Supporting Information Appendix

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Additional Analyses and Results

Classification of Participants into CI vs. NH group. To provide additional evidence supporting the validity of the affected and unaffected brain templates, we conducted a classification analysis with a linear SVM classifier to classify participants into different groups (CI vs. NH Group). We used a 10-fold cross-validation procedure with a feature selection approach (two-sample *t*-tests, approximately 5% of the total voxels were selected on each training set). By using this procedure, we consistently achieved high classification accuracy across tissue types and measures (GM MVPS: 95.9%, WM MVPS: 97.3%, GM density: 97.3%, WM density: 91.9%,). The affected brain areas identified by this classification procedure are largely overlapping with those determined by the univariate group comparisons (see SI Appendix, Fig. S6).

Sex-balanced Cross-validation Procedures. Our 37 children who use CIs consisted of 18 females and 19 males. In the leave-one-participant-out cross-validation (CV) procedure, each participant was treated as a test set once. In this situation, there was no sex bias because each patient would be a testing set. In the 10-fold CV procedure, we randomly selected 90% of the participants (33 out of 37) for training and 10% of the participants (4 out of 37) for testing. For each fold of the CV, we ensured the sex ratio in the testing set was 1:1 (i.e., 2 males and 2 females). Therefore, the sex ratio in the training set was 0.94:1 (16/17) while the testing set was 1:1 (2/2). In other words, there was a slight difference in sex ratio between the training and testing sets. To ensure this was not a confounding factor in our analysis, we used a sex-balanced CV in another classification analysis with 10,000-iteration bootstrapping. We randomly selected 32 participants for training while ensuring that the sex ratio was 1:1 (i.e., 16:16) and the remaining 2 females and 2 male participants for testing in each CV fold. We found that this sex-balanced CV procedure yielded very similar classification performance as those reported in the main text (median of the classification accuracies: GM MVPS: 76%, WM MVPS: 81%, GM density: 53%, WM density: 48%). These results confirmed that the slight difference in sex ratio between the training and testing set did not affect our results.

The Relationship between Duration of Hearing-aid Use and Brain reorganization. To further examine whether duration of hearing-aid use (the time between hearing-aid fitting and MRI scan) was correlated with those neuroanatomical measures (both GM density and similarity), we conducted group-level regression analyses while controlling for effects of other non-neural variables (i.e., age of implant, sex, and SES). No significant correlation between duration of hearing-aid use and any brain measures in the auditory cortices was found. This is true even after a less conservative threshold was used (e.g., uncorrected voxel-level $P = 0.01$).

Table S1. Brain regions in gray matter that showed significant differences in VBM density and MVPS measures between children in the CI and NH groups.

Regions	BA	MNI x	MNI y	MNI z	Peak *t*-value	Number of voxels	Direction
GM MVPS							
L. Superior Frontal Gyrus	8	-24	18	58	5.02	172	WN>BW
L. Inferior Frontal Gyrus	47	-36	20	-10	5.68	126	WN>BW
L. Superior Temporal Gyrus	21	-66	-14	-12	6.78	387	WN>BW
L. Medial Frontal Gyrus	11	-2	52	-10	6.00	278	WN>BW
L. Middle Cingulate Gyrus	31	0	-26	42	7.06	418	WN>BW
R. Middle Frontal Gyrus	6	50	-4	46	5.82	235	WN>BW
R. Superior Temporal Gyrus	22	50	0	2	7.13	432	WN>BW
R. Middle Temporal Pole	21	62	-4	-14	6.31	144	WN>BW
R. Precuneus	7	4	-66	12	7.45	588	WN>BW
GM Density							
L. Superior Temporal Gyrus	22	-56	4	0	5.65	122	NH > CI
L. Heschl Gyrus	13	-46	-30	16	4.95	149	NH > CI
L. Medial Frontal Gyrus	32	-8	48	2	5.95	238	NH > CI
L. Precuneus	31	-6	-24	46	6.55	255	NH > CI
L. Lingual Gyrus	18	-16	-102	-16	8.10	150	NH > CI
L. Parahippocampa Gyrus	-	-26	-42	-2	6.10	111	NH > CI
R. Superior Temporal Gyrus	22	56	4	0	6.67	272	NH > CI
R. Heschl Gyrus	13	32	-22	18	5.20	117	NH > CI
R. SupraMarginal Gyrus	3	32	-36	46	5.24	197	NH > CI
R. Middle Cingulate Gyrus	31	6	-24	48	6.82	188	NH > CI
R. Superior Occipital Gyrus	19	28	-70	32	5.13	345	NH > CI
R. Parahippocampal Gyrus	-	32	-36	-6	6.53	124	NH > CI

Note. L = left hemisphere; R = right hemisphere; WN = within-NH-group MVPS; BW = between-group MVPS.

Table S2. Statistical comparisons between each pair of classification models in classification accuracy made by using permutation tests and bootstrapping procedures.

Features	Compared with **permutation-based** null distribution	Compared with bootstrapping-based **non-neural-measure** classification accuracy distribution	Compared with bootstrapping-based **affected-brain-area** classification accuracy distribution	Compared with bootstrapping-based **unaffected-brain-area** classification accuracy distribution
Demographic variables + pre-CI SAT and pre-CI SRI-Q	*P* = .525	-	-	-
GM MVPS				
Affected	*P* = .549	.547	-	-
Unaffected	*P* = .008	< .001	< .001	-
Whole-brain	*P* = .008	< .001	< .001	.731
WM MVPS				
Affected	*P* = .046	< .001	-	-
Unaffected	*P* = .002	< .001	.004	-
Whole-brain	*P* = .004	< .001	.028	.718
GM Density				
Affected	*P* = .449	.324	-	-
Unaffected	*P* = .240	.056	.180	-
Whole-brain	*P* = .317	.153	.371	.741
WM Density				
Affected	*P* = .879	.989	-	-
Unaffected	*P* = .434	.513	.002	-
Whole-brain	*P* = .533	.547	.009	.759

Table S3. Prediction performance based on a linear SVM classifier and rankSVM (see Methods section for details), respectively.

	Linear SVM					Linear RankSVM	
Features	ACC	Sens	Spec	AUC		*rho* (predicted, observed)	*pval*
Non-neural measures (demographic variables, pre-CI SAT, and pre-CI SRI-Q)							
	49%	60%	35%	49%		0.03	*0.47*
GM MVPS							
affected	59%	59%	59%	59%		-0.01	*0.526*
unaffected	76%	71%	82%	79%		0.49	*0.008*
Whole-brain	76%	76%	76%	78%		0.47	*0.014*
WM MVPS							
affected	68%	65%	71%	73%		0.42	*0.030*
unaffected	76%	71%	82%	82%		0.40	*0.034*
Whole-brain	79%	76%	82%	83%		0.47	*0.015*
GM Density							
affected	51%	60%	41%	51%		-0.15	*0.748*
unaffected	57%	70%	41%	59%		-0.11	*0.672*
Whole-brain	54%	65%	41%	58%		-0.11	*0.680*
WM Density							
affected	38%	41%	35%	35%		-0.26	*0.876*
unaffected	51%	60%	41%	47%		-0.08	*0.622*
Whole-brain	49%	55%	41%	44%		-0.22	*0.827*

Note. For all brain models, nested template definition procedure with 10-fold cross-validation (see Methods section for details) was employed, in which different affected/unaffected voxels were selected for each cross-validated fold. Permutation and bootstrapping with 10,000 iterations was applied. $rho_{(predicted,\ observed)}$, median Spearman's rank correlation between predicted and observed scores from the 10,000-iteration distribution derived from bootstrapping approach; *pval*, *p*-value indicating statistical significance derived from a 10,000-iteration permutation test.

Table S4. Classification performance based on linear and nonlinear SVM classifiers. All non-neural measures (demographic variables, pre-CI SAT, and pre-CI SRI-Q) were included as features in the each model.

	Linear SVM					Nonlinear SVM			
Brain Measures	ACC	Sens	Spec	AUC		ACC	Sens	Spec	AUC
GM MVPS									
Affected	32%	35%	29%	33%		59%	70%	47%	58%
Unaffected	73%	75%	71%	76%		68%	75%	59%	75%
Whole-brain	73%	80%	65%	74%		70%	80%	59%	68%
WM MVPS									
Affected	65%	75%	53%	70%		64%	61%	67%	65%
Unaffected	76%	75%	76%	83%		73%	75%	71%	80%
Whole-brain	70%	80%	59%	83%		68%	75%	59%	76%
GM Density									
Affected	49%	55%	41%	51%		49%	90%	0%	41%
Unaffected	57%	70%	41%	57%		54%	100%	0%	31%
Whole-brain	54%	70%	35%	56%		54%	100%	0%	33%
WM Density									
Affected	43%	40%	47%	46%		38%	70%	0%	30%
Unaffected	51%	60%	41%	44%		46%	85%	0%	39%
Whole-brain	43%	55%	29%	41%		49%	90%	0%	27%

Table S5. Classification performance based on a linear SVM classifier with different feature selection procedures. Two widely-used feature selection approaches were employed for verification because different feature selection procedures could filter out different voxels. We selected 5000 voxels (approximately 5% of a total number of voxels) that showed the most significant difference between the two groups (univariate two-sample *t*-tests or SVM-RFE weights) based on each fold of the training data set. As such, each trained model (affected, unaffected or whole-brain) for each LOOCV contained the same number of voxels. This procedure ruled out the potential confound introduced by using a different number of voxels in different models.

	Univariate feature selection					SVM-RFE feature selection			
Features	ACC	Sens	Spec	AUC		ACC	Sens	Spec	AUC
GM MVPS									
affected	46%	50%	41%	51%		49%	55%	41%	50%
unaffected	68%	75%	59%	76%		70%	80%	59%	75%
Whole-brain	65%	75%	53%	75%		65%	85%	41%	71%
WM MVPS									
affected	65%	80%	47%	77%		65%	75%	53%	71%
unaffected	73%	75%	71%	76%		81%	80%	82%	84%
Whole-brain	65%	70%	59%	76%		84%	80%	88%	84%
GM Density									
affected	59%	65%	53%	61%		57%	60%	53%	61%
unaffected	51%	60%	41%	56%		70%	80%	59%	65%
Whole-brain	57%	65%	47%	58%		70%	75%	65%	67%
WM Density									
affected	35%	35%	35%	34%		35%	35%	35%	36%
unaffected	54%	75%	29%	38%		49%	65%	29%	39%
Whole-brain	43%	50%	35%	35%		46%	60%	29%	33%

Table S6. Brain regions in gray matter that contributed significantly to classifying children with CIs into high- vs. low-improvement sub-groups using the searchlight method.

Regions	BA	MNI coordinates			Peak classification accuracy	Cluster size (Number of voxels)
		x	y	z		
GM MVPS						
L. Superior Frontal Gyrus	11	-2	60	-12	87.5%	101
L. Superior Frontal Gyrus	9	-18	46	34	95%	122
L. Middle Frontal Gyrus	6/9	-38	12	42	90%	340
L. Inferior/Middle Frontal Gyrus	10/46	-36	38	18	87.5%	138
L. Thalamus	-	-12	-32	10	90%	103
L. Cerebellum	-	-14	-42	-54	90%	406
R. Superior Frontal Gyrus	6	38	-8	62	92.5%	273
R. Middle Frontal Gyrus	10/46	38	52	2	90%	295
R. Inferior Frontal Gyrus	45/47	54	30	6	87.5%	144
R. Middle Temporal Gyrus	21/38	58	6	-16	90%	125
R. Cuneus	18	0	-70	4	90%	121
R. Middle Occipital Gyrus	19	38	-76	30	90%	167
R. Cerebellum	-	30	-44	-32	90%	439
GM Density						
L. Middle Frontal Gyrus	10	-32	60	0	80%	228
L. Middle Frontal Gyrus	8	-26	18	46	82.5	168
L. Superior Temporal Gyrus	22/6	-50	-10	8	85%	162
L. Inferior Parietal Lobule	40	-54	-44	48	82.5%	199
L. Middle Occipital Gyrus	18	-22	-98	-8	90%	273
L. Cerebellum	-	-12	-76	-28	87.5%	439
R. Superior Temporal Gyrus	22	50	2	-6	82.5%	156
R. Middle Cingulate Gyrus	31	12	-44	50	87.5%	151
R. Cerebellum	-	20	-44	-58	85%	409

Note. The coordinate was extracted based on the centroid of each contiguous mass. BA, Brodmann's Area

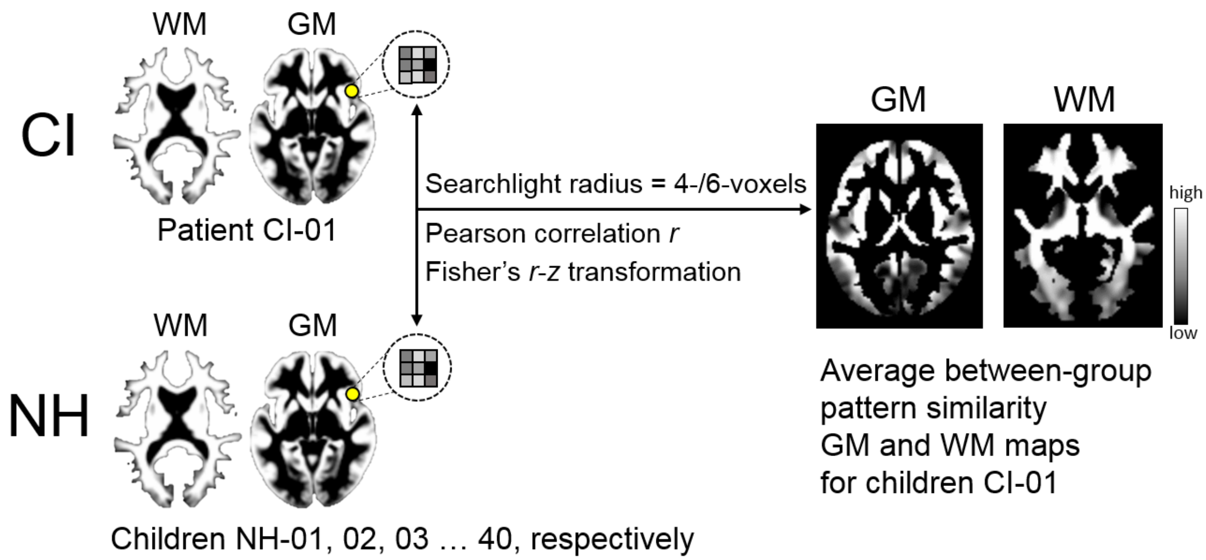

Fig. S1. Between-group searchlight multi-voxel pattern similarity (MVPS) analysis pipeline. "NH-01, 02…" indicates labels of children in the NH group; "CI-01, 02…" indicates labels of children in the CI group. The same procedure was conducted for generating within-NH-group pattern similarity maps (see Methods section for details).

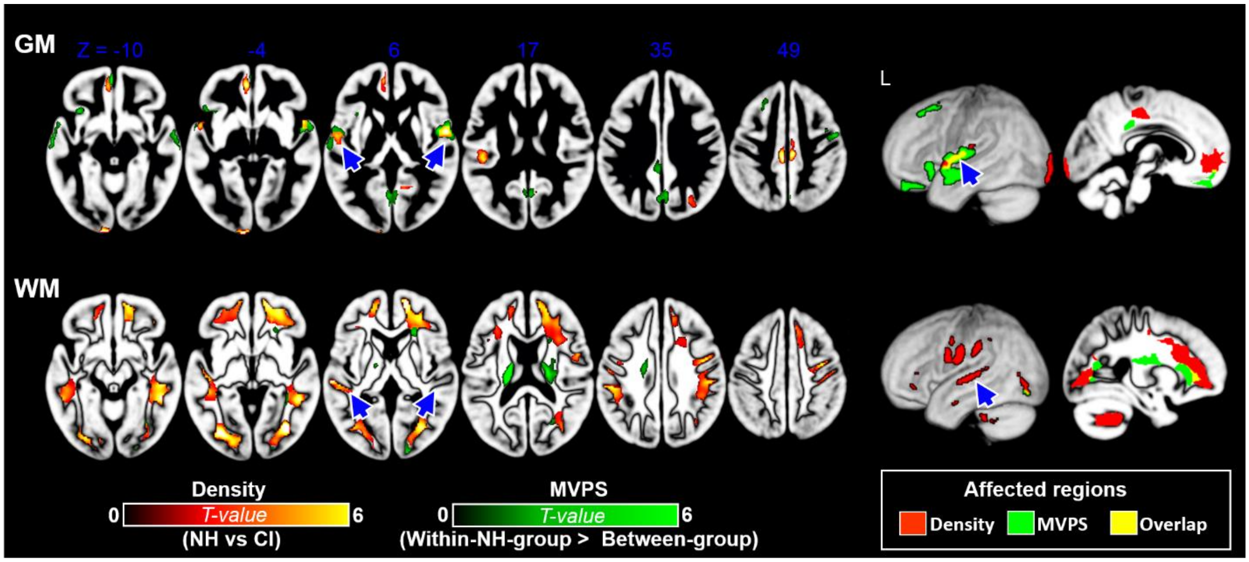

Fig. S2. Group comparisons in density and MVPS without controlling for demographic variables. The pattern of results is largely consistent with Fig. 1. GM = gray matter; WM = white matter.

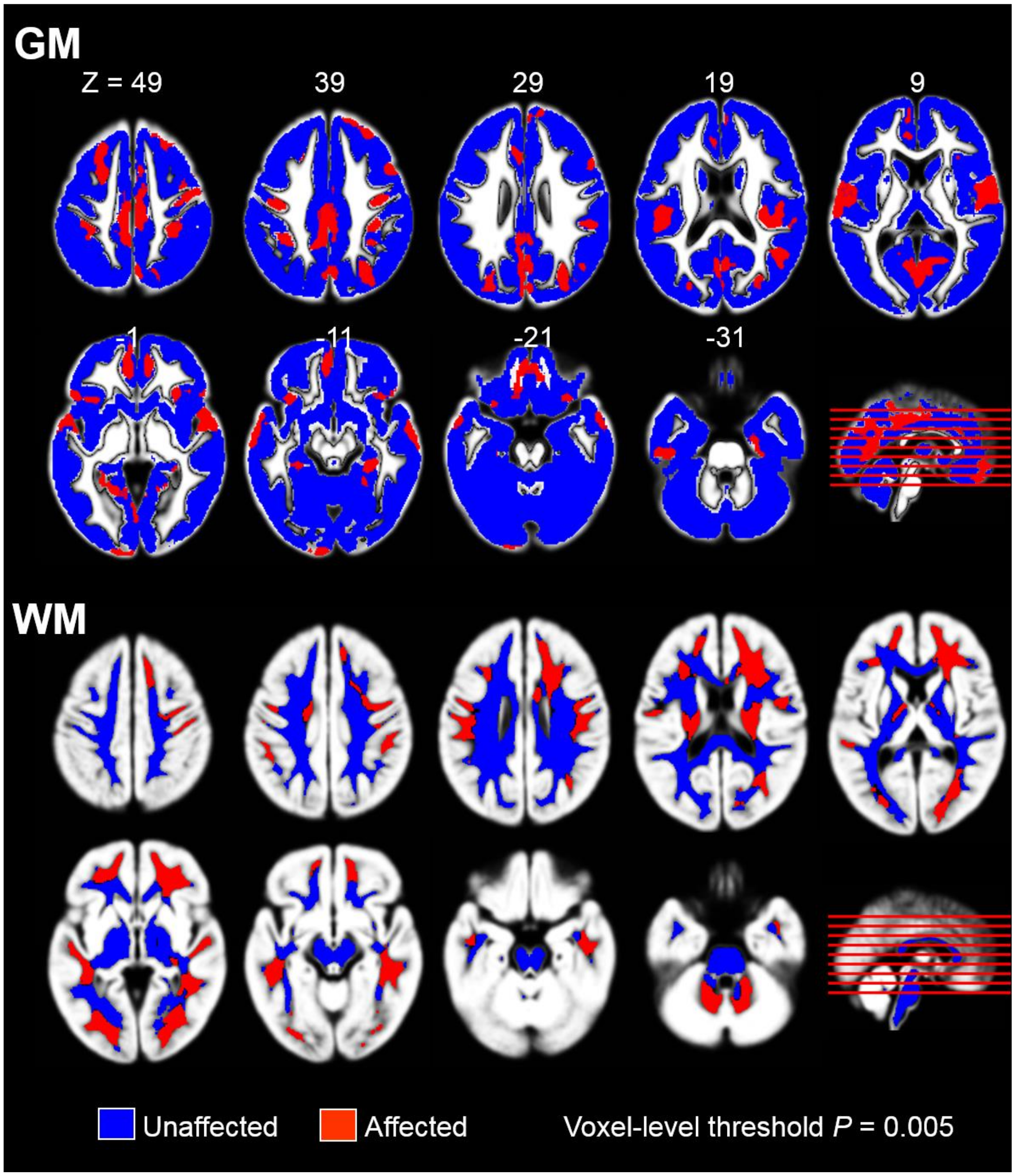

Fig. S3. Affected versus unaffected gray-matter (upper panel) and white-matter regions (lower panel). A less conservative threshold (uncorrected voxel-level threshold P = 0.005) was employed to visualize regions that are potentially different between children in the CI and NH groups.

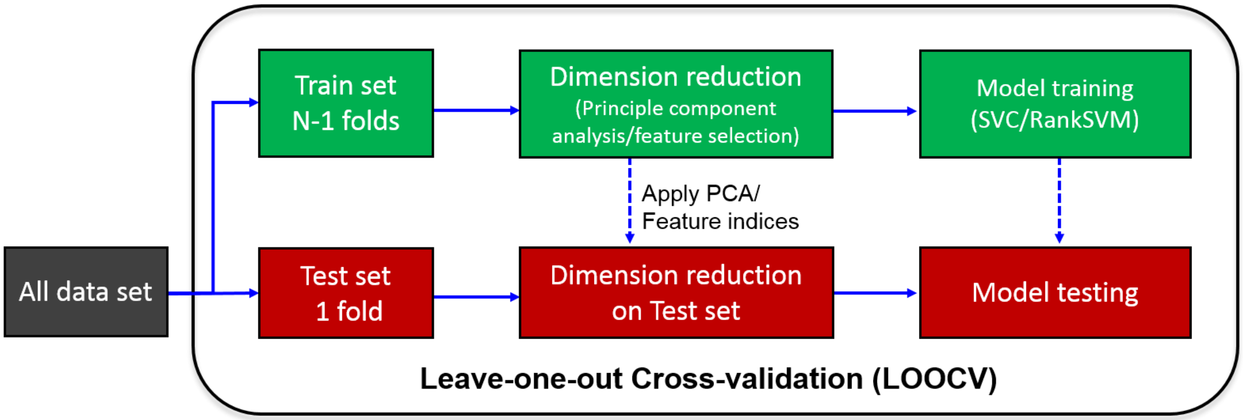

Fig. S4. Three-level nested leave-one-out cross-validation (LOOCV) procedures. Two machine learning algorithms (SVM for Classification [SVC] and RankSVM) were used to verify our findings.

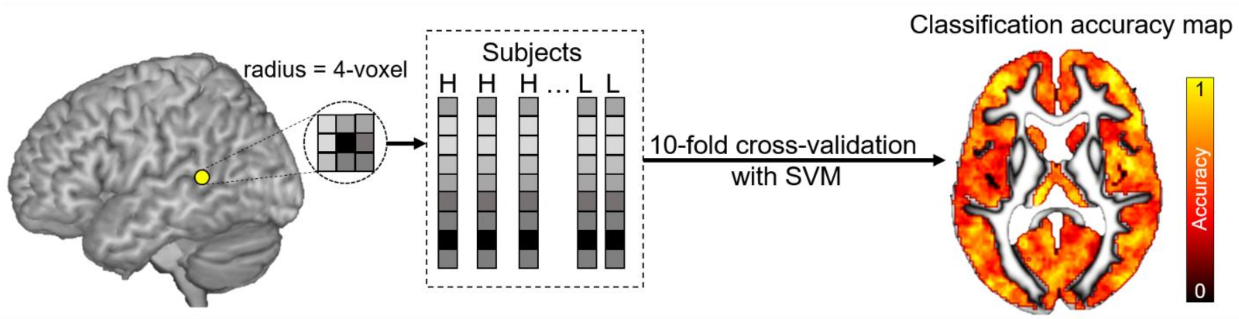

Fig. S5. Whole-brain searchlight outcome-group classification procedure. A balanced 10-fold cross-validation procedure with a linear SVM classifier was employed and used to determine the classification accuracy for each sphere. H = high-improvement child; L = low-improvement child.

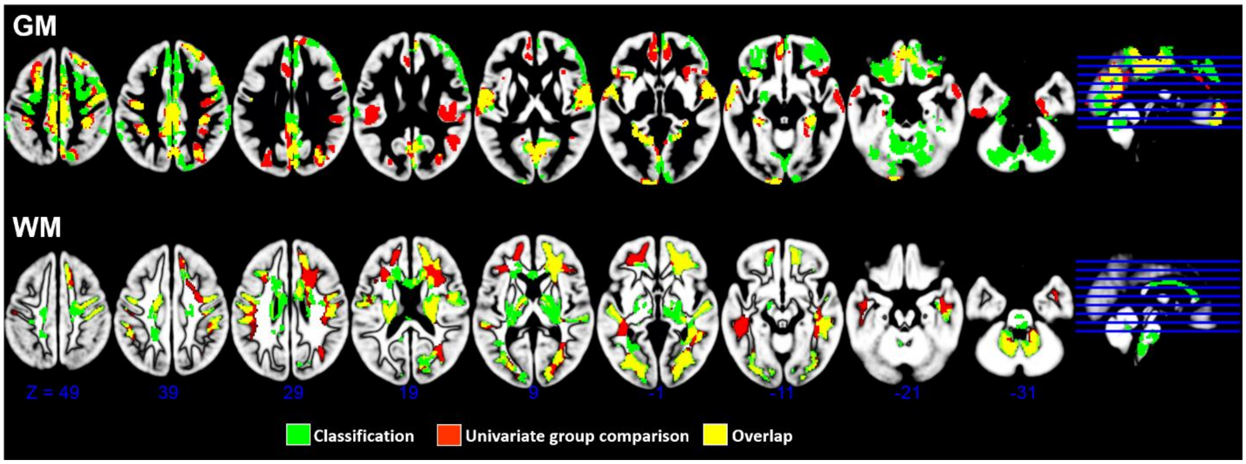

Fig. S6. Brain regions that are distinct between children in the CI and NH groups based on multivariate classification analysis (green) with 10-fold cross-validation and univariate two-sample *t*-tests (red), respectively. Overlapping regions are in yellow. A large proportion of brain areas in both tissue types (GM and WM) overlapped across the two approaches.