The Effects of Epilepsy Surgery on Deep Arousal Structure Functional Connectivity in Temporal Lobe Epilepsy

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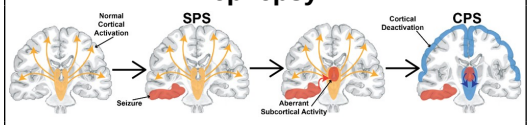
(1) Introduction

Temporal lobe epilepsy (TLE) is associated with widespread brain network perturbations and neurocognitive problems. We hypothesize that seizures lead to interictal dysfunction of brainstem ascending reticular activating system (ARAS) centers, which may contribute to neurocognitive deterioration. This is supported by our recent magnetic resonance imaging (MRI) studies of pre-operative patients with TLE, which showed decreased ARAS connectivity to fronto-parietal neocortical regions that is related to neuropsychological deficits. However, it is not known whether connectivity disturbances can improve in patients after epilepsy surgery.

Network inhibition hypothesis in focal epilepsy



During consciousness-impairing seizures (but not during consciousness-sparing seizures), we have found decreased neuronal activity and decreased cerebral blood flow in rodents and humans. SPS: Simple Partial Seizure, CPS: Complex Partial Seizure. (Modified from [1])

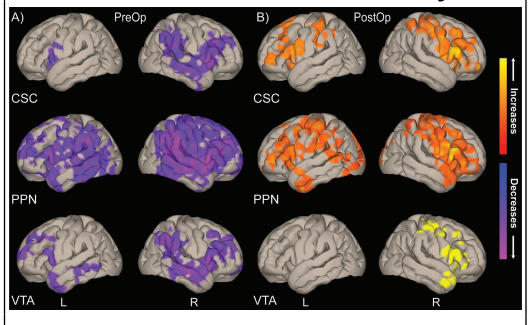
(2) Methods

We evaluated 15 adult TLE patients before and after (> 1 year) surgery, and 15 matched control subjects, and used resting-state functional MRI to measure functional connectivity between three ARAS structures and fronto-parietal neocortex.

(3) Results

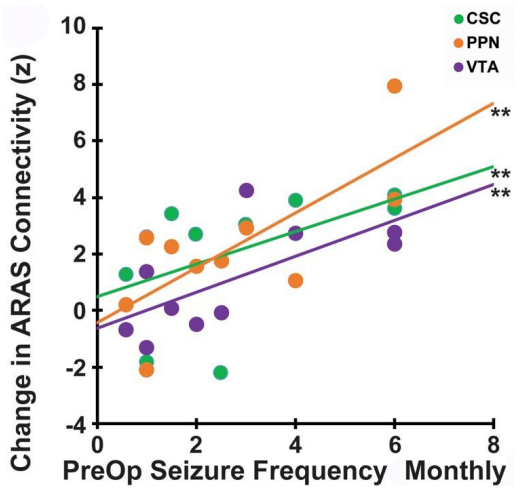
Compared to controls, pre-operative TLE patients demonstrated significant decreases in functional connectivity between ARAS structures and the neocortex ($p < 0.05$, ANOVA, posthoc LSD). After successful epilepsy surgery, the 10 (67%) patients who achieved seizure freedom demonstrated significant increases in connectivity between ARAS structures and the neocortex compared to pre-operative baseline ($p < 0.01$, ANOVA, posthoc LSD), with post-operative connectivity patterns resembling those in controls ($p > 0.6$, ANOVA, posthoc LSD). Certain post-operative connectivity increases were positively correlated with length of time since surgery, while others were positively correlated with pre-operative frequency of complex-partial seizures. Post-operative connectivity recovery was not seen in patients with persistent seizures.

ARAS functional connectivity



Voxel-wise t-tests of ARAS to neocortex connectivity in pre-operative (left) and post-operative patients (right). FDR cluster correction, $p<0.05$, generated with CONN toolbox.

PostOp ARAS connectivity and CPS frequency

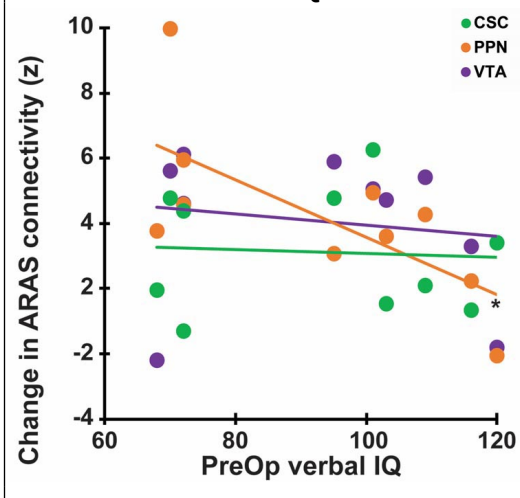


Post-operative functional connectivity increases are correlated with pre-operative complex partial seizure frequency (**p<0.05 corrected).

(4) Conclusions

Impairments in brainstem-neocortical connectivity are observed in TLE, but may recover with successful epilepsy surgery. Some post-operative connectivity patterns may increase with time after surgery, suggesting progressive recovery after achieving seizure freedom. These results are the first to demonstrate connectivity improvements after epilepsy surgery, and may lead to the identification of brainstem neuromodulation targets to address aberrant connectivity patterns and neurocognitive sequelae in this devastating disorder.

PostOP ARAS connectivity & PreOp verbal IQ



Post-operative connectivity increases are correlated with pre-operative verbal IQ. (*p<0.05 uncorrected).

(5) Funding

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(6) References

[1] Englot and Blumenfeld, Prog Brain Res 2009;117:147-70

[2] Englot et al., Brain 2010; 133:3764

[3] Englot et al., J Neurosci 2008; 29:13006-13018

[4] Englot et al., 2018 (In press)

[5] Gonzalez et al., 2018 (Submitted)