Network Modeling of mouse brain fMRI under the effect of different anesthetics

Qasim Bukhari[1], Aileen Schröter[1], and Markus Rudin[1,2]
[1]*Institute of Biomedical Engineering, ETH and University of Zürich, Zürich, Switzerland,* [2]*Institute of Pharmacology and Taxicology, University of Zürich, Zürich, Switzerland*

Purpose

Network modeling is a promising tool for analyzing the brain functional architecture and comparing alteration caused by different physiological or pathological states. While the method is frequently applied to human fMRI data[1] its use in rodent fMRI is still rather limited. In particular it remains to be shown whether the inferior signal-to-noise ratio intrinsic in mouse fMRI is sufficient for applying these tools. In this study we have evaluated the use of dual regression followed by network analysis for detecting differences in mouse functional networks for different anesthetic regimens.

Methods

Network analysis was carried using resting state fMRI data sets of anesthetized mice collected on a Bruker BioSpec 94/30 system operating at 9.4T [2]. Anesthesia regimen included isoflurane (1.0% in air/oxygen, N=11 mice), medetomidine (0.1 mg/kg i.v. followed by infusion of 0.2mg/kg/h, N=13), propofol (30mg/kg i.v followed by infusion of 120-150mg/kg/h, N=6) and urethane (1.5g/kg i.p., N=13) [2]. Data were processed as follows: After preprocessing and realignment, concat-ICA was applied using the MELODIC toolbox of FSL followed by dual regression analysis and 'randomize' with TFCE (Threshold Free Cluster Enhanceent) and Bonferroni correction to provide the final statistically significant maps. These results were used for Network Modeling of the brain networks using FSLNets (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FSLNets) (Fig.1)

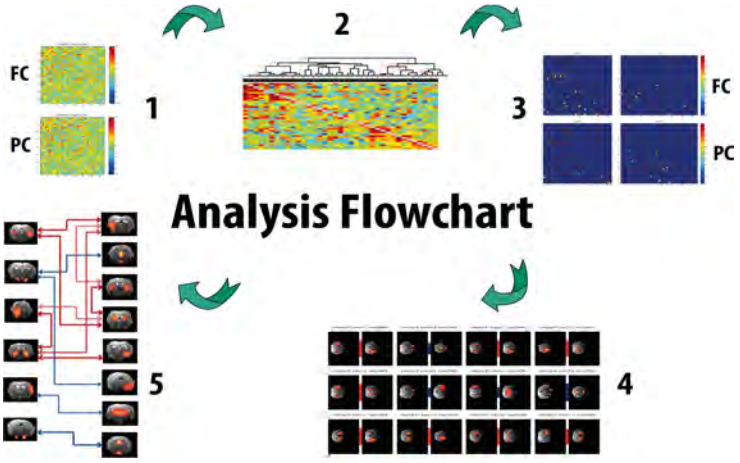

Figure 1: Schematic of network modeling procedure (data are shown for comparison medetomidine vs. urethane). Starting from full (FC) and partial correlation (PC) matrices (1) a dendogram based FC and PC was generated (2) followed by GLM analysis (3). This yielded significant network differences for the functionl networks linked to the two anesthetics (4), which could then be depicted as a network tree (5).

Results

Using dual regression analysis in combination with the network modeling, characteristic anesthesia specific differences could be determined. This is illustrated in Fig.2 displaying network comparisons for several combinations. Comparing network trees significant differences involving 5 to 6 network nodes have been observed between medetomidine anesthetized mice and mice anesthesized with one of the three other anesthesia regimens. In contrast, no or minor differences in the network trees have been found among isoflurane, propofol and urethane anesthetized animals. The results are in close agreement with previous reports [2].
A detailed understanding of anesthesia effects on functional connectivity may help differentiating them from the effect of interest.

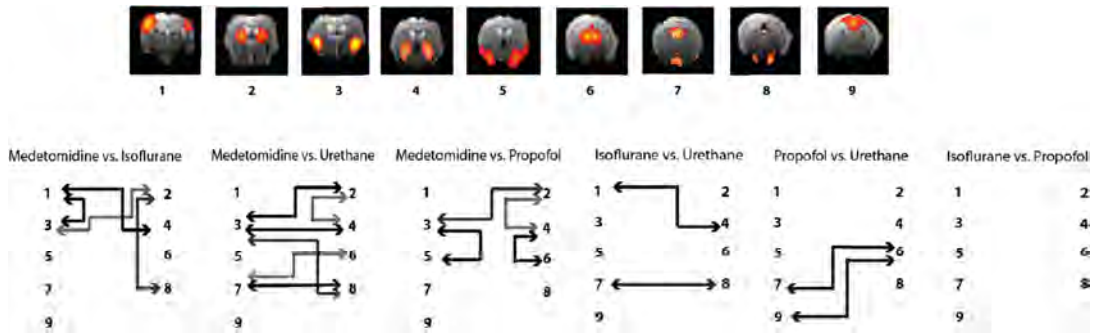

Figure 2: Pairwise comparison of functional networks in mice under four anesthesia regimens (isoflurane, medetomidine, propofol, urethane), Significant network differences between the anesthetics, in particular between medetomidine and the other regimens, have been found using between-network-analysis approach. Numbers indicate network nodes shown in panels on top.

Conclusion

The network modeling approach enables detecting differences in resting state fMRI patterns among different groups of mice (physiological states, treatment groups, pathological states etc.). Here we analyzed the effect of different anesthetics as the example, which illustrates that the method is capable of identifying relatively small differences due to an altered physiological state in mice.

References

1. Smith SM, et al. (2011) Network modelling methods for FMRI. Neuroimage. 54:875-91
2. Grandjean J, Schroeter A, et al. (2014) Optimization of anesthesia protocol for resting-state fMRI studies in mice based on their differential effects on the functional connectivity pattern. NeuroImage 102: 838-47