

Thalamic nuclei segmentation from T1-weighted MRI: unifying and benchmarking state-of-the-art methods

Article

Supplemental Material

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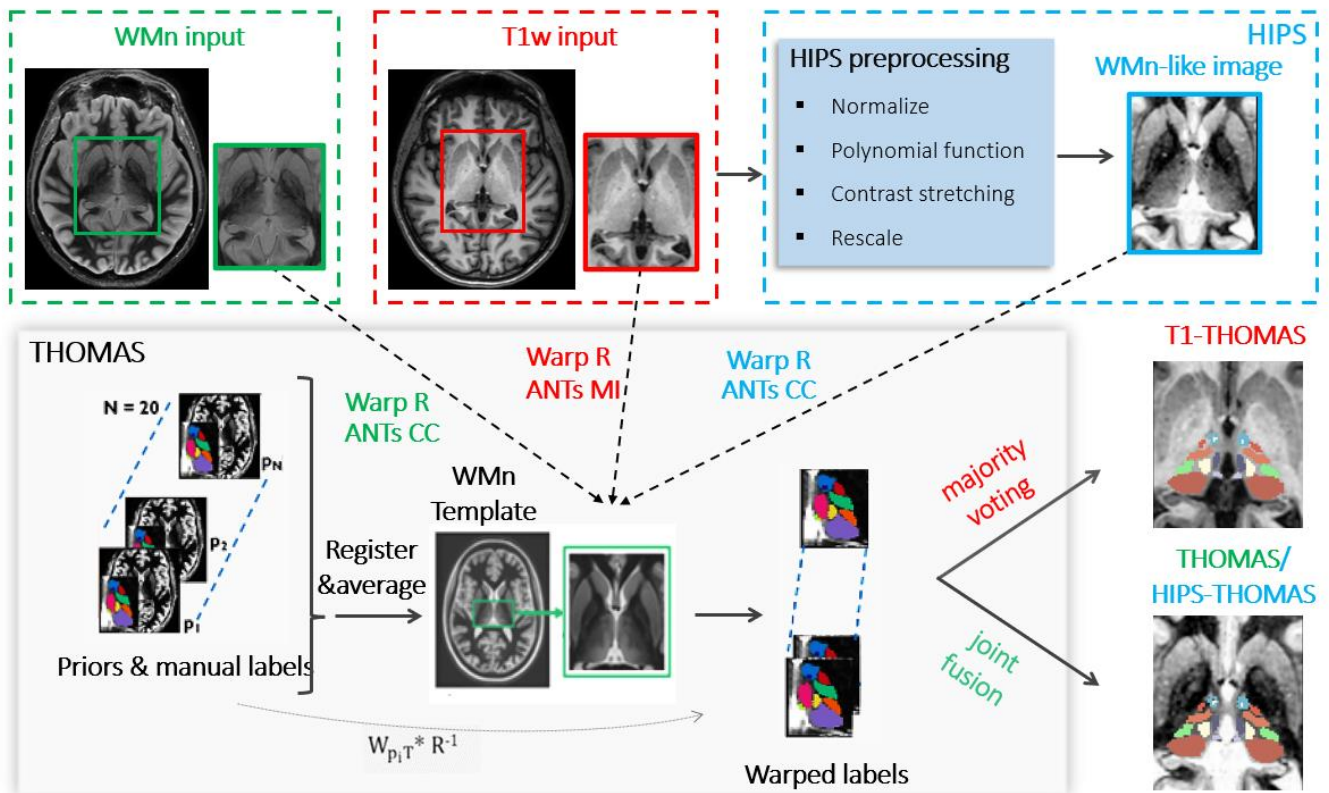
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1 **Supplementary methods**

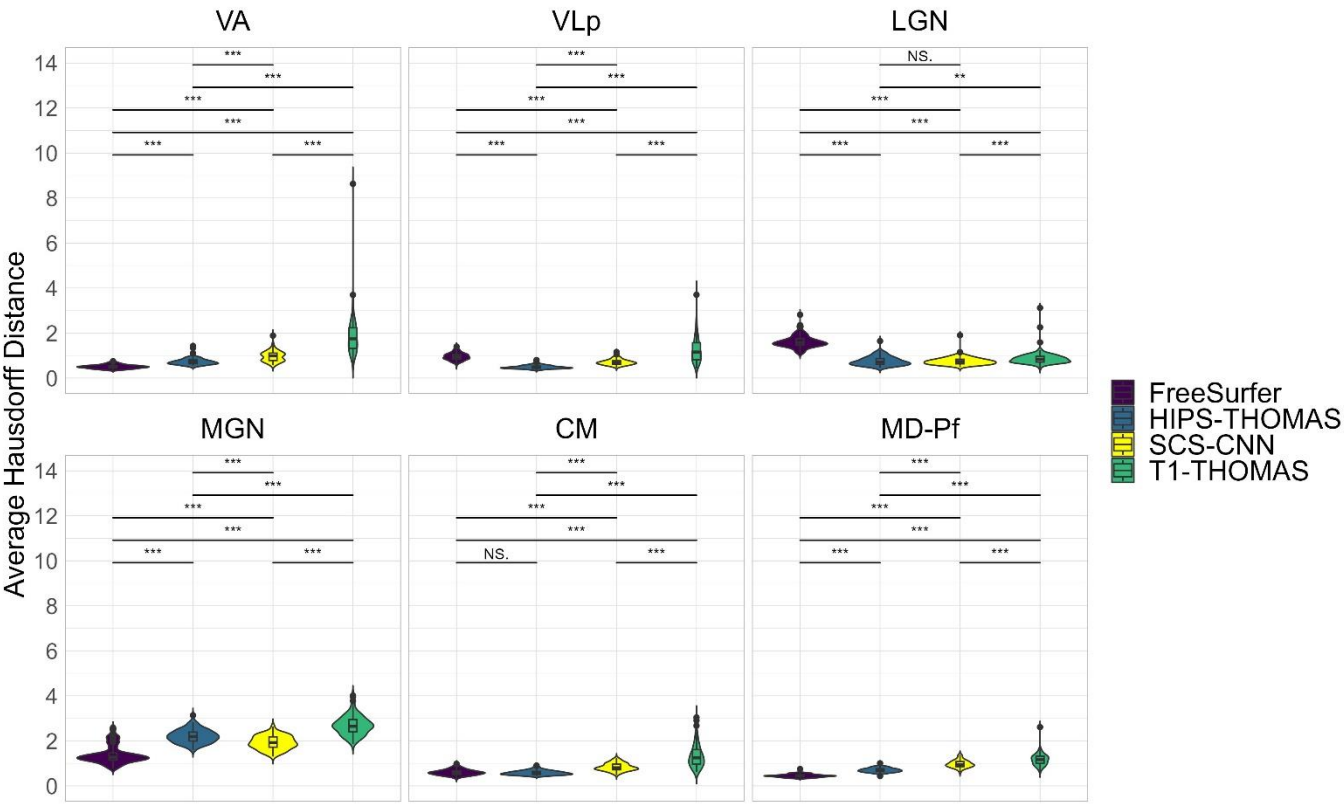
2 **THOMAS pipeline and its variants:** The original THOMAS method that was developed and
3 optimized for WMn-MPRAGE uses a set of 20 WMn-MPRAGE datasets (p_1 - p_{20}) as priors which
4 have been manually segmented using the Moral atlas as guide. The 20 priors are mutually
5 registered and averaged to create a WMn template. The input image is first cropped and
6 registered to a cropped WMn template image using ANTs nonlinear registration (R). The
7 precomputed prior-to-template space warps (W_{piT}) are combined with R^{-1} to warp the 20 prior
8 labels to input space. These labels are then combined using a joint-fusion algorithm to generate
9 a single parcellation in subject space. The WMn-MPRAGE sequence is neither part of standard
10 clinical imaging protocols nor part of extant databases such as ADNI and OASIS. To adapt
11 THOMAS for T1w data, one approach was to replace the cross-correlation (CC) metric with a
12 mutual information (MI) metric in the ANTs nonlinear registration step of THOMAS and replace
13 the joint fusion (JF) with majority voting (MV) in the label fusion step of THOMAS. We refer to this
14 variant as T1-THOMAS. To leverage the improved intrathalamic contrast of WMn-MPRAGE, a
15 polynomial synthesis method (box labelled HIPS) was used to first synthesize WMn-MPRAGE-
16 like images from T1w images before applying the THOMAS algorithm. Note that the WMn-like
17 input enables the use of the more accurate CC metric for nonlinear registration as well as the
18 more sophisticated JF algorithm compared to MV for label fusion. We call this method HIPS-
19 THOMAS. The original THOMAS method and the T1-THOMAS and HIPS-THOMAS variants are
20 shown in Supplemental Figure 1 below, using green, red, and cyan colours to differentiate the
21 three methods.



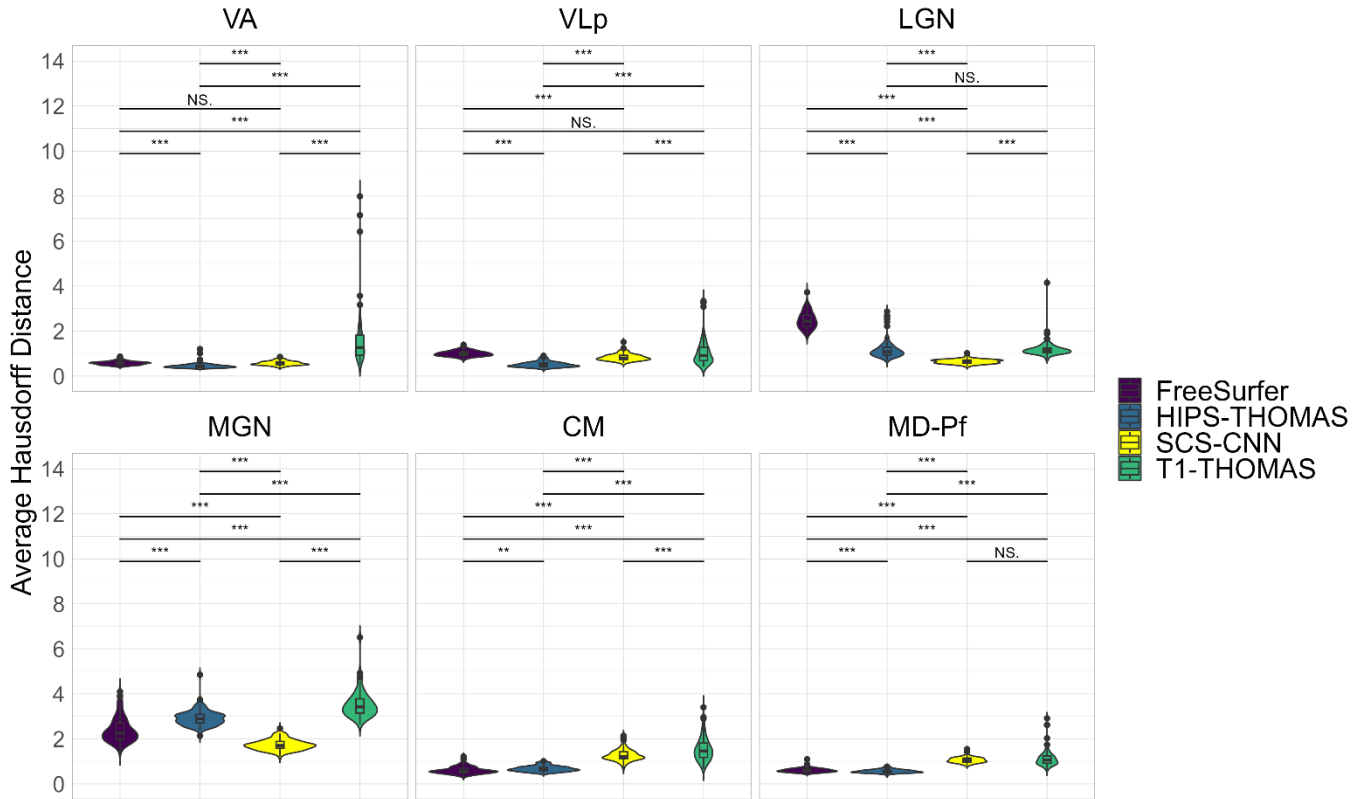
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23 Supplementary Figure 1. Schematic of THOMAS and the two variants- T1-THOMAS and HIPS-
 24 THOMAS. T1-THOMAS (grey text) uses a mutual information metric for nonlinear registration of
 25 input to template and a majority voting algorithm to combine the labels. HIPS-THOMAS (cyan
 26 text) uses a cross-correlation metric for more accurate nonlinear registration of input to template
 27 and a joint fusion algorithm for label fusion.

28 **Supplementary results**

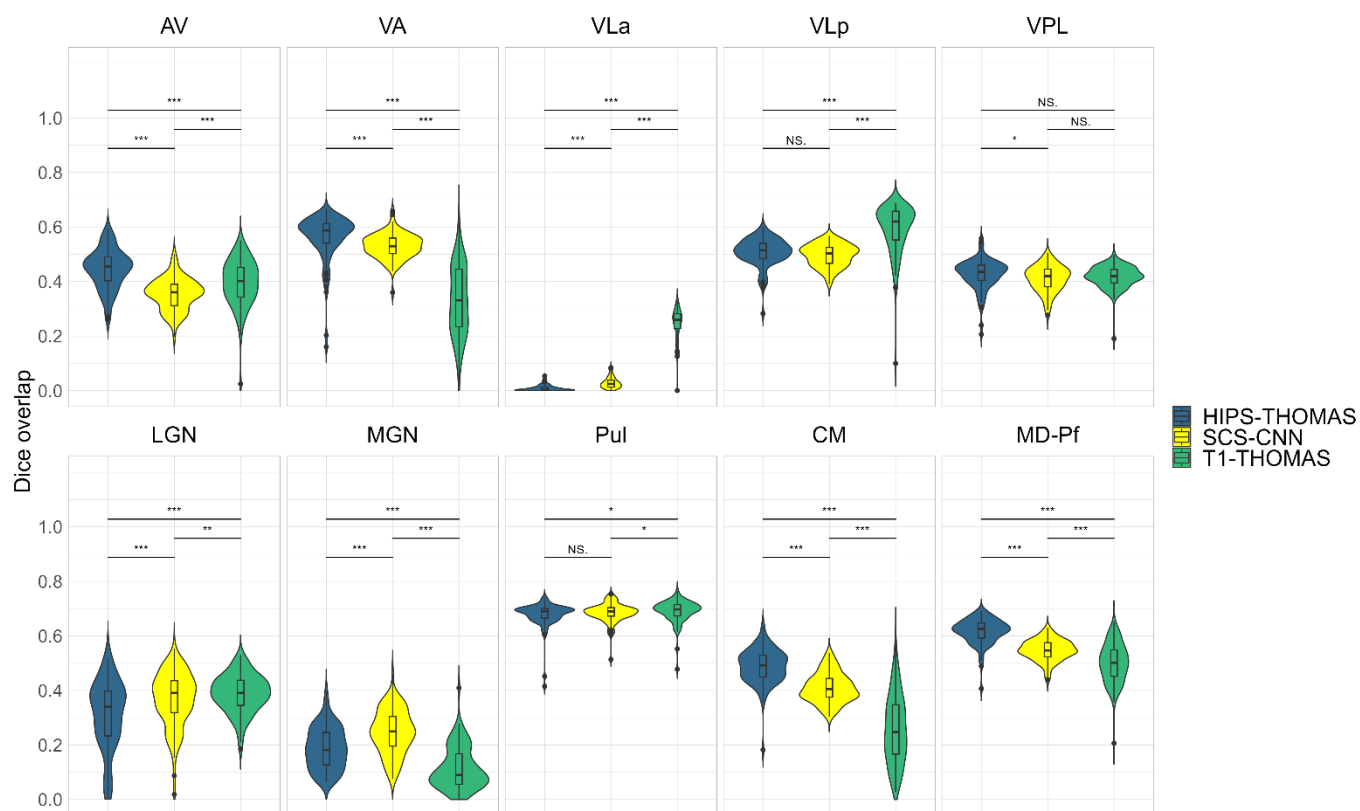


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30 Supplementary Figure 2. Violin plots of left hemisphere nuclei with significantly different Average
31 Hausdorff Distances for nuclei segmented from Human Connectome Project data using
32 FreeSurfer, HIPS-THOMAS, CNN-SCS, and T1-THOMAS approaches. Posthoc t-test results
33 (Bonferroni corrected) are presented to show pairwise difference between segmentation
34 approaches for each nucleus (**p<0.01, ***p<0.001).

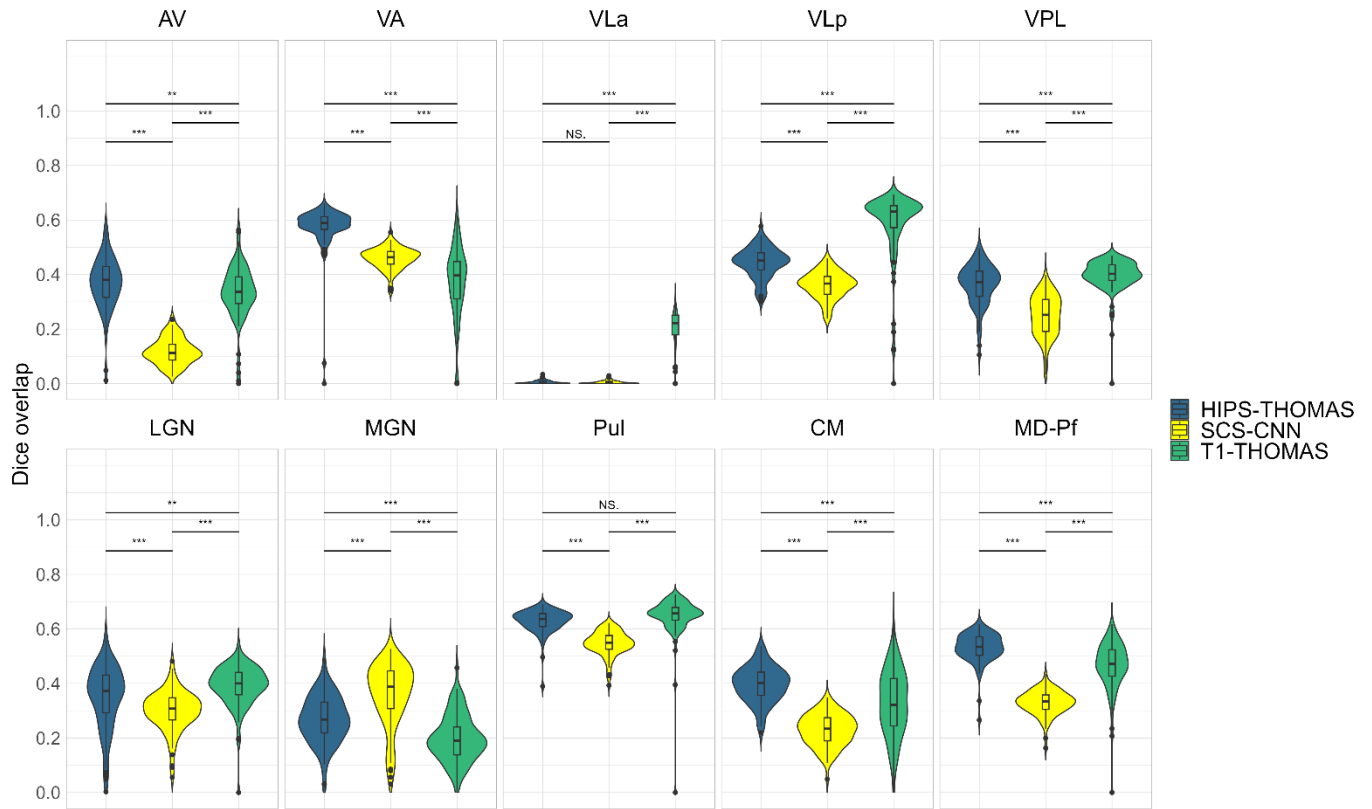


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36 Supplementary Figure 3. Violin plots of right hemisphere nuclei with significantly different Average
 37 Hausdorff Distances for nuclei segmented from Human Connectome Project data using
 38 FreeSurfer, HIPS-THOMAS, CNN-SCS, and T1-THOMAS approaches. Posthoc t-test results
 39 (Bonferroni corrected) are presented to show pairwise difference between segmentation
 40 approaches for each nucleus (**p<0.01, ***p<0.001).

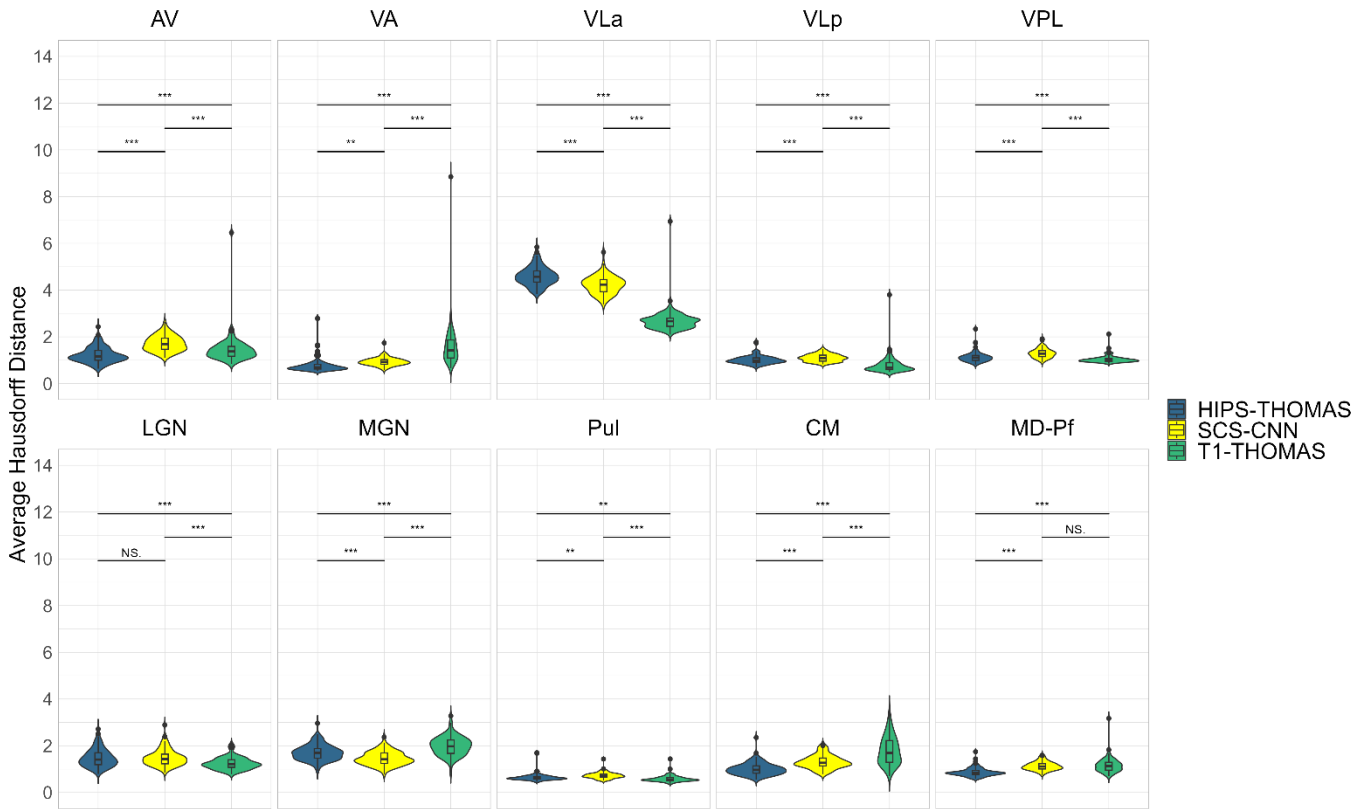


Supplementary Figure 4. Violin plots of left hemisphere Dice overlap using Freesurfer as a reference space for THOMAS-variants with Human Connectome Project data. Posthoc t-test results (Bonferroni corrected) are presented to show pairwise difference between segmentation approaches for each nucleus (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$).



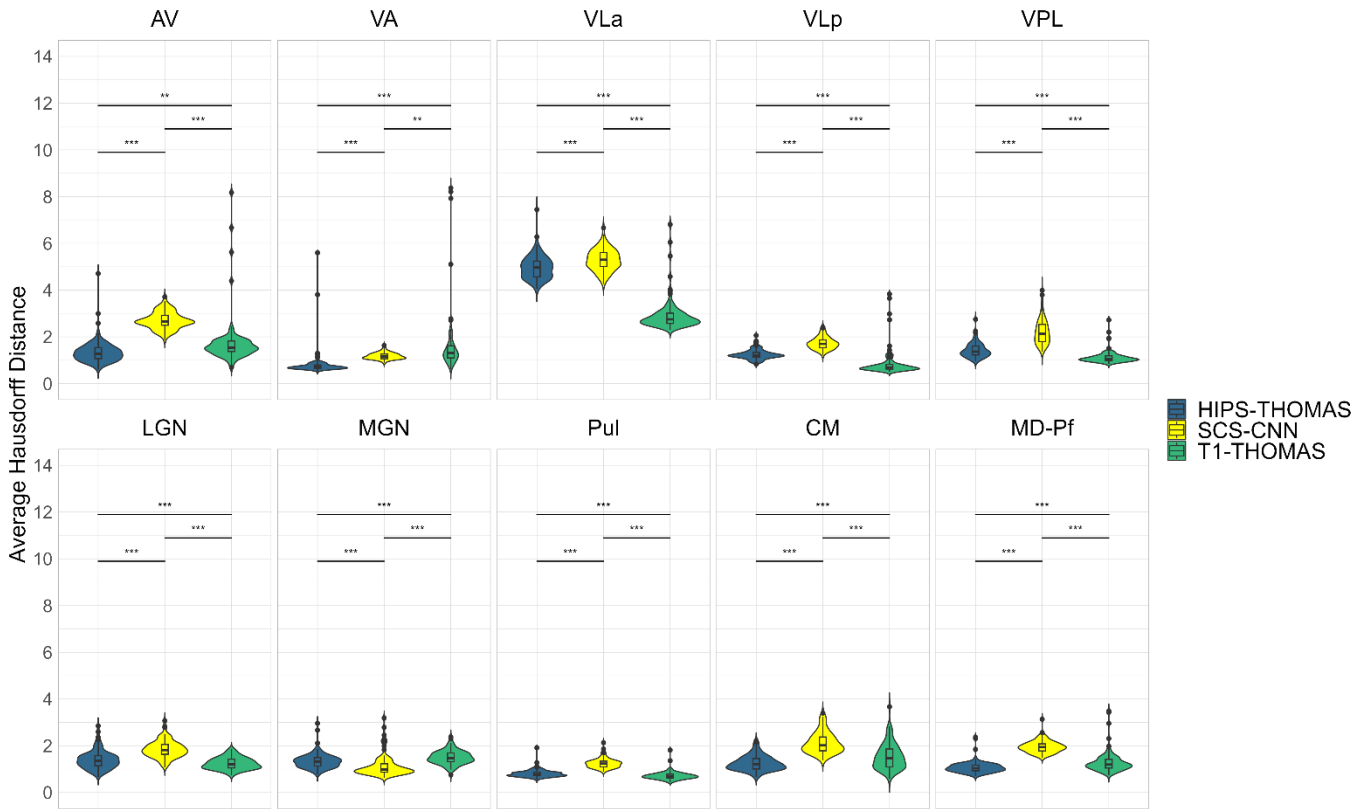
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47 Supplementary Figure 5. Violin plots of right hemisphere Dice overlap using Freesurfer as a
 48 reference space for THOMAS-variants with Human Connectome Project data. Posthoc t-test
 49 results (Bonferroni corrected) are presented to show pairwise difference between segmentation
 50 approaches for each nucleus (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$).



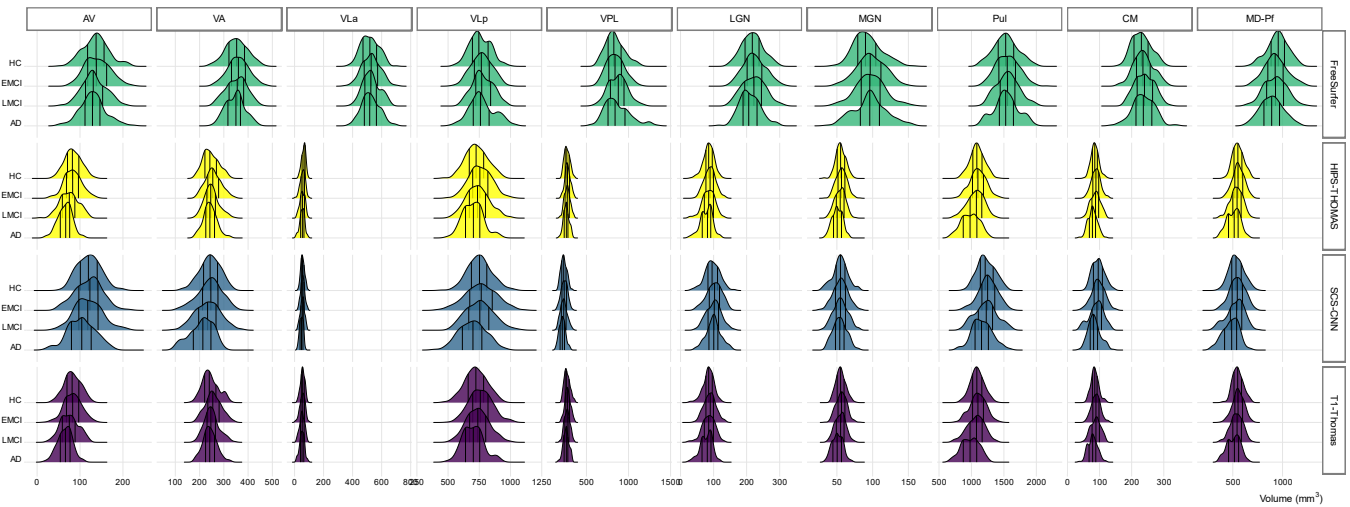
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52 Supplementary Figure 6. Violin plots of left hemisphere Average Hausdorff Distance using
 53 Freesurfer as a reference space for THOMAS-variants with Human Connectome Project data.
 54 Posthoc t-test results (Bonferroni corrected) are presented to show pairwise difference between
 55 segmentation approaches for each nucleus (*p<0.05, **p<0.01, ***p<0.001).



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57 Supplementary Figure 7. Violin plots of right hemisphere Average Hausdorff Distance using
 58 Freesurfer as a reference space for THOMAS-variants with Human Connectome Project data.
 59 Posthoc t-test results (Bonferroni corrected) are presented to show pairwise difference between
 60 segmentation approaches for each nucleus (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$).



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Supplementary Figure 8. Density plots for volumes of segmented thalamic nuclei for data from healthy controls (HC), early minor cognitive impairment (EMCI), late minor cognitive impairment (LMCI), and Alzheimer's disease (AD) using the 4 segmentation methods. Vertical lines for each density plot represent quantiles.

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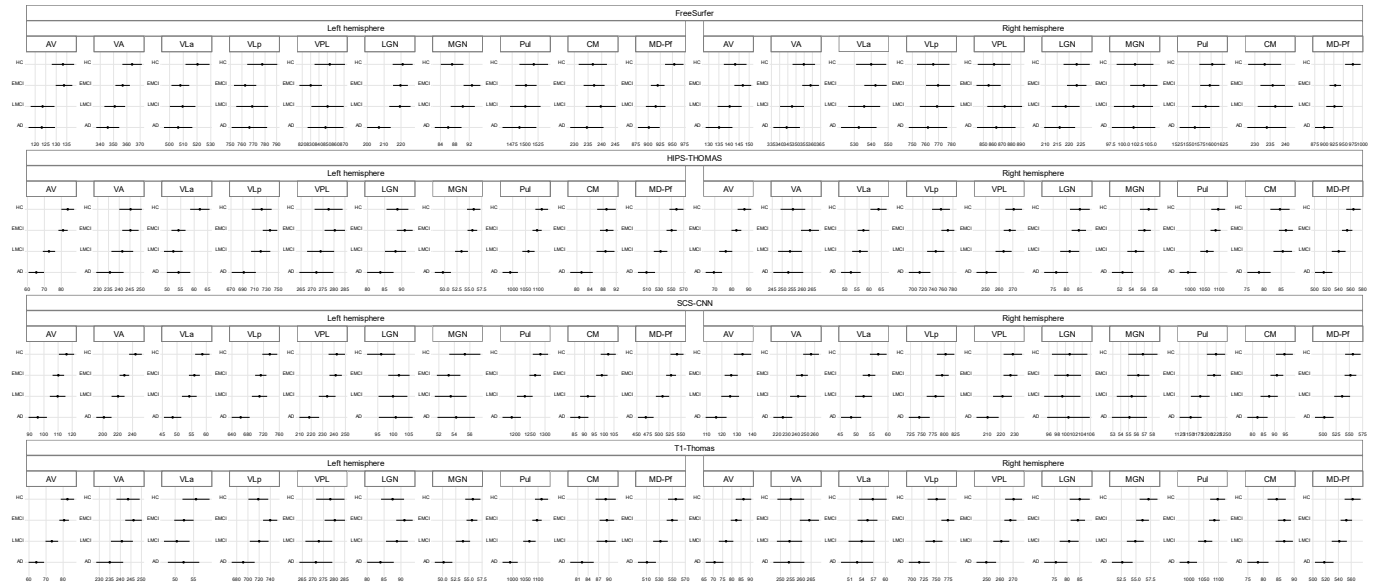
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72 Supplementary table 1. Two-way ANOVA results for HCP dataset analysis in subject space for
73 each nucleus. Significant main effects of segmentation approach (dataset) and hemisphere
74 (side), and interactions were found for all nuclei except for VPL, which did not show a main effect
75 of side.

Effect	DFn	DFd	F	p	p<.05	ges	segmentation
Dataset	2.56	251.05	138.753	3.06E-48	*	0.333	AV
side	1	98	156.403	5.10E-22	*	0.196	AV
Dataset:side	1.9	185.8	110.71	2.50E-31	*	0.199	AV
Dataset	1.35	132.2	596.277	1.24E-57	*	0.719	VA
side	1	98	286.446	7.60E-31	*	0.213	VA
Dataset:side	1.83	179.69	100.781	1.75E-28	*	0.126	VA
Dataset	2.11	206.35	85.01	1.30E-28	*	0.31	VLa
side	1	98	79.947	2.40E-14	*	0.059	VLa
Dataset:side	1.97	192.81	166.994	2.08E-42	*	0.251	VLa
Dataset	1.56	153.36	184.886	1.79E-36	*	0.498	VLp
side	1	98	18.759	3.59E-05	*	0.016	VLp
Dataset:side	1.47	143.99	55.408	3.26E-15	*	0.08	VLp
Dataset	1.72	168.96	75.557	5.91E-22	*	0.275	VPL
side	1	98	0.692	0.407		0.000709	VPL
Dataset:side	1.79	175.34	56.634	2.78E-18	*	0.1	VPL
Dataset	2.74	268.54	407.59	1.34E-95	*	0.593	LGN
side	1	98	357.482	1.83E-34	*	0.267	LGN
Dataset:side	2.57	252.24	92.152	1.79E-36	*	0.202	LGN
Dataset	1.25	122.32	188.742	5.26E-30	*	0.515	MGN
side	1	98	698.738	2.18E-46	*	0.35	MGN
Dataset:side	1.47	143.66	126.936	3.58E-27	*	0.2	MGN
Dataset	2.07	202.89	490.928	1.16E-79	*	0.531	Pul

side	1	98	268.92	7.54E-30	*	0.23	Pul
Dataset:side	1.56	152.6	35.716	2.16E-11	*	0.048	Pul
Dataset	1.65	161.51	523.075	7.27E-66	*	0.74	CM
side	1	98	277.192	2.52E-30	*	0.127	CM
Dataset:side	2.09	205.2	80.828	1.95E-27	*	0.101	CM
Dataset	1.62	159.22	641.411	5.30E-71	*	0.758	MD-Pf
side	1	98	37.576	1.85E-08	*	0.036	MD-Pf
Dataset:side	1.58	155.05	147.22	5.01E-32	*	0.202	MD-Pf