

Temporal Lobe connects Regression and Macrocephaly to Autism Spectrum Disorders

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Table S1 Type of interictal EEG abnormalities according to their site

	Anterior	Posterior	Temporal	Multifocal/Diffuse	Effect size	Test
	n: 53	n:21	n:21	n:59		
EEG Type (n) ***						
Paroxysms (81)	42 (79,2%)	10 (47,6%)	2 (9,5%)	27 (45,8%)	$\phi_c=0.659$	$\chi^2=66.964$
Focal slowing (22)	3 (5,7%)	6 (28,6%)	12 (57,1%)	1 (1,7%)		
Both (51)	8 (15,1%)	5 (23,8%)	7 (33,3%)	31 (52,5%)		

n= number of patients, χ^2 = Pearson chi-squared test; ϕ_c = Cramer's phi coefficient; *** $p \leq 0.001$. Focal paroxysms were prevalent on anterior areas, focal slowing on temporal regions, and both types of EEG abnormalities in multifocal/diffuse localization (***)

Table S2 Correspondence Analysis of Site of interictal EEG abnormalities vs. Type of EEG abnormalities

Summary							
Dimension	Inertia	Chi Square	Sig.	Proportion of Inertia		Confidence Singular Value	
				Accounted for	Cumulative	Standard Deviation	Correlation
1	0.314			0.722	0.722	0.078	-0.008
2	0.121			0.278	1.000	0.074	
Total	0.435	66.964	0.000	1.000	1.000		

Overview Row Points								
Site	Score in Dimension			Contribution				
	1	2	Inertia	Of Point to Inertia of Dimension		Of Dimension to Inertia of Point		
				1	2	1	2	Total
Anterior	-0.498	0.649	0.098	0.152	0.416	0.486	0.514	1.000
Posterior	0.490	0.336	0.024	0.058	0.044	0.774	0.226	1.000
Temporal	1.710	-0.006	0.223	0.712	0.000	1.000	0.000	1.000
Multifocal/ Diffuse	-0.336	-0.700	0.090	0.077	0.540	0.271	0.729	1.000
Active			0.435	1.000	1.000			
Total								

Overview Column Points								
Type	Score in Dimension			Contribution				
	1	2	Inertia	Of Point to Inertia of Dimension		Of Dimension to Inertia of Point		
				1	2	1	2	Total
Paroxysms	-0.477	0.415	0.099	0.214	0.260	0.681	0.319	1.000
Focal slowing	1.756	0.416	0.255	0.786	0.071	0.966	0.034	1.000
Both	0.001	-0.838	0.081	0.000	0.669	0.000	1.000	1.000
Active Total			0.435	1.000	1.000			

CA (two dimensions): **1° Dimension** (72% of total inertia): **in row (Site of EEG abnormalities)**, Temporal has the higher contribution to inertia (71%, positive sign), followed by Anterior (15%, negative sign); **in column (Type of EEG abnormalities)**, Focal slowing has the higher contribution to inertia (79%, positive sign), followed by Paroxysms (21%, negative sign). **2° Dimension** (28% of total inertia): **in row (Site of EEG abnormalities)**, Multifocal/Diffuse has the higher contribution to inertia (54%, negative sign), followed by Anterior (41%, positive sign); **in column (Type of EEG abnormalities)**, Both has the higher contribution to inertia (67%, negative sign), followed by Paroxysms (26%, positive sign)

Table S3 Site and Type of interictal EEG abnormalities according to presence or absence of seizures

	Seizures	No seizures	Effect size	Test
Site				
Anterior	17 (29.3%)	36 (37.5%)	$\phi_c=0.103$	$\chi^2=1.637$
Posterior	10 (17.2%)	11 (11.5%)		
Temporal	8 (13.8%)	13 (13.5%)		
Multifocal/Diffuse	23 (39.7%)	36 (37.5%)		
Type **				
Paroxysms	22 (37.9%)	59 (61.5%)	$\phi_c=0.281$	$\chi^2=12.133$
Focal slowing	7 (12.1%)	15 (15.6%)		
Both	29 (50%)	22 (22.9%)		

χ^2 = Pearson chi-squared test; ϕ_c = Cramer's phi coefficient; ** $p \leq 0.01$.

Patients with seizures displayed a significant association with the concurrence of both types of EEG abnormalities (paroxysms and focal slowing)

Table S4 Analysis of clinical variables in individuals with interictal EEG abnormalities, according to presence or absence of seizures

	Seizures	No seizures	Effect size	Test
Age (mean±SD; range)	9.2±5.0; 2.2-20.8	6.9±3.2; 2.0-17.5	-	t=3.185
Gender				
Male	49 (84.5%)	77 (80.2%)	φc=0.054	χ ² =0.444
Female	9 (15.5%)	19 (19.8%)		
ASD diagnosis				
Autism	20 (34.5%)	29 (30.2%)	φc=0.192	χ ² =5.660
PDDNOS	35 (60.3%)	67 (69.8%)		
Asperger	3 (5.2%)	0		
Language Development				
Normal	14 (24.1%)	19 (19.8%)	φc=0.143	χ ² =3.133
Delayed	23 (39.7%)	52 (54.2%)		
Absent	21 (36.2%)	25 (26%)		
Cognitive Development				
Normal-Borderline	18 (34%)	37 (40.2%)	φc=0.109	χ ² =1.709
Mild-Moderate Delay	19 (35.8%)	36 (39.1%)		
Severe Delay	16 (30.2%)	19 (20.7%)		
Regression				
Yes	26 (47.3%)	39 (41.1%)	φc=0.06	χ ² =0.549
No	29 (52.7%)	56 (58.9%)		
Macrocephaly				
Yes	20 (36.4%)	24 (25.8%)	φc=0.112	χ ² =1.844
No	35 (63.6%)	69 (74.2%)		
Tall stature				
Yes	6 (10.9%)	12 (13.3%)	φc=0.036	χ ² =0.185
No	49 (89.1%)	78 (86.7%)		
Behavioral problems				
Yes	30 (54.5%)	51 (53.7%)	φc=0.008	χ ² =0.010
No	25 (45.5%)	44 (46.3%)		

t=t-test; χ²= Pearson chi-squared test; φc= Cramer's phi coefficient ; ** p≤0.01 Mean age was

higher in individuals with seizures

Table S5 Analysis of clinical variables in individuals with interictal EEG abnormalities (excluding those with only focal slowing), according to presence or absence of seizures

	Seizures	No seizures	Effect size	Test
Age (mean±SD; range)	8.9±4.7; 2.2-19.4	6.7±3.3; 2.0-17.5	-	t=2.860
Gender				
Male	43 (84.3%)	64 (79%)	φc=0.066	χ ² =0.573
Female	8 (15.7%)	17 (21%)		
ASD diagnosis				
Autism	17 (33.3%)	23 (28.4%)	φc=0.205	χ ² =5.560
PDDNOS	31 (60.8%)	58 (71.6%)		
Asperger	3 (5.9%)	0		
Language Development				
Normal	13 (25.5%)	17 (21%)	φc=0.104	χ ² =1.430
Delayed	21 (41.2%)	42 (51.9%)		
Absent	17 (33.3%)	22 (27.1%)		
Cognitive Development				
Normal-Borderline	17 (37%)	33 (42.3%)	φc=0.090	χ ² =0.994
Mild-Moderate Delay	16 (34.8%)	29 (37.2%)		
Severe Delay	13 (28.2%)	16 (20.5%)		
Regression				
Yes	22 (45.8%)	31 (38.8%)	φc=0.070	χ ² =0.620
No	26 (54.2%)	49 (61.2%)		
Macrocephaly				
Yes	16 (32.7%)	19 (24.4%)	φc=0.090	χ ² =1.037
No	33 (67.3%)	59 (75.6%)		
Tall stature				
Yes	6 (12.2%)	9 (12%)	φc=0.004	χ ² =0.002
No	43 (87.8%)	66 (88%)		
Behavioral problems				
Yes	26 (54.2%)	43 (53.8%)	φc=0.004	χ ² =0.002
No	22 (45.8%)	37 (46.2%)		

t=t-test; χ²= Pearson chi-squared test; φc= Cramer's phi coefficient ; ** p≤0.01 Mean age was

higher in individuals with seizures

Table S6 Presence of interictal EEG abnormalities is related to regressive onset of ASD

Onset vs EEG groups *	Regressive (n=82)	Non-Regressive (n=132)	Effect size	Test
ASD-EEG	65 (79.3%)	85 (64.4%)	$\phi_c=0.158$	$\chi^2=5.338$
ASD “simplex”	17 (20.7%)	47 (35.6%)		

χ^2 = Pearson chi-squared test; ϕ_c = Cramer’s phi coefficient; * $p \leq 0.05$.

Regressive onset of ASD was significantly associated to the ASD-EEG group (*)

Table S7 Volumetric analysis at the ROI level

ROI	Regression	Macrocephaly	Descriptive		GLM Univariate Analysis		
			Mean	Std. Deviation	F	p	Partial Eta Squared
Left hemisphere	No	No	0.40298733	0.004632004	0.001	0.974	0.000
		Yes	0.40917733	0.006943139			
	Yes	No	0.39993600	0.020363261			
		Yes	0.40649533	0.002804229			
Right hemisphere	No	No	0.40615733	0.003131560	0.025	0.878	0.004
		Yes	0.40544000	0.002320436			
	Yes	No	0.40304050	0.011253604			
		Yes	0.40115867	0.006762369			
Left Frontal Lobe	No	No	0.14557633	0.002787111	0.951	0.362	0.120
		Yes	0.14719867	0.002258127			
	Yes	No	0.13924050	0.000304763			
		Yes	0.14755133	0.009840529			
Right Frontal Lobe	No	No	0.14637867	0.000658002	3.104	0.121	0.307
		Yes	0.14503067	0.002396949			
	Yes	No	0.13635250	0.002317189			
		Yes	0.14436633	0.007550620			
Left Parietal Lobe	No	No	0.08288400	0.001098603	0.019	0.895	0.003
		Yes	0.08629833	0.003321065			
	Yes	No	0.08332900	0.016085265			
		Yes	0.08561967	0.003823161			
Right Parietal Lobe	No	No	0.08176333	0.001452419	0.146	0.714	0.020
		Yes	0.08411700	0.004379908			
	Yes	No	0.08453450	0.011609986			
		Yes	0.08441100	0.003113454			
Left Limbic Lobe	No	No	0.02302067	0.000375758	1.499	0.260	0.176
		Yes	0.02499633	0.002440135			
	Yes	No	0.02335750	0.000753069			
		Yes	0.02311200	,001140100			
Right Limbic Lobe	No	No	0.02199933	0.000826109	1.193	0.311	0.146
		Yes	0.02400867	0.002270815			
	Yes	No	0.02222500	0.000151321			
		Yes	0.02234967	0.001047550			
Left Occipital Lobe	No	No	0.04144700	0.003523421	0.093	0.769	0.013
		Yes	0.03904033	0.001648448			
	Yes	No	0.04523750	0.004851460			
		Yes	0.04168467	0.002468380			
Right Occipital Lobe	No	No	0.04493033	0.002047379	0.099	0.762	0.014
		Yes	0.04163200	0.001645102			
	Yes	No	0.04684700	0.001374616			
		Yes	0.04423467	0.001808869			

Left Temporal Lobe	No	No	0.11005900	0.003985245	0.271	0.618	0.037
		Yes	0.11164467	0.001657740			
	Yes	No	0.10877150	0.001631295			
		Yes	0.10852733	0.002971575			
Right Temporal Lobe *	No	No	0.11108600	0.002320124	8.029	0.025	0.534
		Yes	0.11065233	0.001050177			
	Yes	No	0.11308200	0.000738219			
		Yes *	0.10579700	0.002623600			
Left Insula	No	No	0.01210700	0.000565833	0.413	0.541	0.056
		Yes	0.01258767	0.000773793			
	Yes	No	0.01233550	0.000482954			
		Yes	0.01233867	0.000503794			
Right Insula	No	No	0.01128333	0.000730871	1.858	0.215	0.210
		Yes	0.01209967	0.000952960			
	Yes	No	0.01153050	0.000020506			
		Yes	0.01118700	0.000496617			
Left Caudato	No	No	0.00514067	0.000112647	0.194	0.673	0.027
		Yes	0.00530433	0.000145225			
	Yes	No	0.00516650	0.000325976			
		Yes	0.00551733	0.000578122			
Right Caudato	No	No	0.00494567	0.000111267	0.030	0.867	0.004
		Yes	0.00505733	0.000154649			
	Yes	No	0.00515500	0.000455377			
		Yes	0.00534800	0.000611532			
Left Putamen	No	No	0.00514000	0.000735268	4.972	0.061	0.415
		Yes	0.00569033	0.000067885			
	Yes	No	0.00622200	0.000441235			
		Yes	0.00543000	0.000450551			
Right Putamen	No	No	0.00514667	0.000793739	3.413	0.107	0.328
		Yes	0.00571267	0.000275558			
	Yes	No	0.00606600	0.000384666			
		Yes	0.00547833	0.000360673			
Cerebellum	No	No	0.13790900	0.006639766	0.061	0.812	0.009
		Yes	0.13004900	0.008946755			
	Yes	No	0.14081700	0.032949762			
		Yes	0.13752367	0.011448932			
Brainstem	No	No	0.00918300	0.000294250	0.023	0.883	0.003
		Yes	0.00888300	0.000626266			
	Yes	No	0.00973150	0.000734684			
		Yes	0.00952300	0.000296565			

ROI= region of interest. Descriptive: mean and SD of the volume ratios (ROI cortex /total gray matter). GLM

Univariate Analysis: F=two-way ANOVA; p= significance; Partial Eta Squared=effect size; * p≤ 0.05 (significant reduction of the volume ratio at the right temporal lobe in patients with both macrocephaly and regression)