Development of Thalamocortical Structural Connectivity in Typically Developing and Psychosis Spectrum Youth

Supplement

SUPPLEMENTARY METHODS

Participants

Participants were part of the PNC (Study Accession phs000607.v3.p2), a publicly available dataset consisting of approximately 9500 individuals (age range: 8-22 years) (1). All subjects provided medical history, clinical, and cognitive data. A subset of participants completed neuroimaging data collection. Of the 1601 participants with neuroimaging data, the diffusion-weighted imaging series was collected on 1396. From this sample, 252 were excluded for a serious medical condition (n = 53), insufficient clinical data to reach a diagnosis (n = 63), or low data quality (n = 136). This resulted in a final sample of 1144 participants. We compared demographic, clinical, and cognitive characteristics between individuals included in the study and those excluded for data that did not meet our quality standards (see Data quality, below). Compared to individuals included in the study, those excluded for data quality were younger (13.1 vs. 15.3, $p < .001$), had fewer years of education (5.9 vs. 8.0, $p < .001$), and had lower global cognition (CNB) scores (-.23 vs .10, $p < .001$). Those excluded were 36 typically-developing youth, 33 psychosis-spectrum youth, and 67 youth with other psychopathology. Individual were not more likely to be excluded based on clinical diagnosis (p=.39). Complete demographics are presented in Supplementary Table S1.

Clinical assessment. Psychopathology self-report and other-report (i.e. parent) ratings and medical histories were completed using GOASSESS, a computerized structured clinical interview.

Neuroimaging Data Acquisition, Preprocessing, and Probabilistic Tractography

High resolution T1-weighted structural scans were acquired using the MPRAGE sequence on a Siemens Tim Trio 3T scanner with a 32-channel head coil with 0.93 x 0.93 x 1 mm voxels (160 slices, TR/TE = 1810/3.5, FOV = 180 x 240 x 160, matrix = 192 x 256 x 160; flip angle = 9°). Diffusion-weighted images were obtained using a twice-refocused spin-echo (TRSE) single-shot EPI sequence (TR = 8100 ms, TE = 82 ms, FOV = 240 x 240 mm, 70 slices, 1.875 x 1.875 x 2 mm resolution, gap = 0, total volumes = 71, GRAPPA factor = 3, bandwidth = 2170 Hz/pixel, PE direction = AP). The complete 64-direction diffusion-weighted imaging set was acquired as two independent 32-direction sequences (b value = 1000 s/mm^2), with a total of 7 interspersed non-diffusion-weighted images (b value = 0 s/mm^2). The two sequences were concatenated prior to preprocessing and the b=0 images were averaged.

Image processing was performed on the Vanderbilt University Institute of Imaging Science Center for Computational Imaging XNAT platform (2) and in MATLAB (version 2018a). Processing pipelines were containerized using Singularity (3) and built at SingularityHub (https://singularity-hub.org), and are available through github (https://github.com/baxpr/freesurfer-singularity/releases/tag/v1.0.0; https://github.com/baxpr/dwipre-PNC/releases/tag/v1.0.0; https://github.com/baxpr/bedpost-singularity/releases/tag/v1.0.0; https://github.com/baxpr/thaltrack-whole/releases/tag/v3.0.3). Each subject's structural T1-weighted image was segmented using FreeSurfer developmental version 6 (4). Cortical ROIs for each participant were defined based on the Desikan-Killiany (DKT) atlas (5) (see Supplementary Table S2 for list of cortical regions). Six bilateral cortical regions-of-interest (ROIs) and the thalamus were used as targets and the seed, respectively, for probabilistic tractography analysis of diffusion-weighted scans. The six cortical ROIs included the: prefrontal cortex (PFC), motor cortex/supplementary motor area, somatosensory cortex, posterior parietal cortex, temporal cortex, and occipital cortex (see Supplementary Figure S1 for an example segmentation). In addition, each subject's T1-weighted anatomical image was segmented into grey matter, white matter, and CSF tissue classes and

DARTEL normalized (6) to Montreal Neurological Institute (MNI) space using the Computational Anatomy Toolbox 12 (CAT12, version 12.5) for Statistical Parametric Mapping 12 (SPM12).

FMRIB's Diffusion Toolbox (FDT) for FSL v5.0.6 software package (http://www.fmrib.ox.ac.uk/fsl/) was used to preprocess the diffusion data and perform probabilistic tractography using the same general approach described by Behrens et al., (7). First, eddy current distortions were corrected using the Eddy tool (8). Fractional anisotropy (FA) and mean diffusivity (MD) images were calculated by fitting a diffusion tensor model at each voxel using DTIFIT. The brain was extracted using the brain extraction tool (BET) (9) and the diffusion parameters were estimated using bedpostx. This method allows for modeling of crossing fibres within each voxel of the brain.

Following preprocessing, the probabilistic fibre tracking tool (probtrackx2) was used to quantify anatomical connectivity between the thalamus and each of the six ipsilateral cortical targets. From each thalamic voxel, 5000 samples were sent through the probability distributions on principle fibre direction. With a curvature threshold of 0.2, 2000 maximum number of steps, step length 0.5 mm, and subsidiary fibre volume threshold of 0.01. Modified Euler streaming and distance correction was used to account for the fact that connectivity distribution drops with distance from the seed mask. The left and right hemispheres were analyzed separately and the contralateral hemisphere was included as an exclusion mask to eliminate streamlines reaching the contralateral hemisphere. For each region, the cortical target was included as a stop mask to ensure that streamlines stopped when reaching the target, and the remaining cortical ROIs from the ipsilateral hemisphere were included as exclusion masks to ensure that only fibres reaching the cortical target directly were included.

From probtrackx2, seed-to-target voxel-wise images were generated, one for each cortical target, in which the value of each voxel within the seed mask (i.e. thalamus) represents the number of samples seeded from that voxel reaching the relevant target mask. The connectivity of each cortical region with the thalamus was calculated by dividing the number of samples reaching that region, summed across all voxels in the thalamus, by the total number of samples within the thalamus reaching all cortical regions. This is a measure of total tractography-defined connectivity from the thalamus to a specific cortical area after controlling for overall connectivity of the thalamus. These values, expressed as "percent total connectivity", served as the dependent variables for the primary analysis. Dividing by total thalamus seeds effectively controls for the potential influence of volume differences across groups.

Each participants' probabilistic tractography map, created as a result of the thalamus-to-cortical targets analysis, were carefully checked for coverage of thalamocortical white matter pathways, normalized using the waytotal value, thresholded for error (1.5%), warped to MNI space using the normalization parameters derived from CAT12, and averaged into group maps representing the spatial overlap of each thalamocortical tract. Group maps were carefully visually inspected and a threshold of >75% participant overlap was selected to capture individual spatial variation in tracts while minimizing the inclusion of voxels with low probability of lying in the tract of interest. Thresholded group maps were transformed to each participant's diffusion space and mean diffusion values (FA, MD) were extracted. Group masks of each thalamocortical tract are presented in Supplementary Figure S2.

Data quality

Prior to preprocessing, all diffusion and T1 scans were carefully visually inspected, blind to demographic and clinical data, for acquisition issues (i.e., partial brain coverage or acquisition artifacts), and 2 participants were excluded. Next, the motion metric of mean relative displacement (rDisp) and the contrast-to-noise ratio (CNR) were calculated. Participants were excluded for excessive motion, defined as a mean rDisp value $\geq$ the 95th percentile (rDisp $\geq$ .73), or for a CNR value $\leq$ the 5th percentile (CNR $\leq$ .46). 80 participants were excluded for excessive motion/low CNR. Motion (rDisp) was included in all analyses as a covariate of no interest. Motion and CNR metrics for included participants are displayed in Supplementary Table S3. Finally, preprocessed diffusion and T1 scans were visually inspected for processing failures (i.e., skull-stripping, coregistration, FreeSurfer, or processing failure), and 54 participants were excluded.

SUPPLEMENTARY RESULTS

Thalamocortical Percent Total Connectivity

Percent total connectivity distributions for the thalamus to each cortical ROI are presented in Supplementary Figure S3A. Streamline counts distributions for the thalamus to each cortical ROI are presented in Supplementary Figure S3B.

Age effects. Age effects of percent total connectivity for each cortical ROI with the thalamus, broken down by hemisphere, are presented in Supplementary Figure S4. Full statistical results are presented in Supplementary Table S4. Linear effects of age were more pronounced in the right hemisphere and largely consistent across hemispheres, with the exception of increased thalamic-motor cortex connectivity, which showed no relationship with age in the left hemisphere.

We performed planned secondary analyses on streamline counts to determine if age effects were consistent across analyses. Age effects of streamline counts for each cortical ROI with the thalamus are presented in Supplementary Figure S5. Full statistical results for streamline counts are presented in Supplementary Table S5. Regression models were repeated as in the primary analysis, with streamline count as the dependent variable, and with an additional covariate of total streamline count for any connection between the thalamus and cortex. Linear effects of age were consistent across analyses. Streamline counts increased linearly with age for the motor and somatosensory cortex, and decreased linearly with age for the temporal and occipital cortex. No other connections showed a linear effect of age for thalamocortical streamline counts. There were also no quadratic effects of age for streamline counts.

Sex effects. Percent total connectivity of each cortical ROI with the thalamus, broken down by hemisphere and sex, are presented in Supplementary Table S6. Females had greater thalamic-occipital cortex percent total connectivity compared to males. There was a trend for greater thalamic-somatosensory cortex percent total connectivity in males than females (p = .01) that did not reach significance at a Bonferroni-corrected $p = .008$. Sex effects were more pronounced in the right hemisphere. Secondary analyses of streamline counts revealed stronger effects compared to the percent total connectivity analysis, with greater thalamic-occipital cortex streamline counts in females and greater thalamic-somatosensory streamline counts in males, and an additional effect of greater thalamic-motor cortex streamline counts in males. Secondary analyses of streamline counts by sex are presented in Supplementary Table S7.

Group differences. Primary analyses for effects of group, presented in Supplementary Table S8, showed no between-group differences in thalamic percent total connectivity for any cortical ROI. Results were consistent across hemispheres. Secondary analyses of streamline counts, presented in Supplementary Table S9, also showed no between-group differences. Mean volumes of the thalamus and cortical ROIs used as seed/target masks for probabilistic tractography are presented in Supplementary Table S10. Cortical and thalamic ROI volumes were larger in the typically developing group compared to the psychosis spectrum group. Volume differences were controlled in the primary analyses by dividing total connectivity by all thalamic connections to any ROI.

Interaction effects. There was a linear interaction between age and sex, with older females showing more thalamic-occipital percent total connectivity than males. The interaction between linear age and sex for total thalamic-occipital connectivity is presented in Supplementary Figure S6.

Cognitive correlates. There were no correlations between cognitive function, as measured by CNB composite scores, and total thalamic connectivity for any cortical ROI. Cognitive correlations are presented in Supplementary Table S11.

Thalamocortical White Matter Microstructure

White matter microstructure (FA) distributions for the thalamus to each cortical ROI are presented in Supplementary Figure S3C.

Age effects. Age effects of FA and MD for each bilateral cortical ROI are presented in Figure 3 and Supplementary Figure S7, respectively. Age effects of FA for each cortical ROI with the thalamus, broken down by hemisphere, are presented in Supplementary Figure S8. Complete statistical results for FA and MD analyses are presented in Supplementary Table S12 and S13, respectively. White matter microstructure, measured as mean FA within thalamocortical tracts, increased linearly with age for all thalamocortical tracts. For each tract, older participants had higher FA values than younger participants. White matter microstructure in tracts linking the thalamus with the motor, somatosensory, posterior parietal, and occipital cortex also showed quadratic associations with age. Higher FA values were observed in late adolescence, while early childhood/early adulthood was associated with lower FA values. Quadratic effects are presented in Supplementary Figure S9. Linear and quadratic effects of age were consistent across hemispheres and when excluding gray matter voxels from tract masks. Follow-up analysis showed that MD values decreased linearly with age across regions. For each region, older participants had lower MD values than younger participants. Follow-up analyses also showed quadratic associations between MD and age across regions (trend effect in thalamic-somatosensory tract). For each pathway, lower MD values were observed in late adolescence, while early childhood/early adulthood was associated with higher MD values. Quadratic effects are presented in Supplementary Figure S10.

Sex effects. White matter microstructure of each cortical ROI with the thalamus, broken down by hemisphere and sex, are presented in Supplementary Tables S14 and S15. Males had higher FA values compared to females in tracts linking the thalamus with the prefrontal, motor, somatosensory, posterior parietal, and occipital cortex. Higher FA values in males were consistent across hemispheres although more pronounced in the left hemisphere. Follow-up analyses showed that males also had lower mean MD in most white matter tracts, with the exception of the thalamic-occipital tract. Sex effects were consistent when excluding gray matter voxels from tract masks.

Group differences. Thalamocortical white matter microstructure analyses for effects of group, presented in Supplementary Tables S16 and S17, showed that typically-developing youth had higher FA values compared to psychosis-spectrum youth in all tracts linking the thalamus and the cortex. Results were consistent across hemispheres and when excluding gray matter voxels from tract masks. Follow-up analysis showed that typically-developing youth also tended to have lower MD values compared to psychosis-spectrum youth across tracts, with significantly lower values in the thalamic-somatosensory and thalamic-posterior parietal tract.

Sensitivity analysis for whole-brain FA. We performed a sensitivity analysis to determine whether age, sex, and group FA effects in thalamocortical tracts were associated with overall whole brain differences in FA. Whole brain FA values were calculated for each participant and entered into each analysis as a covariate of no interest. Statistical results are presented in Supplementary Table S18. Age effects were consistent with the primary analysis across all brain regions except the temporal cortex, which did not show a significant effect of age when controlling for whole brain FA (p = .03). Sex and group effects were consistent with those found in the primary analysis.

Sensitivity analyses for race, parental education, and CNR. Because race, parental education, and CNR differed by diagnostic group, we performed sensitivity analyses to determine whether between-group differences in thalamocortical FA were associated with between-group differences in these demographic and quality characteristics. For each analysis, a matched sample of participants was randomly selected in SAS (PROC SURVEYSELECT) from each diagnostic group (race-matched sample = 96 per diagnostic group, parental education-matched sample = 95 per diagnostic group, CNR-matched sample = 96 per diagnostic group). Statistical results are presented in Supplementary Table S19. Effect sizes for the sensitivity analyses were largely consistent with effect sizes found in the primary analysis of the full sample (ES range:

.011 - .013), with similar or larger between-group effects in all sensitivity analyses (ES range: .010 - .037) with the exception of the somatosensory cortex in the parental education-matched analysis, which was lower (ES = .006) than in the primary analysis (ES = .013).

Interaction effects. There was an interaction between linear age and sex in tracts connecting the thalamus with the prefrontal, motor, somatosensory, and posterior parietal cortex. Older males had higher FA values in thalamic tracts than older females. Interactions are presented in Supplementary Figure S11. Full statistical results are presented in Supplementary Table S20. There were no significant interactions between age and group, or sex and group (all *p*s $\geq$ .10). For reference, FA values are plotted for age by group in Supplementary Figure S12.

Supplementary Table S1. Sample characteristics for individuals included vs. excluded from study

Demographics	**Included**	**Excluded**	**F/X²**	**df**	**p**
Sample size, n	1144	136	--	--	--
Age, years ± SD	15.3 ± 3.4	13.1 ± 3.5	49.67	1,1279	<.001*
Sex, % male	46	52	1.79	1	.18
Race, % W:AA:O	47:43:10	39:13:48	2.82	2	.24
Education, years ± SD	8.0 ± 3.2	5.9 ± 3.2	51.19	1,1279	<.001*
Parental education, years ± SD	14.1 ± 2.3	13.8 ± 2.2	1.37	1,1272	.24
Neuropsychological Functioning					
Global cognition, z-score	0.10 ± .5	-0.23 ± .6	46.26	1,1279	<.001*
WRAT, standard score	100.6 ± 15.1	102.7 ± 16.4	1.98	1,1277	.16

Note: Asterisk denotes significant *p*-value. Standard deviation (SD); White (W); African-American (AA); Other (O).

Supplementary Table S2. Cortical structures included in each cortical region of interest used as a target in probabilistic tractography

Prefrontal Cortex	Label (R, L)
Caudal Anterior Cingulate	1002, 2002
Lateral Orbitofrontal	1012, 2012
Medial Orbitofrontal	1014, 2014
Pars Opercularis	1018, 2018
Pars Orbitalis	1019, 2019
Pars Triangularis	1020, 2020
Rostral Anterior Cingulate	1026, 2026
Rostral Middle Frontal	1027, 2027
Superior Frontal	1028, 2028
Motor Cortex	
Caudal Middle Frontal	1003, 2003
Paracentral	1017, 2017
Precentral	1024, 2024
Somatosensory Cortex	
Postcentral	1022, 2022
Posterior Parietal Cortex	
Inferior Parietal	1008, 2008
Isthmus Cingulate	1010, 2010
Posterior Cingulate	1023, 2023
Precuneus	1025, 2025
Superior Parietal	1029, 2029
Supramarginal	1031, 2031
Temporal Cortex	
Entorhinal	1006, 2006
Fusiform	1007, 2007
Inferior Temporal	1009, 2009
Middle Temporal	1015, 2015
Parahippocampal	1016, 2016
Superior Temporal	1030, 2030
Transverse Temporal	1034, 2034
Occipital Cortex	
Cuneus	1005, 2005
Lateral Occipital	1011, 2011
Lingual	1013, 2013
Pericalcarine	1021, 2021

Note: R=Right; L=Left

Supplementary Table S3. Quality metrics.

	Typically Developing	Psychosis Spectrum	Other Psychopathology	F	df	p	Post-Hoc
Relative displacement (rDisp), mean ± SD	0.21 ± 0.13	0.20 ± 0.10	0.20 ± 0.12	0.48	2,1143	.62	--
CNR, mean ± SD	0.69 ± 0.08	0.66 ± 0.07	0.69 ± 0.07	16.29	2,1143	<.001*	TD,O>PS

Note: Asterisk denotes significant *p*-value. Standard deviation (SD); contrast-to-noise ratio (CNR).

Supplementary Table S4. Linear and quadratic effects of age for thalamocortical percent total connectivity

	Linear Effects				Quadratic Effects			
Cortical Region	F	df	p	Partial η^2	F	df	p	Partial η^2
Average of left and right hemispheres								
Prefrontal	0.11	3,1140	.74	.000	0.79	4,1139	.37	.001
Motor	12.62	3,1140	<.001	.011	0.19	4,1139	.66	.000
Somatosensory	21.48	3,1140	<.001	.019	0.41	4,1139	.52	.000
Temporal	19.93	3,1140	<.001	.017	0.02	4,1139	.88	.000
Posterior parietal	2.83	3,1140	.09	.003	0.25	4,1139	.62	.000
Occipital	11.29	3,1140	<.001	.010	1.01	4,1139	.32	.001
Left								
Prefrontal	0.06	3,1140	.81	.000	3.12	4,1139	.08	.003
Motor	0.41	3,1140	.52	.000	5.59	4,1139	.02	.005
Somatosensory	12.68	3,1140	<.001	.011	0.01	4,1139	.91	.000
Temporal	2.32	3,1140	.13	.002	0.75	4,1139	.39	.001
Posterior parietal	0.76	3,1140	.38	.001	0.46	4,1139	.50	.000
Occipital	2.82	3,1140	.09	.003	0.50	4,1139	.48	.000
Right								
Prefrontal	0.08	3,1140	.77	.000	0.21	4,1139	.65	.000
Motor	30.84	3,1140	<.001	.026	2.44	4,1139	.12	.002
Somatosensory	15.00	3,1140	<.001	.013	1.58	4,1139	.21	.001
Temporal	44.99	3,1140	<.001	.038	2.50	4,1139	.11	.002
Posterior parietal	3.75	3,1140	.05	.003	0.01	4,1139	.92	.000
Occipital	21.68	3,1140	<.001	.019	1.15	4,1139	.28	.001

Note: Asterisk denotes significant *p*-value. Sex and rDisp are included as effects of no interest.

Supplementary Table S5. Linear effects of age for thalamocortical streamline counts

Cortical Region	F	df	p	Partial η^2
Average of left and right hemispheres				
Prefrontal	0.01	4,1139	.93	.000
Motor	21.81	4,1139	<.001*	.018
Somatosensory	28.03	4,1139	<.001*	.024
Temporal	27.38	4,1139	<.001*	.024
Posterior parietal	2.78	4,1139	.10	.002
Occipital	13.52	4,1139	<.001*	.012
Left				
Prefrontal	0.12	4,1139	.74	.000
Motor	0.35	4,1139	.56	.000
Somatosensory	12.58	4,1139	<.001*	.011
Temporal	3.02	4,1139	.08	.003
Posterior parietal	0.70	4,1139	.40	.001
Occipital	2.19	4,1139	.14	.002
Right				
Prefrontal	0.07	4,1139	.79	.000
Motor	39.99	4,1139	<.001*	.034
Somatosensory	22.18	4,1139	<.001*	.019
Temporal	43.89	4,1139	<.001*	.037
Posterior parietal	3.51	4,1139	.06	.003
Occipital	20.60	4,1139	<.001*	.018

Note: Asterisk denotes significant *p*-value. Sex, rDisp, and total streamline count are included as effects of no interest.

Supplementary Table S6. Thalamocortical percent total connectivity values by sex

Cortical Region	Male LSMean ± STDERR	Female LSMean ± STDERR	F	df	p	Partial η^2
Average of left and right hemispheres						
Prefrontal	45.4 ± 0.4	45.1 ± 0.3	0.23	4,1134	.63	.000
Motor	14.1 ± 0.2	13.8 ± 0.2	1.03	4,1134	.31	.001
Somatosensory	9.9 ± 0.2	9.4 ± 0.1	6.46	4,1134	.01	.006
Temporal	4.5 ± 0.1	4.7 ± 0.1	1.89	4,1134	.17	.002
Posterior parietal	18.1 ± 0.2	18.1 ± 0.3	0.01	4,1134	.91	.000
Occipital	8.0 ± 0.2	8.8 ± 0.2	10.83	4,1134	.001*	.009
Left						
Prefrontal	42.5 ± 0.4	42.1 ± 0.4	0.47	4,1134	.49	.000
Motor	11.9 ± 0.2	12.3 ± 0.2	0.73	4,1134	.39	.001
Somatosensory	10.6 ± 0.2	10.1 ± 0.2	3.05	4,1134	.08	.003
Temporal	5.2 ± 0.2	5.2 ± 0.2	0.07	4,1134	.79	.000
Posterior parietal	18.8 ± 0.3	18.9 ± 0.3	0.02	4,1134	.90	.000
Occipital	11.0 ± 0.3	11.5 ± 0.2	2.36	4,1134	.13	.002
Right						
Prefrontal	48.3 ± 0.4	48.2 ± 0.4	0.00	4,1134	.96	.000
Motor	16.3 ± 0.2	15.4 ± 0.2	6.80	4,1134	.009	.006
Somatosensory	9.2 ± 0.2	8.7 ± 0.2	5.64	4,1134	.02	.005
Temporal	3.8 ± 0.1	4.2 ± 0.1	5.57	4,1134	.02	.005
Posterior parietal	17.4 ± 0.2	17.4 ± 0.2	0.00	4,1134	.96	.000
Occipital	5.1 ± 0.2	6.1 ± 0.2	22.32	4,1134	<.001*	.019

Note: Asterisk denotes significant *p*-value. Age, quadratic age, and rDisp are included as effects of no interest.

Supplementary Table S7. Thalamocortical streamline counts by sex

Cortical Region	Male	Female	F	df	p	Partial
	LSMean ± STDERR	LSMean ± STDERR				η^2
Average of left and right hemispheres						
Prefrontal	274306634 ± 2150673	273940216 ± 1987802	0.02	5,1138	.90	.000
Motor	85964701 ± 1201399	80893301 ± 1110416	9.41	5,1138	.002*	.008
Somatosensory	58517880 ± 809018	54203846 ± 747751	15.01	5,1138	<.001*	.013
Temporal	26304034 ± 704721	28604670 ± 651353	5.63	5,1138	.02	.005
Posterior parietal	108267707 ± 1576674	109694962 ± 1457272	0.43	5,1138	.51	.000
Occipital	46075024 ± 1026039	52098985 ± 948337	18.20	5,1138	<.001*	.016
Left						
Prefrontal	232157699 ± 2594971	231439131 ± 2399636	0.04	5,1138	.84	.000
Motor	64829457 ± 1211246	63590273 ± 1120070	0.56	5,1138	.46	.001
Somatosensory	56998878 ± 1026506	53043994 ± 949236	7.88	5,1138	.005*	.007
Temporal	28344921 ± 973648	29746229 ± 900357	1.10	5,1138	.30	.001
Posterior parietal	102518900 ± 1851989	103418604 ± 1712581	0.13	5,1138	.72	.000
Occipital	59554657 ± 1351161	63166282 ± 1249453	3.79	5,1138	.05	.003
Right						
Prefrontal	316003175 ± 2900087	316829068 ± 2680149	0.04	5,1138	.84	.000
Motor	106719095 ± 1547715	98522772 ± 1430339	14.78	5,1138	<.001*	.013
Somatosensory	60056354 ± 1043826	55347007 ± 964664	10.73	5,1138	.001*	.009
Temporal	24721066 ± 791898	27070608 ± 731841	4.64	5,1138	.03	.004
Posterior parietal	114270071 ± 2031386	115753986 ± 1877328	0.28	5,1138	.60	.000
Occipital	32697687 ± 1072055	40944007 ± 990752	31.19	5,1138	<.001*	.027

Note: Asterisk denotes significant *p*-value. Age, quadratic age, rDisp, and total streamline count are included as effects of no interest.

Supplementary Table S8. Thalamocortical percent total connectivity values by group

Cortical Region	Typically Developing LSMean ± STDERR	Psychosis Spectrum LSMean ± STDERR	Other Psychopathology LSMean ± STDERR	F	df	p	Partial η^2	Post-Hoc
Average of left and right hemispheres								
Prefrontal	45.3 ± 0.5	45.4 ± 0.5	45.1 ± 0.4	0.08	6,1137	.92	.000	--
Motor	14.2 ± 0.3	14.2 ± 0.3	13.7 ± 0.2	1.64	6,1137	.20	.003	--
Somatosensory	9.6 ± 0.2	9.8 ± 0.2	9.6 ± 0.2	0.32	6,1137	.72	.001	--
Temporal	4.7 ± 0.2	4.5 ± 0.2	4.6 ± 0.1	0.40	6,1137	.67	.001	--
Posterior parietal	18.0 ± 0.3	17.7 ± 0.3	18.5 ± 0.3	1.60	6,1137	.20	.003	--
Occipital	8.2 ± 0.2	8.4 ± 0.2	8.5 ± 0.2	0.75	6,1137	.47	.001	--
Left								
Prefrontal	42.5 ± 0.6	42.2 ± 0.6	42.1 ± 0.5	0.12	6,1137	.89	.000	--
Motor	12.5 ± 0.3	12.3 ± 0.3	11.7 ± 0.2	2.10	6,1137	.12	.004	--
Somatosensory	10.3 ± 0.3	10.5 ± 0.3	10.3 ± 0.2	0.30	6,1137	.74	.001	--
Temporal	5.3 ± 0.2	5.1 ± 0.2	5.2 ± 0.2	0.25	6,1137	.78	.000	--
Posterior parietal	18.5 ± 0.4	18.6 ± 0.4	19.2 ± 0.4	0.91	6,1137	.40	.002	--
Occipital	10.9 ± 0.3	11.2 ± 0.3	11.5 ± 0.3	1.00	6,1137	.37	.002	--
Right								
Prefrontal	48.1 ± 10.5	48.5 ± 10.5	48.2 ± 9.3	0.16	6,1137	.85	.000	--
Motor	15.8 ± 6.1	16.2 ± 5.8	15.6 ± 5.3	0.66	6,1137	.52	.001	--
Somatosensory	8.8 ± 3.7	9.1 ± 4.2	8.9 ± 3.7	0.12	6,1137	.89	.000	--
Temporal	4.2 ± 3.0	3.8 ± 2.6	4.0 ± 2.8	0.28	6,1137	.75	.001	--
Posterior parietal	17.5 ± 7.1	16.8 ± 6.8	17.8 ± 6.9	1.66	6,1137	.19	.003	--
Occipital	5.6 ± 3.6	5.6 ± 3.8	5.6 ± 3.6	0.29	6,1137	.75	.001	--

Note: Asterisk denotes significant *p*-value. Age, quadratic age, sex, and rDisp are included as effects of no interest.

Supplementary Table S9. Thalamocortical streamline counts by group

Cortical Region	Typically Developing LSMean ± STDERR	Psychosis Spectrum LSMean ± STDERR	Other Psychopathology LSMean ± STDERR	F	df	p	Partial η^2	Post-Hoc
Average of left and right hemispheres								
Prefrontal	273797762 ± 2792829	275985309 ± 2739406	273090931 ± 2196641	0.35	7,1136	.71	.001	--
Motor	85193457 ± 1559069	83507653 ± 1529246	82250532 ± 1226253	1.11	7,1136	.33	.002	--
Somatosensory	56570054 ± 1050828	56028303 ± 1030727	56448899 ± 826507	0.08	7,1136	.93	.000	--
Temporal	28124866 ± 915121	27221322 ± 897616	27181668 ± 719769	0.37	7,1136	.69	.001	--
Posterior parietal	108095122 ± 2045282	106746773 ± 2006158	111035513 ± 1608674	1.55	7,1136	.21	.003	--
Occipital	47654720 ± 1331834	49946620 ± 1306358	49428436 ± 1047526	0.83	7,1136	.44	.002	--
Left								
Prefrontal	231233270 ± 3384570	233174802 ± 3317882	231242958 ± 2659788	0.12	7,1136	.89	.000	--
Motor	66354842 ± 1577885	64149395 ± 1546795	62881022 ± 1239991	1.50	7,1136	.22	.003	--
Somatosensory	55666308 ± 1338806	54729739 ± 1312426	54803993 ± 1052110	0.16	7,1136	.85	.000	--
Temporal	29578324 ± 1269909	28831684 ± 1244888	28847908 ± 997967	0.12	7,1136	.89	.000	--
Posterior parietal	101941107 ± 2414494	101617521 ± 2366920	104524108 ± 1897447	0.60	7,1136	.55	.001	--
Occipital	59630662 ± 1761443	61901372 ± 1726736	62104524 ± 1384242	0.67	7,1136	.51	.001	--
Right								
Prefrontal	316104664 ± 3756065	319084995 ± 3685662	314837326 ± 2959805	0.41	7,1136	.67	.001	--
Motor	104026625 ± 2004342	102945849 ± 1966773	101506909 ± 1579435	0.51	7,1136	.60	.001	--
Somatosensory	57478825 ± 1352251	57319302 ± 1326905	58098679 ± 1065583	0.13	7,1136	.88	.000	--
Temporal	26893670 ± 1025397	25347655 ± 1006178	25623801 ± 808020	0.67	7,1136	.51	.001	--
Posterior parietal	114544091 ± 2628032	111596280 ± 2578773	117585984 ± 2070908	1.67	7,1136	.19	.003	--
Occipital	35419574 ± 1387784	38173366 ± 1361772	36814748 ± 1093584	0.97	7,1136	.38	.002	--

Note: Asterisk denotes significant *p*-value. Age, quadratic age, sex, rDisp, and total streamline count are included as effects of no interest.

Supplementary Table S10. Seed/target Volumes (mm^3)

Brain Region	Region of Interest	Typically Developing	Psychosis Spectrum	Other Psychopathology	F	df	p	Post-Hoc
		Mean ± SD	Mean ± SD	Mean ± SD				
Average of left and right hemispheres								
Thalamus	Seed	6921 ± 711	6678 ± 739	6816 ± 723	9.13	2,1143	<.001*	TD,OP>PS
Prefrontal cortex	Target	82292 ± 9561	77651 ± 9967	80153 ± 9380	18.94	2,1143	<.001*	TD>OP>PS
Motor cortex	Target	27188 ± 3344	25588 ± 3414	26487 ± 3182	19.20	2,1143	<.001*	TD>OP>PS
Somatosensory cortex	Target	11578 ± 1635	10876 ± 1679	11303 ± 1625	15.10	2,1143	<.001*	TD,OP>PS
Temporal cortex	Target	62625 ± 7193	59184 ± 7523	61478 ± 6850	19.76	2,1143	<.001*	TD,OP>PS
Posterior parietal cortex	Target	57281 ± 7459	53792 ± 7853	55741 ± 7259	17.67	2,1143	<.001*	TD>OP>PS
Occipital cortex	Target	27310 ± 3388	25640 ± 3614	26591 ± 3378	19.12	2,1143	<.001*	TD>OP>PS
Left								
Thalamus	Seed	6619 ± 622	6374 ± 679	6510 ± 648	11.51	2,1143	<.001*	TD>O>PS
Prefrontal cortex	Target	81890 ± 9523	77218 ± 10130	79693 ± 9278	19.18	2,1143	<.001*	TD>O>PS
Motor cortex	Target	27878 ± 3559	26309 ± 3477	27269 ± 3337	17.24	2,1143	<.001*	TD>O>PS
Somatosensory cortex	Target	11991 ± 1773	11229 ± 1783	11692 ± 1787	15.13	2,1143	<.001*	TD>O>PS
Temporal cortex	Target	63234 ± 7454	59636 ± 7683	62060 ± 7026	20.55	2,1143	<.001*	TD,O>PS
Posterior parietal cortex	Target	56163 ± 7540	52596 ± 7749	54484 ± 7195	18.54	2,1143	<.001*	TD>O>PS
Occipital cortex	Target	26940 ± 3279	25442 ± 3517	26442 ± 3444	16.34	2,1143	<.001*	TD,O>PS
Right								
Thalamus	Seed	7222 ± 853	6982 ± 846	7121 ± 852	6.52	2,1143	.002*	TD,O>PS
Prefrontal cortex	Target	82694 ± 9737	78083 ± 9938	80612 ± 9657	18.13	2,1143	<.001*	TD>O>PS
Motor cortex	Target	26498 ± 3378	24868 ± 3531	25704 ± 3257	18.90	2,1143	<.001*	TD>O>PS
Somatosensory cortex	Target	11166 ± 1706	10523 ± 1705	10914 ± 1652	12.06	2,1143	<.001*	TD,O>PS
Temporal cortex	Target	62016 ± 7054	58731 ± 7454	60895 ± 6824	18.28	2,1143	<.001*	TD,O>PS
Posterior parietal cortex	Target	58398 ± 7618	54987 ± 8143	56998 ± 7580	15.88	2,1143	<.001*	TD>O>PS
Occipital cortex	Target	27680 ± 3668	25839 ± 3846	26740 ± 3499	20.56	2,1143	<.001*	TD>O>PS

Note: Asterisk denotes significant *p*-value. No covariates were included in between-group volume comparisons.

Supplementary Table S11. Association between cognition and thalamocortical percent total connectivity

	CNB Composite Score			
Cortical Region	**F**	**df**	**p**	**Partial η^2**
Average of left and right hemispheres				
Prefrontal	0.28	10,1133	.60	.000
Motor	0.28	10,1133	.60	.000
Somatosensory	0.27	10,1133	.60	.000
Temporal	0.28	10,1133	.60	.000
Posterior parietal	0.28	10,1133	.60	.000
Occipital	0.28	10,1133	.60	.000

Note: Asterisk denotes significant *p*-value. For each region tested, all other regions, along with age, sex, group, and rDisp are included as effects of no interest.

Supplementary Table S12. Linear and quadratic effects of age for thalamocortical FA

	Linear Effects				Quadratic Effects			
Cortical Region	**F**	**df**	**p**	**Partial η^2**	**F**	**df**	**p**	**Partial η^2**
Average of left and right hemispheres								
Prefrontal	122.90	3,1140	<.001*	.097	0.17	4,1139	.68	.000
Motor	28.79	3,1140	<.001*	.025	6.58	4,1139	.01	.006
Somatosensory	38.83	3,1140	<.001*	.033	6.14	4,1139	.01	.005
Temporal	33.48	3,1140	<.001*	.029	0.24	4,1139	.63	.000
Posterior parietal	64.70	3,1140	<.001*	.054	15.79	4,1139	<.001*	.014
Occipital	23.19	3,1140	<.001*	.020	9.61	4,1139	.002*	.008
Left								
Prefrontal	113.70	3,1140	<.001*	.091	0.26	4,1139	.61	.000
Motor	23.97	3,1140	<.001*	.021	5.68	4,1139	.02	.005
Somatosensory	38.02	3,1140	<.001*	.032	4.80	4,1139	.03	.004
Temporal	41.19	3,1140	<.001*	.035	1.09	4,1139	.30	.001
Posterior parietal	57.53	3,1140	<.001*	.048	13.00	4,1139	<.001*	.011
Occipital	25.74	3,1140	<.001*	.022	9.91	4,1139	.002*	.009
Right								
Prefrontal	122.37	3,1140	<.001*	.097	0.09	4,1139	.76	.000
Motor	30.07	3,1140	<.001*	.026	6.65	4,1139	.01	.006
Somatosensory	33.46	3,1140	<.001*	.029	6.62	4,1139	.01	.006
Temporal	18.32	3,1140	<.001*	.016	0.02	4,1139	.89	.000
Posterior parietal	65.51	3,1140	<.001*	.054	17.08	4,1139	<.001*	.015
Occipital	18.02	3,1140	<.001*	.016	8.05	4,1139	.005*	.007

Note: Asterisk denotes significant *p*-value. Sex and rDisp are included as effects of no interest.

Supplementary Table S13. Linear and quadratic effects of age for thalamocortical MD

	Linear Effects				Quadratic Effects			
Cortical Region	**F**	**df**	**p**	**Partial η^2**	**F**	**df**	**p**	**Partial η^2**
Average of left and right hemispheres								
Prefrontal	368.37	3,1140	<.001*	.244	7.03	4,1139	.008*	.006
Motor	173.48	3,1140	<.001*	.132	17.21	4,1139	<.001*	.015
Somatosensory	93.10	3,1140	<.001*	.076	6.69	4,1139	.01	.006
Temporal	77.68	3,1140	<.001*	.064	6.75	4,1139	.01	.006
Posterior parietal	153.72	3,1140	<.001*	.119	14.45	4,1139	<.001*	.013
Occipital	111.36	3,1140	<.001*	.089	13.07	4,1139	<.001*	.011

Note: Asterisk denotes significant *p*-value. Sex and rDisp are included as effects of no interest.

Supplementary Table S14. Thalamocortical FA values by sex

	Male	Female				
Cortical Region	LSMean ± STDERR	LSMean ± STDERR	F	df	p	Partial η^2
Average of left and right hemispheres						
Prefrontal	0.440 ± 0.001	0.432 ± 0.001	31.79	4,1139	<.001*	.027
Motor	0.469 ± 0.002	0.457 ± 0.002	35.52	4,1139	<.001*	.028
Somatosensory	0.450 ± 0.002	0.440 ± 0.001	24.79	4,1139	<.001*	.021
Temporal	0.443 ± 0.001	0.443 ± 0.001	0.61	4,1139	.43	.001
Posterior parietal	0.468 ± 0.001	0.462 ± 0.001	9.59	4,1139	.002*	.008
Occipital	0.513 ± 0.001	0.508 ± 0.001	7.57	4,1139	.006*	.007
Left						
Prefrontal	0.442 ± 0.001	0.432 ± 0.001	36.98	4,1139	<.001*	.031
Motor	0.467 ± 0.002	0.454 ± 0.002	33.42	4,1139	<.001*	.029
Somatosensory	0.445 ± 0.002	0.436 ± 0.002	17.62	4,1139	<.001*	.015
Temporal	0.447 ± 0.001	0.446 ± 0.001	0.37	4,1139	.54	.000
Posterior parietal	0.458 ± 0.001	0.453 ± 0.001	5.33	4,1139	.02	.005
Occipital	0.500 ± 0.001	0.495 ± 0.001	6.36	4,1139	.01	.006
Right						
Prefrontal	0.439 ± 0.001	0.431 ± 0.001	24.52	4,1139	<.001*	.021
Motor	0.472 ± 0.002	0.460 ± 0.002	27.57	4,1139	<.001*	.024
Somatosensory	0.455 ± 0.002	0.443 ± 0.001	28.95	4,1139	<.001*	.025
Temporal	0.438 ± 0.001	0.441 ± 0.001	4.13	4,1139	.04	.004
Posterior parietal	0.478 ± 0.001	0.470 ± 0.001	13.75	4,1139	<.001*	.012
Occipital	0.526 ± 0.001	0.521 ± 0.001	7.63	4,1139	.006*	.007

Note: Asterisk denotes significant *p*-value. Age, quadratic age, and rDisp are included as effects of no interest.

Supplementary Table S15. Thalamocortical MD values by sex

Cortical Region	Male	Female				
	LSMean ± STDERR	LSMean ± STDERR	F	df	p	Partial η^2
Average of left and right hemispheres						
Prefrontal	7.448e-4 ± 1.00e-6	7.514e-4 ± 9.3e-7	22.75	4,1139	<.001*	.020
Motor	6.991e-4 ± 1.40e-6	7.084e-4 ± 1.30e-6	23.73	4,1139	<.001*	.020
Somatosensory	7.167e-4 ± 1.52e-6	7.262e-4 ± 1.41e-6	20.67	4,1139	<.001*	.018
Temporal	7.912e-4 ± 2.26e-6	8.120e-4 ± 2.09e-6	45.62	4,1139	<.001*	.039
Posterior parietal	7.530e-4 ± 1.81e-6	7.628e-4 ± 1.68e-6	15.68	4,1139	<.001*	.014
Occipital	7.674e-4 ± 1.41e-6	7.701e-4 ± 1.30e-6	1.91	4,1139	.17	.002

Note: Asterisk denotes significant *p*-value. Age, quadratic age, and rDisp are included as effects of no interest.

Supplementary Table S16. Thalamocortical FA values by group

Cortical Region	Typically Developing	Psychosis Spectrum	Other Psychopathology	F	df	p	Partial η^2	Post-Hoc
	LSMean ± STDERR	LSMean ± STDERR	LSMean ± STDERR					
Average of left and right hemispheres								
Prefrontal	0.439 ± 0.001	0.431 ± 0.001	0.437 ± 0.001	6.90	6,1137	.001*	.012	TD,OP>PS
Motor	0.468 ± 0.002	0.457 ± 0.002	0.464 ± 0.002	7.38	6,1137	.001*	.013	TD,OP>PS
Somatosensory	0.450 ± 0.002	0.439 ± 0.002	0.445 ± 0.002	7.18	6,1137	.001*	.013	TD,OP>PS
Temporal	0.445 ± 0.001	0.440 ± 0.001	0.444 ± 0.001	6.13	6,1137	.002*	.011	TD,OP>PS
Posterior parietal	0.469 ± 0.002	0.460 ± 0.002	0.466 ± 0.002	6.94	6,1137	.001*	.012	TD,OP>PS
Occipital	0.515 ± 0.002	0.506 ± 0.002	0.510 ± 0.001	6.77	6,1137	.001*	.012	TD>OP>PS
Left								
Prefrontal	0.439 ± 0.002	0.432 ± 0.002	0.438 ± 0.001	6.07	6,1137	.002*	.011	TD,OP>PS
Motor	0.466 ± 0.002	0.455 ± 0.002	0.461 ± 0.002	6.61	6,1137	.001*	.012	TD,OP>PS
Somatosensory	0.446 ± 0.002	0.434 ± 0.002	0.441 ± 0.002	7.22	6,1137	.001*	.013	TD>OP>PS
Temporal	0.449 ± 0.001	0.442 ± 0.001	0.448 ± 0.001	6.92	6,1137	.001*	.012	TD,OP>PS
Posterior parietal	0.460 ± 0.002	0.451 ± 0.002	0.456 ± 0.002	6.20	6,1137	.002*	.011	TD,OP>PS
Occipital	0.501 ± 0.002	0.494 ± 0.002	0.497 ± 0.001	5.50	6,1137	.004*	.010	TD>OP,PS
Right								
Prefrontal	0.438 ± 0.001	0.431 ± 0.001	0.436 ± 0.001	7.23	6,1137	.001*	.013	TD,OP>PS
Motor	0.470 ± 0.002	0.459 ± 0.002	0.468 ± 0.002	7.55	6,1137	.001*	.013	TD,OP>PS
Somatosensory	0.453 ± 0.002	0.444 ± 0.002	0.450 ± 0.002	6.06	6,1137	.002*	.011	TD,OP>PS
Temporal	0.441 ± 0.001	0.437 ± 0.001	0.441 ± 0.001	3.86	6,1137	.02	.007	TD,OP>PS
Posterior parietal	0.469 ± 0.002	0.479 ± 0.002	0.475 ± 0.002	6.99	6,1137	.001*	.012	TD,OP>PS
Occipital	0.528 ± 0.002	0.518 ± 0.002	0.524 ± 0.001	7.11	6,1137	.001*	.012	TD,OP>PS

Note: Asterisk denotes significant *p*-value. Age, quadratic age, sex, and rDisp are included as effects of no interest.

Supplementary Table S17. Thalamocortical MD values by group

	Typically Developing	Psychosis Spectrum	Other Psychopathology					
Cortical Region	LSMean ± STDERR	LSMean ± STDERR	LSMean ± STDERR	**F**	**df**	**p**	**Partial η^2**	**Post-Hoc**
Average of left and right hemispheres								
Prefrontal	7.476e-4 ± 1.30e-6	7.500e-4 ± 1.28e-6	7.471e-4 ± 1.03e-6	1.63	6,1137	.20	.003	--
Motor	7.008e-4 ± 1.82e-6	7.079e-4 ± 1.79e-6	7.028e-4 ± 1.44e-6	4.18	6,1137	0.02	.007	--
Somatosensory	7.166e-4 ± 1.97e-6	7.268e-4 ± 1.93e-6	7.210e-4 ± 1.56e-6	6.81	6,1137	.001*	.012	PS>TD,OP
Temporal	7.973e-4 ± 2.95e-6	8.068e-4 ± 2.89e-6	8.009e-4 ± 2.33e-6	2.65	6,1137	.07	.005	--
Posterior parietal	7.533e-4 ± 2.36-e6	7.641e-4 ± 2.31e-6	7.568e-4 ± 1.86e-6	5.54	6,1137	.004*	.010	PS>TD,OP
Occipital	7.660e-4 ± 1.83e-6	7.726e-4 ± 1.80e-6	7.680e-4 ± 1.45e-6	3.49	6,1137	0.03	.006	--

Note: Asterisk denotes significant *p*-value. Age, quadratic age, sex, and rDisp are included as effects of no interest.

Supplementary Table S18. Sensitivity analysis for age, sex, and group effects of FA controlling for whole brain FA

				Age Effects	
Cortical Region	**F**	**df**	**p**	**Partial η^2**	
Prefrontal	76.97	4,1139	<.001*	.063	
Motor	19.00	4,1139	<.001*	.016	
Somatosensory	22.67	4,1139	<.001*	.020	
Temporal	4.78	4,1139	.03	.004	
Posterior parietal	36.82	4,1139	<.001*	.031	
Occipital	8.71	4,1139	.003*	.008	
				Sex Effects	
Cortical Region	**F**	**df**	**p**	**Partial η^2**	
Prefrontal	33.18	5,1138	<.001*	.028	
Motor	32.76	5,1138	<.001*	.028	
Somatosensory	25.25	5,1138	<.001*	.022	
Temporal	0.58	5,1138	.45	.001	
Posterior parietal	9.97	5,1138	.002*	.009	
Occipital	7.90	5,1138	.005*	.007	
				Group Effects	
Cortical Region	**F**	**df**	**p**	**Partial η^2**	**Post-Hoc**
Prefrontal	6.90	7,1136	.001*	.012	TD,OP>PS
Motor	7.31	7,1136	.001*	.013	TD,OP>PS
Somatosensory	7.06	7,1136	.001*	.012	TD,OP>PS
Temporal	6.65	7,1136	.001*	.012	TD,OP>PS
Posterior parietal	6.82	7,1136	.001*	.012	TD,OP>PS
Occipital	6.61	7,1136	.001*	.012	TD,OP>PS

Note: Asterisk denotes significant *p*-value. rDisp and whole brain FA are included as effects of no interest for all analyses. Additional effects of no interest by model are: age model: sex; sex model: age and quadratic age; group model: age, quadratic age, and sex.

Supplementary Table S19. Sensitivity analysis for group effects of FA controlling for race, parental education, and CNR

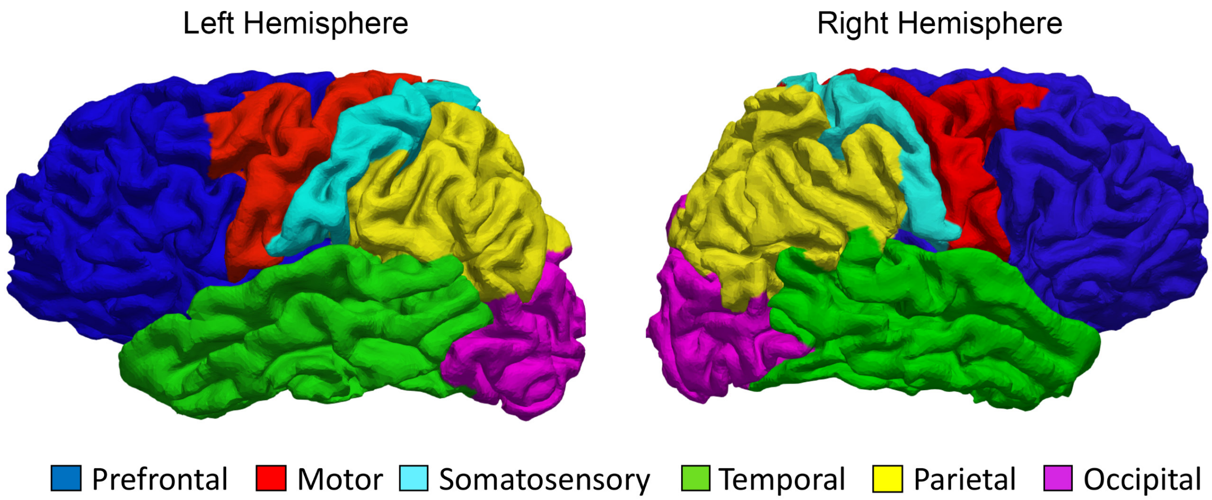
	Race-Matched Groups (n = 288)				Parent Education-Matched Groups (n = 285)				CNR-Matched Groups (n = 288)			
Cortical Region	**F**	**df**	**p**	**Partial η^2**	**F**	**df**	**p**	**Partial η^2**	**F**	**df**	**p**	**Partial η^2**
Average of left and right hemispheres												
Prefrontal	3.17	6,281	.04	.022	2.13	6,278	.12	.015	2.42	6,281	.09	.017
Motor	3.11	6,281	.05	.022	1.38	6,278	.25	.010	5.41	6,281	.005	.037
Somatosensory	3.51	6,281	.03	.024	3.21	6,278	.46	.006	3.67	6,281	.03	.025
Temporal	2.92	6,281	.06	.020	2.65	6,278	.07	.019	2.11	6,281	.12	.015
Posterior parietal	2.27	6,281	.11	.016	2.57	6,278	.08	.018	3.59	6,281	.03	.025
Occipital	4.34	6,281	.01	.030	2.20	6,278	.11	.016	1.57	6,281	.21	.011

Supplementary Table S20. Interaction effects in thalamocortical white matter microstructure

	Linear Age by Sex				Linear Age by Group				Sex by Group			
Cortical Region	F	df	p	Partial η^2	F	df	p	Partial η^2	F	df	p	Partial η^2
Average of left and right hemispheres												
Prefrontal	9.32	10,1133	.002*	.008	0.65	10,1133	.52	.001	2.05	10,1133	.13	.004
Motor	12.42	10,1133	<.001*	.011	0.39	10,1133	.68	.001	1.79	10,1133	.17	.003
Somatosensory	8.15	10,1133	.004*	.007	0.76	10,1133	.47	.001	0.05	10,1133	.95	.000
Temporal	0.00	10,1133	.96	.000	2.27	10,1133	.10	.004	1.77	10,1133	.17	.003
Posterior parietal	9.48	10,1133	.002*	.008	1.31	10,1133	.27	.002	0.06	10,1133	.94	.000
Occipital	4.91	10,1133	.03	.004	1.37	10,1133	.25	.002	0.34	10,1133	.71	.001

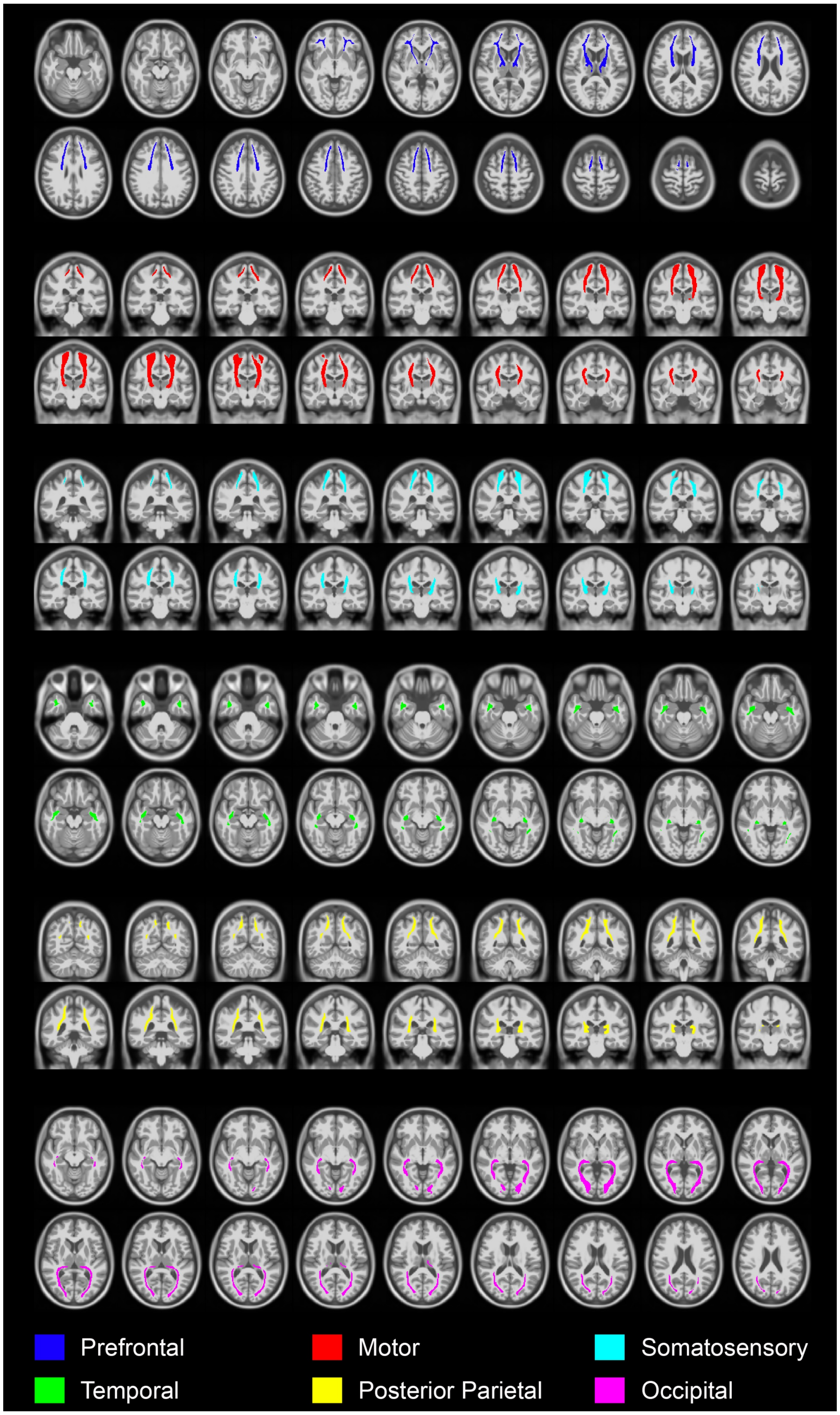
Note: Asterisk denotes significant *p*-value. Sex, group, and rDisp are included as effects of no interest.

Supplementary Figure S1. Cortical segmentation



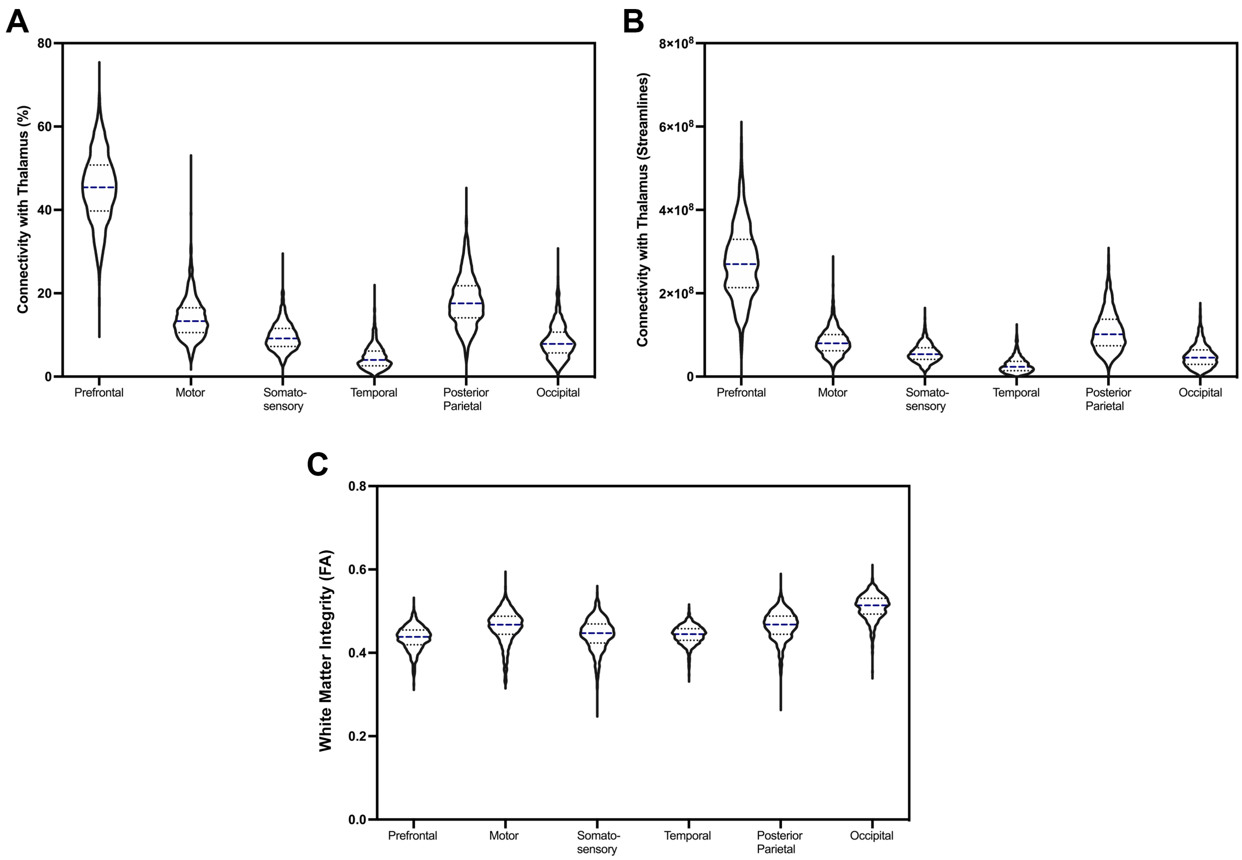
Supplementary Figure S1. Six bilateral cortical regions were included as thalamic targets for the probabilistic tractography analysis.

Supplementary Figure S2. White matter tracts between the thalamus and cortical ROIs



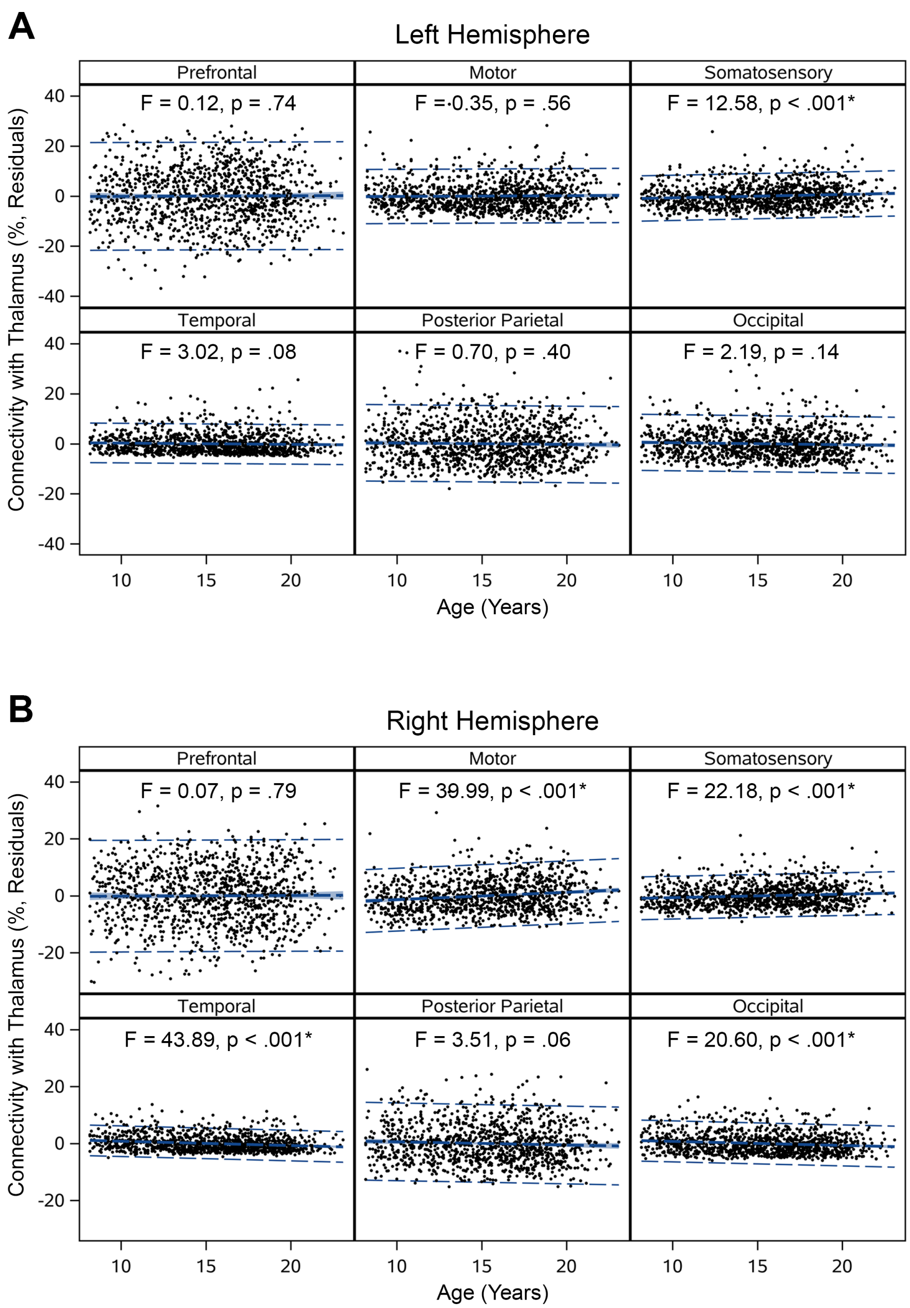
Supplementary Figure S2. Group masks for each thalamocortical white matter tract are overlaid on a T1 template.

Supplementary Figure S3. Connectivity distribution by cortical region



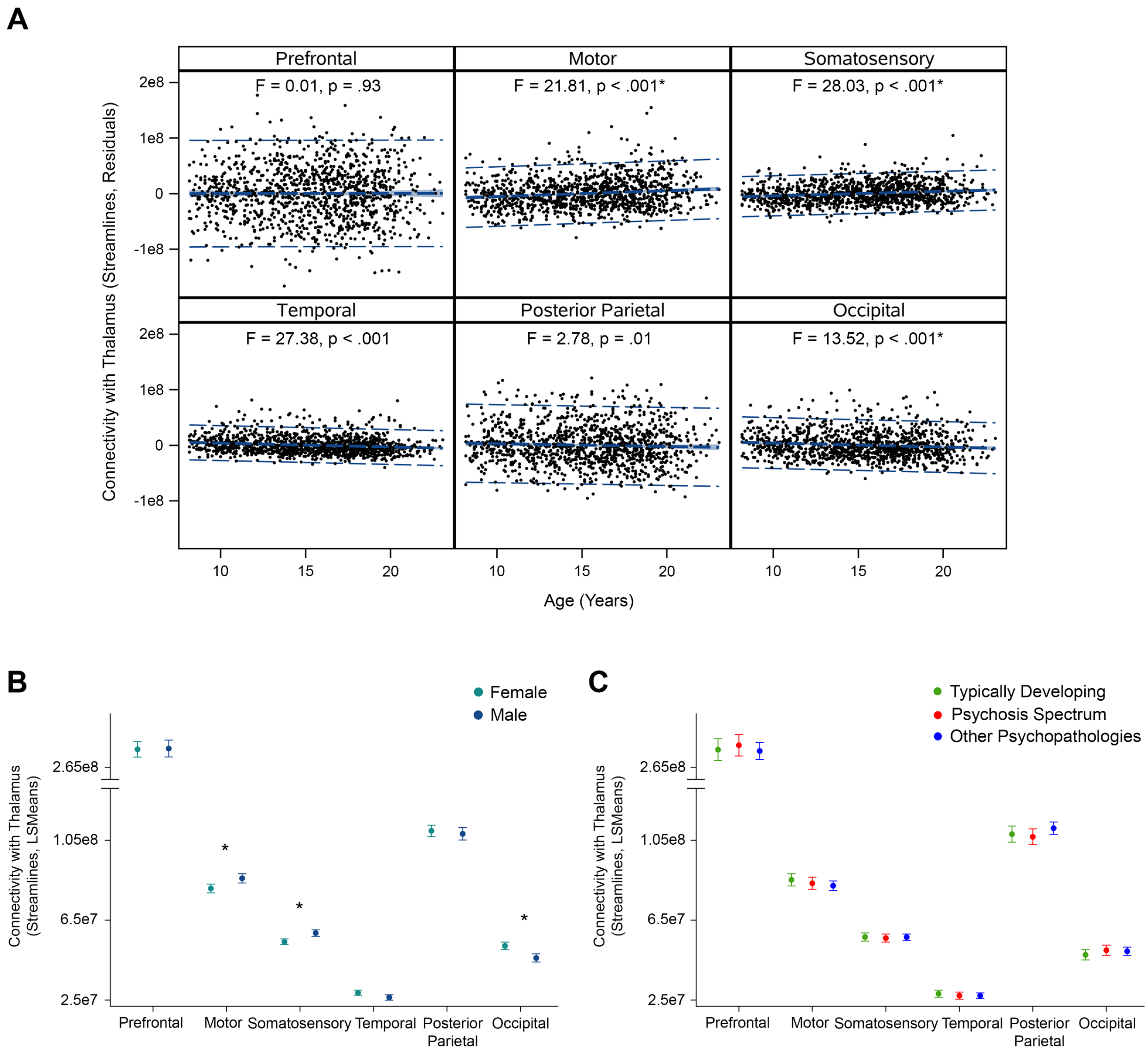
Supplementary Figure S3. Distribution of thalamocortical percent total connectivity values (A), streamline counts (B), and white matter FA (C) by cortical target.

Supplementary Figure S4. Age effects of thalamocortical percent total connectivity, by hemisphere



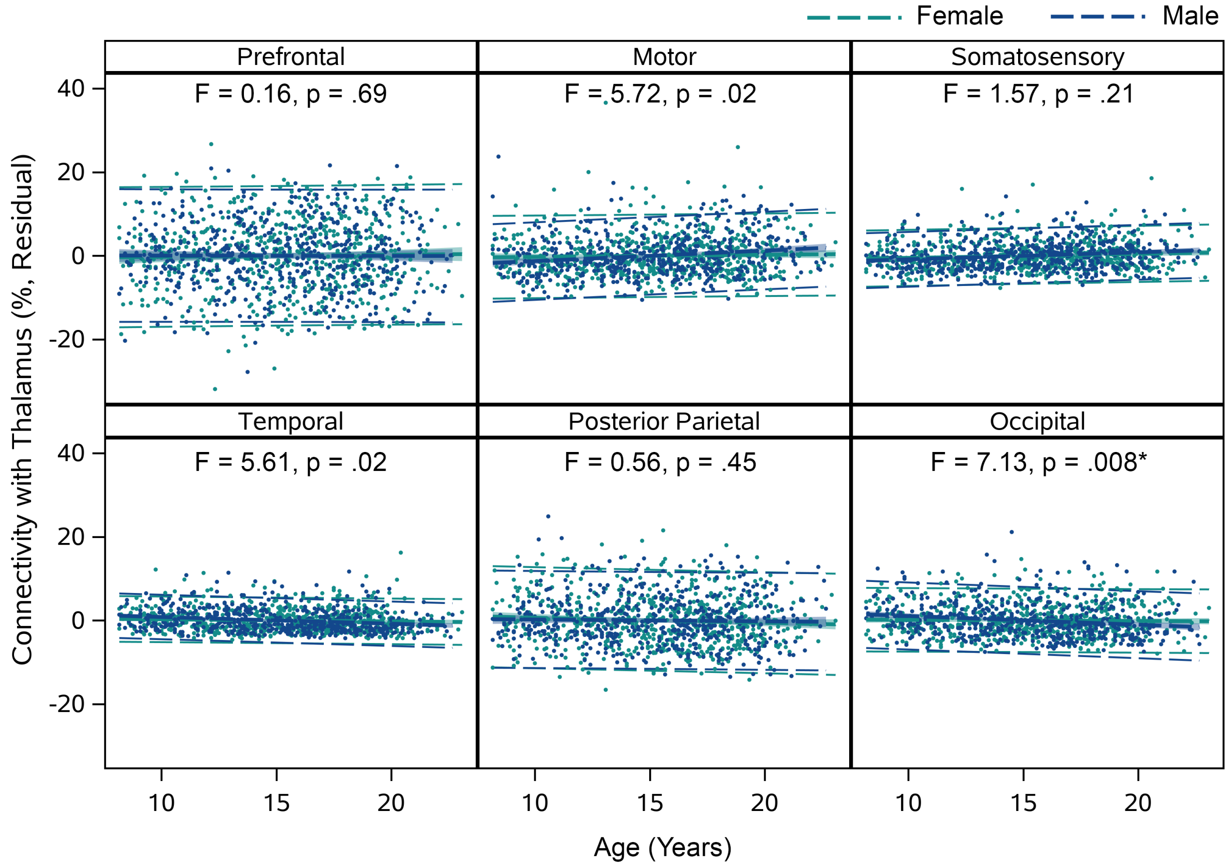
Supplementary Figure S4. Linear effects of age were less pronounced in the left hemisphere (A) than the right hemisphere (B).

Supplementary Figure S5. Effects of age, sex, and group for thalamocortical streamline counts



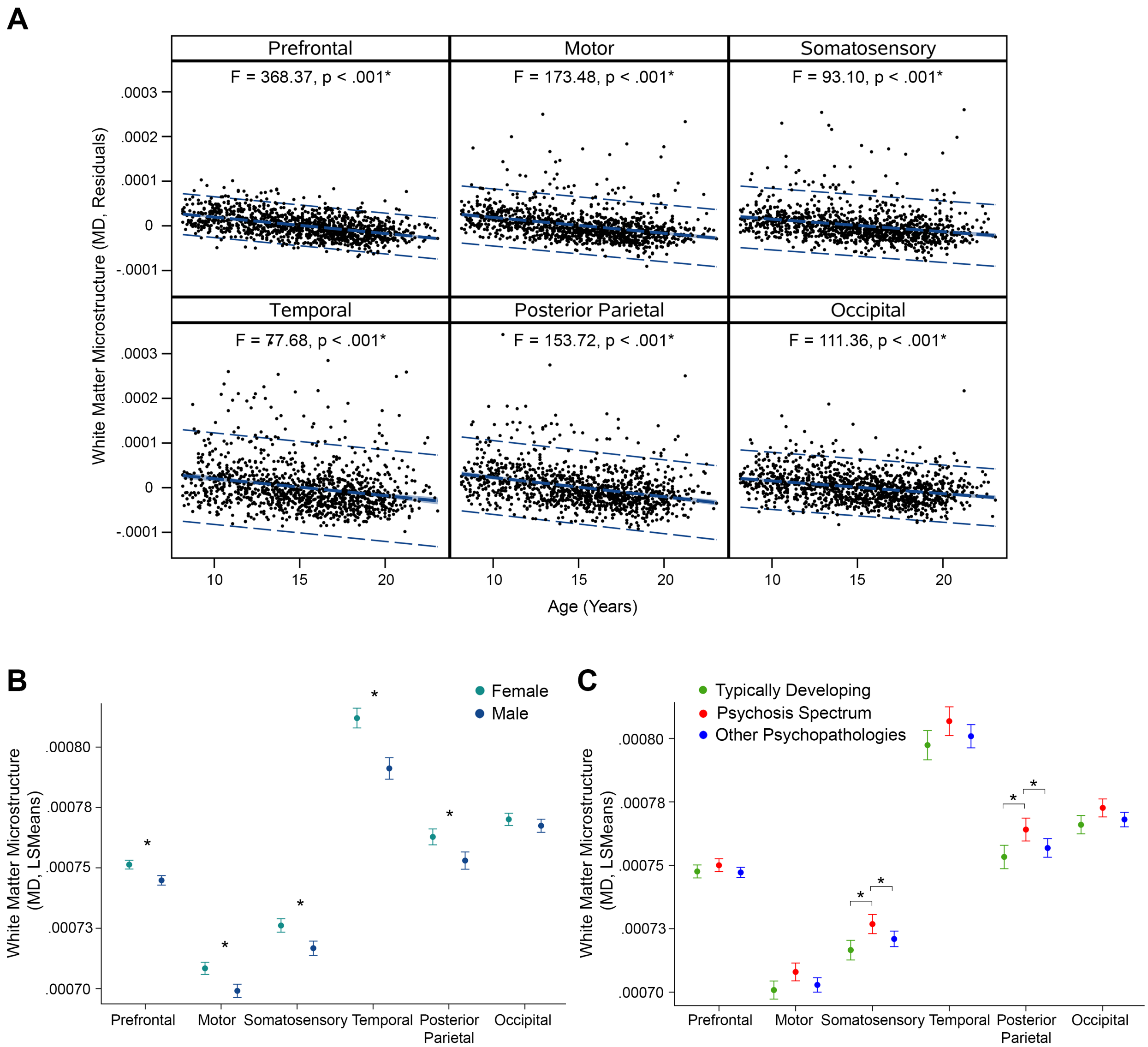
Supplementary Figure S5. Streamline count analyses showed similar age and group effects as percent total connectivity analyses. Sex effects were stronger, with one additional cortical region (motor cortex) showing greater streamline counts in males. 95% confidence intervals are shown for sex and group effects.

Supplementary Figure S6. Interaction of linear age and sex for thalamic-occipital percent total connectivity



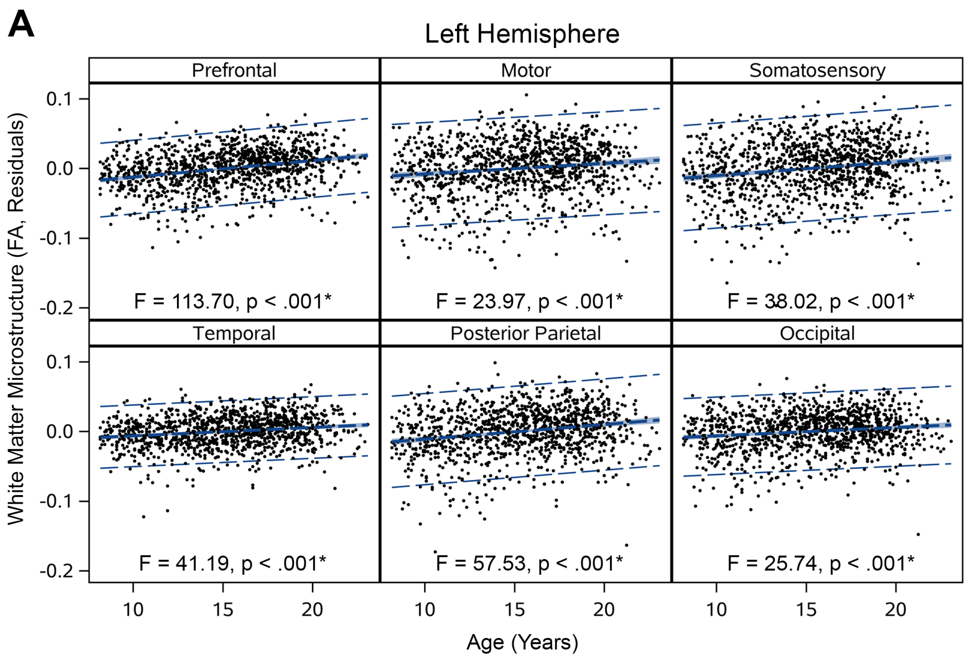
Supplementary Figure S6. There was a linear interaction between age and sex, with older females showing more thalamic-occipital percent total connectivity than males.

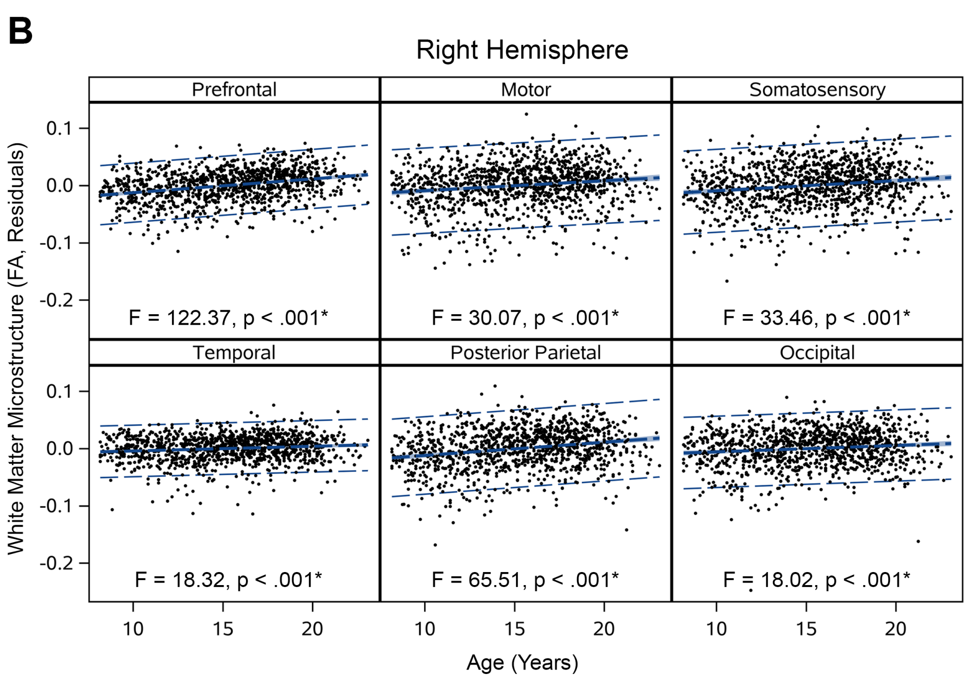
Supplementary Figure S7. Effects of linear age, sex, and group for MD values



Supplementary Figure S7. (A) MD values decreased linearly with age across regions. (B) Males had lower mean MD in most white matter tracts, with the exception of the thalamic-occipital tract. (C) Typically-developing youth and youth with other psychopathologies had lower MD values compared to psychosis-spectrum youth in the thalamic-somatosensory and thalamic-posterior parietal tract. 95% confidence intervals are shown for sex and group effects.

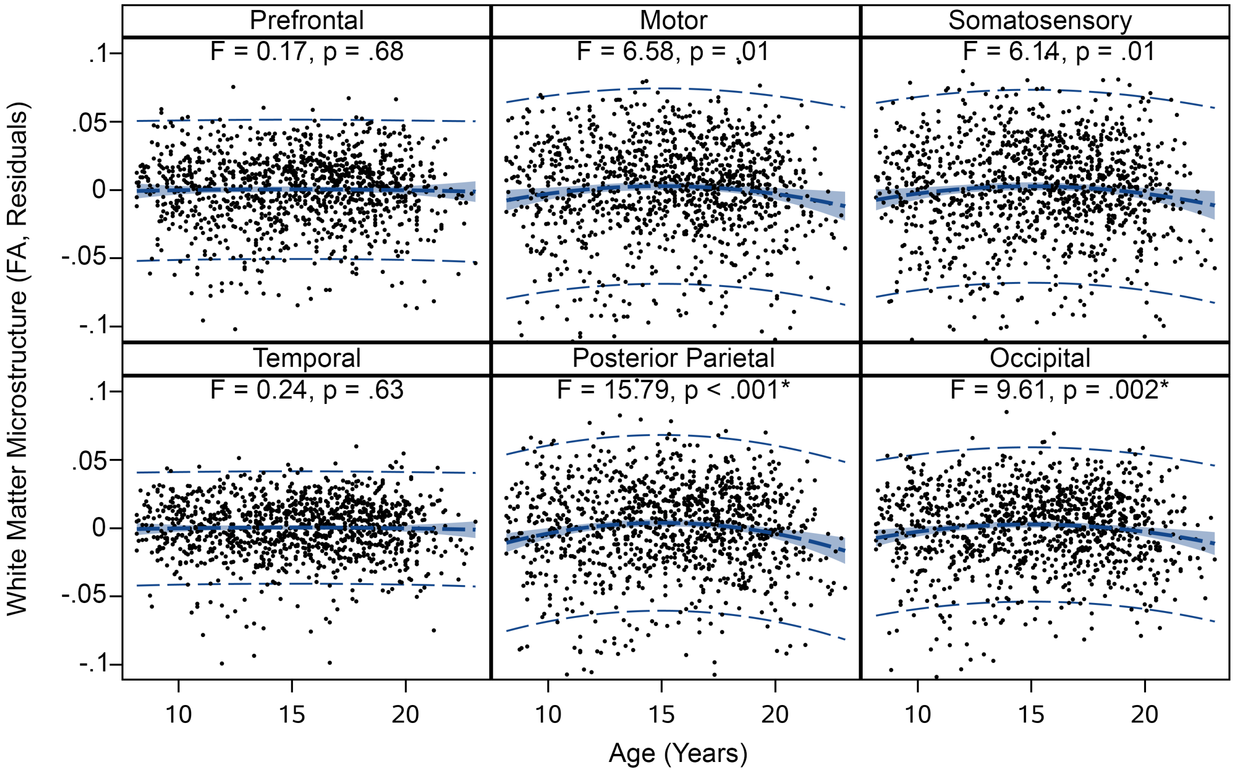
Supplementary Figure S8. Linear age effects of thalamocortical FA values, by hemisphere





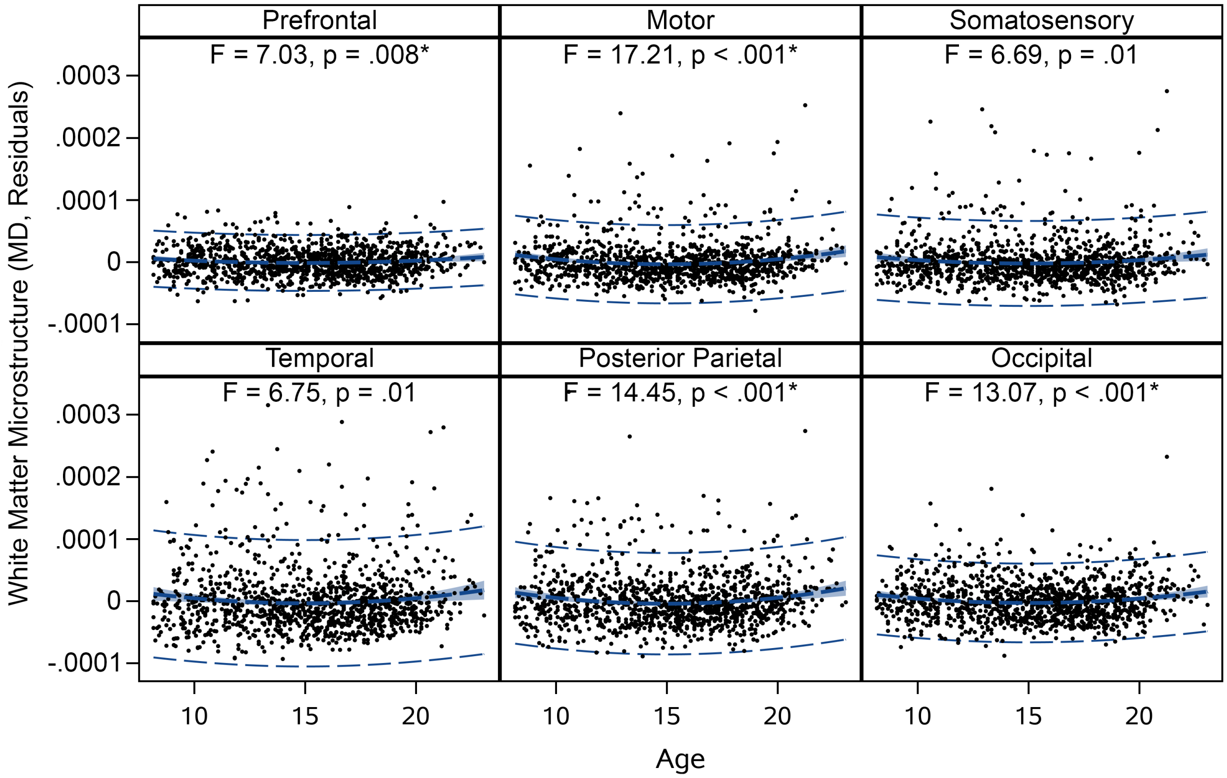
Supplementary Figure S8. Linear effects of age were consistent across left (A) and right (B) hemispheres for FA values.

Supplementary Figure S9. Quadratic age effects of thalamocortical FA values



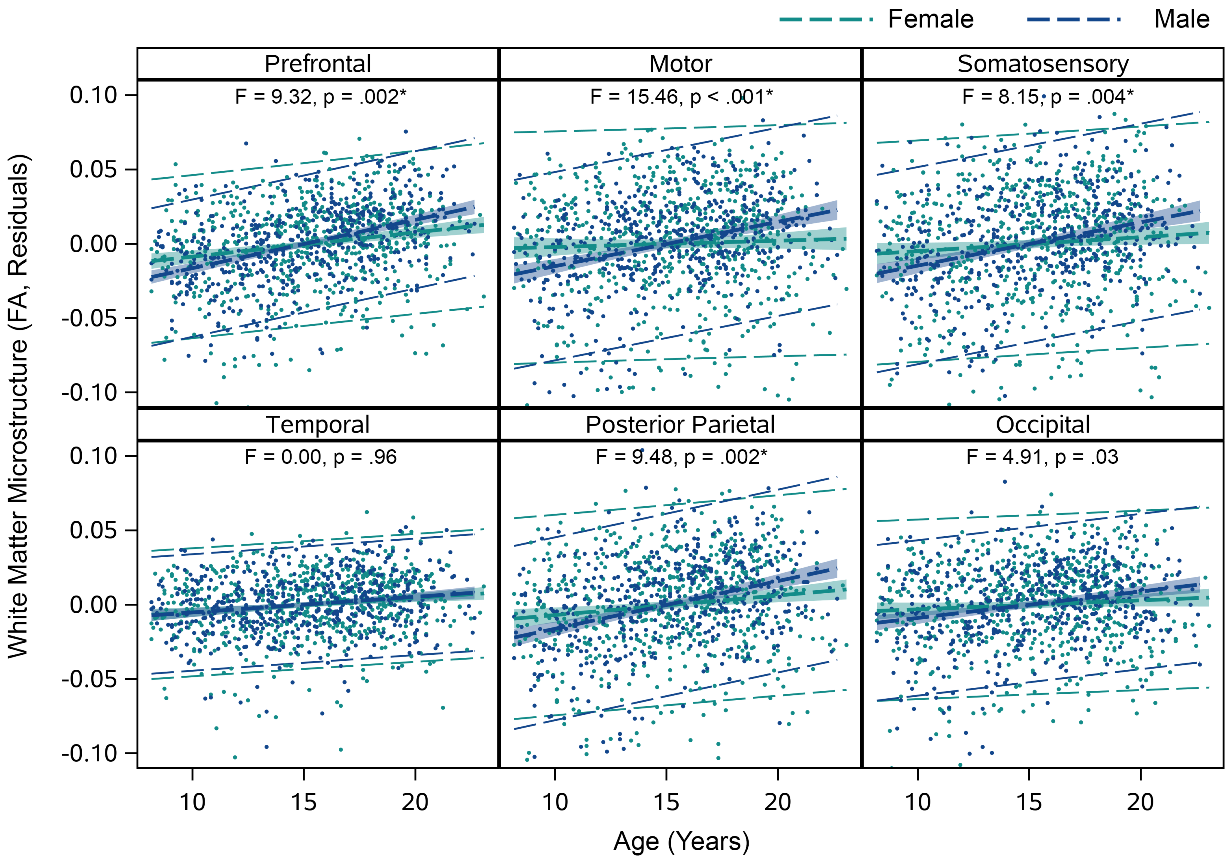
Supplementary Figure S9. FA values in the thalamic-posterior parietal and thalamic-occipital tracts followed and inverted-U shape, with higher FA values observed during adolescence and lower FA values in childhood and early adulthood.

Supplementary Figure S10. Quadratic age effects of thalamocortical MD values



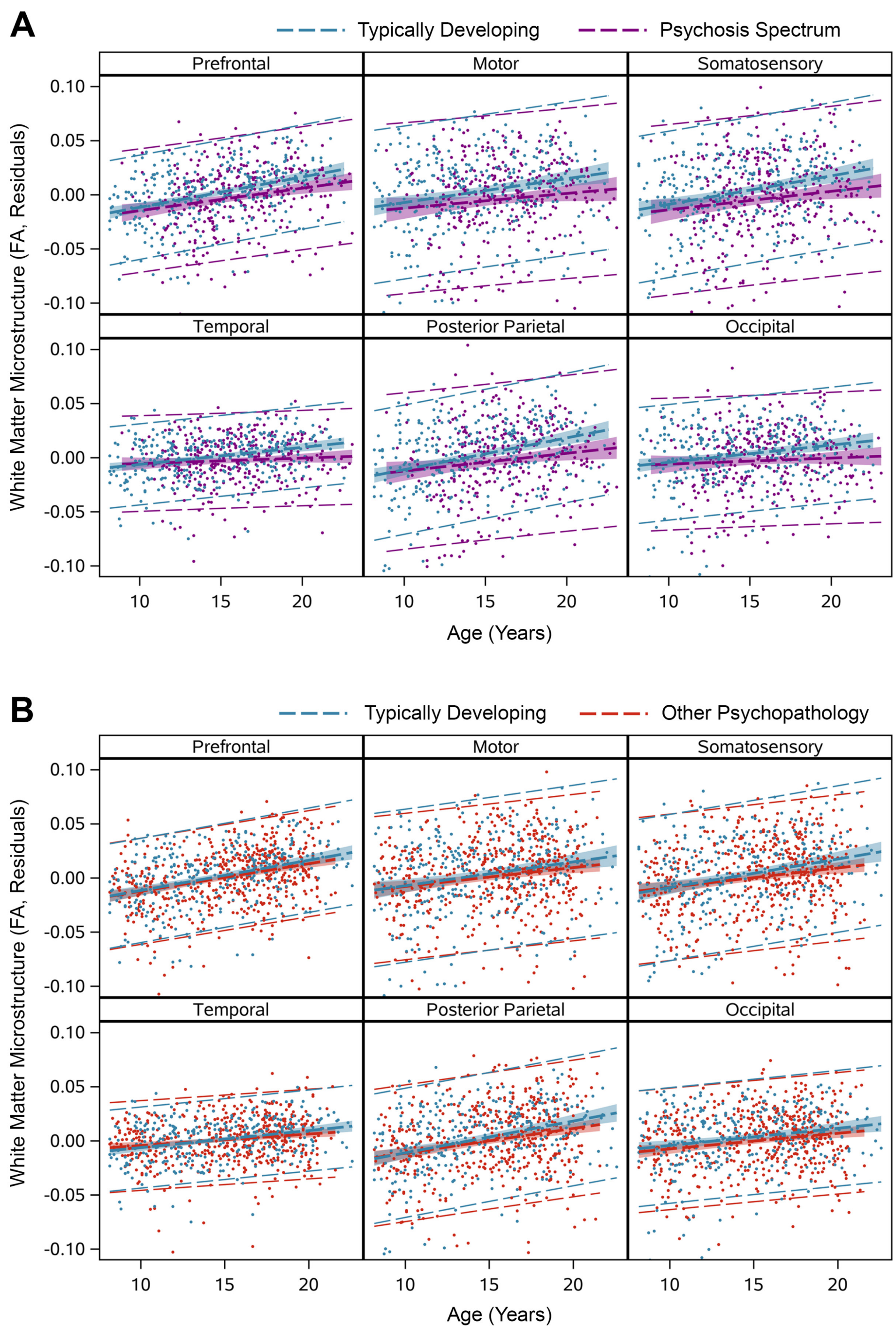
Supplementary Figure S10. MD values followed a U-shaped curve, with lower MD values observed during adolescence and higher MD values in childhood and early adulthood.

Supplementary Figure S11. Interactions of linear age and sex for thalamocortical FA values



Supplementary Figure S11. Older males had higher FA values than older females in tracts connecting the thalamus with the prefrontal motor, somatosensory, and posterior parietal cortex.

Supplementary Figure S12. Linear age by group for thalamocortical FA values



Supplementary Figure S12. Age effects are plotted by (A) typically-developing and psychosis-spectrum youth and (B) typically-developing youth and youth with other psychopathologies.

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