

Appendix 1 to Hegarty JP, Lazzeroni LC, Raman MM, et al. Genetic and environmental influences on corticostriatal circuits in twins with autism. *J Psychiatry Neurosci* 2019.

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Supplementary Materials

This supplement includes more detailed information for the results outlined in *Genetic and Environmental Influences on Cortico-Striatal Circuits in Twins with Autism*.

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Table S1. Group comparisons between twins with ASD and TD controls.

Region	ASD (n=78 twins)		TD (n=68 twins)		ASD vs TD		ASD vs TD (TBV)		ASD vs TD (TBV & age)		Add. Comps
	M	SD	M	SD	t	p	F	p	F	p	
<i>Cortical</i>											
ACC WM Vol	10931.03	1585.07	10731.97	1012.06	0.89	0.38	1.35	0.25	0.32	0.57	
ACC GM Area	2944.82	561.80	2835.34	363.83	1.38	0.17	2.70	0.10	1.05	0.31	
ACC GM Thick	3.05	0.21	3.10	0.17	-1.74	0.08	3.00	0.09	0.18	0.68	
OFC WM Vol	19733.67	2595.19	19833.58	2005.56	-0.26	0.80	0.61	0.44	1.61	0.21	a
OFC GM Area	9067.26	1065.45	8982.62	820.90	0.53	0.60	0.28	0.60	0.17	0.69	a
OFC GM Thick	3.03	0.21	3.10	0.16	-2.10	0.04*	4.38	0.04*	0.35	0.56	
<i>Striatal</i>											
Caudate GM Vol	8341.88	1209.57	8197.19	874.42	0.82	0.42	0.71	0.40	2.25	0.14	a,d
Putamen GM Vol	12540.97	1471.23	12109.16	1033.99	2.02	0.05*	5.20	0.02*	4.59	0.03*	d
Pallidum GM Vol	3602.84	463.52	3516.88	353.91	1.25	0.22	1.62	0.21	2.63	0.11	b
<i>Thalamic</i>											
Thalamus GM Vol	15602.55	1650.03	15793.24	1448.18	-0.74	0.46	1.59	0.21	4.54	0.04*	a,b,c

Group comparisons were completed with independent samples t tests and ANCOVA, adjusted for total brain volume (TBV) and age, between twins with autism spectrum disorder (ASD) and typically-developing (TD) controls. Regional brain measures were generated with FreeSurfer¹ based on the Desikan-Killiany atlas.² Significant two-tailed comparison at *p < 0.05 or † False Discovery Rate³ corrected across the tests within each column are indicated. a = MZ ASD vs. DZ ASD p ≤ 0.05, b = MZ TD vs. DZ TD p ≤ 0.05, c = MZ ASD vs. MZ TD p ≤ 0.05, d = DZ ASD vs. DZ TD p ≤ 0.05.

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Table S2. Group comparisons within twin pairs discordant for ASD.

Region	ASD (n=18 twins)		Co-twin (n=18 twins)		ASD vs Co-twin		ASD vs Co-twin (TBV)		ASD vs Co-twin (TBV & age)		Add. Comps
	M	SD	M	SD	t	p	F	p	F	p	
<i>Cortical</i>											
ACC WM Vol	10747.12	1576.63	10852.18	1320.79	-0.28	0.78	2.96	0.10	0.12	0.73	
ACC GM Area	2913.06	442.57	2928.11	510.84	-0.11	0.92	2.10	0.17	1.95	0.18	
ACC GM Thick	3.10	0.14	3.02	0.19	2.25	0.04*	4.08	0.06	0.47	0.50	
OFC WM Vol	19834.17	2684.04	20020.47	2685.28	-0.30	0.78	0.99	0.34	0.34	0.57	
OFC GM Area	9137.33	958.20	9072.22	971.43	0.22	0.83	1.88	0.19	2.88	0.11	
OFC GM Thick	3.09	0.17	2.97	0.20	2.90	0.01*	5.76	0.03*	0.88	0.36	b
<i>Striatal</i>											
Caudate GM Vol	8251.98	1229.26	8571.21	1201.66	-1.28	0.22	0.28	0.60	0.57	0.46	
Putamen GM Vol	12398.03	1745.76	12621.36	1477.25	-0.61	0.55	0.20	0.66	0.07	0.79	
Pallidum GM Vol	3594.28	546.87	3727.45	429.72	-1.26	0.22	0.31	0.59	0.26	0.62	
<i>Thalamic</i>											
Thalamus GM Vol	15397.84	2182.10	16523.70	1482.09	-2.71	0.02*	5.37	0.03*	0.04	0.85	a

Group comparisons were completed with paired samples t tests and ANCOVA, adjusted for total brain volume (TBV) and age, between twins with autism spectrum disorder (ASD) and their unaffected co-twins. Regional brain measures were generated with FreeSurfer¹ based on the Desikan-Killiany atlas.² Significant two-tailed comparison at *p < 0.05 or † False Discovery Rate³ corrected across the tests within each column are indicated. a = MZ ASD vs. MZ TD p ≤ 0.05, b = DZ ASD vs. DZ TD p ≤ 0.05.

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Table S3. ICCs within all twin pairs.

	All Twin Pairs				MZ vs DZ	
	MZ (n=78 twins/39 pairs)		DZ (n=86 twins/43 pairs)		z	p
	ICC [95% CI]	p	ICC [95% CI]	p		
<i>Cortical</i>						
ACC WM Vol	0.93 [0.85,1.01]	<0.001 †	0.95 [0.91,0.99]	<0.001 †	-1.09	0.28
ACC GM Area	0.95 [0.91,1.03]	<0.001 †	0.92 [0.86,0.99]	<0.001 †	1.52	0.13
ACC GM Thick	0.65 [0.44,0.86]	<0.001 †	0.53 [0.30,0.76]	<0.001 †	1.16	0.25
OFC WM Vol	0.90 [0.84,0.96]	<0.001 †	0.80 [0.68,0.91]	<0.001 †	2.35	0.02 †
OFC GM Area	0.83 [0.74,0.93]	<0.001 †	0.47 [0.28,0.67]	<0.001 †	4.26	<0.001 †
OFC GM Thick	0.71 [0.48,0.95]	<0.001 †	0.48 [0.21,0.75]	<0.001 †	2.29	0.02 †
<i>Striatal</i>						
Caudate GM Vol	0.83 [0.73,0.92]	<0.001 †	0.70 [0.56,0.83]	<0.001 †	2.01	0.04*
Putamen GM Vol	0.97 [0.94,1.00]	<0.001 †	0.84 [0.75,0.93]	<0.001 †	5.47	<0.001 †
Pallidum GM Vol	0.99 [0.98,1.00]	<0.001 †	0.97 [0.93,1.00]	<0.001 †	3.48	<0.001 †
<i>Thalamic</i>						
Thalamus GM Vol	0.88 [0.80, 0.96]	<0.001 †	0.73 [0.52, 0.94]	<0.001 †	2.81	0.01 †

Intra-class correlation coefficients (ICC), adjusted for sex and diagnosis, are compared with Fisher's z transformation⁴ between monozygotic (MZ) and dizygotic (DZ) twin pairs. Regional brain measures were generated with FreeSurfer¹ based on the Desikan-Killiany atlas.² Significant correlation or two-tailed group comparison at *p < 0.05 or † False Discovery Rate³ corrected across the tests within each column are indicated.

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Table S4. ICCs in concordant ASD and TD twin pairs.

	ASD				TD				ASD vs TD			
	MZ		DZ		MZ		DZ		z(MZ)	p	z(DZ)	p
	(n=30 twins/15 pairs) ICC [95% CI]	p	(n=30 twins/15 pairs) ICC [95% CI]	p	(n=40 twins/20 pairs) ICC [95% CI]	p	(n=28 twins/14 pairs) ICC [95% CI]	p				
<i>Cortical</i>												
ACC WM Vol	0.91 [0.79,1.03]	<0.001 †	0.59 [0.28,0.90]	<0.001 †	0.49 [0.13,0.84]	0.01 †	0.09 [-0.41,0.59]	0.73	3.92	<0.001 †	2.12	0.03*
ACC GM Area	0.91 [0.77,1.05]	<0.001 †	0.59 [0.23,0.94]	0.001 †	0.60 [0.26,0.94]	<0.001 †	-0.02 [-0.52,0.48]	0.94	3.30	0.001 †	2.51	0.01*
ACC GM Thick	0.35 [-0.03,0.73]	0.07	0.50 [0.18,0.81]	0.002 †	0.81 [0.62,1.01]	<0.001 †	0.17 [-0.28,0.62]	0.47	-3.01	0.003 †	1.36	0.17
OFC WM Vol	0.77 [0.49,1.05]	<0.001 †	0.12 [-0.38,0.62]	0.63	0.78 [0.58,0.99]	<0.001 †	-0.25 [-0.66,0.17]	0.24	-0.10	0.92	1.35	0.18
OFC GM Area	0.72 [0.35,1.09]	<0.001 †	0.39 [-0.02,0.80]	0.06	0.80 [0.67,0.94]	<0.001 †	-0.16 [-0.54,0.23]	0.42	-0.75	0.45	2.07	0.04*
OFC GM Thick	0.65 [0.17,1.12]	0.01 †	0.55 [0.06,1.04]	0.03*	0.52 [0.24,0.80]	<0.001 †	0.36 [-0.11,0.83]	0.13	0.79	0.43	0.87	0.38
<i>Striatal</i>												
Caudate GM Vol	0.91 [0.78,1.03]	<0.001 †	0.40 [0.03,0.76]	0.03*	0.69 [0.42,0.97]	<0.001 †	0.24 [-0.24,0.71]	0.33	2.68	0.01 †	0.64	0.52
Putamen GM Vol	0.90 [0.74,1.05]	<0.001 †	0.18 [-0.25,0.60]	0.42	0.71 [0.54,0.88]	<0.001 †	0.45 [0.19,0.71]	0.001 †	2.31	0.02 †	-1.09	0.28
Pallidum GM Vol	0.72 [0.27,1.17]	0.002 †	0.15 [-0.25,0.55]	0.48	0.55 [0.27,0.82]	<0.001 †	0.36 [-0.001,0.73]	0.05*	1.14	0.25	-0.81	0.42
<i>Thalamic</i>												
Thalamus GM Vol	0.78 [0.56,0.99]	<0.001 †	-0.05 [-0.62,0.51]	0.85	0.90 [0.82,0.97]	<0.001 †	0.36 [-0.12,0.85]	0.14	-1.69	0.09	-1.54	0.12

Intra-class correlation coefficients (ICC), adjusted for sex, are compared with Fisher's z transformation⁴ between monozygotic (MZ) and dizygotic (DZ) twin pairs in which both twins were diagnosed with autism spectrum disorder (ASD) or were typically-developing (TD) controls. Regional brain measures were generated with FreeSurfer¹ based on the Desikan-Killiany atlas.² Significant correlation or two-tailed group comparison at *p < 0.05 or † False Discovery Rate³ corrected across the tests within each column are indicated.

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