

Data Supplement for van Rooij et al., Cortical and Subcortical Brain Morphometry Differences Between Patients With Autism Spectrum Disorder and Healthy Individuals Across the Lifespan: Results From the ENIGMA-ASD Working Group. Am J Psychiatry (doi: 10.1176/appi.ajp.2017.17010100)

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FIGURE S1. Locations of the ENIGMA-ASD Working Groups That Contributed to the Study by Sharing Data, Knowledge, or Resources



Supplementary Methods

Quality Control of Freesurfer segmentation

Quality control of the Freesurfer segmentation was performed using the standardized ENIGMA protocols, which can be found at <http://enigma.ini.usc.edu/protocols/imaging-protocols/>. All participating cohorts ran the Freesurfer pipeline on site, and followed the protocol to determine low quality segmentations. To detect low quality segmentations, a script was run to flag all outlying individual brain volumes (volumes with a value 2.689 standard deviation from the mean). Additionally, a script was run to produce histograms of distribution of volumes for each brain region, to further indicate anomalous values. Subsequently, a script was run to provide 3D images of all the subcortical volumes within the reconstructed native space brain template of each subject. The researchers visually inspected all flagged and anomalous individual brain volumes. If low quality segmentations were found, the researchers chose to either remove a single volume from the analysis, or remove an entire subject from further analyses. This QC led to the final exclusion of 117 subjects (5.4%), and the additional exclusion of 223 single volumes (0.64%). Of the excluded subjects, 73 had an ASD diagnosis (62%) and 44 were healthy controls (38%). Of the removed volumes, 133 were from subjects with ASD (60%) and 90 from healthy controls (40%). These percentages were not significantly different between subjects with ASD and healthy controls.

TABLE S1. Demographics for All Participating Cohorts. Medication status indicates whether the presence of medication information for this cohort was available, Comorbidity status indicates whether information on comorbid disorders was available. These both also include samples where medication use and/or comorbidity were used as exclusion criteria. ADOS scores indicates the availability of classic ADOS total scores for this sample.

Name Site	N Patients	N Controls	Age (Mean)	% Female	Scanner Type	Field Strength	IQ	Medication Status	Comorbidity Info	ADOS Scores
ABIDE_CALTECH	19	19	28.16	0.21	Siemens Trio	3T	Yes	No	No	Yes
ABIDE_KKI	22	33	10.1	0.24	Philips Achieva	3T	Yes	No	No	Yes
ABIDE_LEUVEN_1	14	15	22.59	0	Philips Interna	3T	Yes	No	No	No
ABIDE_LEUVEN_2	15	20	14.16	0.23	Philips Interna	3T	Yes	No	No	No
ABIDE_MAX_MUN	24	33	26.16	0.12	Siemens Verio	3T	Yes	No	No	Yes
ABIDE_NYU	79	105	15.25	0.2	Siemens Allegra	3T	Yes	No	No	Yes
ABIDE_OHSU	7	11	10.25	0	Siemens Trio	3T	Yes	No	No	Yes
ABIDE_OLIN	20	16	16.81	0.14	Siemens Allegra	3T	Yes	No	No	Yes
ABIDE_PITT	30	27	18.9	0.14	Siemens Allegra	3T	Yes	No	No	Yes
ABIDE_SBL	15	15	34.37	0	Philips Intera	3T	Yes	No	No	Yes
ABIDE_SDSU	20	16	14.41	0.19	GE MR750	3T	Yes	No	No	Yes
ABIDE_STANFORD	24	16	9.96	0.2	GR Signa	3T	Yes	No	No	Yes
ABIDE_UM_1	54	52	13.41	0.25	GE Signa	3T	Yes	No	No	Yes
ABIDE_UM_2	13	16	15.53	0.07	GE Signa	3T	Yes	No	No	Yes
ABIDE_USM	54	42	22.01	0	Siemens Trio	3T	Yes	No	No	Yes
ABIDE_YALE	28	27	12.72	0.29	Siemens Magnetom	3T	Yes	No	No	Yes
ABIDEII-BNI_1	29	29	38.5	0.00	Philips Ingenia	3T	Yes	Yes	No	Yes
ABIDEII-EMC_1	27	27	8.09	0.21	GE MR750	3T	Yes	Yes	No	Yes
ABIDEII-ETH_1	13	24	22.7	0.00	Philips Achieva	3T	Yes	Yes	No	Yes
ABIDEII-GU_1	51	54	10.65	0.26	Siemens TriTim	3T	Yes	Yes	No	Yes
ABIDEII-IP_1	32	22	20.41	0.56	Siemens TriTim	1.5T	Yes	Yes	No	Yes
ABIDEII-IU_1	20	20	24.37	0.23	Philips Achieva	3T	Yes	Yes	No	Yes
ABIDEII-KKI_1	54	154	10.34	0.34	Philips Achieva	3T	Yes	Yes	No	Yes
ABIDEII-KUL_3	28	0	23.57	0.00	Philips Achieva	3T	Yes	Yes	No	Yes

ABIDEII-NYU_1	47	30	9.88	0.09	Siemens Allegra	3T	Yes	Yes	No	Yes
ABIDEII-NYU_2	27	0	6.78	0.11	Siemens Allegra	3T	Yes	Yes	No	Yes
ABIDEII-OHSU_1	37	56	10.94	0.39	Siemens Skyra	3T	Yes	Yes	No	Yes
ABIDEII-OILH_2	21	34	23.2	0.35	Siemens TriTim	3T	Yes	Yes	No	Yes
ABIDEII-SDSU_1	33	25	13.04	0.16	GE MR750	3T	Yes	Yes	No	Yes
ABIDEII-TCD_1	21	21	15.19	0.00	Philips Achieva	3T	Yes	Yes	No	Yes
ABIDEII-UCD_1	17	14	14.86	0.26	Siemens TriTim	3T	Yes	Yes	No	Yes
ABIDEII-UCLA_1	15	16	10.73	0.19	Siemens TriTim	3T	Yes	Yes	No	Yes
ABIDEII-USM_1	17	15	21.35	0.16	Siemens TriTim	3T	Yes	Yes	No	Yes
BRC	19	33	27.12	0	GE Signa HDx	3T	Yes	Excluded	No	Yes
CMU	13	14	16.9	0.13	Siemens Magnetom	3T	Yes	Yes	Excluded	Yes
FRANKFURT	13	12	18.08	0.15			Yes	Excluded	No	No
FSM	40	40	4.1	0.5	GE Signa	1.5T	Yes	Excluded	Excluded	Yes
MRC	74	74	9.57	0.14	GE Signa HDx	3T	Yes	Yes	Yes	Yes
MYAD	59	1	4.78	0	Siemens symphony	1.5T	No	Excluded	No	Yes
NIJMEGEN1	25	17	14.95	0.15	Siemens Avanto	1.5T	Yes	No	No	No
NIJMEGEN2	46	15	16.39	0.11	Siemens Avanto	1.5T	Yes	No	No	No
NIJMEGEN3	53	41	26.29	0.38	Siemens Avanto	1.5T	No	Yes	No	No
SAO PAULO	15	20	12.31	0	Philips	3T	Yes	No	No	No
OHSU	41	40	11.46	0.26	Siemens Trio	3T	Yes	Yes	Yes	Yes
ParelladaHGGM	35	31	12.51	0.05	Philips Intera	1.5T	Yes	No	No	no
PITT	45	44	14.6	0	Siemens Allegra	3T	Yes	Yes	Yes	Yes
TCD	23	16	26.59	0.22	Philips Achieva	3T	Yes	Excluded	Excluded	Yes
TORONTO	102	144	12.06	0.37	Siemens Trio	3T	No	No	No	No
UMCU	36	38	14.22	0.09	Philips	1.5T	Yes	No	No	No
MEGA analysis	1651	1579								
META analysis	1644	1551								

Supplementary Results

Influence of ASD status on subcortical volumes, performed with classic meta-analysis

TABLE S2. Meta-Analysis ASD v Control Comparison for Mean Subcortical Volume Outcomes. All subcortical volumes are corrected for total ICV. Bold values indicate significant effects (p-values are FDR corrected). I² values indicate the heterogeneity of the effects between sites.

Subcortical	N patients	N controls	Cohen's d	Corrected p	I ²
Lateral Ventricles	985	1071	0.11	0.031	46.45
Thalamus	982	1070	-0.09	0.043	21.33
Caudate	984	1070	-0.05	0.460	64.63
Putamen	985	1071	-0.03	0.039	42.25
Pallidum	983	1071	-0.03	0.556	33.66
Hippocampus	981	1069	-0.03	0.667	66.9
Amygdala	980	1068	-0.06	0.282	48.21
Nucleus accumbens	984	1071	-0.05	0.291	34.58
ICV	985	1071	0.10	0.036	37.78
Frontal					
Superior Frontal	977	1059	0.11	0.016	27.17
Rostral Middle Frontal	976	1060	0.11	0.013	37.76
Caudal Middle Frontal	977	1059	0.06	0.147	40.74
Pars Triangularis	975	1056	0.05	0.305	34.31
Pars Orbitalis	977	1058	0.04	0.352	20.48
Pars Opercularis	976	1057	-0.03	0.489	34.41
Medial Orbitofrontal	977	1058	0.08	0.063	22.92
Lateral Orbitofrontal	977	1057	0.00	0.947	29.27
Precentral	974	1058	0.09	0.050	26.25
Paracentral	977	1056	-0.05	0.233	38.04
Frontal Pole	975	1059	0.04	0.372	41.15
Insula					
	976	1058	-0.09	0.045	32.08
Cingulate					
Rostral Anterior (Frontal)	976	1056	0.01	0.777	34
Caudal Anterior (Frontal)	974	1056	0.03	0.463	27.85
Posterior (Parietal)	973	1060	0.05	0.313	28.38
Isthmus (Parietal)	976	1056	0.05	0.294	27.97
Parietal					
Superior Parietal	976	1058	-0.09	0.057	40.22
Inferior Parietal	977	1060	-0.05	0.298	30.55
Supramarginal	976	1056	-0.09	0.036	42.3
Postcentral	973	1058	-0.07	0.108	15.19
Precuneus	977	1060	-0.08	0.089	26.4

Temporal					
Superior temporal	975	1058	-0.15	0.001	23.64
Middle temporal	976	1060	-0.12	0.009	44.13
Inferior temporal	976	1059	-0.16	0.000	26.5
Banks of the Superior Temporal Sulcus	976	1060	-0.07	0.126	17.27
Fusiform	975	1059	-0.19	0.000	20.04
Transverse Temporal	977	1059	-0.24	0.000	22.72
Entorhinal	973	1058	-0.24	0.000	31.93
Temporal Pole	972	1057	-0.14	0.001	43.66
Parahippocampal	974	1059	-0.11	0.019	43.98
Occipital					
Lateral Occipital	975	1056	-0.02	0.083	33.6
Lingual	976	1058	-0.02	0.147	35.3
Cuneus	977	1057	-0.06	0.177	33.6
Pericalcarine	977	1057	-0.01	0.083	38.57

Sensitivity analysis with correction for total grey matter volume

Following the main ASD vs Control mega-analysis, the same model was run again for the subcortical volumes without correction for ICV, but instead correcting for total intracranial grey matter (total subcortical grey matter and total cortical grey matter output from Freesurfer). This since ICV potentially does not accurately reflect the current total grey matter volume. The results are depicted in Table S3. The correlation between ICV and total grey matter values is 0.78.

TABLE S3. Mega-Analysis of Diagnosis on Subcortical Volumes, Corrected for Gender, Age, IQ, and Total Grey Matter Volume. Bold values indicate significant effects (p-values are FDR corrected).

	N Controls	N Patients	Cohen's d	Corrected p
Lateral Ventricles	1606	1522	0.249	0.016
Thalamus	1569	1482	0.074	0.448
Caudate	1597	1494	-0.130	0.206
Putamen	1604	1517	-0.268	0.012
Pallidum	1600	1518	-0.191	0.069
Hippocampus	1596	1509	-0.023	0.793
Amygdala	1595	1507	-0.093	0.375
Nucleus accumbens	1601	1508	-0.263	0.012

Results remain largely the same as in the main analysis where we corrected for ICV, only the pallidum volume is now just marginally significantly different between subjects with ASD and healthy controls after correction for FDR.

Main ASD analysis with groups matched on gender and IQ.

An additional sensitivity analysis as performed to exclude the potential influence of gender and IQ imbalances in the sample on the main effects. To this end, the full cohort was matched on IQ and Gender distribution using the MatchIt package in R (Ho, Imai, King, & Stuart, 2011). After matching, 1073 controls and 976 subjects with ASD remained in the analysis. Average IQ was 110.3 for controls and 107.28 for subjects with ASD respectively, with 17.17% females in the control groups and 13.81% females in the ASD group. The mega-analysis testing the main effect of diagnosis was subsequently repeated, with age added as a covariate in all analyses (see Table S4). The outcome of this sensitivity analyses indicate that the main effects of ASD on brain morphometry is robust, and is largely uninfluenced by the observed imbalance in IQ and gender distribution in our sample. Interestingly, some effects of cortical thickness in the parietal and occipital lobes are now also observed, indicating a more widespread posterior reduction in cortical thickness in this matched sample.

TABLE S4. Mega-Analysis With Groups Matched on IQ and Gender, ASD v Control Comparison Model Outcomes. All subcortical volumes are corrected for total ICV. Bold values indicate significant effects (p-values are FDR corrected).

Subcortical	N controls	N patients	Cohen's d	Corrected p
Lateral Ventricles	1358	1229	0.16	0.004
Thalamus	1386	1262	0.02	0.683
Caudate	1388	1264	-0.08	0.151
Putamen	1386	1262	-0.24	0.000
Pallidum	1383	1255	-0.18	0.001
Hippocampus	1378	1252	-0.03	0.671
Amygdala	1385	1253	-0.09	0.012
Nucleus accumbens	1381	1263	-0.23	0.000
ICV	1358	1229	0.18	0.002
Frontal				
Superior Frontal	1241	1173	-0.01	0.879
Rostral Middle Frontal	1240	1173	0.07	0.127
Caudal Middle Frontal	1241	1173	-0.05	0.281
Pars Triangularis	1239	1168	0.16	0.009
Pars Orbitalis	1240	1172	0.01	0.830
Pars Opercularis	1239	1169	0.12	0.005
Medial Orbitofrontal	1240	1171	0.08	0.096
Lateral Orbitofrontal	1241	1172	-0.06	0.208
Precentral	1238	1172	0.13	0.003
Paracentral	1241	1168	0.12	0.006
Frontal Pole	1237	1170	0.05	0.281
Insula				
	1240	1170	-0.13	0.004
Cingulate				
Rostral Anterior (Frontal)	1238	1169	-0.02	0.646

Caudal Anterior (Frontal)	1237	1171	-0.03	0.546
Posterior (Parietal)	1237	1173	0.05	0.285
Isthmus (Parietal)	1240	1169	0.04	0.366
Parietal				
Superior Parietal	1240	1171	-0.13	0.003
Inferior Parietal	1241	1173	-0.01	0.120
Supramarginal	1241	1171	-0.16	0.001
Postcentral	1238	1173	-0.01	0.100
Precuneus	1241	1173	-0.01	0.100
Temporal				
Superior temporal	1240	1173	-0.15	0.001
Middle temporal	1241	1170	-0.16	0.001
Inferior temporal	1240	1173	-0.19	0.000
Banks of the Superior Temporal Sulcus	1238	1171	-0.11	0.016
Fusiform	1241	1171	-0.21	0.000
Transverse Temporal	1241	1170	-0.16	0.001
Entorhinal	1238	1167	-0.25	0.000
Temporal Pole	1233	1165	-0.15	0.001
Parahippocampal	1237	1168	-0.15	0.001
Occipital				
Lateral Occipital	1239	1172	-0.14	0.002
Lingual	1240	1172	-0.13	0.003
Cuneus	1239	1171	-0.03	0.460
Pericalcarine	1238	1166	-0.06	0.208

Main ASD subcortical analysis with groups matched on ICV

An additional sensitivity analysis as performed to further exclude any potential influences of the total ICV difference on subcortical ASD diagnostic effects. To this end, the full cohort was matched on ICV between subjects with ASD and controls using the MatchIt package in R. After matching, 1388 controls and 1264 patients were included in the analysis. The results (see Table S5) verify that the reported subcortical effects are robust after matching for total ICV.

TABLE S5. Mega-Analysis With Groups Matched on ICV, ASD v Control Comparison Model Outcomes Corrected for Age, Sex, and Scan Site. Bold values indicate significant effects (p-values are FDR corrected).

Subcortical	Cohen's d	N controls	N patients	Corrected p
Lateral Ventricles	0.11	1358	1229	0.014
Thalamus	0.01	1386	1262	0.761
Caudate	-0.05	1388	1264	0.271
Putamen	-0.12	1386	1262	0.007
Pallidum	-0.11	1383	1255	0.015
Hippocampus	-0.03	1378	1252	0.555
Amygdala	-0.06	1385	1253	0.218
Nucleus accumbens	-0.15	1381	1263	0.002
ICV	0.11	1358	1229	0.014
Frontal				
Superior Frontal	0.02	1483	1456	0.664
Rostral Middle Frontal	0.06	1482	1457	0.168
Caudal Middle Frontal	-0.03	1483	1456	0.446
Pars Triangularis	0.01	1481	1452	0.880
Pars Orbitalis	0.02	1482	1456	0.582
Pars Opercularis	-0.08	1481	1453	0.060
Medial Orbitofrontal	0.07	1481	1455	0.074
Lateral Orbitofrontal	-0.04	1483	1454	0.352
Precentral	-0.13	1480	1455	0.002
Paracentral	-0.09	1483	1452	0.031
Frontal Pole	0.04	1477	1454	0.352
Insula				
	-0.12	1482	1453	0.003
Cingulate				
Rostral Anterior (Frontal)	-0.03	1478	1452	0.541
Caudal Anterior (Frontal)	-0.01	1475	1450	0.910
Posterior (Parietal)	0.07	1477	1456	0.094
Isthmus (Parietal)	0.04	1481	1449	0.362
Parietal				
Superior Parietal	-0.10	1482	1455	0.012
Inferior Parietal	-0.09	1483	1457	0.033
Supramarginal	-0.14	1482	1453	0.001
Postcentral	-0.11	1479	1455	0.008
Precuneus	-0.08	1482	1457	0.068
Temporal				
Superior temporal	-0.14	1480	1454	0.001
Middle temporal	-0.15	1482	1455	0.000
Inferior temporal	-0.17	1482	1455	0.000

Banks of the Superior Temporal Sulcus	-0.10	1479	1455	0.021
Fusiform	-0.21	1482	1454	0.000
Transverse Temporal	-0.16	1483	1454	0.000
Entorhinal	-0.25	1480	1452	0.000
Temporal Pole	-0.17	1475	1449	0.000
Parahippocampal	-0.14	1479	1452	0.001
Occipital				
Lateral Occipital	-0.12	1480	1453	0.003
Lingual	-0.10	1481	1454	0.016
Cuneus	0.00	1480	1452	0.953
Pericalcarine	-0.03	1480	1447	0.501

Sensitivity analysis without corrections for IQ.

By excluding potential influence of IQ on the diagnostic effects, it may also be possible to remove variance of interest, especially when IQ and the diagnostic status (ASD or healthy control) may be conceptually linked. To exclude this possibility, the main mega-analysis model was run performed again without IQ included in the covariance list, as depicted in Table S5. The results do not significantly differ from the model corrected for IQ, again confirming that the between-group diagnostic results are not influenced by the differences in IQ between these groups.

TABLE S6. Mega-Analysis With Correction for and Gender, Age, and Scan Site, But No Correction for IQ. Bold values indicate significant effects (p-values are FDR corrected).

Subcortical	N controls	N patients	Cohen's d	Corrected p
Lateral Ventricles	1575	1485	0.13	0.003
Thalamus	1603	1497	0.05	0.348
Caudate	1610	1520	0.00	0.990
Putamen	1606	1521	-0.07	0.168
Pallidum	1602	1512	-0.09	0.046
Hippocampus	1601	1510	-0.01	0.807
Amygdala	1607	1511	-0.09	0.036
Nucleus accumbens	1602	1521	-0.10	0.019
ICV	1612	1525	0.06	0.016
Frontal				
Superior Frontal	1527	1532	0.17	0.000
Rostral Middle Frontal	1526	1533	0.23	0.000
Caudal Middle Frontal	1527	1532	0.10	0.026
Pars Triangularis	1525	1528	0.13	0.005
Pars Orbitalis	1526	1531	0.13	0.005
Pars Opercularis	1525	1529	0.03	0.576
Medial Orbitofrontal	1525	1531	0.14	0.002

Lateral Orbitofrontal	1527	1530	0.04	0.438
Precentral	1524	1531	-0.03	0.576
Paracentral	1527	1528	-0.01	0.847
Frontal Pole	1521	1530	0.12	0.006
Insula				
	1525	1529	-0.07	0.135
Cingulate				
Rostral Anterior (Frontal)	1522	1528	0.03	0.576
Caudal Anterior (Frontal)	1519	1526	0.03	0.576
Posterior (Parietal)	1521	1532	0.13	0.005
Isthmus (Parietal)	1525	1525	0.08	0.087
Parietal				
Superior Parietal	1526	1531	-0.03	0.567
Inferior Parietal	1527	1533	0.00	0.963
Supramarginal	1526	1529	-0.07	0.114
Postcentral	1523	1531	-0.02	0.665
Precuneus	1526	1533	-0.01	0.835
Temporal				
Superior temporal	1524	1530	-0.06	0.176
Middle temporal	1526	1530	-0.10	0.037
Inferior temporal	1526	1531	-0.16	0.000
Banks of the Superior Temporal Sulcus	1523	1531	-0.02	0.635
Fusiform	1525	1530	-0.20	0.000
Transverse Temporal	1527	1530	-0.08	0.076
Entorhinal	1523	1527	-0.22	0.000
Temporal Pole	1518	1523	-0.12	0.007
Parahippocampal	1522	1528	-0.09	0.039
Occipital				
Lateral Occipital	1524	1529	-0.08	0.091
Lingual	1525	1530	-0.06	0.206
Cuneus	1524	1528	0.02	0.646
Pericalcarine	1524	1523	-0.02	0.646

Sensitivity analyses on the effects of medication use and comorbidity.

For all samples, information about medication use and comorbidity were collected where available. Medication use was available for 858 subjects with ASD (625 without prescribed medication, 233 with prescribed medication). Due to the large variation of medication types (e.g. stimulants, atypical antipsychotics, antidepressants, anxiolytics), no further subdivision on medication type was possible. A linear mixed effects model was run to see if these two groups differed on subcortical brain volumes differences, with age, gender and IQ added as covariates and site as a random factor. No significant effects of medication use on brain volumes were observed (Table S7).

Similarly, information on comorbid disorders was available for 951 subjects with ASD (803 without comorbid disorders, 148 subjects with some kind of comorbidity). Given the large variety of comorbidities (e.g. Depression, ADHD, OCD, Anxiety, Tourettes), no further useful subdivisions could be made within this sample. Hence, a linear mixed effects model was run to investigate the effect of comorbidity on subcortical brain volumes. Age, gender and IQ were added as covariates and Site was added as a random factor. No significant differences were observed between subjects with and without comorbidities (Table S7).

TABLE S7. Mega-Analysis of Effects of Medication Use (yes/no) and Comorbidities (yes/no) on the Subcortical Volumes and Cortical Thickness. All models corrected for sex, age, IQ and scan -site. Bold values indicate significant effects (p-values are FDR corrected).

Subcortical	Cohen's d Medication	Corrected p Medication	Cohen's d Comorbidity	Corrected p Comorbidity
Lateral Ventricles	-0.21	0.507	-0.14	0.429
Thalamus	-0.15	0.638	-0.21	0.261
Caudate	-0.14	0.638	0.16	0.381
Putamen	-0.25	0.448	-0.32	0.073
Pallidum	-0.07	0.838	0.09	0.604
Hippocampus	-0.10	0.787	0.04	0.828
Amygdala	0.02	0.948	0.02	0.916
Nucleus accumbens	-0.32	0.293	0.06	0.722
ICV	0.01	0.948	-0.05	0.774
Frontal				
Superior Frontal	-0.07	0.724	-0.39	0.143
Rostral Middle Frontal	-0.24	0.277	-0.35	0.208
Caudal Middle Frontal	-0.19	0.328	-0.30	0.220
Pars Triangularis	-0.18	0.328	-0.26	0.264
Pars Orbitalis	-0.18	0.328	-0.72	0.001
Pars Opercularis	-0.22	0.289	-0.27	0.251
Medial Orbitofrontal	-0.36	0.108	-0.21	0.317
Lateral Orbitofrontal	-0.37	0.108	-0.43	0.124
Precentral	-0.33	0.129	-0.46	0.095
Paracentral	-0.11	0.574	-0.22	0.317
Frontal Pole	-0.29	0.172	-0.30	0.220
Insula				
	-0.36	0.108	-0.30	0.220
Cingulate				
Rostral Anterior (Frontal)	-0.10	0.574	-0.14	0.476
Caudal Anterior (Frontal)	-0.10	0.574	-0.09	0.634
Posterior (Parietal)	0.02	0.896	-0.15	0.450
Isthmus (Parietal)	-0.04	0.795	-0.34	0.220
Parietal				
Superior Parietal	-0.13	0.500	-0.15	0.450

Inferior Parietal	-0.18	0.328	-0.20	0.317
Supramarginal	-0.19	0.328	-0.42	0.124
Postcentral	-0.29	0.172	-0.31	0.220
Precuneus	-0.11	0.574	-0.21	0.317
Temporal				
Superior temporal	-0.32	0.140	-0.29	0.223
Middle temporal	-0.34	0.129	-0.27	0.251
Inferior temporal	-0.48	0.020	-0.23	0.317
Banks of the Superior Temporal Sulcus	-0.27	0.201	-0.20	0.317
Fusiform	-0.26	0.229	-0.31	0.220
Transverse Temporal	-0.19	0.328	-0.22	0.317
Entorhinal	-0.20	0.328	-0.15	0.450
Temporal Pole	-0.22	0.289	-0.21	0.317
Parahippocampal	-0.31	0.152	-0.33	0.220
Occipital				
Lateral Occipital	-0.19	0.328	-0.23	0.317
Lingual	-0.22	0.292	-0.41	0.129
Cuneus	-0.24	0.277	-0.21	0.317
Pericalcarine	-0.05	0.772	-0.30	0.220

Main ASD analysis split by hemisphere.

Given previous findings on lateralization effects of morphometric features in ASD, the main ASD vs Controls analysis was repeated split by hemisphere. The model was kept identical to the main group analysis. In general, both subcortical volume and cortical thickness effects are robust over both hemispheres, with decreased striatal volumes and temporal cortical thickness observed in subjects with ASD over both hemispheres, as well as increased frontal cortical thickness.

TABLE S8. Mega-Analysis of Main ASD Effect Split by Hemisphere. Separate models were run for each hemisphere. L indicates left hemisphere, R indicates hemisphere. All models corrected for sex, age, IQ and scan -site. Bold values indicate significant effects (p-values are FDR corrected).

		N	N	Cohen's	Corrected		N	N	Cohen's	Corrected
Subcortical		Controls	Patients	d	p		s	Patients	d	p
Lateral Ventricles	L	1112	1035	0.11	0.028	R	457	447	0.13	0.054
Thalamus	L	1123	1030	-0.01	0.868	R	474	464	-0.02	0.755
Caudate	L	1127	1051	-0.08	0.101	R	477	466	-0.01	0.922
Putamen	L	1124	1052	-0.10	0.036	R	476	466	-0.12	0.052
Pallidum	L	1123	1044	-0.09	0.076	R	473	465	-0.09	0.164
Hippocampus	L	1122	1045	-0.03	0.616	R	473	462	-0.13	0.052
Amygdala	L	1128	1046	-0.08	0.101	R	473	462	-0.14	0.034
Nucleus accumbens	L	1124	1054	-0.14	0.008	R	472	464	-0.15	0.026
Frontal										
Superior Frontal	L	1574	1659	0.10	0.019	R	1574	1657	0.20	0.000
Rostral Middle Frontal	L	1573	1659	0.14	0.000	R	1573	1658	0.22	0.000
Caudal Middle Frontal	L	1574	1657	0.05	0.275	R	1574	1658	0.09	0.038
Pars Triangularis	L	1573	1657	0.09	0.038	R	1573	1655	0.10	0.029
Pars Orbitalis	L	1573	1658	0.07	0.087	R	1574	1657	0.13	0.002
Pars Opercularis	L	1574	1658	-0.01	0.897	R	1572	1655	0.02	0.633
Medial Orbitofrontal	L	1572	1658	0.08	0.076	R	1574	1657	0.18	0.000
Lateral Orbitofrontal	L	1574	1657	0.05	0.287	R	1574	1656	0.03	0.454
Precentral	L	1570	1657	-0.06	0.151	R	1572	1657	-0.05	0.249
Paracentral	L	1574	1657	0.01	0.803	R	1574	1655	-0.04	0.438
Frontal Pole	L	1570	1658	0.08	0.067	R	1571	1656	0.09	0.029
Insula										
	L	1570	1656	-0.01	0.792	R	1570	1654	-0.10	0.027
Cingulate										
Rostral Anterior (Frontal)	L	1570	1658	-0.05	0.255	R	1573	1653	0.09	0.040
Caudal Anterior (Frontal)	L	1571	1658	0.02	0.633	R	1569	1652	0.02	0.680
Posterior (Parietal)	L	1572	1659	0.06	0.215	R	1570	1657	0.15	0.000
Isthmus (Parietal)	L	1573	1653	0.02	0.653	R	1573	1655	0.13	0.002
Parietal										
Superior Parietal	L	1573	1656	0.02	0.697	R	1573	1655	-0.04	0.438
Inferior Parietal	L	1573	1659	0.01	0.889	R	1573	1657	0.03	0.574
Supramarginal	L	1572	1656	-0.04	0.370	R	1574	1654	-0.08	0.067
Postcentral	L	1572	1657	-0.02	0.633	R	1571	1656	-0.03	0.574
Precuneus	L	1574	1659	0.04	0.427	R	1573	1658	0.01	0.828
Temporal										
Superior temporal	L	1570	1655	-0.09	0.040	R	1573	1655	-0.05	0.244
Middle temporal	L	1570	1656	-0.09	0.029	R	1574	1655	-0.09	0.040
Inferior temporal	L	1571	1657	-0.05	0.256	R	1574	1657	-0.19	0.000
Banks of the Superior Temporal Sulcus	L	1569	1650	0.00	0.986	R	1566	1655	-0.05	0.235
Fusiform	L									

Transverse Temporal	L	1574	1658	-0.06	0.142	R	1574	1656	-0.13	0.001
Entorhinal	L	1567	1654	-0.15	0.000	R	1562	1642	-0.23	0.000
Temporal Pole	L	1570	1654	-0.09	0.032	R	1569	1652	-0.15	0.000
Parahippocampal	L	1572	1656	-0.08	0.065	R	1571	1656	-0.10	0.019
Occipital										
Lateral Occipital	L	1569	1655	-0.01	0.828	R	1574	1655	-0.08	0.045
Lingual	L	1572	1658	-0.01	0.859	R	1574	1656	-0.06	0.180
Cuneus	L	1573	1655	0.06	0.217	R	1572	1654	0.07	0.094
Pericalcarine	L	1572	1654	0.01	0.842	R	1573	1652	0.00	0.986

Sensitivity analyses on the effects of ASD severity

ASD severity was collected for all subjects with ASD where available in our cohort. The most commonly available measure was the total ADOS_G score (Lord et al., 2000), which was available for 1545 subjects with ASD. Additionally, the Social Responsiveness Scale (SRS), was available for 1302 subjects with ASD. A simple regression was performed, predicting subcortical brain volumes based on ADOS total scores, with age, gender and scansite added as covariates. The results of this analysis are depicted in Table S6. Results are mostly consistent with the direction of the group contrast, i.e. in ICV and lateral ventricles higher ADOS scores are associated with larger volume, while higher ADOS scores are associated with lower volumes in the amygdala, thalamus and nucleus accumbens. Greater thickness is associated with higher ADOS scores in the frontal areas, and lower thickness with higher ADOS scores in the temporal areas. Interestingly, insular, cingulate, parietal and occipital regions also show associations with ADOS scores, with higher ADOS scores generally associated with increased thickness in cingulate, parietal and occipital regions, while lower cortical thickness is associated with higher ADOS scores in the insula. SRS showed no significant associations with subcortical volumes or cortical thickness in any of the partitions.

TABLE S9. Mega-Analytic Regression Analysis of ADOS Scores With Subcortical Volumes. All subcortical volumes are corrected for total ICV, age and gender were added as covariates. Bold values indicate significant effects (p-values are FDR corrected).

Subcortical	n	Estimate (ADOS)	Corrected p (ADOS)	R ² (ADOS)
Lateral Ventricles	1538	87.85	0.000	0.059
Thalamus	1538	-21.37	0.000	0.034
Caudate	1538	-4.84	0.059	0.004
Putamen	1538	7.25	0.059	0.004
Pallidum	1538	-0.41	0.726	0.001
Hippocampus	1538	-21.29	0.000	0.074
Amygdala	1538	-11.88	0.000	0.093
Nucleus accumbens	1538	-3.40	0.000	0.000
ICV	1538	352.38	0.007	0.071
Frontal				
Superior Frontal	1545	0.000	0.598	0.73
Rostral Middle Frontal	1545	0.005	0.000	0.70
Caudal Middle Frontal	1545	0.003	0.000	0.68
Pars Triangularis	1545	0.004	0.000	0.69
Pars Orbitalis	1545	-0.002	0.065	0.61
Pars Opercularis	1545	0.001	0.103	0.69
Medial Orbitofrontal	1545	0.000	0.735	0.53
Lateral Orbitofrontal	1545	0.007	0.000	0.67
Precentral	1545	0.003	0.000	0.57
Paracentral	1545	-0.002	0.000	0.64
Frontal Pole	1545	0.005	0.000	0.39
Insula				
	1545	-0.003	0.000	0.43
Cingulate				
Rostral Anterior (Frontal)	1545	0.009	0.000	0.36
Caudal Anterior (Frontal)	1545	0.014	0.000	0.24
Posterior (Parietal)	1545	0.013	0.000	0.45
Isthmus (Parietal)	1545	-0.011	0.071	0.03
Parietal				
Superior Parietal	1545	0.001	0.069	0.76
Inferior Parietal	1545	0.001	0.080	0.83
Supramarginal	1545	0.002	0.000	0.84
Postcentral	1545	0.004	0.000	0.60
Precuneus	1545	-0.006	0.000	0.79
Temporal				
Superior temporal	1545	-0.002	0.002	0.51
Middle temporal	1545	0.001	0.081	0.61

Inferior temporal	1545	-0.001	0.157	0.56
Banks of the Superior Temporal Sulcus	1545	-0.001	0.054	0.57
Fusiform	1545	-0.006	0.000	0.56
Transverse Temporal	1545	-0.002	0.020	0.39
Entorhinal	1545	-0.018	0.000	0.17
Temporal Pole	1545	-0.014	0.000	0.13
Parahippocampal	1545	-0.014	0.000	0.23
Occipital				
Lateral Occipital	1545	0.003	0.000	0.52
Lingual	1545	0.003	0.000	0.33
Cuneus	1545	0.006	0.000	0.37
Pericalcarine	1545	0.010	0.000	0.20

Mega analysis of Diagnosis effects split by Adult and Children

In order to further explore the development of subcortical volumes and cortical thickness in ASD, the cohort was subdivided in subjects above and below 18 years of age. The results of the mega-analysis are reported in Table S10. As can be observed, the strongest effects are generally observed in children, which also constitute the largest part of the sample. Nevertheless, the overall pattern of result are stable and robust over this subdivision, with similar volumes reductions observed in the subcortical volumes in ASD as well as higher cortical thickness in frontal areas and reduced cortical thickness in temporal areas.

TABLE S10. Mega-Analytic Regression Analysis Split by Adults (18+) and Children (18-). All subcortical volumes are corrected for total ICV, sex, age, IQ and scan-site were added as covariates. Bold values indicate significant effects (p-values are FDR corrected).

Subcortical	N	N	Cohen's	Corrected	N	N	Cohen's	Corrected
	Controls Children	Patients Children	d Children		p Children	Controls Adults	Patients Adults	
Lateral Ventricles	1112	1035	0.11	0.028	457	447	0.13	0.054
Thalamus	1123	1030	-0.01	0.868	474	464	-0.02	0.755
Caudate	1127	1051	-0.08	0.101	477	466	-0.01	0.922
Putamen	1124	1052	-0.10	0.036	476	466	-0.12	0.052
Pallidum	1123	1044	-0.09	0.076	473	465	-0.09	0.164
Hippocampus	1122	1045	-0.03	0.616	473	462	-0.13	0.052
Amygdala	1128	1046	-0.08	0.101	473	462	-0.14	0.034
Nucleus accumbens	1124	1054	-0.14	0.008	472	464	-0.15	0.026
Frontal								
Superior Frontal	992	1016	0.144	0.001	468	438	0.273	0.063
Rostral Middle Frontal	991	1016	0.180	0.000	468	439	0.262	0.009
Caudal Middle Frontal	992	1015	0.062	0.172	468	439	0.110	0.000
Pars Triangularis	991	1012	0.022	0.629	467	438	0.356	0.734
Pars Orbitalis	992	1015	0.087	0.054	467	439	0.218	0.124

Pars Opercularis	991	1014	-0.037	0.414	468	437	0.146	0.018
Medial Orbitofrontal	990	1015	0.096	0.033	468	438	0.213	0.001
Lateral Orbitofrontal	992	1015	-0.022	0.623	468	437	0.186	0.985
Precentral	991	1014	-0.022	0.631	467	439	-0.105	0.185
Paracentral	992	1012	0.000	0.998	468	438	-0.001	0.323
Frontal Pole	988	1014	0.093	0.039	466	438	0.179	0.225
Insula								
	992	1012	-0.104	0.021	466	439	0.028	0.225
Cingulate								
Rostral Anterior (Frontal)	989	1013	-0.009	0.841	466	437	0.129	0.401
Caudal Anterior (Frontal)	985	1010	0.018	0.694	467	438	0.078	0.024
Posterior (Parietal)	989	1015	0.117	0.010	467	439	0.161	0.000
Isthmus (Parietal)	990	1010	0.101	0.025	468	437	0.031	0.118
Parietal								
Superior Parietal	992	1015	0.017	0.707	468	438	-0.090	0.140
Inferior Parietal	992	1016	0.085	0.060	468	439	-0.154	0.310
Supramarginal	992	1013	-0.094	0.037	467	438	-0.057	0.225
Postcentral	990	1014	-0.011	0.815	466	439	-0.067	0.000
Precuneus	991	1016	0.069	0.128	468	439	-0.023	0.240
Temporal								
Superior temporal	991	1014	-0.085	0.059	466	438	-0.080	0.684
Middle temporal	992	1014	-0.110	0.015	467	438	-0.107	0.000
Inferior temporal	991	1014	-0.113	0.013	468	439	-0.247	0.002
Banks of the Superior Temporal Sulcus	992	1015	-0.037	0.419	464	438	-0.050	0.000
Fusiform	990	1013	-0.163	0.000	468	439	-0.273	0.006
Transverse Temporal	992	1015	-0.123	0.006	468	437	-0.101	0.225
Entorhinal	989	1012	-0.207	0.000	468	437	-0.185	0.021
Temporal Pole	988	1012	-0.128	0.005	463	434	-0.128	0.225
Parahippocampal	987	1013	-0.129	0.004	468	437	-0.085	0.748
Occipital								
Lateral Occipital	989	1014	-0.026	0.572	468	437	-0.157	0.211
Lingual	990	1013	-0.050	0.274	468	439	-0.069	0.032
Cuneus	989	1011	0.076	0.094	468	439	0.083	0.649
Pericalcarine	989	1008	0.021	0.641	468	438	-0.022	0.059

Fractional Polynomial Fit of Age for subcortical and cortical partitions

TABLE S11. Fractional Polynomial Best Model Fits for the Entire Sample, for both subjects with ASD and healthy controls separately, showing their coefficients after fitting. The optimal one- or two-term model was selected with the possible powers of -2, -1, -0.5, 0, 0.5, 1, 2 and 3. The “I()” model indicates the use of a specific power function ‘as is’ in the model , without incorporating lower order powers of the same variable.

	Model ASD	Model Controls
Thalamus	$\log((\text{Age}/10)) + I(\log((\text{Age}/10))^2)$	$\log((\text{Age}/10)) + I((\text{Age}/10)^{0.5})$
Caudate	$I((\text{Age}/10)^{-2})$	$\log((\text{Age}/10)) + I(\log((\text{Age}/10))^2)$
Putamen	$I((\text{Age}/10)^{-2})$	$\log((\text{Age}/10)) + I((\text{Age}/10)^{0.5})$
Amygdala	$\log((\text{Age}/10)) + I(\log((\text{Age}/10))^2)$	$\log((\text{Age}/10)) + I((\text{Age}/10)^{0.5})$
Nucleus accumbens	$\log((\text{Age}/10)) + I(\log((\text{Age}/10))^2)$	$\log((\text{Age}/10)) + I((\text{Age}/10)^{0.5})$
Lateral Ventricles	$I((\text{Age}/10)^2) + I((\text{Age}/10)^3)$	$I((\text{Age}/10)^1)$
ICV	$I((\text{Age}/10)^{-2}) + I((\text{Age}/10)^{-2} * \log((\text{Age}/10)))$	$I((\text{Age}/10)^{-1})$
Superior Frontal	$I((\text{Age}/10)^{-0.5}) + I((\text{Age}/10)^3)$	$I((\text{Age}/10)^{-2}) + I((\text{Age}/10)^{0.5})$
Rostral Middle Frontal	$I((\text{Age}/10)^{-0.5}) + I((\text{Age}/10)^3)$	$I((\text{Age}/10)^{-2}) + I((\text{Age}/10)^1)$
Caudal Middle Frontal	$I((\text{Age}/10)^{-0.5}) + I((\text{Age}/10)^3)$	$I((\text{Age}/10)^{-2}) + I((\text{Age}/10)^1)$
Pars Triangularis	$\log((\text{Age}/10)) + I((\text{Age}/10)^3)$	$I((\text{Age}/10)^{-2}) + I((\text{Age}/10)^{0.5})$
Pars Orbitalis	$\log((\text{Age}/10))$	$I((\text{Age}/10)^{-2}) + \log((\text{Age}/10))$
Medial Orbitofrontal	$I((\text{Age}/10)^{-1}) + I((\text{Age}/10)^3)$	$I((\text{Age}/10)^{-2}) + \log((\text{Age}/10))$
Frontal Pole	$I((\text{Age}/10)^{-1}) + I((\text{Age}/10)^3)$	$\log((\text{Age}/10)) + I((\text{Age}/10)^3)$
Posterior (parietal) Cingulate	$I((\text{Age}/10)^1) + I((\text{Age}/10)^2)$	$I((\text{Age}/10)^{-1}) + I((\text{Age}/10)^{-1} * \log((\text{Age}/10)))$
Isthmus (parietal) Cingulate	$I((\text{Age}/10)^{-0.5}) + I((\text{Age}/10)^{-0.5} * \log((\text{Age}/10)))$	$I((\text{Age}/10)^{-1}) + I((\text{Age}/10)^{-1} * \log((\text{Age}/10)))$
Middle temporal	$I((\text{Age}/10)^{-1}) + I((\text{Age}/10)^{-1} * \log((\text{Age}/10)))$	$I((\text{Age}/10)^{-2}) + I((\text{Age}/10)^{-1})$
Inferior temporal	$I((\text{Age}/10)^{-2}) + I((\text{Age}/10)^{-1})$	$I((\text{Age}/10)^{-2}) + I((\text{Age}/10)^{-1})$
Fusiform	$I((\text{Age}/10)^{0.5}) + I((\text{Age}/10)^1)$	$I((\text{Age}/10)^{-1}) + I((\text{Age}/10)^{-1} * \log((\text{Age}/10)))$
Transverse Temporal	$I((\text{Age}/10)^{-0.5}) + \log((\text{Age}/10))$	$I((\text{Age}/10)^{-1}) + I((\text{Age}/10)^{-1} * \log((\text{Age}/10)))$
Entorhinal	$I((\text{Age}/10)^{0.5}) + I((\text{Age}/10)^2)$	$I((\text{Age}/10)^2) + I((\text{Age}/10)^2 * \log((\text{Age}/10)))$
Temporal Pole	$I((\text{Age}/10)^{-1}) + I((\text{Age}/10)^3)$	$I((\text{Age}/10)^2) + I((\text{Age}/10)^2 * \log((\text{Age}/10)))$
Parahippocampal	$I((\text{Age}/10)^{-1}) + I((\text{Age}/10)^{-0.5})$	$I((\text{Age}/10)^2) + I((\text{Age}/10)^2 * \log((\text{Age}/10)))$

Permutation based mega-analysis of ASD vs Control effect.

In order to directly compare the current results to the effects reported by (Haar, Berman, Behrmann, & Dinstein, 2014), who also employed the ABIDE cohort, we repeated the main diagnostic effect analysis using a permutation based method. For this randomization test, the labels of ASD vs Control were randomly shuffled across rows for a particular morphometric feature, and the difference measure between the two groups was calculated. This process was repeated 10000 times to create a distribution of differences expected by chance. The true distribution was compared to the random distribution, and the place of the observed effect in the distribution was translated to a p-value, which were subsequently FDR corrected for multiple comparisons. A corrected p-value of <.05 indicates a diagnosis effect significantly different from the expected averrandom effect.

TABLE S12. FDR Corrected p Values Calculated by Permutation Based Randomization Test. Bold values indicate a group difference significantly different from the random distribution mean.

Subcortical	Permutation (p value)
Lateral Ventricles	0.001
Thalamus	0.775
Caudate	0.188
Putamen	0.0417
Pallidum	0.0760
Hippocampus	0.2703
Amygdala	0.0417
Nucleus accumbens	0.0207
Frontal	
Superior Frontal	0.116
Rostral Middle Frontal	0.044
Caudal Middle Frontal	0.049
Pars Triangularis	0.030
Pars Orbitalis	0.031
Pars Opercularis	0.044
Medial Orbitofrontal	0.044
Lateral Orbitofrontal	0.034
Precentral	0.051
Paracentral	0.031
Frontal Pole	0.452
Insula	
	0.525
Cingulate	
Rostral Anterior (Frontal)	0.089
Caudal Anterior (Frontal)	0.205
Posterior (Parietal)	0.031
Isthmus (Parietal)	0.260
Parietal	
Superior Parietal	0.148
Inferior Parietal	0.139

Supramarginal	0.084
Postcentral	0.030
Precuneus	0.044
Temporal	
Superior temporal	0.188
Middle temporal	0.260
Inferior temporal	0.450
Banks of the Superior Temporal Sulcus	0.030
Fusiform	0.035
Transverse Temporal	0.202
Entorhinal	0.008
Temporal Pole	0.450
Parahippocampal	0.200
Occipital	
Lateral Occipital	0.638
Lingual	0.260
Cuneus	0.187
Pericalcarine	0.187

Meta analysis results split by site

In Table S13 we present the effects sizes of the meta-analysis on subcortical volumes split by participating site. Differences in both the direction and the size of the effects can be observed for all volumes. It is to be noted that many if not most of the individual samples do not show a significant main effect of diagnosis on cortical thickness or subcortical volumes. This demonstrates the care needed to be taken when interpreting findings in small homogenous samples of ASD subjects.

TABLE S13. Effects Sizes (Cohen's d) for Frontal and Temporal Cortical Thickness Partitions That Showed a Significant Group Effect in the Main Mega-Analysis, As Well As All Subcortical Volumes for All Participating Sites. Significant effects are bold and in color. Red values indicate a negative d-value, with lower thickness/volume in ASD. Green values indicate a positive d-value, with greater thickness or volume values in ASD.

Frontal Partitions	Superior Frontal	Rostral Middle Frontal	Caudal Middle Frontal	Pars Triangularis	Pars Orbitalis	Medial Orbitofrontal	Frontal Pole	Posterior (Parietal)	Isthmus (Parietal)
ABIDE_CALTECH	-0.78	-0.53	-0.78	-0.52	-0.64	0.04	-0.40	-0.24	0.11
ABIDE_KKI	-0.30	-0.05	-0.34	0.05	-0.07	0.03	-0.19	0.14	0.22
ABIDE_LEUVEN_1	0.24	0.21	0.42	-0.17	0.19	-0.44	-0.11	0.46	0.25
ABIDE_LEUVEN_2	0.77	0.48	1.05	0.58	0.93	-0.13	-0.56	0.90	0.04
ABIDE_MAX_MUN	0.31	-0.32	-0.08	0.41	0.08	0.69	0.10	-0.19	-0.43
ABIDE_NYU	1.25	1.84	1.04	0.95	0.55	0.84	0.75	1.10	0.88
ABIDE_OHSU	0.22	-0.04	0.12	0.05	-0.16	-0.09	-0.26	0.86	0.58
ABIDE_OLIN	0.17	0.25	0.36	0.12	-0.01	-0.23	0.26	-0.19	0.08
ABIDE_PITT	1.35	1.21	1.45	0.68	0.90	0.43	1.04	0.28	-0.20
ABIDE_SBL	0.48	0.11	-0.07	0.47	0.50	0.68	0.30	0.42	0.17
ABIDE_SDSU	-0.80	-1.34	-1.28	-1.14	-1.09	-0.42	0.07	-0.29	0.20
ABIDE_STANFORD	-0.23	-0.01	0.04	0.13	-0.12	0.43	-0.33	0.73	0.89
ABIDE_UM_1	0.25	0.32	0.06	0.20	0.36	0.03	0.17	-0.07	-0.20
ABIDE_UM_2	-0.06	-0.36	-0.41	-0.14	-0.60	0.29	-0.24	-0.03	0.27
ABIDE_USM	-0.04	0.68	0.04	0.35	0.63	0.35	0.66	-0.88	-0.63
ABIDE_YALE	-1.85	-2.44	-1.83	-2.28	-2.04	-2.76	-2.51	-1.35	-1.13
ABIDEII-BNI_1	-0.10	-0.31	-0.44	0.12	-0.03	-0.38	-0.20	0.08	0.15
ABIDEII-EMC_1	0.04	0.27	0.14	0.25	0.27	0.39	0.31	0.13	0.20
ABIDEII-ETH_1	-0.07	0.32	-0.37	0.30	0.03	0.37	0.24	0.30	0.22
ABIDEII-GU_1	-0.52	-0.39	-0.56	-0.60	-0.49	-0.20	-0.27	0.05	0.02
ABIDEII-IP_1	-0.20	-0.25	-0.43	-0.14	-0.26	-0.16	0.23	0.04	0.16
ABIDEII-IU_1	0.26	0.24	0.19	-0.16	0.11	0.06	0.28	0.67	-0.01
ABIDEII-KKI_1	-0.42	-0.27	-0.43	-0.20	-0.19	-0.22	0.15	-0.12	0.01

ABIDEII-NYU_1	-0.31	0.07	-0.10	-0.07	0.16	0.14	-0.08	0.37	0.06
ABIDEII-OHSU_1	-0.20	-0.04	-0.25	0.00	0.15	0.05	-0.05	-0.11	0.06
ABIDEII-OILH_2	0.36	0.28	0.32	0.58	0.29	0.20	0.62	-0.31	-0.31
ABIDEII-SDSU_1	-0.06	0.03	0.05	-0.34	0.04	0.30	-0.08	0.31	-0.16
ABIDEII-TCD_1	-0.42	-0.18	-0.70	-0.35	-0.01	0.12	0.09	0.21	-0.42
ABIDEII-UCD_1	-0.47	-0.46	-0.46	-0.24	0.11	-0.13	-0.25	0.67	0.01
ABIDEII-UCLA_1	-0.11	0.33	-0.06	0.07	0.31	0.77	0.20	0.05	0.18
ABIDEII-USM_1	-0.40	-0.81	-0.41	-0.39	-0.40	-0.23	0.05	0.06	0.08
BRC	0.04	0.06	0.17	-0.25	-0.05	0.20	-0.35	0.21	-0.24
CMU	0.06	-0.38	0.73	-0.18	-0.76	0.07	-0.20	0.17	-0.28
FRANKFURT	0.23	-0.21	0.56	0.18	0.45	0.44	0.94	-0.18	0.20
FSM	0.34	0.09	0.37	-0.20	0.03	-0.28	0.11	0.03	0.09
MRC	0.19	0.26	0.28	0.24	0.04	-0.08	0.01	0.15	0.00
MYAD	0.28	0.27	0.37	0.05	-0.07	0.40	0.32	-0.02	0.21
NIJMEGEN1	0.35	0.28	0.23	-0.21	0.26	0.28	-0.02	-0.05	-0.28
NIJMEGEN2	0.43	0.21	0.41	0.29	-0.43	0.57	-0.08	0.40	0.28
NIJMEGEN3	-0.14	-0.22	-0.13	-0.30	-0.08	-0.13	-0.34	0.58	-0.40
SAO PAULO	0.87	-0.51	0.78	-0.47	-0.26	-0.48	-0.18	-0.44	0.19
OHSU	0.20	0.17	0.03	0.19	0.29	0.31	0.06	-0.02	0.12
ParelladaHGGM	-0.20	-0.46	0.45	-0.23	-0.30	-0.47	-0.09	-0.07	0.08
PITT	-0.24	0.06	0.34	-0.15	-0.40	0.43	-0.33	-0.12	0.17
TCD	-0.33	-0.27	0.46	0.07	0.19	-0.08	-0.07	0.04	0.11
TORONTO	0.50	-0.06	0.03	0.34	-0.14	0.19	0.80	0.52	0.44
UMCU	-0.09	-0.08	-0.11	-0.02	0.13	0.03	0.21	-0.15	0.18
META	0.11	0.11	0.06	0.05	0.04	0.08	0.04	0.05	0.05
MEGA	0.17	0.20	0.08	0.11	0.12	0.15	0.10	0.13	0.08

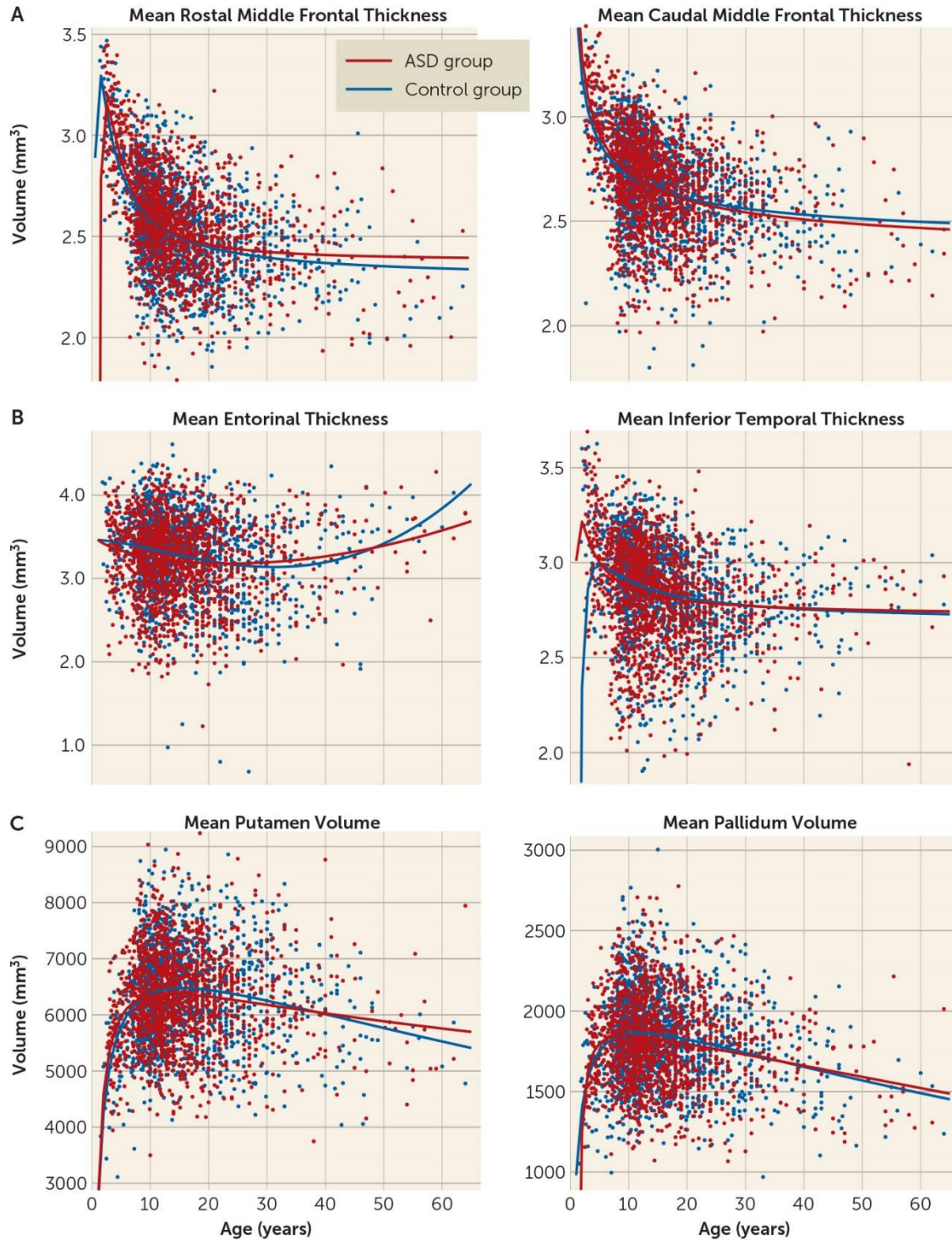
Temporal Partitions	Middle	Inferior	Transverse		Temporal			Overall Mean Thickness
	Temporal	Temporal	Fusiform	Temporal	Entorhinal	Pole	Parahippocampal	
ABIDE_CALTECH	-0.92	-0.53	-0.31	-0.28	-0.31	-0.17	-0.44	-0.68
ABIDE_KKI	0.12	0.33	0.33	-0.24	0.14	-0.03	-0.02	0.16
ABIDE_LEUVEN_1	0.24	0.09	0.25	-0.03	0.17	0.10	0.05	0.11
ABIDE_LEUVEN_2	0.97	0.88	0.62	0.05	0.03	0.51	0.12	0.83
ABIDE_MAX_MUN	0.88	0.72	0.72	0.65	1.52	1.01	1.09	0.42
ABIDE_NYU	-1.03	-1.17	-1.13	-1.43	-2.01	-1.36	-0.77	-0.14
ABIDE_OHSU	0.48	0.59	0.41	0.61	-0.18	0.11	0.47	0.44
ABIDE_OLIN	0.62	0.47	0.38	-0.58	0.33	0.51	-0.26	0.20
ABIDE_PITT	-0.19	0.29	-0.18	-0.61	-0.38	0.05	-0.46	0.72
ABIDE_SBL	-0.08	0.25	0.62	0.51	0.10	-0.02	0.91	0.64
ABIDE_SDSU	-0.97	-0.84	-0.24	-0.27	0.30	0.42	-0.32	-0.99
ABIDE_STANFORD	0.68	0.64	0.92	0.40	0.22	0.38	0.41	0.58
ABIDE_UM_1	-0.29	-0.37	-0.61	-0.43	-0.38	-0.17	-0.25	-0.38
ABIDE_UM_2	-0.33	-0.25	-0.34	0.29	-0.46	-0.67	0.31	-0.14
ABIDE_USM	0.18	-0.20	-0.47	-0.53	-0.20	-0.01	-0.45	-0.34
ABIDE_YALE	-1.98	-2.14	-1.67	-1.80	-0.86	-1.23	-1.03	-2.40
ABIDEII-BNI_1	0.08	0.20	0.06	0.28	-0.44	-0.08	-0.54	-0.04
ABIDEII-EMC_1	-0.10	-0.14	-0.06	-0.45	0.18	0.17	0.04	0.14
ABIDEII-ETH_1	-0.70	-0.35	-0.66	0.51	-0.50	0.04	0.12	-0.04
ABIDEII-GU_1	-0.49	-0.51	-0.53	-0.25	-0.37	-0.50	-0.33	-0.56
ABIDEII-IP_1	-0.38	-0.53	-0.56	0.07	-0.47	-1.00	-0.36	-0.40
ABIDEII-IU_1	-0.20	0.02	-0.25	-0.24	-0.54	-0.50	0.19	0.01
ABIDEII-KKI_1	-0.39	-0.36	-0.36	0.02	-0.32	-0.41	-0.30	-0.42
ABIDEII-NYU_1	-0.05	-0.10	0.01	0.18	-0.23	0.09	-0.06	0.00
ABIDEII-OHSU_1	-0.07	0.38	-0.14	-0.03	0.04	-0.12	-0.06	-0.12
ABIDEII-OILH_2	0.12	-0.37	-0.27	0.65	-0.21	-0.29	-0.54	0.14
ABIDEII-SDSU_1	-0.21	-0.18	-0.14	0.25	-0.46	-0.37	-0.37	0.06
ABIDEII-TCD_1	-0.07	-0.30	-0.15	-0.11	-0.42	-0.23	0.16	-0.25

ABIDEII-UCD_1	-0.53	-0.24	-0.21	0.82	-0.15	0.37	-0.36	-0.11
ABIDEII-UCLA_1	-0.18	-0.22	-0.23	-0.24	-0.29	-0.44	-1.22	-0.08
ABIDEII-USM_1	0.04	0.08	0.01	0.42	-0.09	0.06	0.96	0.00
BRC	-0.01	-0.08	-0.18	0.17	0.05	-0.13	0.53	0.05
CMU	-0.12	-0.41	-0.57	-0.49	-0.62	-0.29	-0.46	-0.68
FRANKFURT	0.15	0.36	0.24	0.78	0.44	-0.11	-0.31	0.55
FSM	-0.14	-0.70	-0.48	0.10	-0.40	-0.56	0.10	0.03
MRC	-0.05	-0.12	-0.16	0.03	-0.15	-0.12	-0.10	0.06
MYAD	0.38	-0.15	-0.15	-0.02	-0.07	0.12	-0.28	0.36
NIJMEGEN1	0.32	0.42	0.15	0.19	0.29	0.29	0.17	0.44
NIJMEGEN2	0.01	-0.07	0.32	0.00	0.49	0.26	0.28	0.33
NIJMEGEN3	-0.32	-0.03	-0.14	-0.28	-0.05	-0.06	-0.28	-0.18
SAO PAULO	-0.12	-0.08	-0.55	-0.42	-0.25	-0.14	-0.33	-0.66
OHSU	0.03	0.07	-0.17	0.39	-0.19	0.06	0.29	0.10
ParelladaHGGM	-0.24	-0.32	-0.18	-0.35	-0.14	-0.11	-0.09	-0.37
PITT	-0.21	-0.13	-0.05	-0.09	-0.58	-0.08	-0.13	-0.20
TCD	-0.19	-0.01	0.01	0.05	-0.44	-0.21	-0.28	-0.04
TORONTO	0.87	0.58	0.50	0.50	-0.12	-1.02	0.02	0.41
UMCU	-0.10	0.10	-0.12	0.00	-0.03	-0.14	0.24	0.01
META	-0.12	-0.16	-0.19	-0.24	-0.24	-0.14	-0.11	-0.07
MEGA	-0.10	-0.14	-0.19	-0.12	-0.21	-0.13	-0.10	-0.41

Subcortical Volumes	Thalamus	Caudate	Putamen	Pallidum	Hippocampus	Amygdala	Accumbens	Lateral Ventricles	ICV
ABIDE_CALTECH	0.23	-0.02	-0.11	0.75	-0.04	-0.42	-0.06	0.17	0.31
ABIDE_KKI	0.24	-0.19	-0.17	0.71	-0.52	0.18	-0.38	-0.18	1.03
ABIDE_LEUVEN_1	0.14	-0.04	0.51	0.84	0.27	0.6	0.17	-0.12	0.47
ABIDE_LEUVEN_2	0.56	0.46	0.18	-0.04	-0.21	-0.1	0.93	-0.35	0.49
ABIDE_MAX_MUN	-0.15	-0.4	-0.58	0.76	-0.27	0.3	0.01	0.14	0.8
ABIDE_NYU	-0.21	-0.23	-0.68	-0.79	0.17	-0.39	-1.01	0.08	-0.52
ABIDE_OHSU	-0.15	0.86	0.54	0.1	-0.27	0.3	0.75	0.82	0.54
ABIDE_OLIN	-0.6	-0.05	-0.43	-0.64	-0.84	0.08	-0.38	0.62	-0.17
ABIDE_PITT	0.43	-0.36	-0.81	-0.52	0.63	-0.76	-0.92	0.13	-0.29
ABIDE_SBL	-0.18	-0.19	0.82	0.58	-0.44	0.44	0.26	-1.03	0.26
ABIDE_SDSU	0.31	-0.12	0.46	-0.38	1.07	1.17	1.1	0.39	-0.29
ABIDE_STANFORD	0.18	0.23	-0.05	0.96	-0.15	0.08	0.42	0.13	1.24
ABIDE_UM_1	0.55	0.19	-0.73	0.08	-0.61	-0.73	-0.4	0.21	0.33
ABIDE_UM_2	0.07	0.28	0.04	0.16	0.37	0.02	-0.4	0.32	-0.48
ABIDE_USM	0.26	-0.29	-1.33	-0.52	-0.09	-0.59	-1.35	0.36	0.93
ABIDE_YALE	-0.47	-0.34	0.22	-0.52	-0.48	0.25	0.99	1.11	-0.59
ABIDEII-BNI_1	-0.52	0.11	0.03	-0.01	-0.48	-0.30	-0.17	0.60	0.00
ABIDEII-EMC_1	0.60	0.21	0.02	0.10	0.15	-0.04	-0.48	0.27	-0.32
ABIDEII-ETH_1	0.32	0.21	-0.28	0.29	0.00	-0.02	-0.40	0.40	-0.22
ABIDEII-GU_1	-0.62	-0.11	-0.03	0.14	-0.25	-0.31	0.09	0.19	0.13
ABIDEII-IP_1	-0.35	-0.06	0.16	0.12	0.15	-0.22	-0.23	-0.13	0.72
ABIDEII-IU_1	-0.14	0.06	0.60	-0.21	-0.37	-0.09	0.32	-0.02	-0.53
ABIDEII-KKI_1	0.10	0.16	0.29	0.11	0.16	0.10	0.32	0.07	0.14
ABIDEII-NYU_1	0.21	-0.18	0.11	0.06	0.20	0.01	-0.07	0.08	-0.03
ABIDEII-OHSU_1	0.19	-0.33	-0.35	-0.47	0.36	-0.09	-0.36	-0.06	0.14
ABIDEII-OILH_2	0.18	0.77	0.48	0.19	-0.17	0.27	0.51	0.41	-0.05
ABIDEII-SDSU_1	-0.08	0.15	0.36	0.15	-0.18	-0.19	-0.21	-0.02	-0.19
ABIDEII-TCD_1	0.08	-0.13	-0.39	-0.06	-0.14	0.24	0.12	0.15	0.70
ABIDEII-UCD_1	0.26	0.76	-0.36	-0.27	-0.03	-0.12	-0.08	0.83	0.20

ABIDEII-UCLA_1	0.59	0.87	0.57	0.56	-0.23	-0.58	0.39	-0.01	-0.04
ABIDEII-USM_1	0.38	-0.10	0.34	0.37	-0.03	-0.43	0.35	0.23	0.50
BRC	0	0.08	-0.05	-0.49	0.19	-0.52	-0.17	-0.38	0.17
CMU	-0.05	-0.17	-0.2	0.01	0.61	-0.08	-0.12	0.37	-0.14
FRANKFURT	-0.04	0.19	0.85	0.81	0.35	0.45	0.79	-0.63	0.22
FSM	-0.24	0.1	-0.28	0.42	-0.2	0.04	-0.13	-0.25	0.74
MRC	-0.05	0.08	0.16	-0.2	-0.1	-0.11	0.13	0.29	0.04
MYAD	0.34	-0.32	0.27	0	0.23	0.01	-0.35	0.02	0.04
NIJMEGEN1	-0.02	-0.39	-0.3	-0.09	-0.03	-0.27	0.02	-0.58	0.15
NIJMEGEN2	-0.17	0.04	-0.1	-0.14	-0.55	-0.01	-0.08	0.46	0.51
NIJMEGEN3	-0.11	-0.33	0.4	0.11	-0.22	-0.18	-0.19	0.06	0.1
SAO PAULO	-0.82	-0.88	-0.75	-0.97	-0.31	-0.11	-0.27	0.76	0.15
OHSU	0.22	0.08	-0.15	-0.36	0.36	0.35	-0.24	-0.39	0.05
ParelladaHGGM	0.13	0.50	-0.07	0.27	-0.32	-0.02	-0.13	0.28	0.03
PITT	-0.46	-0.04	-0.04	-0.29	0.11	0.36	-0.33	0.47	0.11
TCD	0.46	0.08	-0.2	-0.06	0.03	-0.49	-0.2	NA	-0.02
TORONTO	-0.28	-0.54	-0.01	-0.2	-0.39	-0.26	-0.2	0.16	-0.08
UMCU	0.19	0.55	0.79	0.47	0.12	-0.3	0.22	0.14	0.28
META	-0.09	-0.05	-0.03	-0.03	-0.03	-0.06	-0.05	0.11	0.10
MEGA	0.00	-0.05	-0.10	-0.08	-0.05	-0.08	-0.13	0.11	0.13

FIGURE S2. Additional Fractional Polynomial Best Model Fits for Age in a Mega-Analysis of Brain Morphometry in Patients With Autism Spectrum Disorder (ASD) and Healthy Control Subjects. These plots are in addition to those presented in Figure 3 in the main article. Models are shown (with separate fits for the ASD and control groups) for frontal cortical thickness (panel A), temporal cortical thickness (panel B), and subcortical volumes with significant diagnosis and age or age-by-diagnosis effects (panel C).



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