

A Description of Subcortical Functional Connectivity Gradients in Temporal Lobe Epilepsy

Supplementary Figures and Tables

Supplementary Table 1 – Regression coefficients and corresponding p-values for linear model of disease factors predicting the z-scored mean of gradient 1 at each subcortical ROI

I-Hippocampus					C-Hippocampus				
	Laterality	MTS	BTCS	Duration		Laterality	MTS	BTCS	Duration
β	-0.0197	-0.0032	-0.0035	-0.0003	β	-0.0082	0.0004	0.0014	-0.0002
p-value	0.004	0.665	0.631	0.332	p-value	0.151	0.955	0.828	0.323
I-Amygdala					C-Amygdala				
	Laterality	MTS	BTCS	Duration		Laterality	MTS	BTCS	Duration
β	-0.0133	0.0027	-0.0002	0.0002	β	-0.0036	0.0107	0.002	0.0002
p-value	0.164	0.799	0.983	0.655	p-value	0.637	0.206	0.811	0.554
I-Thalamus					C-Thalamus				
	Laterality	MTS	BTCS	Duration		Laterality	MTS	BTCS	Duration
β	-0.0041	-0.0025	-0.0122	-0.0005	β	0.0041	0.0004	-0.0078	-0.0003
p-value	0.58	0.757	0.135	0.121	p-value	0.626	0.968	0.392	0.39
I-Caudate					C-Caudate				
	Laterality	MTS	BTCS	Duration		Laterality	MTS	BTCS	Duration
β	0.0096	-0.0034	0.029	0.0006	β	0.0046	0.0005	0.0159	0.0008
p-value	0.351	0.765	0.012	0.13	p-value	0.652	0.962	0.161	0.071
I-Putamen					C-Putamen				
	Laterality	MTS	BTCS	Duration		Laterality	MTS	BTCS	Duration
β	0.0122	-0.0003	0.0058	0.0004	β	0.0067	0.0003	0.0005	0.0002
p-value	0.047	0.96	0.377	0.119	p-value	0.371	0.972	0.953	0.567
I-Pallidum					C-Pallidum				
	Laterality	MTS	BTCS	Duration		Laterality	MTS	BTCS	Duration
β	0.002	0.0076	-0.0083	-0.0002	β	-0.0063	0.0021	-0.0089	-0.0001
p-value	0.674	0.152	0.113	0.39	p-value	0.423	0.81	0.299	0.697

Supplementary Table 2 – Regression coefficients and corresponding p-values for linear models of disease factors predicting the z-scored variance of gradient 1 at each subcortical ROI

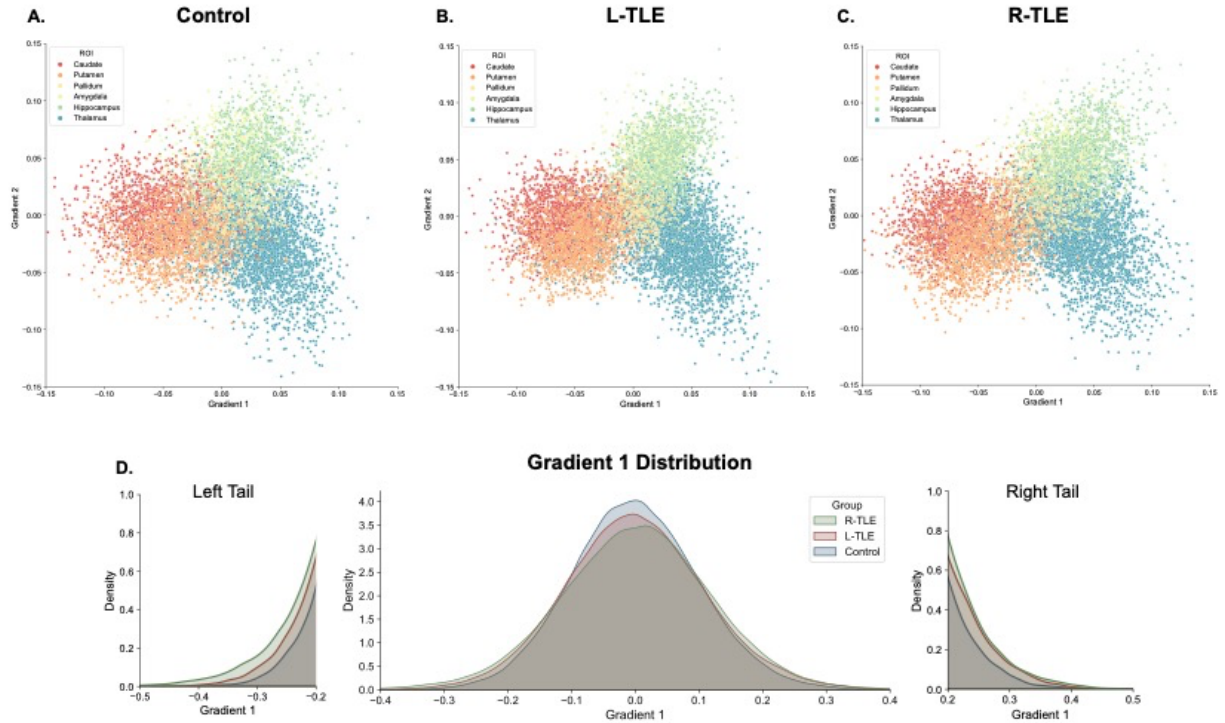
I-Hippocampus					C-Hippocampus				
	Laterality	MTS	BTCS	Duration		Laterality	MTS	BTCS	Duration
β	-0.0034	-0.0027	-0.0005	-4.04E-05	β	-0.0027	-0.0024	0.0004	-7.75E-05
p-value	0.01	0.058	0.705	0.435	p-value	0.041	0.108	0.789	0.146
I-Amygdala					C-Amygdala				
	Laterality	MTS	BTCS	Duration		Laterality	MTS	BTCS	Duration
β	-0.0033	-0.0026	-0.0024	-0.0001	β	-0.0025	-0.0019	-0.0005	-8.04E-05
p-value	0.034	0.132	0.152	0.087	p-value	0.063	0.211	0.757	0.137
I-Thalamus					C-Thalamus				
	Laterality	MTS	BTCS	Duration		Laterality	MTS	BTCS	Duration
β	-0.0032	-0.0028	0.0013	-7.32E-05	β	-0.0024	-0.0028	0.0011	-8.64E-05
p-value	0.029	0.088	0.431	0.213	p-value	0.151	0.126	0.554	0.199
I-Caudate					C-Caudate				
	Laterality	MTS	BTCS	Duration		Laterality	MTS	BTCS	Duration
β	-0.001	-0.0013	6.35E-05	-2.33E-05	β	-0.0015	-0.0014	0.0006	-2.59E-05
p-value	0.397	0.333	0.961	0.627	p-value	0.189	0.255	0.63	0.571
I-Putamen					C-Putamen				
	Laterality	MTS	BTCS	Duration		Laterality	MTS	BTCS	Duration
β	-0.002	-0.0014	0.0005	-2.81E-05	β	-0.0018	-0.0015	0.0001	-7.69E-05
p-value	0.161	0.379	0.738	0.623	p-value	0.175	0.316	0.929	0.161
I-Pallidum					C-Pallidum				
	Laterality	MTS	BTCS	Duration		Laterality	MTS	BTCS	Duration
β	-0.002	-0.0019	-0.0003	-3.23E-05	β	-0.0032	-0.0031	0.0015	-8.03E-05
p-value	0.055	0.093	0.783	0.428	p-value	0.033	0.061	0.347	0.184

Supplementary Table 3 - Regression coefficients and corresponding p-values for linear models of disease factors predicting the global variance of gradient 1 across all subcortical ROIs

	Global Variance			
	Laterality	MTS	BTCS	Duration
β	-0.8413	-0.9904	0.3233	-0.0155
p-value	0.086	0.069	0.542	0.427

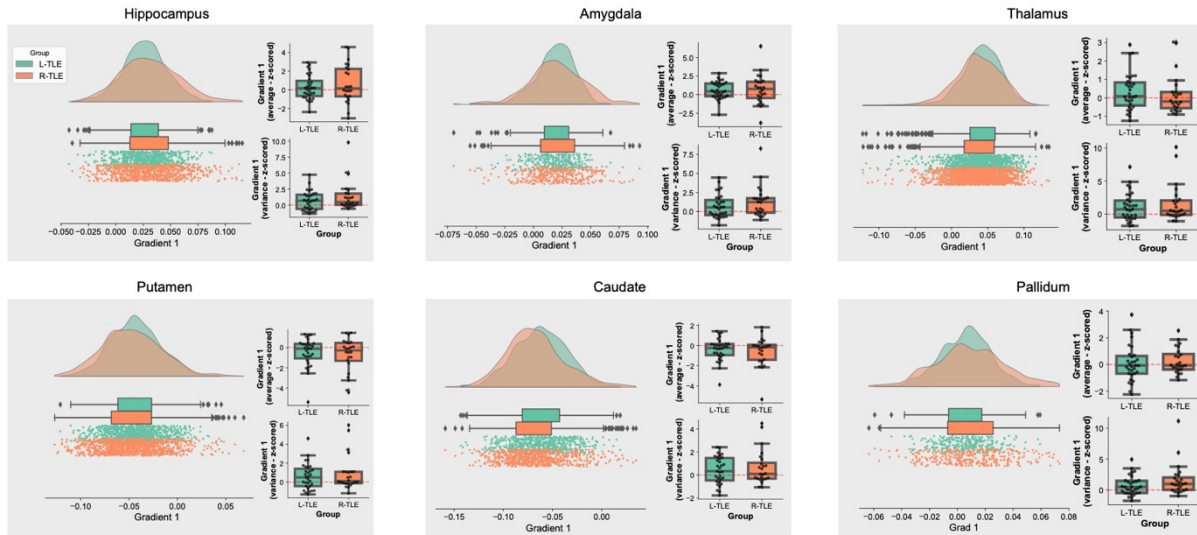
Supplementary Table 4 - Bhattacharyya Distance and corresponding p-value between the 2D distribution generated by gradient 1 and gradient 2 in L-TLE and R-TLE subjects in the ipsilateral hippocampus, computed using different similarity metrics and dimensionality reduction approaches for gradient estimation. DM: Diffusion mapping. LE: Laplacian embedding. PCA: principal component analysis.

Method	Bhattacharyya Distance	p-value
Cosine-DM	0.107963972	0.010989011
Gaussian-DM	0.095780277	0.020979021
Norm. Angle-DM	0.106681173	0.01998002
Pearson-DM	0.097407341	0.018981019
Spearman-DM	0.065434815	0.03996004
Cosine-LE	0.02770632	0.087912088
Gaussian-LE	0.034955792	0.042957043
Norm. Angle-LE	0.044388407	0.047952048
Pearson-LE	0.025584961	0.116883117
Spearman-LE	0.022037481	0.084915085
Cosine-PCA	0.1069308	0.022977023
Gaussian-PCA	0.059444441	0.06993007
Norm. Angle-PCA	0.111091021	0.016983017
Pearson-PCA	0.10620882	0.016983017
Spearman-PCA	0.031851973	0.228771229

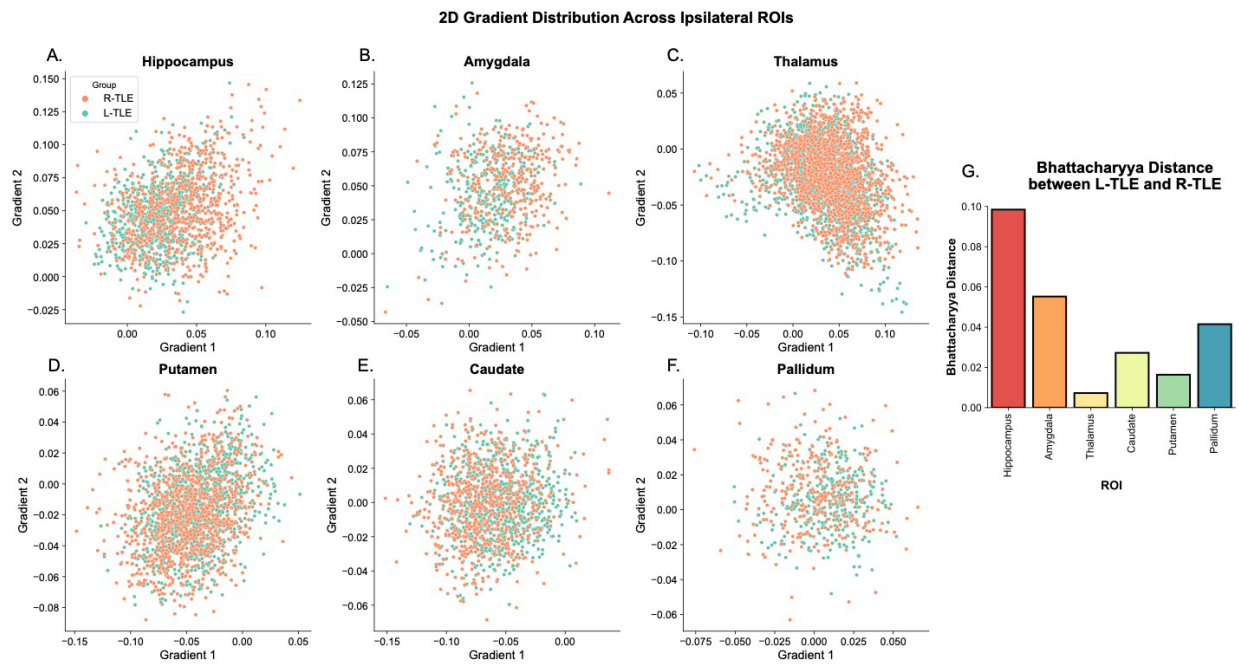


Supplementary Figure 2 - Overview of the Subcortical Functional Gradient Across ROIs in Healthy Controls, L-TLE and R-TLE: **A-C.** Average gradient space generated by principal gradient 1 and 2 across all **A.** control subjects, **B.** L-TLE subjects and **C.** R-TLE subjects. Ipsilateral and contralateral structures are assigned the same color in this representation. **D.** Distribution of Gradient 1 across all subjects and ROIs for each subgroup. The left and right tail show an expansion of gradient 1 for left and right TLE relative to controls.

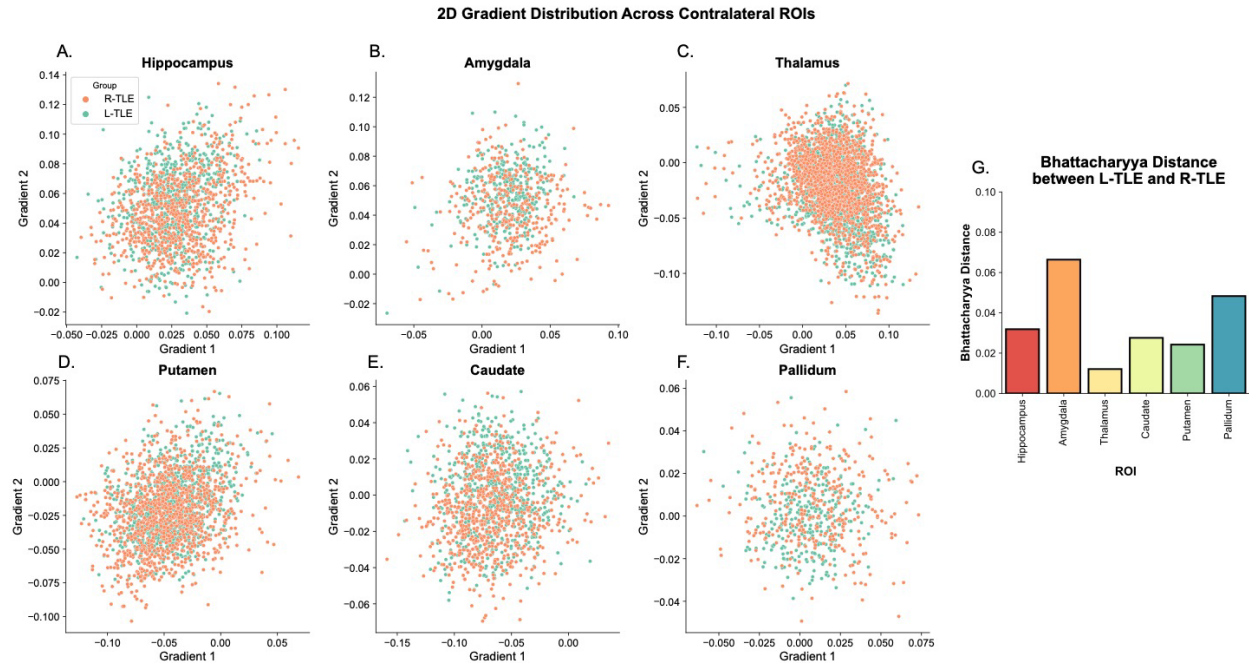
Gradient 1 Values Across Contralateral ROIs



Supplementary Figure 3 - Principal Gradient 1 Across Contralateral Subcortical ROIs: A-F. Each panel represents a different subcortical ROI, and they show both, the average distribution in gradient space for gradient 1 across subjects in each group (left), and the distribution of individual gradient 1 mean and variance for subjects in each group (right). The individual subject mean and variance were z-scored relative to the distribution of gradient 1 mean and variance for controls in the same ROI, but across bilateral regions.



Supplementary Figure 4 – 2-Dimensional Gradient Distribution Across Ipsilateral ROIs: A-F. Group average 2-dimensional distribution generated by subcortical functional gradient 1 and 2 of R-TLE and L-TLE across ipsilateral ROIs. **G.** Bhattacharyya distance between the distribution of L-TLE and R-TLE across ROIs.



Supplementary Figure 5 – 2-Dimensional Gradient Distribution Across Contralateral ROIs: A-F. Group average 2-dimensional distribution generated by subcortical functional gradient 1 and 2 of R-TLE and L-TLE across contralateral ROIs. **G.** Bhattacharyya distance between the distribution of L-TLE and R-TLE across ROIs.