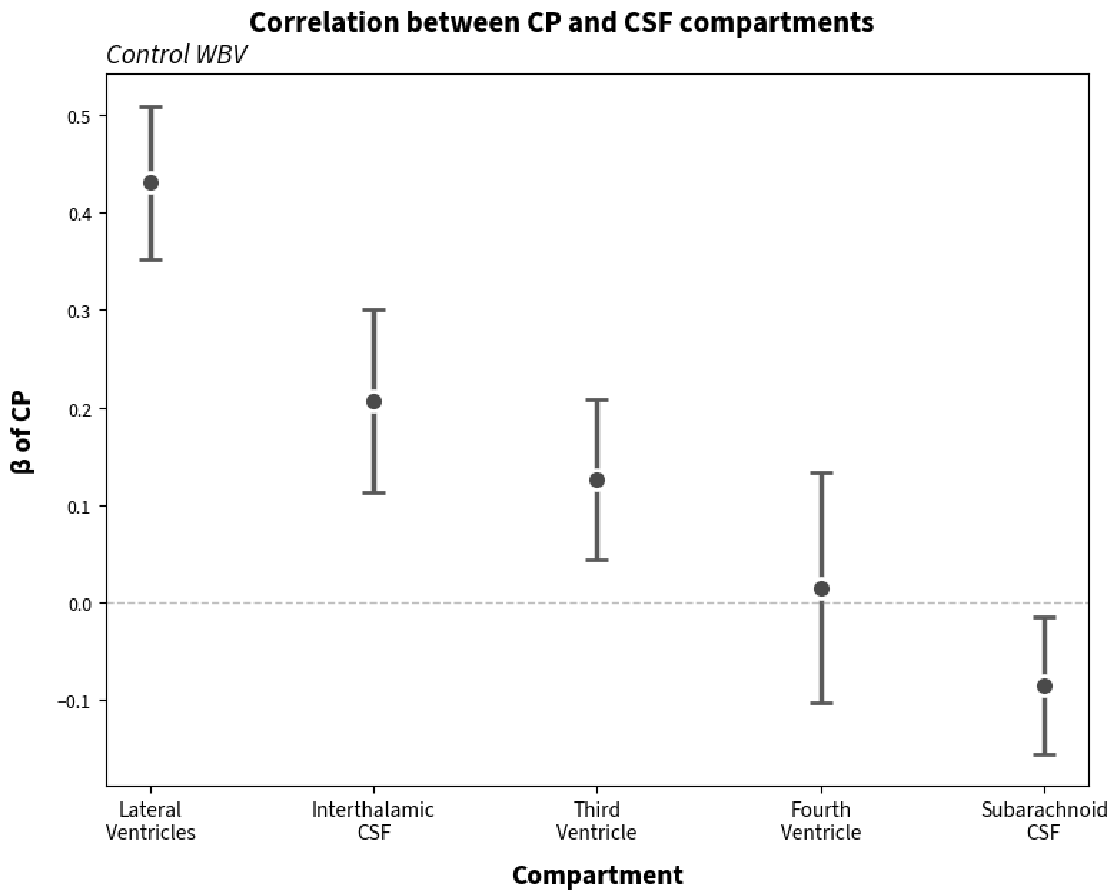
```
outcome ~ CP + WBV + age + Female + tiv
```

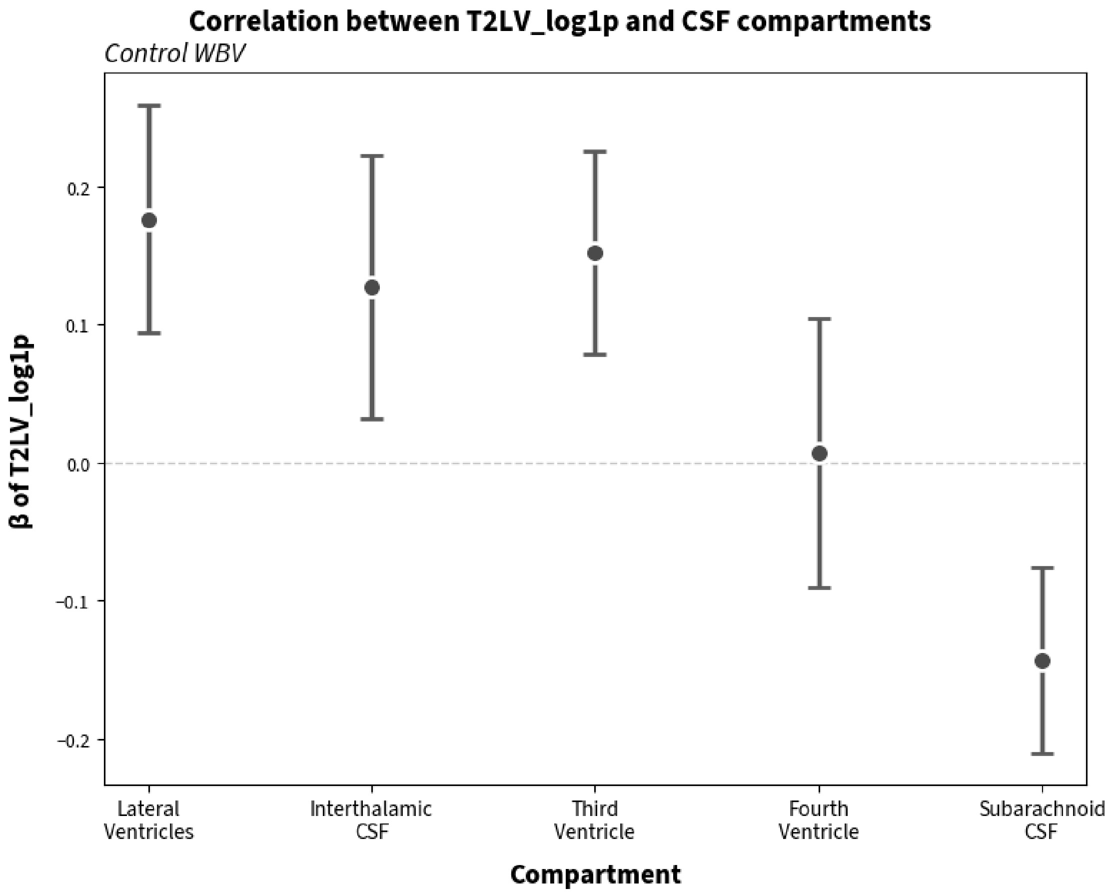
outcome	coef	p_fdr	se	ci	R2
LV_log	0.4309	7.4e-26	0.0404	[0.352, 0.51]	0.65
interCSF_log	0.2067	4.1e-05	0.048	[0.113, 0.301]	0.39
thirdV_log	0.1258	0.0048	0.0422	[0.0431, 0.208]	0.52
fourthV_log	0.0142	0.81	0.0604	[-0.104, 0.133]	0.22
periCSF_log	-0.086	0.02	0.0357	[-0.156, -0.016]	0.67

```
outcome ~ T2LV_log1p + WBV + age + Female + tiv
```

outcome	coef	p_fdr	se	ci	R2
LV_log	0.1764	7.5e-05	0.0423	[0.0935, 0.259]	0.57
thirdV_log	0.1521	8.7e-05	0.0376	[0.0784, 0.226]	0.52
interCSF_log	0.1272	0.011	0.0486	[0.032, 0.222]	0.38
fourthV_log	0.0073	0.88	0.0497	[-0.0901, 0.105]	0.22
periCSF_log	-0.1432	7.5e-05	0.0343	[-0.21, -0.076]	0.68

Plot the betas of CP wrt to CSF compartments





CP predicts CSF expansion after controlling for atrophy After controlling for WBV, both CP abd T2LV retained significant associations with all CSF compartment except fourthV.

After controlling for WTV, CP retained significant associations with all CSF compartment, but T2LV with none.

Effect of CP on outcomes after accounting for brain and THALAMUS_1 as well

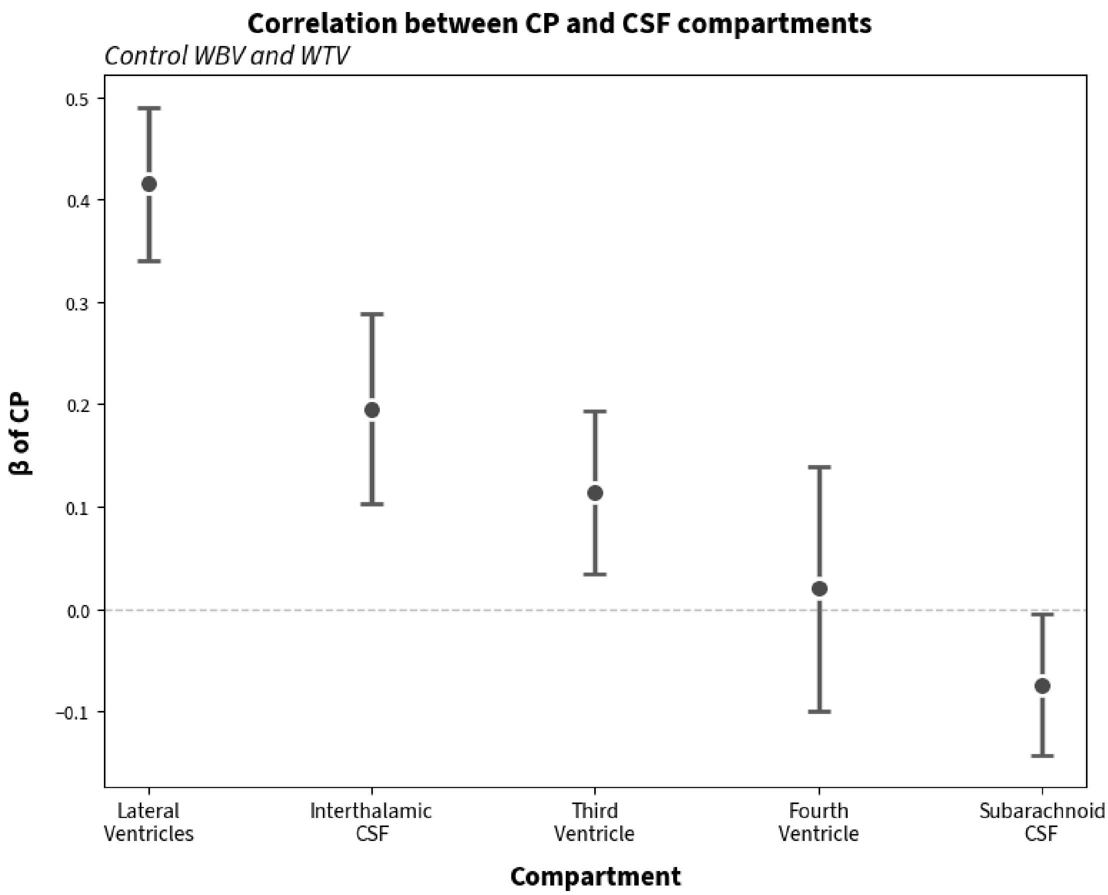
`outcome ~ CP + WTV + WBV + age + Female + tiv`

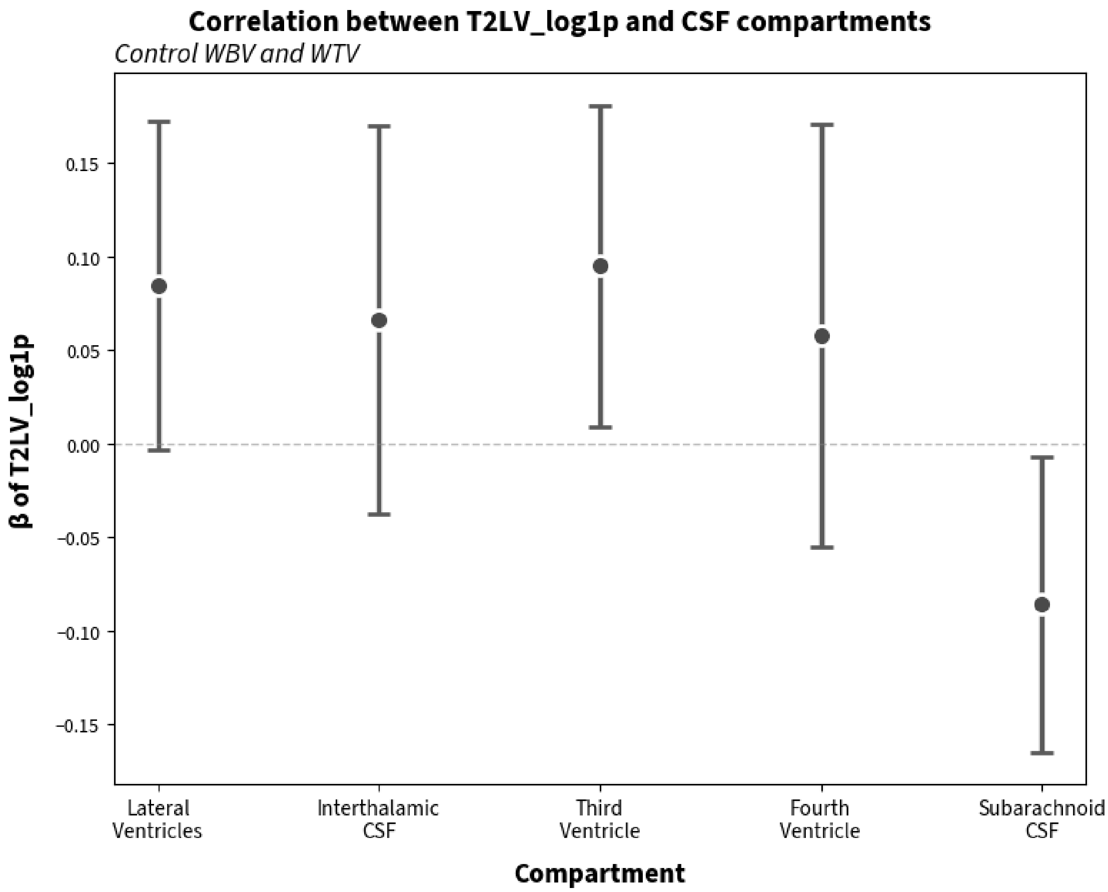
outcome	coef	p_fdr	se	ci	R2
LV_log	0.4152	8.8e-27	0.0382	[0.34, 0.49]	0.68
interCSF_log	0.1955	9.4e-05	0.0474	[0.103, 0.289]	0.4
thirdV_log	0.1136	0.0086	0.0406	[0.034, 0.193]	0.53
fourthV_log	0.0199	0.74	0.061	[-0.0997, 0.139]	0.23
periCSF_log	-0.074	0.043	0.0349	[-0.142, -0.00547]	0.69

Effect of T2LV_log1p on outcomes after accounting for brain and THALAMUS_1 as well

```
outcome ~ T2LV_log1p + WTV + WBV + age + Female + tiv
```

outcome	coef	p_fdr	se	ci	R2
LV_log	0.0846	0.098	0.0448	[-0.00323, 0.172]	0.59
interCSF_log	0.0662	0.26	0.0529	[-0.0376, 0.17]	0.38
thirdV_log	0.0952	0.083	0.0439	[0.00927, 0.181]	0.53
fourthV_log	0.0578	0.32	0.0577	[-0.0552, 0.171]	0.23
periCSF_log	-0.0858	0.083	0.0403	[-0.165, -0.00693]	0.69





CSF compartment volumes predict PRL count

`PRL ~ *predictor* + age + Female + tiv`

predictor	coef	p_fdr	se	ci	R2
periCSF_log	0.5135	0.00017	0.1345	[0.25, 0.777]	0.29
thirdV_log	0.4199	2.7e-06	0.0849	[0.254, 0.586]	0.31
LV_log	0.407	2.7e-06	0.0835	[0.243, 0.571]	0.3
interCSF_log	0.3263	3.5e-05	0.0767	[0.176, 0.477]	0.28
fourthV_log	0.2988	0.00034	0.0835	[0.135, 0.462]	0.27

`PRL ~ *predictor* + CP + age + Female + tiv`

predictor	coef	p_fdr	se	ci	R2
periCSF_log	0.4004	0.01	0.1298	[0.146, 0.655]	0.36
thirdV_log	0.2806	0.013	0.1007	[0.0832, 0.478]	0.35
fourthV_log	0.2142	0.013	0.0805	[0.0563, 0.372]	0.34
LV_log	0.1978	0.096	0.1187	[-0.0348, 0.43]	0.33

predictor	coef	p_fdr	se	ci	R2
interCSF_log	0.1855	0.036	0.085	[0.0189, 0.352]	0.33

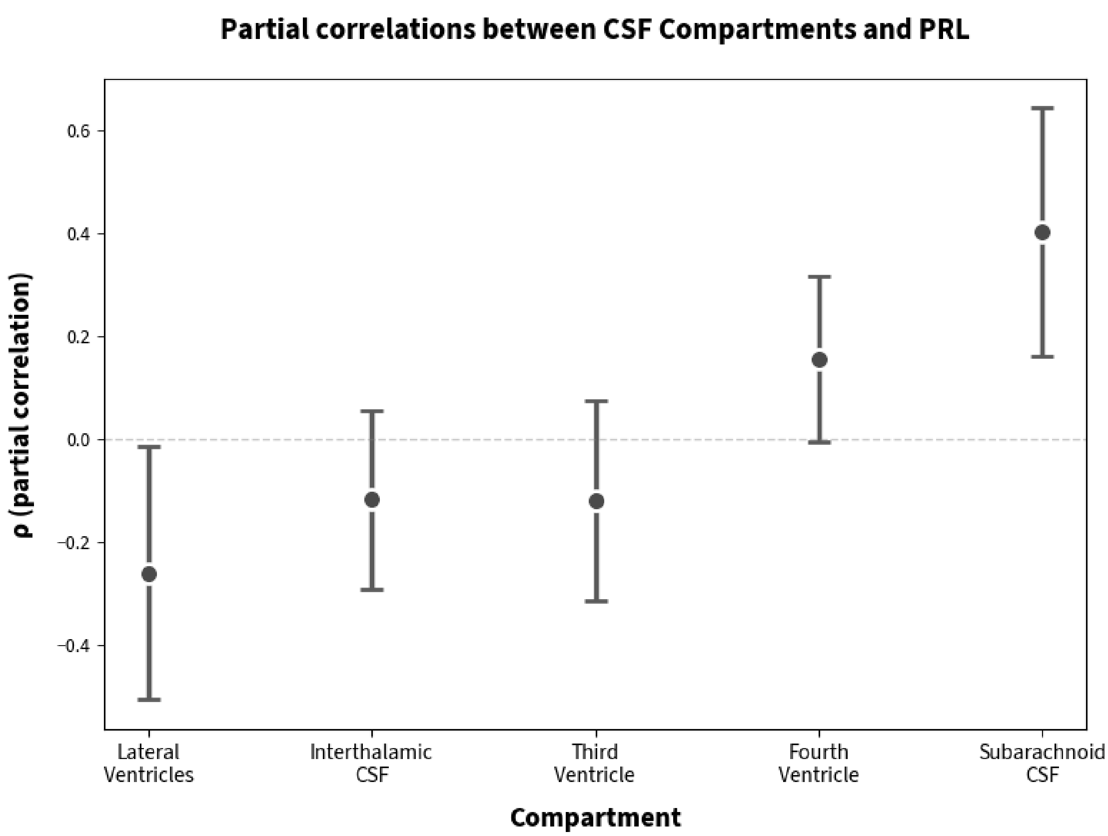
```
PRL ~ *predictor* + T2LV_log1p + age + Female + tiv
```

predictor	coef	p_fdr	se	ci	R2
periCSF_log	0.4073	0.0025	0.117	[0.178, 0.636]	0.56
fourthV_log	0.1648	0.11	0.0825	[0.0031, 0.326]	0.54
LV_log	-0.1055	0.38	0.0981	[-0.298, 0.0868]	0.53
interCSF_log	-0.0777	0.38	0.0791	[-0.233, 0.0773]	0.53
thirdV_log	-0.0757	0.38	0.0863	[-0.245, 0.0934]	0.53

```
PRL ~ *predictor* + CP + T2LV_log1p + age + Female + tiv
```

predictor	coef	p_fdr	se	ci	R2
periCSF_log	0.4023	0.0052	0.1226	[0.162, 0.642]	0.56
LV_log	-0.2598	0.094	0.1255	[-0.506, -0.0138]	0.54
fourthV_log	0.1565	0.094	0.0821	[-0.00446, 0.317]	0.54
thirdV_log	-0.1186	0.23	0.0993	[-0.313, 0.0761]	0.53
interCSF_log	-0.1169	0.23	0.0888	[-0.291, 0.0572]	0.53

Plot the betas of CSF compartments wrt to PRL



CP predicts these compartment volumes after controlling for brain and thalamus, but t2lv does not

Sanity check on peripheral CSF The following is more of a sanity check. If all the CSF volumes are defined properly, particulary peripheral CSF, we'd expect thalamic volume to be related more to the central CSF compartments and for brain volume to be related more to the peripheral CSF volume. This is borne out. Peripheral CSF has a much stronger relationship to WBV and LV has a much stronger relationship to thalamus

periCSF brain+thalamus

`periCSF ~ brain + THALAMUS_1 + age + Female + tiv`

	coef	pval	se	ci	R2
Intercept	-0.1526	0.04	0.0744	[-0.298, -0.00681]	0.62
Female[T.1]	0.1985	0.02	0.085	[0.0319, 0.365]	0.62
brain	-0.2327	7.2e-11	0.0357	[-0.303, -0.163]	0.62
THALAMUS_1	-0.1109	0.013	0.0445	[-0.198, -0.0237]	0.62
age	0.0609	0.074	0.0341	[-0.00597, 0.128]	0.62
tiv	0.8337	4.1e-109	0.0376	[0.76, 0.907]	0.62

LV_log brain+thalamus

`LV_log ~ brain + THALAMUS_1 + age + Female + tiv`

	coef	pval	se	ci	R2
Intercept	-0.0549	0.46	0.0743	[-0.201, 0.0908]	0.52
Female[T.1]	0.073	0.42	0.0901	[-0.104, 0.25]	0.52
brain	-0.0151	0.72	0.0426	[-0.0987, 0.0685]	0.52
THALAMUS_1	-0.6317	8.7e-59	0.0391	[-0.708, -0.555]	0.52
age	0.2105	1.3e-09	0.0347	[0.142, 0.279]	0.52
tiv	0.4906	2.2e-29	0.0436	[0.405, 0.576]	0.52

Note: brain has a significant association with LV_log before controlling for THALAMUS_1

```
notebook controller is DISPOSED.

View Jupyter <a href='command:jupyter.viewOutput'>log</a> for further details.
```

1.1.2 Central CSF Expansion

Does the relationship between CP and LV volumes represent a global process whereby CP influences overall atrophy or CSF hydrodynamics, or is CP causing regional changes? With the degree of preferential central expansion defined as the central CSF ratio (CCR):

$CCR = LV/periCSF$

CCR baseline associations with atrophy and inflammation *Note*: Cortical thickness has inverse association with CCR, indicating that atrophy occurs quicker centrally than peripherally as a general pattern

```
CCR2_log ~ *predictor* + age + Female + tiv
```

predictor	coef	p_fdr	se	ci	R2
CP	0.6355	6.7e-74	0.0347	[0.567, 0.704]	0.51
T2LV_log1p	0.4215	4.6e-22	0.0436	[0.336, 0.507]	0.35
WTV	-0.6295	2.8e-65	0.0367	[-0.701, -0.557]	0.47
WBV	-1.2634	4e-51	0.0837	[-1.43, -1.1]	0.47
WMV	-0.8923	6e-31	0.0768	[-1.04, -0.742]	0.36
GMV	-0.8214	4.5e-10	0.1317	[-1.08, -0.563]	0.37
cortical_thickness	-0.4595	7.4e-28	0.0419	[-0.542, -0.377]	0.35

```
CCR2_log ~ CP + age + Female + tiv
R2=0.51, AIC=997.93, BIC=1018.67

CCR2_log ~ WBV + age + Female + tiv
R2=0.47, AIC=1038.43, BIC=1059.18

CCR2_log ~ WTV + age + Female + tiv
R2=0.47, AIC=1035.40, BIC=1056.14
```

Does CP predict CCR beyond atrophy? CP is associated with increasing CCR, beyond what is predicted by brain or thalamus volumes.

T2LV explains CCR independently of CP when controlling for WBV, but not when controlling for both WBV and WTV. WTV actually mediates the effect of T2LV on CCR, suggesting that T2LV's role is to produce thalamic atrophy via Wallerian degeneration.

WBV + WTV

```
CCR2_log ~ WBV + WTV + age + Female + tiv
```

	coef	p_fdr	se	ci	R2
WBV	-0.7168	1.7e-09	0.1144	[-0.942, -0.492]	0.51
WTV	-0.3695	5.5e-10	0.0567	[-0.481, -0.258]	0.51

CP + WBV + WTV

```
CCR2_log ~ CP + WBV + WTV + age + Female + tiv
```

	coef	p_fdr	se	ci	R2
CP	0.4268	4.3e-24	0.039	[0.35, 0.503]	0.61
WBV	-0.27	0.025	0.1099	[-0.486, -0.054]	0.61
WTV	-0.3304	6.4e-10	0.0507	[-0.43, -0.231]	0.61

CP + T2LV + WBV

```
CCR2_log ~ CP + T2LV_log1p + WBV + age + Female + tiv
```

	coef	p_fdr	se	ci	R2
CP	0.4256	5.9e-23	0.04	[0.347, 0.504]	0.59
T2LV_log1p	0.1613	1.3e-05	0.0355	[0.0915, 0.231]	0.59
WBV	-0.5889	8.1e-10	0.0913	[-0.768, -0.41]	0.59

CP + T2LV + WBV + WTV

```
CCR2_log ~ CP + T2LV_log1p + WBV + WTV + age + Female + tiv
```

	coef	p_fdr	se	ci	R2
CP	0.4217	1.8e-23	0.0391	[0.345, 0.498]	0.61
T2LV_log1p	0.0645	0.11	0.04	[-0.0141, 0.143]	0.61
WBV	-0.277	0.024	0.1098	[-0.493, -0.0612]	0.61
WTV	-0.2836	6.4e-06	0.0583	[-0.398, -0.169]	0.61

CP + T2LV + PRL

```
CCR2_log ~ PRL + WBV + age + Female + tiv
```

	coef	p_fdr	se	ci	R2
PRL	0.0115	0.85	0.0202	[-0.0282, 0.0512]	0.47
WBV	-1.2503	3.6e-40	0.0843	[-1.42, -1.08]	0.47

F-tests to determine whether CP adds explanatory power beyond atrophy

	base model	full model	ΔR	F-statistic	pval	df
0	WBV + WTV	CP + WBV + WTV	0.0998	119.785	6.1e-25	1
1	CP + WBV	CP + T2LV + WBV	0.0172	20.6182	7.2e-06	1
2	CP + WBV + WTV	CP + T2LV + WBV + WTV	0.0013	2.5989	0.11	1

WTV fully mediates the effect of T2LV on expanding CCR when controlling CP.

```
================================================================================

Direct effect of T2LV_log1p on CCR2_log:

  Effect     SE      t      p    LLCI   ULCI
  0.0645 0.0400 1.6121 0.1076 -0.0139 0.1429

Indirect effect of T2LV_log1p on CCR2_log:

       Effect  Boot SE  BootLLCI  BootULCI
  WBV  0.0385   0.0190    0.0055    0.0794
  WTV  0.1402   0.0306    0.0814    0.2028


================================================================================
```

CCR and regional thalamic atrophy

Partial correlations between CCR, WTV, and nuclei groups

Patients with MS Assess CCR2_log and control for WBV, age, Female, tiv

Pearson correlations of residualized thalamic nuclei and CCR2_log:

```
THALAMUS_1: r=-0.29, p=1.53e-10
medial: r=-0.397, p=3.84e-19
posterior: r=-0.315, p=2.96e-12
anterior: r=-0.118, p=1.04e-02
ventral: r=-0.0301, p=5.16e-01
```

Comparisons between thalamic nuclei and whole thalamus:

```
+ medial > THALAMUS_1: p=7.47e-06
  posterior = THALAMUS_1: p=2.44e-01
- anterior < THALAMUS_1: p=8.93e-05
- ventral < THALAMUS_1: p=4.04e-22
```

Comparisons between thalamic nuclei:

```
+ medial > posterior: p=8.02e-03
+ medial > anterior: p=2.94e-09
+ medial > ventral: p=2.05e-19
+ posterior > anterior: p=1.91e-05
+ posterior > ventral: p=4.33e-11
  anterior = ventral: p=6.97e-02
```

Patients with MS **Pearson correlations of residualized thalamic nuclei and CP:**

```
THALAMUS_1: r=-0.0304, p=5.12e-01
medial: r=-0.0928, p=4.47e-02
posterior: r=-0.0945, p=4.11e-02
```

```
anterior: r=0.0206, p=6.57e-01
ventral: r=0.107, p=2.04e-02
```

Comparisons between thalamic nuclei and whole thalamus:

```
+ medial > THALAMUS_1: p=1.86e-02
+ posterior > THALAMUS_1: p=5.57e-03
  anterior = THALAMUS_1: p=2.64e-01
- ventral < THALAMUS_1: p=3.37e-07
```

Comparisons between thalamic nuclei:

```
  medial = posterior: p=9.63e-01
+ medial > anterior: p=2.35e-02
+ medial > ventral: p=2.04e-06
+ posterior > anterior: p=1.66e-02
+ posterior > ventral: p=5.14e-06
  anterior = ventral: p=7.58e-02
```

CCR and all thalamic + deep grey

```
thalamic nucleus ~ *CCR2_log* + WBV + age + Female + tiv
```

outcome	coef	p_fdr	se	ci	R2
MD_Pf_12	-0.3524	1.3e-15	0.0422	[-0.435, -0.27]	0.65
LGN_9	-0.3326	1.6e-08	0.056	[-0.442, -0.223]	0.44
Pul_8	-0.275	7.7e-09	0.0448	[-0.363, -0.187]	0.59
MGN_10	-0.2497	9.6e-08	0.0448	[-0.338, -0.162]	0.57
CM_11	-0.1724	0.00047	0.0459	[-0.262, -0.0825]	0.53
AV_2	-0.1257	0.026	0.0508	[-0.225, -0.026]	0.41
VLP_6	-0.0512	0.32	0.0461	[-0.142, 0.0391]	0.56
VPL_7	-0.0458	0.36	0.0484	[-0.141, 0.0491]	0.49
VA_4	0.0622	0.24	0.0434	[-0.0229, 0.147]	0.54
VLa_5	0.0658	0.25	0.0503	[-0.0327, 0.164]	0.48

```
deep grey ~ *CCR2_log* + WBV + age + Female + tiv
```

outcome	coef	p_fdr	se	ci	R2
Acc_26	-0.2553	1.6e-08	0.0432	[-0.34, -0.171]	0.59
Cla_28	-0.2165	2.9e-06	0.0441	[-0.303, -0.13]	0.6
Hb_13	-0.1517	0.028	0.063	[-0.275, -0.0282]	0.17
Put_31	-0.1337	0.013	0.0479	[-0.228, -0.0397]	0.52
RN_32	-0.0594	0.25	0.0464	[-0.15, 0.0316]	0.54
Cau_27	-0.0122	0.78	0.0435	[-0.0974, 0.073]	0.4
GPe_29	0.0505	0.36	0.053	[-0.0533, 0.154]	0.39
GPi_30	0.0704	0.25	0.0539	[-0.0354, 0.176]	0.31
MTT_14	0.1639	0.017	0.0619	[0.0425, 0.285]	0.31

```
thalamic nucleus ~ *CCR2_log* + WBV + age + Female + tiv
```

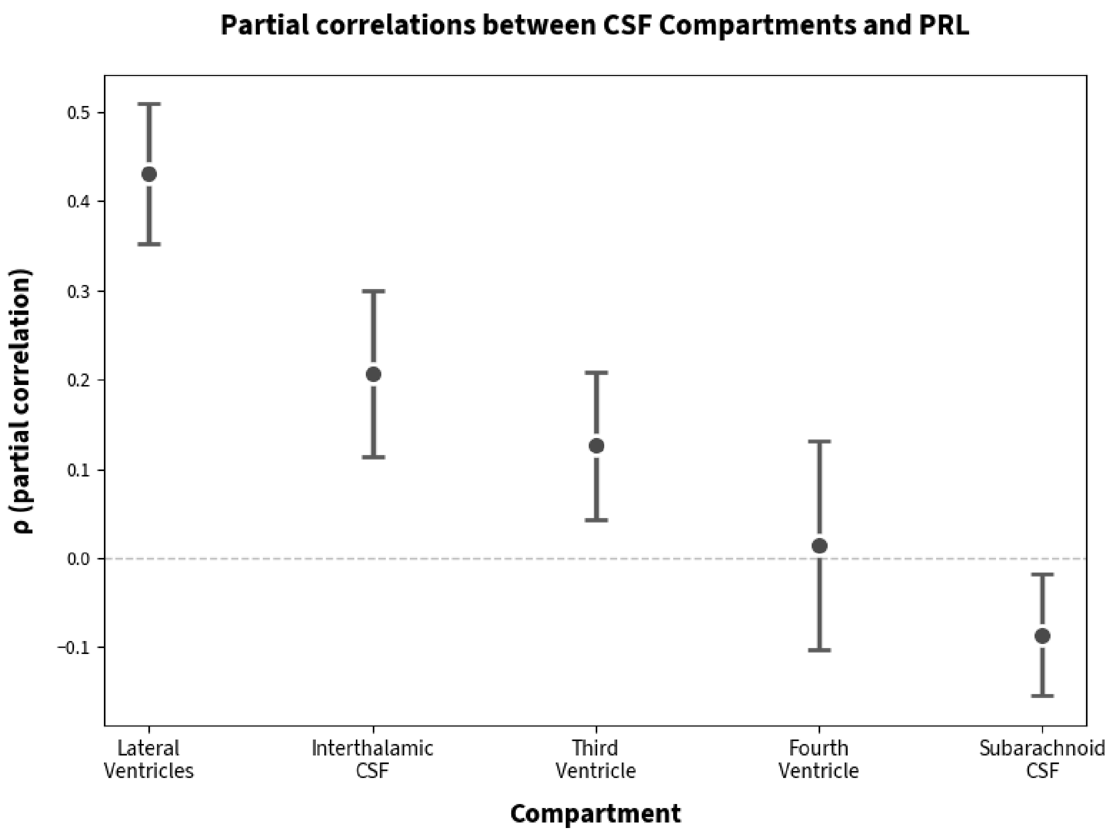
outcome	coef	p_fdr	ci
MD_Pf_12	-0.3967	8.3e-18	[-0.47, -0.32]
LGN_9	-0.3085	8.5e-11	[-0.39, -0.22]
Pul_8	-0.2987	2.7e-10	[-0.38, -0.21]
MGN_10	-0.2677	1.5e-08	[-0.35, -0.18]
CM_11	-0.1814	0.00021	[-0.27, -0.09]
AV_2	-0.1184	0.018	[-0.21, -0.03]
VLP_6	-0.0563	0.27	[-0.15, 0.03]
VPL_7	-0.0466	0.33	[-0.14, 0.04]
VLa_5	0.0664	0.22	[-0.02, 0.16]
VA_4	0.0667	0.22	[-0.02, 0.16]

```
deep grey ~ *CCR2_log* + WBV + age + Female + tiv
```

outcome	coef	p_fdr	ci
Acc_26	-0.2797	3.5e-09	[-0.36, -0.19]
Cla_28	-0.2411	4.1e-07	[-0.32, -0.15]
Put_31	-0.1393	0.0053	[-0.23, -0.05]
Hb_13	-0.1209	0.017	[-0.21, -0.03]
RN_32	-0.0638	0.23	[-0.15, 0.03]
Cau_27	-0.0115	0.8	[-0.1, 0.08]
GPe_29	0.0472	0.33	[-0.04, 0.14]
GPi_30	0.0616	0.23	[-0.03, 0.15]
MTT_14	0.1424	0.0048	[0.05, 0.23]

Other check If I define another ratio of `LV / (thirdV + interCSF)`, I actually see the coefficient for WBV flip once CP and WTV are controlled.

1.1.3 Partial Correlations



1.1.4 Unstandardized Regressions

To get a sense of the scale of each compartment

```
Raw volumes:
LV          : 19454.91 ± 14852.40
interCSF    : 963.13 ± 347.66
thirdV      : 954.28 ± 483.20
fourthV     : 1747.36 ± 511.06
periCSF     : 344944.62 ± 34932.04

Log volumes:
LV_log      : 9.64 ± 0.69
interCSF_log : 6.81 ± 0.36
thirdV_log   : 6.74 ± 0.48
fourthV_log  : 7.43 ± 0.28
periCSF_log  : 12.75 ± 0.10

Raw volumes:
CCR           : 0.06 ± 0.04
```

```
CCR2          : 0.06 ± 0.04
CCR_norm      : 1.02 ± 0.77
CCR2_norm     : 1.02 ± 0.75
CCR2_norm2    : 2.03 ± 1.19

Log volumes:
CCR_log       : -3.11 ± 0.67
CCR2_log      : -3.05 ± 0.65
CCR_norm_log  : -0.21 ± 0.67
CCR2_norm_log : -0.20 ± 0.65
CCR2_norm2_log : 0.57 ± 0.52
```

```
<IPython.core.display.HTML object>
```

Outcomes are raw values and predictors are Z-scored. Betas represent the change in mm3 of the compartment with 1SD change in the predictor

```
LV Mean: 19492.70 ± 14859.00
```

```
LV ~ *predictor* + age + Female + tiv
```

predictor	coef	p_fdr	se	ci	R2
CP	6666.82	1.6e-31	567.059	[5.56e+03, 7.78e+03]	0.37
t2lv_log	5566.21	3.7e-11	841.397	[3.92e+03, 7.22e+03]	0.33
THALAMUS_1	-9449.65	3.8e-40	706.051	[-1.08e+04, -8.07e+03]	0.49
brain	-16883.3	1.8e-13	2283.94	[-2.14e+04, -1.24e+04]	0.33
cortical_thickness	-7251.02	1.4e-19	796.084	[-8.81e+03, -5.69e+03]	0.39

```
interCSF Mean: 964.45 ± 348.45
```

```
interCSF ~ *predictor* + age + Female + tiv
```

predictor	coef	p_fdr	se	ci	R2
CP	150.587	1.1e-22	15.219	[1.21e+02, 1.8e+02]	0.25
t2lv_log	105.765	2.1e-06	22.2847	[62.1, 1.49e+02]	0.18
THALAMUS_1	-202.174	2.1e-32	16.8671	[-2.35e+02, -1.69e+02]	0.34
brain	-431.114	2.2e-20	46.3175	[-5.22e+02, -3.4e+02]	0.24
cortical_thickness	-156.704	7.3e-17	18.7257	[-1.93e+02, -1.2e+02]	0.25

```
thirdV Mean: 955.76 ± 483.74
```

```
thirdV ~ *predictor* + age + Female + tiv
```

predictor	coef	p_fdr	se	ci	R2
CP	176.9	3.6e-18	20.1136	[1.37e+02, 2.16e+02]	0.32
t2lv_log	163.38	5.4e-09	28.0096	[1.08e+02, 2.18e+02]	0.32
THALAMUS_1	-289.863	2.8e-45	20.3622	[-3.3e+02, -2.5e+02]	0.47
brain	-541.141	2.2e-16	65.6896	[-6.7e+02, -4.12e+02]	0.34

predictor	coef	p_fdr	se	ci	R2
cortical_thickness	-221.976	1e-17	25.7135	[-2.72e+02, -1.72e+02]	0.38

`fourthV Mean: 1749.45 ± 512.52`

`fourthV ~ *predictor* + age + Female + tiv`

predictor	coef	p_fdr	se	ci	R2
CP	114.646	1.5e-05	25.7823	[64.1, 1.65e+02]	0.14
t2lv_log	76.3952	0.0042	26.6602	[24.1, 1.29e+02]	0.12
THALAMUS_1	-137.983	2.9e-06	28.3918	[-1.94e+02, -82.3]	0.16
brain	-401.058	1.7e-06	78.6161	[-5.55e+02, -2.47e+02]	0.16
cortical_thickness	-124.168	1.6e-05	28.4583	[-1.8e+02, -68.4]	0.15

`periCSF Mean: 345018.14 ± 34930.85`

`periCSF ~ *predictor* + age + Female + tiv`

predictor	coef	p_fdr	se	ci	R2
CP	5204.57	2.7e-05	1224.08	[2.81e+03, 7.6e+03]	0.58
t2lv_log	1671.48	0.2	1305.53	[-8.87e+02, 4.23e+03]	0.56
THALAMUS_1	-7081.38	4e-06	1502.19	[-1e+04, -4.14e+03]	0.59
brain	-49197.5	6e-64	2897.82	[-5.49e+04, -4.35e+04]	0.75
cortical_thickness	-10687.1	5.2e-10	1681.39	[-1.4e+04, -7.39e+03]	0.63

Predictors are Z-scored but the outcomes are just log transformed.

`LV_log Mean: 9.64 ± 0.69`

`LV_log ~ *predictor* + age + Female + tiv`

predictor	coef	p_fdr	se	ci	R2
CP	0.4421	2.9e-84	0.0226	[0.398, 0.486]	0.57
t2lv_log	0.2738	2.3e-13	0.0374	[0.201, 0.347]	0.38
THALAMUS_1	-0.4374	2.6e-76	0.0236	[-0.484, -0.391]	0.53
brain	-0.7154	1e-16	0.0859	[-0.884, -0.547]	0.34
cortical_thickness	-0.3364	2.7e-33	0.0279	[-0.391, -0.282]	0.42

`interCSF_log Mean: 6.81 ± 0.36`

`interCSF_log ~ *predictor* + age + Female + tiv`

predictor	coef	p_fdr	se	ci	R2
CP	0.168	2.2e-25	0.016	[0.137, 0.199]	0.27
t2lv_log	0.1011	1.2e-05	0.0231	[0.0558, 0.146]	0.17
THALAMUS_1	-0.2017	5.8e-41	0.0149	[-0.231, -0.172]	0.32

predictor	coef	p_fdr	se	ci	R2
brain	-0.4379	5.8e-21	0.0464	[-0.529, -0.347]	0.24
cortical_thickness	-0.1536	1.2e-19	0.0169	[-0.187, -0.121]	0.23

`thirdV_log Mean: 6.74 ± 0.49`

`thirdV_log ~ *predictor* + age + Female + tiv`

predictor	coef	p_fdr	se	ci	R2
CP	0.206	2.1e-23	0.0205	[0.166, 0.246]	0.35
t2lv_log	0.1605	7e-09	0.0277	[0.106, 0.215]	0.31
THALAMUS_1	-0.2837	1.4e-60	0.0172	[-0.317, -0.25]	0.45
brain	-0.5334	9.4e-21	0.0569	[-0.645, -0.422]	0.32
cortical_thickness	-0.2214	1.2e-21	0.023	[-0.267, -0.176]	0.37

`fourthV_log Mean: 7.43 ± 0.28`

`fourthV_log ~ *predictor* + age + Female + tiv`

predictor	coef	p_fdr	se	ci	R2
CP	0.0628	9.2e-06	0.0138	[0.0357, 0.0899]	0.14
t2lv_log	0.0427	0.0022	0.0139	[0.0154, 0.07]	0.12
THALAMUS_1	-0.0724	3.5e-06	0.015	[-0.102, -0.043]	0.15
brain	-0.216	5.2e-07	0.0406	[-0.296, -0.136]	0.16
cortical_thickness	-0.0657	2.6e-05	0.0155	[-0.096, -0.0354]	0.15

`periCSF_log Mean: 12.75 ± 0.10`

`periCSF_log ~ *predictor* + age + Female + tiv`

predictor	coef	p_fdr	se	ci	R2
CP	0.0156	2.1e-05	0.0036	[0.00848, 0.0227]	0.57
t2lv_log	0.0041	0.28	0.0038	[-0.00341, 0.0117]	0.56
THALAMUS_1	-0.0198	9.2e-06	0.0044	[-0.0283, -0.0113]	0.58
brain	-0.1421	4.2e-60	0.0086	[-0.159, -0.125]	0.74
cortical_thickness	-0.0311	5.8e-10	0.0049	[-0.0407, -0.0215]	0.62

`LV_log Mean: 9.64 ± 0.69`

`LV_log ~ *predictor* + age + Female + tiv + periCSF`

predictor	coef	p_fdr	se	ci	R2
CP	0.6681	1.2e-82	0.0345	[0.6, 0.736]	0.45
t2lv_log	0.4353	1.5e-13	0.059	[0.32, 0.551]	0.19
THALAMUS_1	-0.629	1.4e-78	0.0334	[-0.695, -0.563]	0.39
brain	-0.4601	1e-24	0.0447	[-0.548, -0.372]	0.21

predictor	coef	p_fdr	se	ci	R2
cortical_thickness	-0.5236	4.3e-30	0.0458	[-0.613, -0.434]	0.27

`interCSF_log Mean: 6.81 ± 0.36`

`interCSF_log ~ *predictor* + age + Female + tiv + periCSF`

predictor	coef	p_fdr	se	ci	R2
CP	0.4079	1.2e-21	0.0422	[0.325, 0.491]	0.16
t2lv_log	0.2731	1.6e-05	0.0632	[0.149, 0.397]	0.073
THALAMUS_1	-0.4595	2.6e-32	0.0384	[-0.535, -0.384]	0.21
brain	-0.3091	1.1e-12	0.0433	[-0.394, -0.224]	0.094
cortical_thickness	-0.326	8.2e-13	0.0451	[-0.414, -0.238]	0.1

`thirdV_log Mean: 6.74 ± 0.49`

`thirdV_log ~ *predictor* + age + Female + tiv + periCSF`

predictor	coef	p_fdr	se	ci	R2
CP	0.4051	1.3e-20	0.0431	[0.321, 0.49]	0.16
t2lv_log	0.3489	1.2e-08	0.0611	[0.229, 0.469]	0.12
THALAMUS_1	-0.5332	1e-53	0.0343	[-0.6, -0.466]	0.28
brain	-0.3491	3e-15	0.0441	[-0.436, -0.263]	0.12
cortical_thickness	-0.4159	3e-16	0.0505	[-0.515, -0.317]	0.17

`fourthV_log Mean: 7.43 ± 0.28`

`fourthV_log ~ *predictor* + age + Female + tiv + periCSF`

predictor	coef	p_fdr	se	ci	R2
CP	0.187	0.00023	0.0478	[0.0933, 0.281]	0.033
t2lv_log	0.1466	0.0041	0.0511	[0.0465, 0.247]	0.019
THALAMUS_1	-0.1987	0.00017	0.048	[-0.293, -0.105]	0.037
brain	-0.1903	0.00025	0.0502	[-0.289, -0.0918]	0.034
cortical_thickness	-0.1669	0.0012	0.0506	[-0.266, -0.0678]	0.026

`periCSF_log Mean: 12.75 ± 0.10`

`periCSF_log ~ *predictor* + age + Female + tiv + periCSF`

predictor	coef	p_fdr	se	ci	R2
CP	0.0418	0.44	0.045	[-0.0463, 0.13]	-0.0004
t2lv_log	-0.0962	0.1	0.0469	[-0.188, -0.00436]	0.0071
THALAMUS_1	0.1071	0.1	0.0481	[0.0128, 0.201]	0.0093
brain	0.0981	0.19	0.0617	[-0.0229, 0.219]	0.0075

predictor	coef	p_fdr	se	ci	R2
cortical_thickness	0.0249	0.63	0.0519	[-0.0769, 0.127]	-0.0015

1.2 PRL Analysis

PRL count is predicted most strongly by the peripheral CSF volume. This variable has an even stronger association with PRL than CP and T2LV.

CSF compartment volumes predict PRL count

```
PRL ~ *predictor* + T2LV_log1p + age + Female + tiv
```

predictor	coef	p_fdr	se	ci	R2
periCSF_log	0.4515	0.0011	0.1225	[0.211, 0.692]	0.55
fourthV_log	0.1779	0.074	0.0817	[0.0177, 0.338]	0.52
LV_log	-0.0438	0.97	0.1091	[-0.258, 0.17]	0.51
interCSF_log	-0.0248	0.97	0.0925	[-0.206, 0.157]	0.51
thirdV_log	-0.0039	0.97	0.1079	[-0.215, 0.208]	0.51

```
PRL ~ *predictor* + CP + age + Female + tiv
```

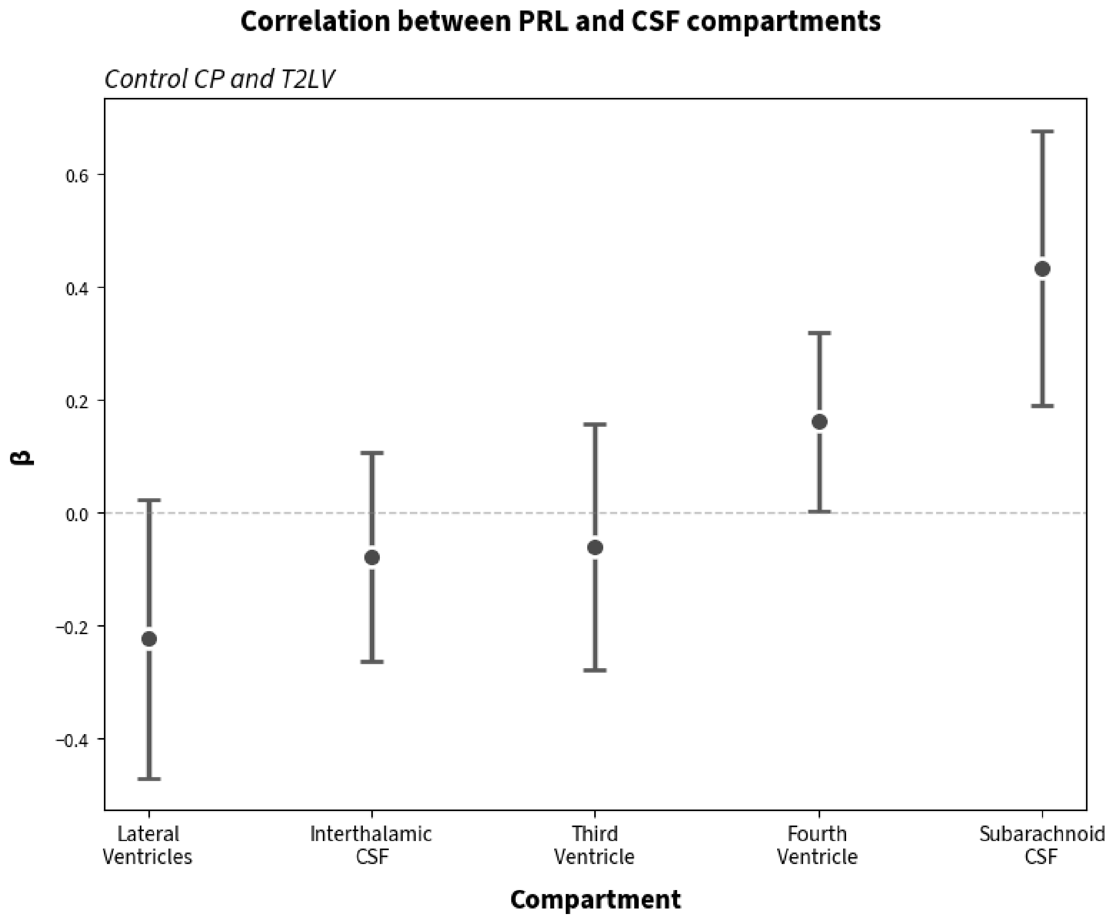
predictor	coef	p_fdr	se	ci	R2
periCSF_log	0.4004	0.01	0.1298	[0.146, 0.655]	0.36
thirdV_log	0.2806	0.013	0.1007	[0.0832, 0.478]	0.35
fourthV_log	0.2142	0.013	0.0805	[0.0563, 0.372]	0.34
LV_log	0.1978	0.096	0.1187	[-0.0348, 0.43]	0.33
interCSF_log	0.1855	0.036	0.085	[0.0189, 0.352]	0.33

```
PRL ~ *predictor* + CP + T2LV_log1p + age + Female + tiv
```

predictor	coef	p_fdr	se	ci	R2
periCSF_log	0.4323	0.0025	0.1243	[0.189, 0.676]	0.55
LV_log	-0.2231	0.13	0.1253	[-0.469, 0.0225]	0.52
fourthV_log	0.1612	0.11	0.0806	[0.00323, 0.319]	0.53
interCSF_log	-0.0782	0.51	0.0945	[-0.263, 0.107]	0.52
thirdV_log	-0.0605	0.59	0.1114	[-0.279, 0.158]	0.52

Plot the betas of CSF compartments wrt to PRL

```
Text(0.0, 1.0, 'Control CP and T2LV')
```




```
PRL ~ *predictor* + CP + t2lv_log + age + Female + tiv
```

predictor	coef	pval	p_fdr	ci
periCSF_log	0.1292	0.0051	0.026	[0.04, 0.22]
fourthV_log	0.0978	0.034	0.086	[0.01, 0.19]
thirdV_log	0.0692	0.13	0.22	[-0.02, 0.16]
interCSF_log	0.0521	0.26	0.33	[-0.04, 0.14]
LV_log	0.0121	0.79	0.79	[-0.08, 0.1]

Explore some more models for PRL count

1.3 Analysis around MS Status

1.3.1 CCR increases in MS

Is CCR specific for MS pathology? Logistic regression of MS status on CCR, controlling for age, sex, and tiv. CCR is increased in MS patients

CP `MS ~ CP + age + Female + tiv`

	coef	p_fdr	se	ci
Intercept	2.193	5.1e-11	0.3223	[1.56, 2.82]
Female[T.1]	-0.6504	0.084	0.359	[-1.35, 0.0532]
CP	0.2251	0.084	0.1302	[-0.03, 0.48]
age	-0.2616	0.072	0.1295	[-0.515, -0.00784]
tiv	-0.388	0.012	0.1381	[-0.659, -0.117]

LV_log `MS ~ LV_log + age + Female + tiv`

	coef	p_fdr	se	ci
Intercept	2.2577	1.3e-11	0.3227	[1.63, 2.89]
Female[T.1]	-0.7125	0.045	0.3561	[-1.41, -0.0145]
LV_log	0.3349	0.02	0.1371	[0.0661, 0.604]
age	-0.3255	0.02	0.1352	[-0.59, -0.0606]
tiv	-0.4576	0.004	0.1449	[-0.742, -0.174]

CCR2_log `MS ~ CCR_log + age + Female + tiv`

	coef	p_fdr	se	ci
Intercept	2.2539	1.3e-11	0.3223	[1.62, 2.89]
Female[T.1]	-0.7089	0.046	0.3558	[-1.41, -0.0116]
CCR_log	0.3179	0.023	0.1327	[0.0578, 0.578]
age	-0.3135	0.023	0.1334	[-0.575, -0.052]
tiv	-0.4192	0.0076	0.1414	[-0.696, -0.142]

periCSF `MS ~ periCSF + age + Female + tiv`

	coef	p_fdr	se	ci
Intercept	2.2524	8.2e-12	0.319	[1.63, 2.88]
Female[T.1]	-0.7433	0.058	0.3526	[-1.43, -0.0522]
periCSF	0.0587	0.74	0.1772	[-0.289, 0.406]
age	-0.188	0.16	0.1228	[-0.429, 0.0527]
tiv	-0.4051	0.058	0.1893	[-0.776, -0.034]

periCSF_ratio_log `MS ~ periCSF_ratio_log + age + Female + tiv`

	coef	p_fdr	se	ci
Intercept	2.2539	1.3e-11	0.3223	[1.62, 2.89]
Female[T.1]	-0.7089	0.046	0.3558	[-1.41, -0.0116]
periCSF_ratio_log	-0.3179	0.023	0.1327	[-0.578, -0.0578]

	coef	p_fdr	se	ci
age	-0.3135	0.023	0.1334	[-0.575, -0.052]
tiv	-0.4192	0.0076	0.1414	[-0.696, -0.142]

1.4 Scratch

1.4.1 Plotting CP vs CSF compartments, various controls

Patients with MS Pearson correlations of residualized thalamic nuclei and CCR2_log:

```
THALAMUS_1: r=-0.29, p=1.53e-10
medial: r=-0.397, p=3.84e-19
posterior: r=-0.315, p=2.96e-12
anterior: r=-0.118, p=1.04e-02
ventral: r=-0.0301, p=5.16e-01
```

Comparisons between thalamic nuclei and whole thalamus:

```
+ medial > THALAMUS_1: p=7.47e-06
  posterior = THALAMUS_1: p=2.44e-01
- anterior < THALAMUS_1: p=8.93e-05
- ventral < THALAMUS_1: p=4.04e-22
```

Comparisons between thalamic nuclei:

```
+ medial > posterior: p=8.02e-03
+ medial > anterior: p=2.94e-09
+ medial > ventral: p=2.05e-19
+ posterior > anterior: p=1.91e-05
+ posterior > ventral: p=4.33e-11
  anterior = ventral: p=6.97e-02
```

Patients with MS Pearson correlations of residualized thalamic nuclei and CP:

```
THALAMUS_1: r=-0.0304, p=5.12e-01
medial: r=-0.0928, p=4.47e-02
posterior: r=-0.0945, p=4.11e-02
anterior: r=0.0206, p=6.57e-01
ventral: r=0.107, p=2.04e-02
```

Comparisons between thalamic nuclei and whole thalamus:

```
+ medial > THALAMUS_1: p=1.86e-02
+ posterior > THALAMUS_1: p=5.57e-03
  anterior = THALAMUS_1: p=2.64e-01
- ventral < THALAMUS_1: p=3.37e-07
```

Comparisons between thalamic nuclei:

```
  medial = posterior: p=9.63e-01
+ medial > anterior: p=2.35e-02
+ medial > ventral: p=2.04e-06
+ posterior > anterior: p=1.66e-02
+ posterior > ventral: p=5.14e-06
  anterior = ventral: p=7.58e-02
```

1.4.2 So linters stfu about unused imports

I might want to use these ones at some point