

Reorganization of Thalamic Intrinsic Connectivity Following Anterior Temporal Lobectomy

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Rationale:

The thalamus has played a crucial role in determining surgical outcome following anterior temporal lobectomy (ATL) in temporal lobe epilepsy (TLE) (He, et al., 2017). Before successfully quantifying the impact of the thalamus on ATL outcomes, this structure's own intrinsic connectivity must be understood. Accordingly, we characterize thalamic intrinsic connectivity through resting-state fMRI (rsfMRI) longitudinally, exploring its change pre- to post-surgery.

Methods:

Subjects: Twenty-six unilateral TLE patients and 28 matched healthy controls were enrolled in this study. All patients received standard en bloc ATL and remained seizure free (Engel Class I, Engel, et al., 1993) at 1 year postoperatively.

Data Collection: Two 5 min rsfMRI scans were performed, one prior to ATL, and the second postoperatively (~1 year). One identical 5 min rsfMRI scan was administered to matched healthy controls.

Table 1. Sample demographic and clinical characteristics.

Sample Group (N)	Good Outcome TLE (26)	Healthy Controls (28)
Epileptogenic Temporal Lobe (L/R)	14/12	N.A.
Age (M±SD)	41.37±12.86	38.84±12.62
Gender (M/F)	15/11	14/14
Handedness (R/L)	21/5	23/5
Age at Epilepsy Onset (M±SD)	26.29±11.87	N.A.
Duration of Epilepsy (M±SD)	15.08±14.07	N.A.
Seizure Focality (With/Without GS or 2nd GS)	16/10	N.A.
Interictal Spike (Ipsilateral/Bilateral)	21/5	N.A.
Temporal Pathology (NB/MTS/Other)	10/10/6	N.A.

Abbreviations & Definitions: TLE, temporal lobe epilepsy; NB, normal brain; MTS, mesial temporal sclerosis; Other, other temporal pathologies (heterotopia, dysplasia, tumor, etc.)

Data Preprocessing: RsfMRI data was preprocessed using a standard pipeline in SPM12.

Testing Hypotheses:

(1) Since slow fluctuations in activity are a fundamental feature of the resting brain, and their presence is key to determining correlated activity between brain regions, we tested for the power of low frequency oscillation (0.01-0.1 Hz) with an amplitude of low frequency fluctuation (ALFF) measure in thalamus. **We hypothesized that post-ATL seizure freedom would be associated with increase in ictal-sided thalamic neural activities, tested via by ALFF, specifically considering ictal-sided thalamic hypometabolism is frequently seen in these patients.**

(2) As seizures tend to propagate and spread through bilateral thalami, we hypothesized that post-ATL seizure freedom would be associated with reorganization in the inter-talk between the bilateral thalami. To test this theory, we estimated the intrinsic connectivity contrasts (ICC) for each thalamus. First, voxel-to-voxel functional connectivity were calculated for both thalami. Then for each thalamic voxel, its intra-thalamic intrinsic connectivity was estimated by the mean square root of all connections to the ipsilateral thalamus, while its inter-thalamic intrinsic connectivity was estimated by the mean square root of all connections to the contralateral thalamus. ICC, is later defined as the contrast between the intra- vs. inter- thalamic intrinsic connectivity at each voxel.

Analysis Summary: Analyses reported here only involve ATL patients with a **good outcome**. Mean values of ALFF and ICC were extracted for thalamic subdivisions (8 each side), using a multimodal connectome based atlas (Fan et al., 2016). Deviation scores (Z) relative to healthy controls' for each division were then calculated. Lastly, data of the RTLEs were flipped right-to-left to maintain clear access to the ictal-sided vs. nonictal-sided thalamus. Note, the use of Z scores instead of raw measures insured comparability after L/R flipping.

Results:

Repeated-measures ANOVA on ALFF and ICC revealed significant session (pre/post) by side (ictal-sided/nonictal-sided) by thalamic subdivisions (8 in total) interactions for both measures:

(1) **ALFF:** $F(3.744, 93.597) = 5.118, P = 0.001$ (Greenhouse-Geisser corrected)

(2) **HCC:** $F(1.730, 43.253) = 9.085, P = 0.001$ (Greenhouse-Geisser corrected)

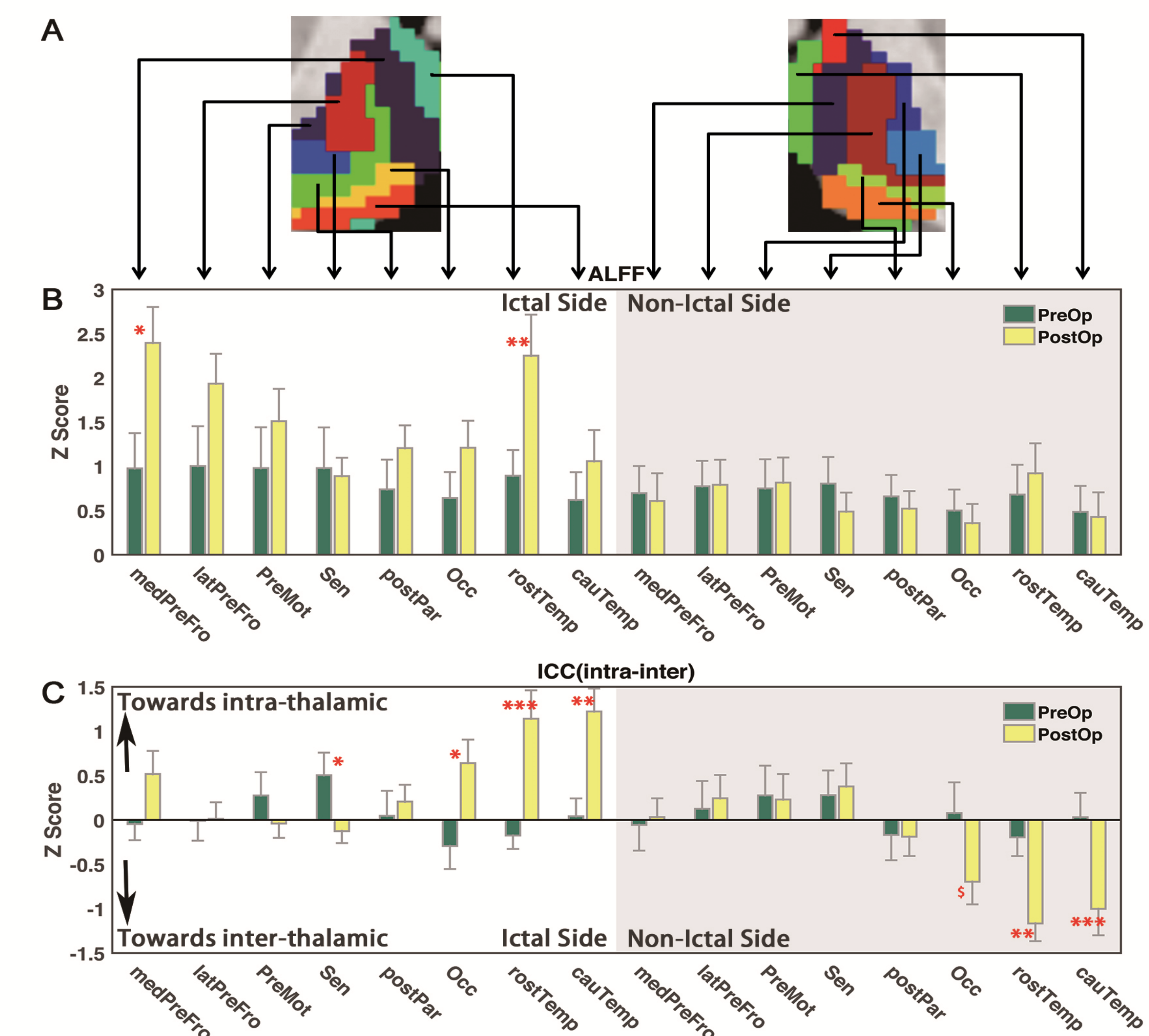


Figure 1. A) Thalamic subdivisions are coded based upon the cortical regions they found to be connected to, according to a multimodal connectome based atlas (Fan et al., 2016). Pre- vs. Postoperative comparison of ALFF (B) and ICC (C) area shown. Both panels show the Deviation Z Scores of the data from TLE patients in reference to the data from healthy controls (Z=0). Significant differences are marked: *, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$; §, $P = 0.07$. Abbreviations: Preop, preoperative patients; Postop, postoperative patients; medPreFro, medial prefrontal lobe; latPreFro, lateral prefrontal lobe; PreMot, premotor area; Sen, sensory area; PostPar, posterior parietal lobe; Occ, occipital lobe; rostTemp, rostral temporal lobe; cauTemp, caudal temporal lobe.

Conclusion:

- Significant increase in ALFF was found after surgery, specifically involving two ictal subdivisions (medial portion, connecting to medial prefrontal and rostral temporal areas).
- Post-surgery, ICC (intra-inter) increased in ictal-sided and decreased in nonictal-sided homologous subdivisions (occipital, rostral and caudal temporal).

After the surgery, the medial, and posterior portions of ictal-sided thalamus displayed increased intrinsic neural activities (ALFF) and preference for intra-thalamic communications (ICC), implying release from the deleterious signaling previously coming from epileptogenic tissue, now removed. In the homologous thalamic subdivisions from the nonictal side, a reversed preference in intrinsic connectivity (towards cross-hemisphere thalamic connections) emerged post-surgery. These changes indicate that a form of diaschisis can occur after ATL, presumed to be adaptive in the setting of good surgical outcome. These data suggest that when epileptogenic tissue is removed, changes in thalamic neural activity and the balance of intra- vs. inter-thalamic connections can occur, with the nature of these changes varying for the ictal and nonictal side.

References:

- Engel J., et al. (1993) Outcome with respect to epileptic seizures. Raven, New York. P. 609-621.
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