Introduction
Epilepsy is a neurological disease characterized by recurring spontaneous seizures caused by intracranial neuronal firing. It was previously shown that the epileptogenic zone exhibits abnormal anatomical and functional brain connectivity of clinical and prognostic value (Kramer and Cash, 2012).

Our aim is to evidence the changes in effective connectivity induced by epilepsy in temporal lobe structures, using cortico-cortical evoked potentials (CCEPs).

Methods
45 patients undergoing SEEG presurgical evaluation with temporal lobe epilepsy (TLE) and non-temporal lobe epilepsy (NTE).

- 535 pairs of stimulation/sampling, 80 brain structures from both hemispheres (Fig. 1).
- Surgical Outcome in 36 out of 45 patients who had surgery.

Results

Cortico-Cortical Evoked Potentials Reveal Abnormal Effective Connectivity Patterns of Temporal Lobe Structures

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Epilepsy A structure width)

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Methods

45 patients undergoing SEEG presurgical evaluation with temporal lobe epilepsy (TLE) and non-temporal lobe epilepsy (NTE).

- SEEG patients (red contacts are inside EZ, green contacts outside EZ).
- epileptogenic structures defined by experienced epileptologists using interictal and ictal SEEG data.
- single pulse electrical stimulation (20 biphasic pulses, 0.25-5mA, 3ms pulse width) (Valentin et al., 2002, Donos et al. 2016a, Donos et al. 2016b) (Fig 2)
- cortico-cortical evoked potentials (CCEPs) - quantified as RMS over 10-110ms post-stimulation.
- criteria for contact activation (Donos et al. 2016b)

- significant Spearman correlation between the CCEP amplitudes and the stimulation currents
- CCEP amplitudes higher than the 3rd quartile (12.5) of all amplitudes observed within a patient

- CCEP analysis: contacts are sorted by epileptogenicity, then grouped at structure level for each patient (Fig 3).
- The effective connectivity strength at the patient level is obtained by averaging CCEPs and normalizing to the patient’s O3 value (Donos et al. 2016b).
- the effective connectivity analysis is performed at the group level, by averaging connections from individual patients.

- an Epileptogenicity Modulation Index (EMI) (Donos et al. 2017) quantifies the relationship between the effective connectivity of temporal structures when part of the epileptogenic network (EZ) or not (NEZ).

$$ EMI = \frac{R^2_{A,B} - R^2_{A,B'}}{R^2_{A,B}} $$

where $E MI$ is the connectivity between structures $A$ and $B$, calculated according to the method described in Donos et al. 2016b, defined in the subset of patients where structure $A$ is part of EZ and $R^2_{A,B}$ is the connectivity between the same structures when $A$ is not part of NEZ.

Results

Shown below (Fig. 5) are the results of the differential analysis of the effective connectivity of epileptogenic vs non-epileptogenic temporal lobe structures, quantified by EMI values, represented using circular graphs.

The two circles of the circular graphs contain information about the number of patients in which the structure was probed in EZ (red color scale) and NEZ (blue color scale) conditions. The inner circle shows the number of patients for the left hemisphere structures, while the outer circle shows the same for left hemisphere structures. The circle drawn outside the structure labels the population. To provide a better visualization of the EMI values, we color-coded the values in blue-white-red color scale, and its absolute magnitude in the size of the segments.

The EMI values inside and the outside of the circle are represented for the right and left hemisphere structures, respectively. The direction of effective connections are shown as arcs having the same color as the EMI. The direction of the effective connections is from the stimulated structure (green arrow of the arc) to the other structures in which significant CCEP activations were observed.

Discussion
An area widespread, affecting connections of pathological structures with other structures outside the EZ. Such changes in connectivity with remote structures that don’t need to be included in the resection volume have been observed across multiple modalities (Engel et al. 2010). Effective connectivity of homologous structures is impacted differently, for example a) pathological left amygdala has stronger connections to ipsilateral hippocampus and entorhinal cortex than pathological right amygdala; b) pathological left hippocampus has weaker connections with all contralateral modalities (Engel et al. 2010).

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References

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