Investigating the Impact of Cortical Lesions on Brain Complexity *in silico*

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Introduction

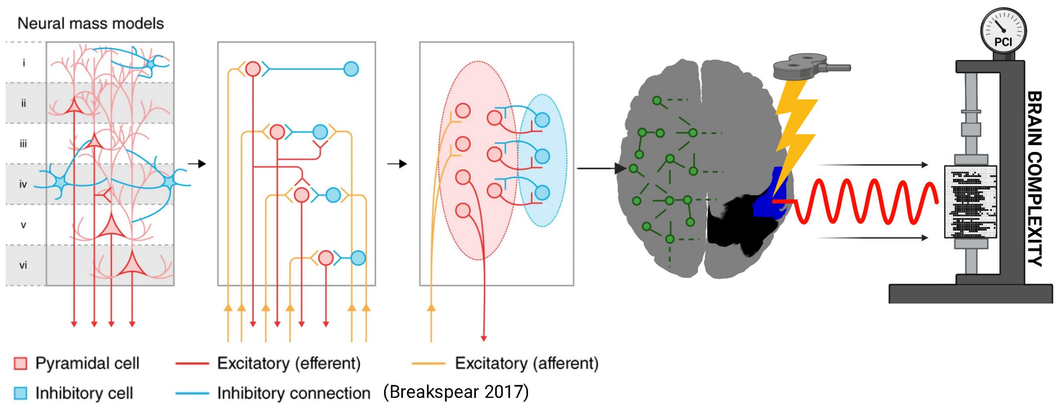
Cortical lesions are thought to result in largescale network effects that extend beyond the damaged area.
From a theoretical perspective, an efficient brain information processing can be characterized in terms of an optimal balance between functional integration and functional differentiation. This balance, also called brain complexity, is likely altered following brain injuries. The Perturbation Complexity Index (PCI) is a reliable index of brain complexity.

Aim of the study

We used a perturbational approach to quantify the complexity of the deterministic component of the response to stimulation using The Virtual Brain (TVB) platform and tested the effect of different cortical lesions on the spatiotemporal complexity of the evoked responses, quantified with PCI.

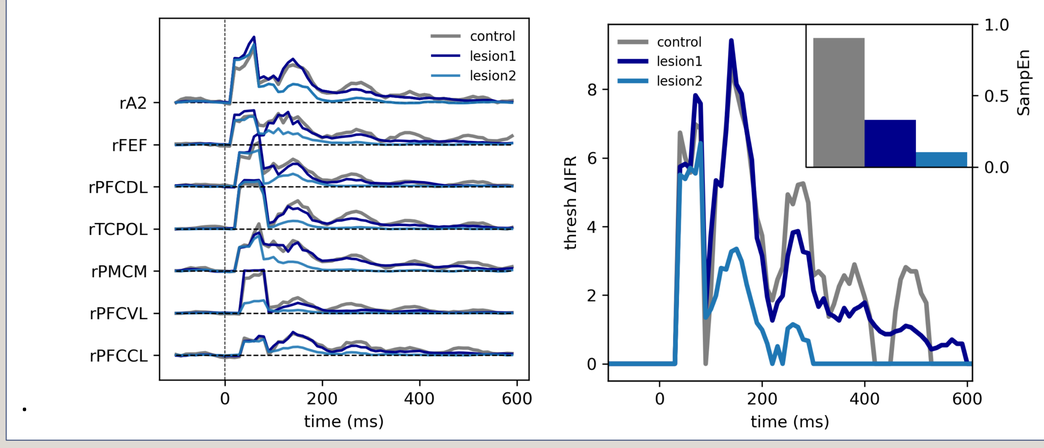
Methods and Materials

We used a directional connectome (1) and each node was modelled with the Larter-Breakspear model (LB) (2). LB is a neural mass model which describes the interaction of excitatory and inhibitory neurons.
We simulated control and lesion conditions (4) and analysed the response to a stimulation in terms of the instantane1ous firing rate (IFR) of each node (5). Next, we extracted a binary spatiotemporal matrix of significant post-stimulus IFR relative to baseline. Finally, we measured brain complexity by applying the Lempel-Ziv algorithm to the matrix, normalized the result, and obtained PCI (6).



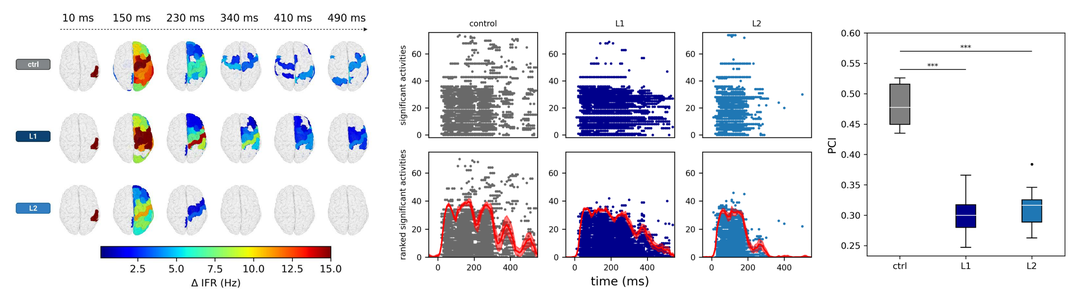
Results I

Left panel: Activity evoked by the stimulation pulse at t=0 in some representative regions of the stimulated hemisphere (and damaged in the lesion conditions). The ΔIFR, averaged across trials, obtained by subtracting the mean firing rate (MFR) at baseline from the IFR (ΔIFR = IFR(t) - MFRbaseline), is reported on the y-axis; right panel: thresholded ΔIFR (the threshold is the 99th percentile of pre-stimulus activity) and Sample Entropy (SampEn) of the rPFCCL response.



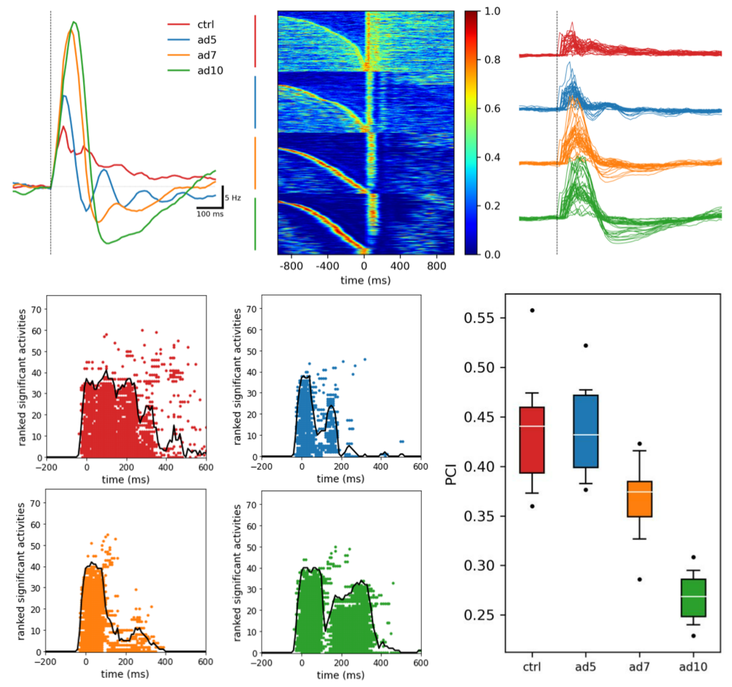
Results 2

In **control** the evoked activity is integrated and differentiated often involving the non-stimulated hemisphere (left hemisphere); in **L1** the activity is sustained but **redundant** and **local**; in **L2** the activity is **local** and dissipates rapidly. Consistently, **PCI values in lesions are lower than ctrl.**



Results 3

Adaptation mechanisms in the stimulated region affect its evoked response. Increasing the number of regions with adaptation leads to a more global slow-oscillatory regime where the stimulus triggers a full-fledged **slow-wave** (up-state followed by a silent period) in several areas. Consistently, **the more global the adaptation the less complex the global response**, as measured by PCI.



Discussion

Consistent with empirical work on focal brain injury, we found that compared to control conditions most of the lesions affected the evoked responses over the affected hemisphere (e.g., by reducing stimulus-related oscillations, Fig. 1).
Interestingly, lesions result in a loss of the richness of the response to stimulation, quantified by Sample Entropy, resulting in a more regular and redundant evoked response compared to control (Fig. 2).
Furthermore, the spatiotemporal complexity of the response to a perturbation quantified via PCI was significantly lower in the lesion condition (Fig. 4), indicating a loss of brain complexity following brain injury.
Most important, we found that PCI values correlated with the amount of significant activations observed distant from the stimulated site (R-squared=0.68, not shown). Indeed, cortical lesions resulted in network responses that remained mostly confined to the stimulated hemisphere.

Conclusions

These results highlight the possibility of exploiting computational models to explore the impact of brain injury on complexity, and open further perspectives for investigating the network underpinnings that sustain brain complexity as well as the precise mechanisms for its recovery following brain injury.

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