

6. SUPPLEMENTARY MATERIAL

Table S1.

Pairwise comparison of \sqrt{DTS} means between ROIs using double nested bootstrap in each patient group and for each segmentation.

Segm	Group	V1	V2	ΔM	95% CI	p		
VB	FAS	Caudate	Putamen	-10.46	[-15.32,-5.45]	.002		
			Globus pallidus	-1.11	[-5.50,3.31]	.298		
			Thalamus	-8.65	[-13.11,-4.73]	.002		
			Accumbens	-12.43	[-18.34,-6.31]	.002		
			Globus pallidus	9.35	[5.64,13.06]	.002		
			Putamen	Thalamus	1.81	[-2.02,5.37]	.215	
		Globus pallidus	Accumbens	-1.97	[-6.97,4.03]	.259		
			Thalamus	-7.54	[-10.66,-4.23]	.002		
			Accumbens	-11.33	[-16.66,-6.00]	.002		
			Thalamus	Accumbens	-3.78	[-9.12,1.14]	.116	
				Putamen	-8.21	[-12.01,-4.25]	.002	
				Globus pallidus	-1.84	[-5.28,1.65]	.179	
	NS-FASD	Caudate	Thalamus	-7.48	[-10.90,-4.25]	.002		
			Accumbens	-10.45	[-15.18,-5.65]	.002		
			Globus pallidus	6.37	[3.51,9.36]	.002		
			Putamen	Thalamus	0.73	[-2.26,3.65]	.340	
				Accumbens	-2.24	[-6.43,2.35]	.179	
				Thalamus	-5.64	[-8.14,-3.18]	.002	
		Globus pallidus	Accumbens	-8.61	[-12.86,-4.64]	.002		
			Thalamus	Accumbens	-2.97	[-7.01,1.02]	.110	
		Segm	Group	V1	V2	ΔM	95% CI	p
		FS	FAS	Caudate	Putamen	-9.54	[-14.00,-5.20]	.002
					Globus pallidus	-2.89	[-7.10,1.63]	.105
Thalamus	-4.25				[-8.37,-0.30]	.027		
Accumbens	-8.37				[-12.97,-3.97]	.002		
Putamen	Globus pallidus			6.65	[3.59,9.73]	.002		
	Thalamus			5.29	[2.25,8.18]	.002		
	Accumbens			1.18	[-2.07,4.67]	.264		
Globus	Thalamus			-1.36	[-4.52,1.32]	.211		

		pallidus	Accumbens	-5.47	[-8.78,-2.29]	.002
	Thalamus		Accumbens	-4.11	[-7.29,-0.63]	.022
NS-FASD	Caudate		Putamen	-9.36	[-12.94,-5.85]	.002
			Globus pallidus	-4.87	[-8.27,-1.65]	.004
			Thalamus	-5.57	[-8.78,-2.27]	.002
			Accumbens	-8.93	[-12.37,-5.36]	.002
	Putamen		Globus pallidus	4.49	[2.12,6.81]	.002
			Thalamus	3.80	[1.29,6.16]	.002
			Accumbens	0.43	[-2.25,3.35]	.410
	Globus pallidus		Thalamus	-0.69	[-2.93,1.49]	.319
			Accumbens	-4.06	[-6.75,-1.47]	.002
	Thalamus		Accumbens	-3.37	[-6.07,-0.58]	.009

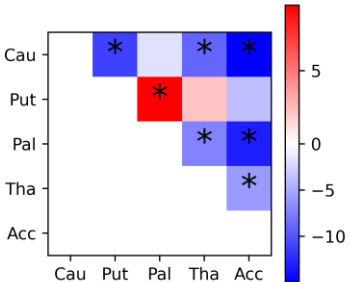
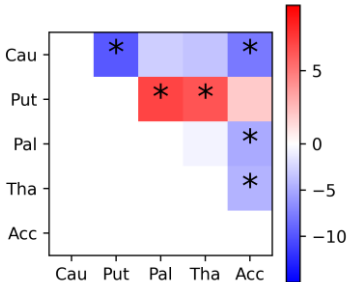
Segm	Group	V1	V2	ΔM	95% CI	<i>p</i>
FSL	FAS	Caudate	Putamen	-8.87	[-13.89,-3.49]	.010
			Globus pallidus	-4.38	[-9.71,0.84]	.071
			Thalamus	-5.69	[-10.01,-1.49]	.013
			Accumbens	-11.05	[-17.25,-4.84]	.010
		Putamen	Globus pallidus	4.49	[-0.63,9.22]	.071
			Thalamus	3.18	[-1.28,7.43]	.088
			Accumbens	-2.18	[-7.93,3.49]	.253
		Globus pallidus	Thalamus	-1.31	[-5.34,2.71]	.253
			Accumbens	-6.68	[-12.78,-0.78]	.045
		Thalamus	Accumbens	-5.36	[-10.91,0.28]	.058
	NS-FASD	Caudate	Putamen	-7.98	[-12.29,-3.62]	.003
			Globus pallidus	-3.63	[-7.51,0.25]	.053
			Thalamus	-6.15	[-9.57,-2.81]	.003
			Accumbens	-8.99	[-13.82,-4.18]	.003
		Putamen	Globus pallidus	4.35	[0.68,7.96]	.024
			Thalamus	1.83	[-1.60,5.30]	.142
			Accumbens	-1.00	[-5.68,3.49]	.350
		Globus pallidus	Thalamus	-2.52	[-5.36,0.35]	.059
			Accumbens	-5.36	[-10.15,-0.91]	.024
		Thalamus	Accumbens	-2.84	[-7.37,1.39]	.134

Note. Segm, segmentation; VB, volBrain-vol2Brain; FS, Freesurfer-SAMSEG; FSL, FSL-FIRST; FAS, fetal alcohol syndrome; NS-FASD, non-syndromic fetal alcohol spectrum disorders; ΔM , mean difference; 95% CI, 95% confidence interval; p, FDR-adjusted p-value.

Table S2.

Estimation of the deep grey matter pattern of undersizing in patients with FAS data not harmonized for age and sex.

A	volBrain-vol2Brain	Freesurfer-SAMSEG	FSL-FIRST
	M [CI95%] ^p	M [CI95%] ^p	M [CI95%] ^p
caudate	-12.60 [-16.13,-9.09]**	-12.30 [-15.70,-9.14]**	-17.60 [-21.14,-14.28]***
putamen	-1.35 [-4.20,1.48] ^{ns}	-2.61 [-4.82;-0.52]*	-7.78 [-11.22,-4.67]***
Globus pallidus	-10.80 [-12.93,-8.72]**	-9.45 [-11.42,-7.48]**	-12.60 [-15.73,-9.45]***
thalamus	-3.53 [-5.51,-1.62]**	-8.87 [-10.85,-6.90]**	-11.40 [-13.39,-9.43]***
accumbens	2.52 [-2.26,7.02] ^{ns}	-4.53 [-7.02,-2.02]**	-6.21 [-11.19,-1.55]*
total deep grey matter volume	-5.58 [-7.16;-4.11]**	-7.51 [-9.12,-5.96]**	-11.60 [-13.30,-10.10]***

B	volBrain-vol2Brain	Freesurfer-SAMSEG	FSL-FIRST
	Pairwise mean comparisons		

Note. (A) VB, volBrain-vol2Brain; FS, Freesurfer-SAMSEG; FSL, FSL-FIRST; M, mean volume Deviation from Typical Scaling (\sqrt{DTS}); CI95%, 95% confidence interval of the mean \sqrt{DTS} ; p, FDR-adjusted p-value; (B) Pairwise bootstrapped mean comparison matrices between deep grey matter \sqrt{DTS} for each segmentation method. The color bar represents the magnitude and the direction of the \sqrt{DTS} mean difference, and * indicates significant false discovery rate adjusted p-values ($p \leq .05$). The bluer the cell, the smaller the nucleus \sqrt{DTS} represented on the y-axis is compared to the one on the x-axis. Conversely, the redder the cell, the larger the nucleus \sqrt{DTS} on the y-axis is compared to the one on the x-axis. Cau, Caudate; Put, Putamen; Pal, Globus pallidus; Tha, Thalamus; Acc, Accumbens.

Table S3.

Mean Dice coefficients between segmentation methods for deep grey matter in total sample.

	Mean Dice coefficients (in %)		
	volBrain-vol2Brain – Freesurfer-SAMSEG	volBrain-vol2Brain – FSL-FIRST	Freesurfer-SAMSEG – FSL-FIRST
	<i>M (SD)</i>	<i>M (SD)</i>	<i>M (SD)</i>
Caudate	85.19 (3.67)	84.26 (3.84)	86.50 (5.03)
Putamen	86.10 (2.34)	89.70 (1.89)	86.45 (3.24)
Globus pallidus	86.43 (4.16)	86.28 (3.62)	84.86 (5.16)
Thalamus	84.84 (3.19)	86.61 (2.29)	84.16 (3.92)
Accumbens	68.03 (5.45)	67.53 (5.33)	74.70 (8.51)

Table S4.

Pearson correlation coefficients between segmentation methods for deep grey matter in total sample.

	Pearson's correlations coefficients		
	volBrain-vol2Brain ~ Freesurfer-SAMSEG	volBrain-vol2Brain ~ FSL-FIRST	Freesurfer-SAMSEG ~ FSL-FIRST
	<i>r</i>	<i>r</i>	<i>r</i>
Caudate	.92	.91	.87
Putamen	.94	.90	.92
Globus pallidus	.96	.93	.93
Thalamus	.85	.86	.86
Accumbens	.69	.45	.66
Total deep grey matter volume	.94	.94	.94

Table S5.

Mean comparisons of volume deviation from typical scaling ($\sqrt{\text{DTS}}$) between segmentation methods in the fetal alcohol syndrome group.

	volBrain-vol2Brain	Freesurfer-SAMSEG	FSL-FIRST	mean comparisons
ROIs	$\sqrt{\text{DTS}}$ (%)	$\sqrt{\text{DTS}}$ (%)	$\sqrt{\text{DTS}}$ (%)	
Caudate	-12.66	-12.75	-17.27	VB \approx FS > FSL
Putamen	-2.21	-3.22	-8.43	VB \approx FS > FSL
Globus pallidus	-11.48	-9.78	-12.84	FS > VB \approx FSL
Thalamus	-3.98	-8.45	-11.58	VB > FS > FSL

Accumbens	-0.13	-4.35	-6.15	VB > FS ≈ FSL
Total deep grey matter volume	-6.10	-7.64	-11.82	VB > FS > FSL

Note. The “≈” indicates no significant bootstrapped mean difference between the $\sqrt{\text{DTS}}$ while the “>” sign indicates a significant difference and shows the direction of the difference. All p-values are false discovery rate adjusted. More details in Table S6.

Table S6.

Pairwise comparison of $\sqrt{\text{DTS}}$ between segmentations using double nested bootstrap in the FAS group.

Nucleus	V1	V2	ΔM	95% CI	p
Caudate	VB	FS	0.10	[-1.97, 1.99]	.460
	VB	FSL	4.66	[2.88, 6.46]	.002
	FS	FSL	4.57	[2.14, 7.11]	.002
Putamen	VB	FS	1.01	[-0.64, 2.58]	.134
	VB	FSL	6.25	[3.46, 8.73]	.002
	FS	FSL	5.24	[2.75, 7.73]	.002
Globus pallidus	VB	FS	-1.69	[-3.39, -0.16]	.021
	VB	FSL	1.40	[-1.18, 4.12]	.171
	FS	FSL	3.08	[0.40, 6.08]	.020
Thalamus	VB	FS	4.50	[1.89, 6.98]	.002
	VB	FSL	7.63	[5.23, 9.93]	.002
	FS	FSL	3.13	[1.11, 5.36]	.002
Accumbens	VB	FS	4.17	[0.68, 7.64]	.009
	VB	FSL	6.05	[-.046, 11.73]	.032
	FS	FSL	1.88	[-3.13, 6.56]	.233

Note. Segm, segmentation; VB, volBrain-vol2Brain; FS, Freesurfer-SAMSEG; FSL, FSL-FIRST; FAS, fetal alcohol syndrome; NS-FASD, non-syndromic fetal alcohol spectrum disorders; ΔM , mean difference; 95% CI, 95% confidence interval; p, FDR-adjusted p-value.

Table S7.

Comparison of diagnostic classifiers using either the total deep grey matter volume deviation from typical scaling ($\sqrt{\text{DTS}}$) only or adding the individual nuclear $\sqrt{\text{DTS}}$.

models features	Total deep grey matter	Total deep grey matter + caudate + putamen + globus pallidus + thalamus + accumbens
AIC	161.69	104.58
BIC	167.69	110.58
Model comparison		$\chi^2(5) = 57.11, p < .001$
AUC	75.73	91.48
AUC _{cv} , M, SD	74.96 (7.27)	89.38 (3.47)
Specificity _{cv} M, SD	93.68 (3.94)	93.68 (3.94)
Sensitivity _{cv} M, SD	48.91 (15.60)	66.00 (10.08)

Accuracy_{cv} *M, SD*

77.68 (6.96)

83.75 (4.13)

Note. AIC, Akaike information criterion; BIC, Bayesian information criterion; model comparison test of Likelihood ratio; AUC, area under the curve; _{cv}, 5-fold cross-validation.

Table S8.

Comparison of performance metrics for the three nested logistic models.

Model features	TBV	TBV + total deep grey matter	TBV + total deep grey matter + pattern
AIC	107.10	97.52	74.64
BIC	113.10	103.51	80.63
AUC	91.52	92.97	95.49
AUC _{cv} , <i>M, SD</i>	91.37 (5.08)	91.71 (3.80)	93.06 (3.33)
Specificity _{cv} <i>M, SD</i>	93.68 (3.94)	94.74 (3.33)	93.68 (5.16)
Sensitivity _{cv} <i>M, SD</i>	67.64 (10.58)	73.09 (12.42)	81.27 (9.82)
Accuracy _{cv} <i>M, SD</i>	84.41 (4.77)	87.10 (4.67)	89.22 (2.40)

Note. TBV, total brain volume distance from typical volume; total deep grey matter volume deviation from typical scaling (_vDTS), pattern, deep grey matter pattern of _vDTS ; AIC, Akaike information criterion; BIC, Bayesian information criterion; AUC, area under the curve; _{cv}, 5-fold cross-validation.

Table S9.

Comparison of the goodness of fit of power-law vs. proportional linear models for each deep grey matter structure in the TD group.

	R ²	χ ²	p-value
Caudate	25.10	5.01	.025
Putamen	29.11	10.30	.003
Globus pallidus	43.29	9.09	.004
Thalamus	57.11	13.23	<.001
Accumbens	16.20	5.34	.02
Total deep grey matter volume	58.40	20.20	<.001

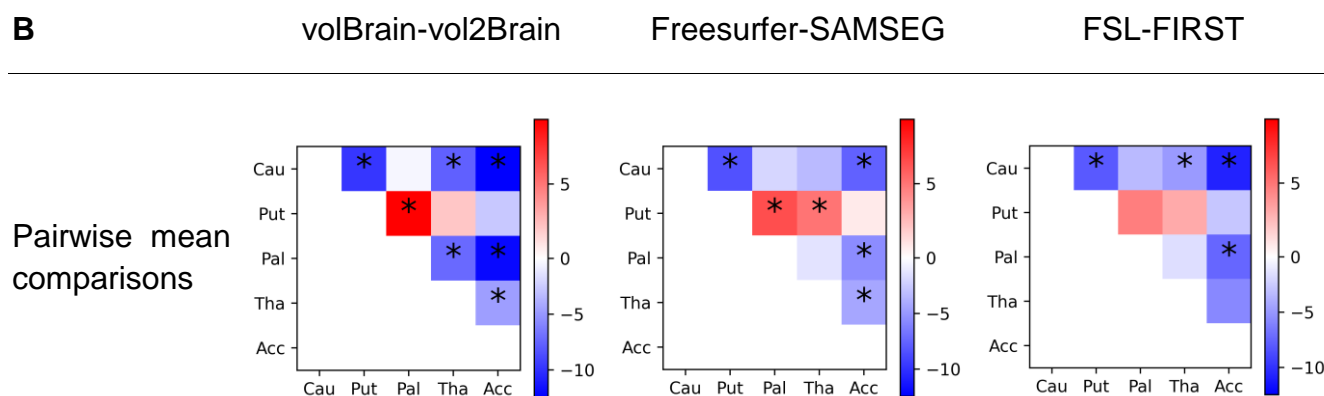
Note. Adjusted R² from scaling models. P-values are *false discovery rate*-adjusted for multiple comparisons from Likelihood ratio tests.

Table S10.

Estimation of the deep grey matter pattern of undersizing in patients with FAS data harmonized for site using neuroCombat harmonization and for age and sex using adjusted residuals harmonization.

A	volBrain-vol2Brain	Freesurfer-SAMSEG	FSL-FIRST
	<i>M [CI95%]^p</i>	<i>M [CI95%]^p</i>	<i>M [CI95%]^p</i>
caudate	-11.69 [-15.36,-8.20]**	-11.45 [-15.20,-8.30]**	-15.98 [-20.04,-12.58]**

putamen	-1.89 [-4.97, 1.06] ^{ns}	-3.00 [-5.08,-0.80]*	-8.26 [-11.42,-4.52]**
Globus pallidus	-11.15 [-13.65,-8.64]**	-9.35 [-11.67,-7.21]**	-12.96 [-16.77,-9.27]**
thalamus	-3.93 [-5.93,-1.92]**	-8.06 [-10.09,-5.97]**	-11.14 [-13.35,-8.79]**
accumbens	0.86 [-3.70,4.97] ^{ns}	-3.78 [-6.23,-1.40]**	-5.36 [-10.98,0.04] ^{ns}
total deep grey matter volume	-5.02 [-6.85,-3.07]**	-6.54 [-8.44,-4.51]**	-10.83 [-12.94,-8.68]**



Note. (A) VB, volBrain-vol2Brain; FS, Freesurfer-SAMSEG; FSL, FSL-FIRST; M, mean volume Deviation from Typical Scaling ($\sqrt{\text{DTS}}$); CI95%, 95% confidence interval of the mean $\sqrt{\text{DTS}}$; p, FDR-adjusted p-value; (B) Pairwise bootstrapped mean comparison matrices between deep grey matter $\sqrt{\text{DTS}}$ for each segmentation method. The color bar represents the magnitude and the direction of the $\sqrt{\text{DTS}}$ mean difference, and * indicates significant false discovery rate adjusted p-values ($p \leq .05$). The bluer the cell, the smaller the nucleus $\sqrt{\text{DTS}}$ represented on the y-axis is compared to the one on the x-axis. Conversely, the redder the cell, the larger the nucleus $\sqrt{\text{DTS}}$ on the y-axis is compared to the one on the x-axis. Cau, Caudate; Put, Putamen; Pal, Globus pallidus; Tha, Thalamus; Acc, Accumbens.