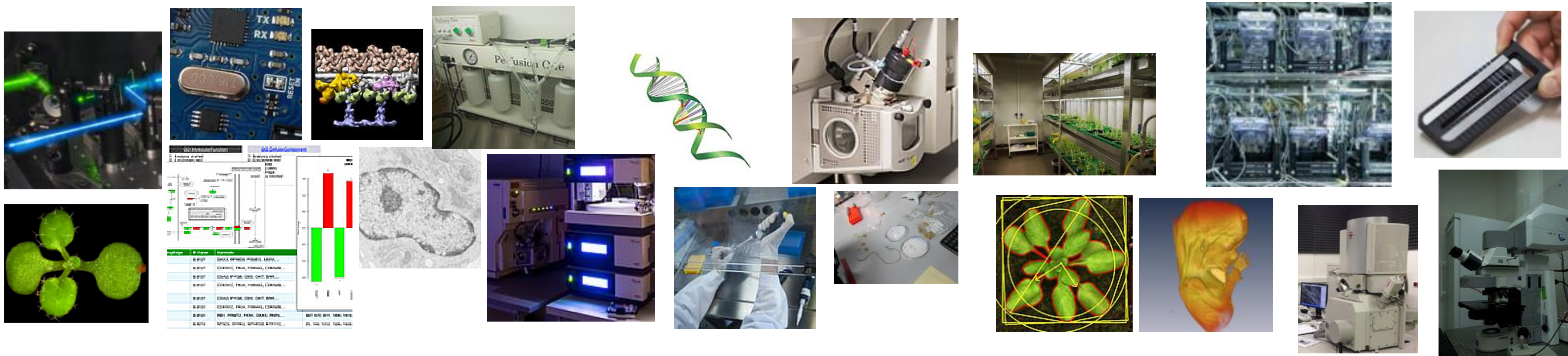

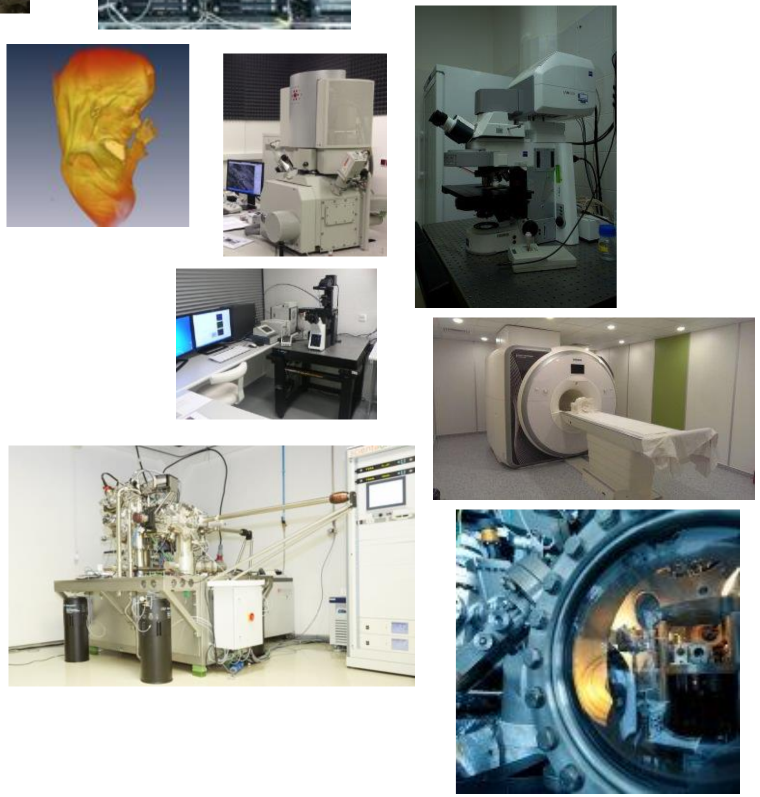

High field improvements for BOLD fMRI in mouse models

Michal Mikl (CEITEC-MU), Jelena Zinnanti (VBCF)

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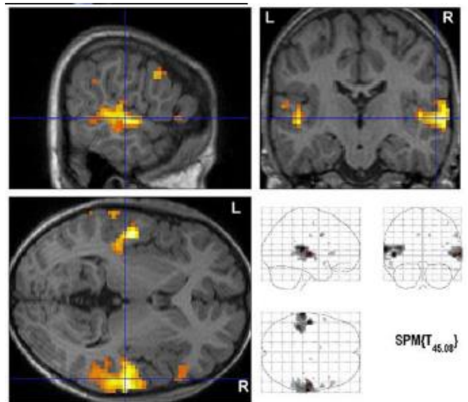
European Regional Development Fund

Pilot project introduction

- *Project partners:*
  - *VBCF (pcIMAG)*
  - *CEITEC (MAFIL)*

- *pcIAMG equipment/expertise:*
  - *Ultra-high field (15T) animal scanner*
  - *Experiences with high-field animal MR imaging*

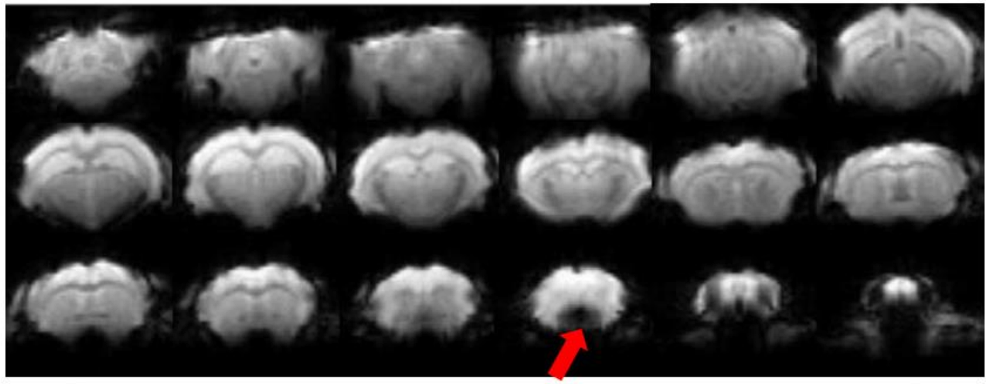
- *MAFIL equipment/expertise:*
  - *Long-term experiences with analysis of human fMRI data (from 1.5T and 3T scanners)*
  - *Experiences with optimization of data processing methods, development and implementation of new methods*

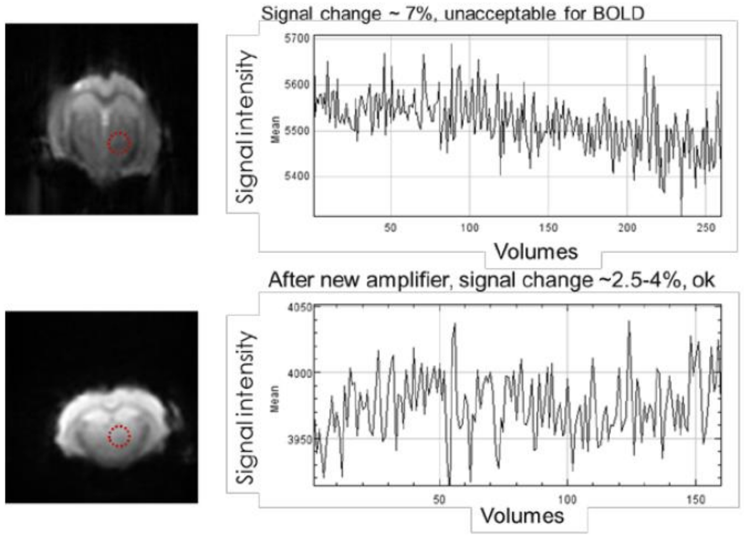


Pilot project introduction

- *Functional imaging at ultra-high filed very challenging due to susceptibility-related artifacts (image distortion) near tissue-air interfaces*

- *State of the art shimming system – to improve Bo homogeneity*
- *State of the art amplifier to reduce noise*





- *Improve image quality (acquisition, VBCF) → improve geometric distortion (post processing, VBCF, MAFIL) → apply advanced image algorithms for data analysis (MAFIL)*

Pilot project introduction

- ***The goal of the project is to bring together experts in functional imaging at CEITEC and apply their knowledge for successful adaptation of BOLD fMRI to mouse studies and high magnetic field***

    - *Added value for MAFIL –new experiences with high-field animal data, improved ability for cooperation with local researchers and institutions*

- *Potential end-users:*
    - *Academic users in the field of preclinical and translational research working with animal and human MRI*

Project implementation

- *Advanced fMRI data analysis*
- *5 staff exchanges and visits so far*

1. *Visits (Jelena Zinnanti and Peter Opriessnig visit to MAFIL) Introduction and general discussion of the project and milestones.*

2. *Staff Exchange –Martin Gajdoš visits VBCF*

   - *Comparison of common steps in data acquisition and analysis*
   - *Implementation and consultation of data analyses –fMRI preprocessing, GLM, dynamic connectivity*

3. *Staff Exchange –Raphaela Höfl visits MAFIL*
   - *Implementation of preprocessing, GLM and group analysis on mouse data with electric stimulation*

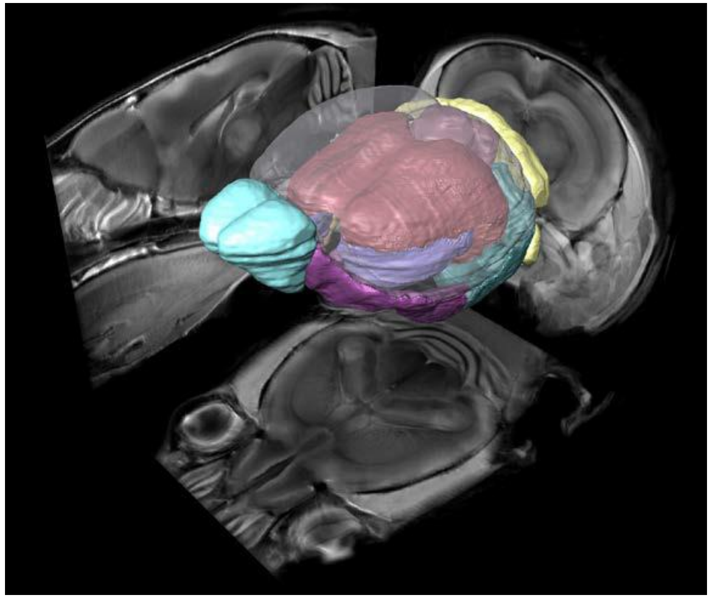
Project description

***Biological significance**: determine differences in brain processing that lead to pain suppression in KO mice*

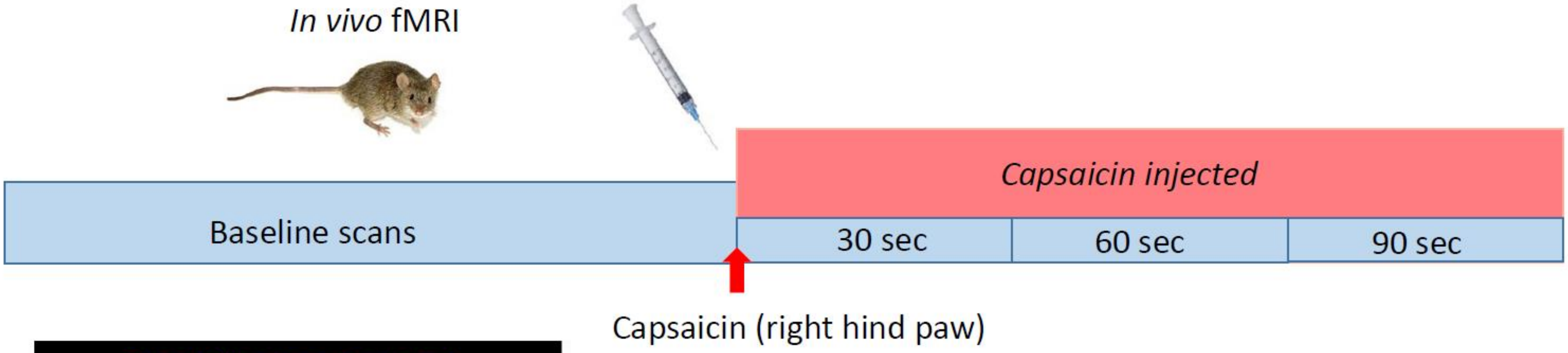
Methods

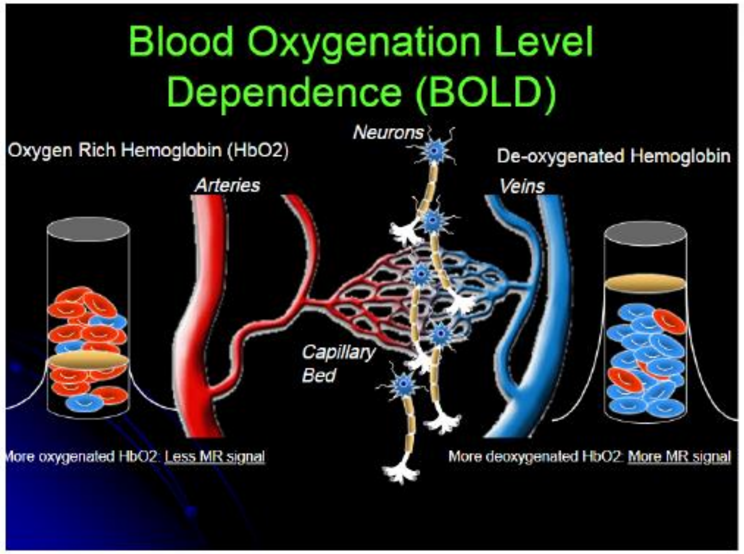
- 7 genetically modified pain resistant mice (KO)

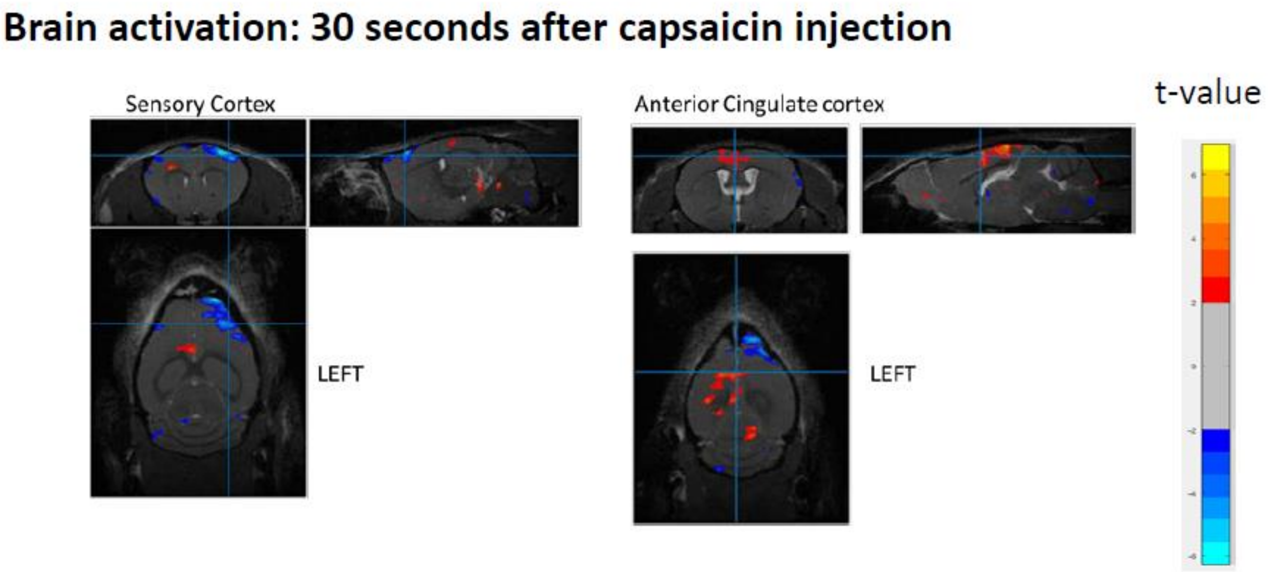
  and 5 pain sensitive mice (WT)
- 15.2 T Bruker BioSpec 152/11 MR scanner
- resting state BOLD fMRI (TR=2 s, vx= 0.125 x 0.125 x 1 mm)
- 120 scans - capsaicin injection in front paw - 360 scans



Project description

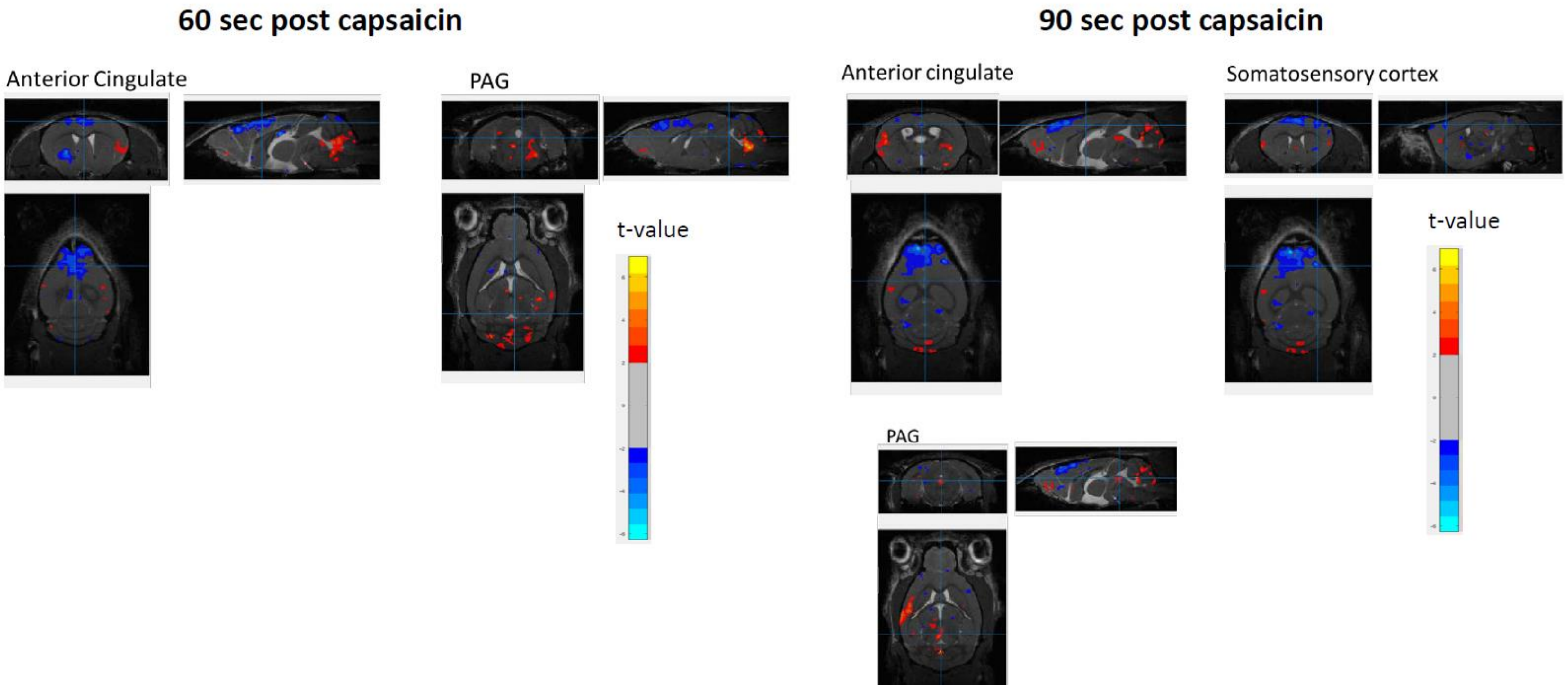




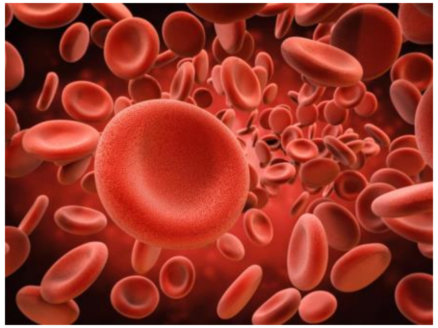


High field improvements for BOLD fMRI in mouse models

Project results – effect of capsaicin



Project results – effect of capsaicin



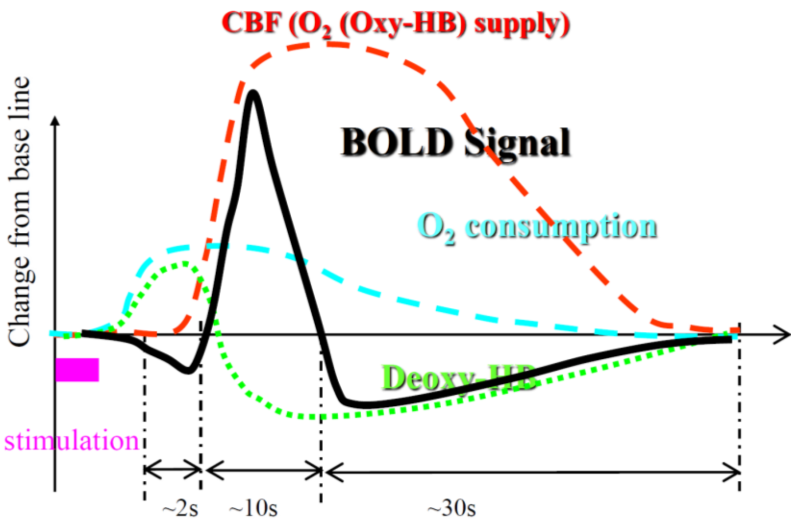
Theory

BOLD fMRI

- BOLD = blood oxygenation level dependent
- fMRI = functional magnetic resonance imaging
- Functional connectivity

BSFA

- BSFA = Bayesian switching factor analysis (Tahgia 2017)
- Time-varying functional connectivity
- Based on Bayesian fitting and Hidden Markov models



Project results – effect of capsaicin

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BOLD fMRI

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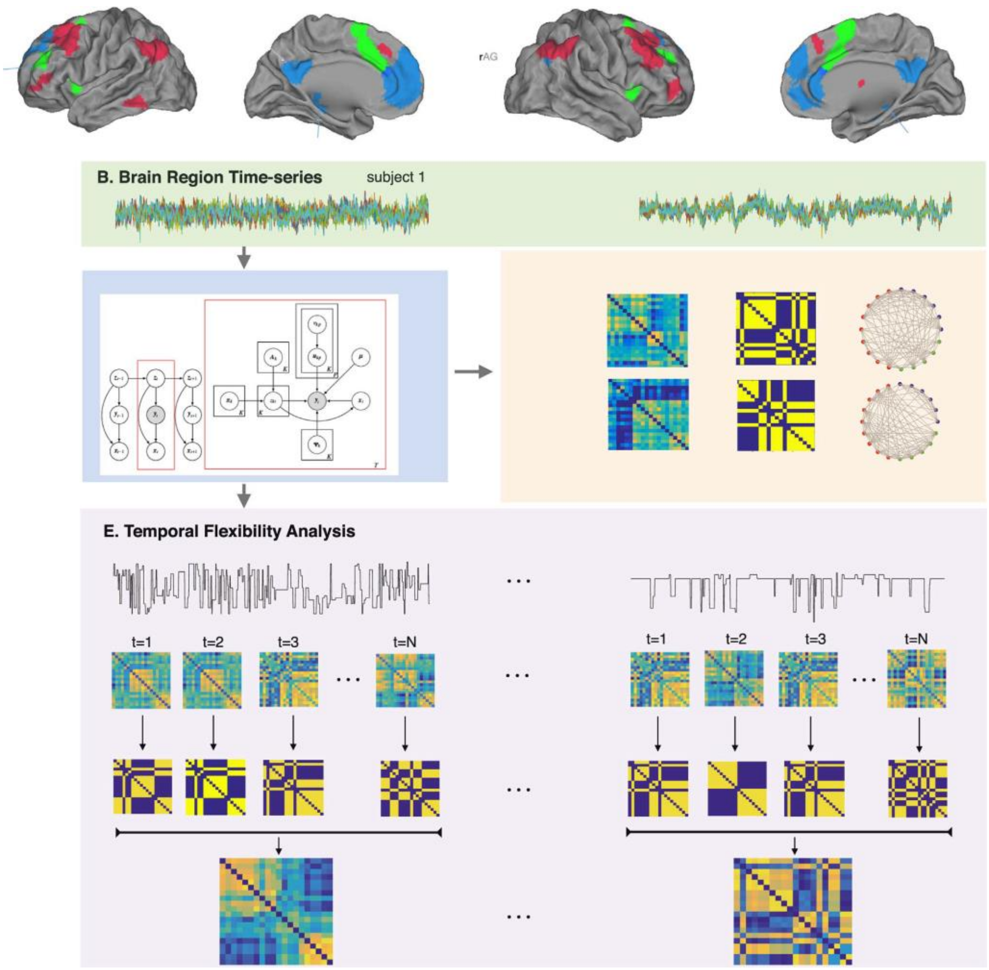
- BSFA = Bayesian switching factor analysis (Tahgia 2017)
- Time-varying functional connectivity
- Based on Bayesian fitting and Hidden Markov models
- Estimates dominant states of network in time

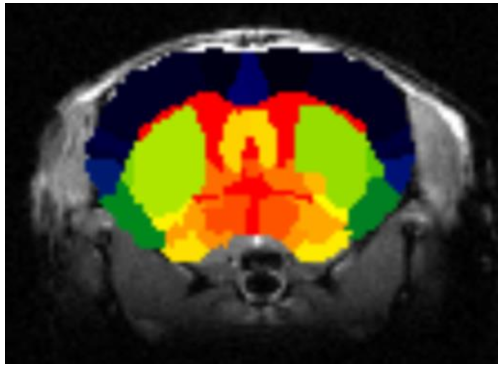


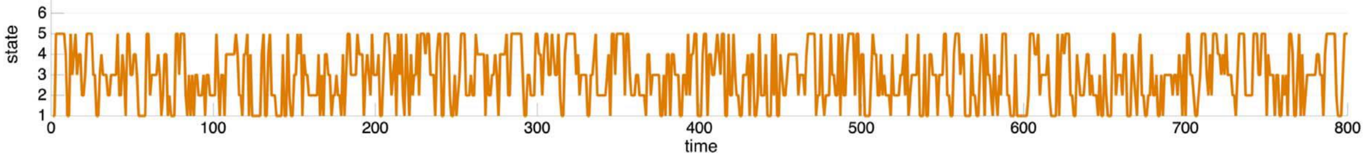
Tahgia 2017

Project results – effect of capsaicin

Analysis

1. Preprocessing of the data with DPABI pipeline
   - slice timing correction, realign, normalization, smoothing, detrend and regression of nuisance covariates
2. Parcellation based on in-house anatomical atlas of mouse brain
3. Representative signals from 4 ROIs: left and right thalamus (TH) and left and right periaqueductal grey (PAG)
4. BSFA
5. Evaluation of within and between groups differences on BSFA parameters (paired and independent t-tests)





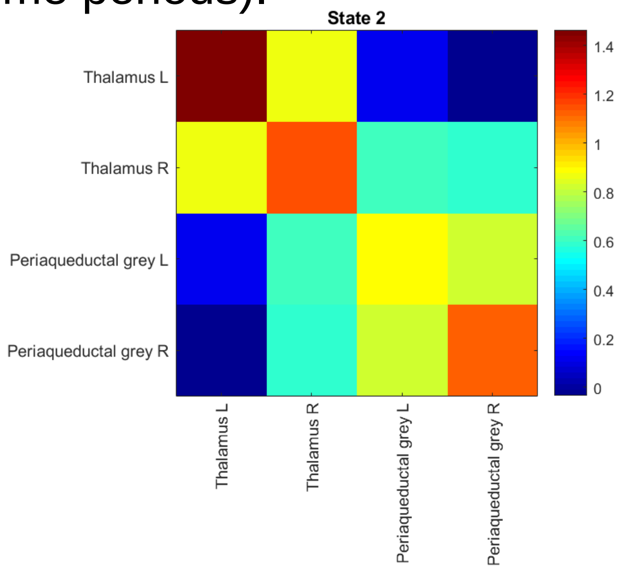
Tahgia 2017

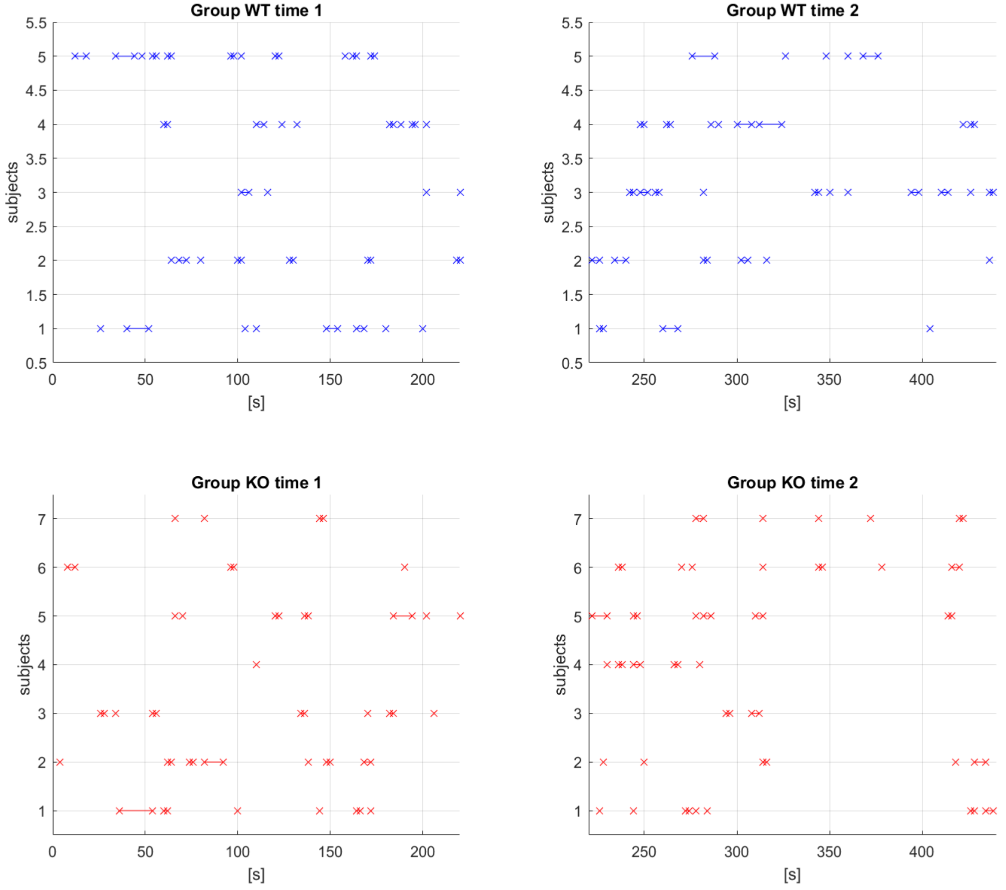
Project results – effect of capsaicin

Results

- Each state is characterized with covariance matrix (covariance between ROIs) and temporal evolution of the state.
- BSFA estimated across our fMRI mice data 6 dominant states

1. State 2
    - significant increase in mean time of stay in state 2 in WT group immediately after capsaicin injection (comparing 220s time periods).



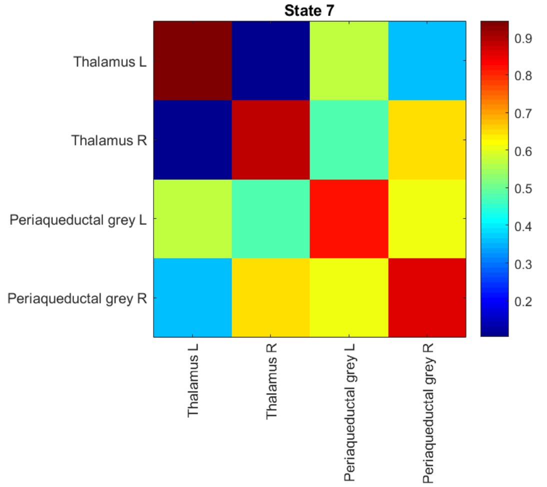


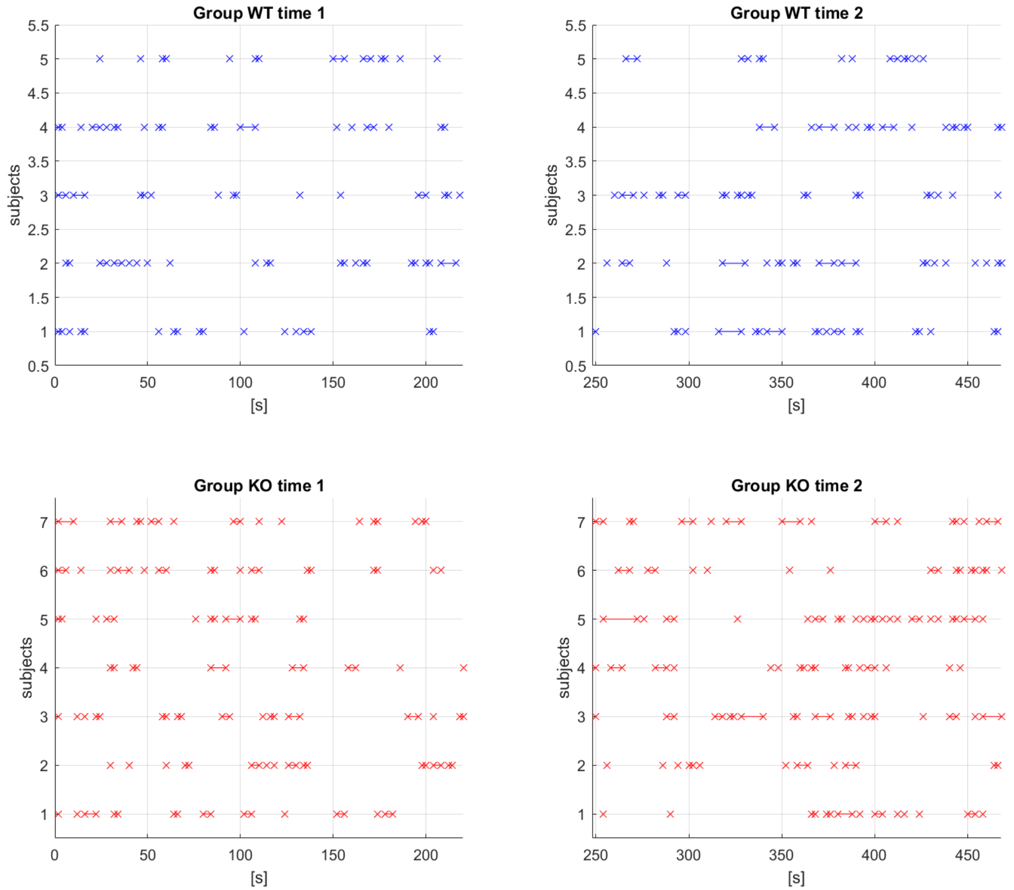
Project results – effect of capsaicin

Results

- Each state is characterized with covariance matrix (covariance between ROIs) and temporal evolution of the state.
- BSFA estimated across our fMRI mice data 6 dominant states

2. State 7
    - significant decrease of median length of stay in KO group in time period starting 220 seconds after capsaicin injection (in 220s time period) when comparing with 220s time period before capsaicin injection.

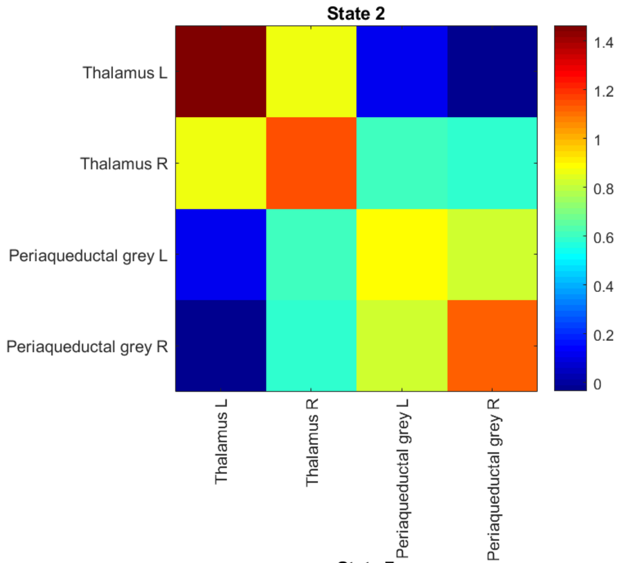


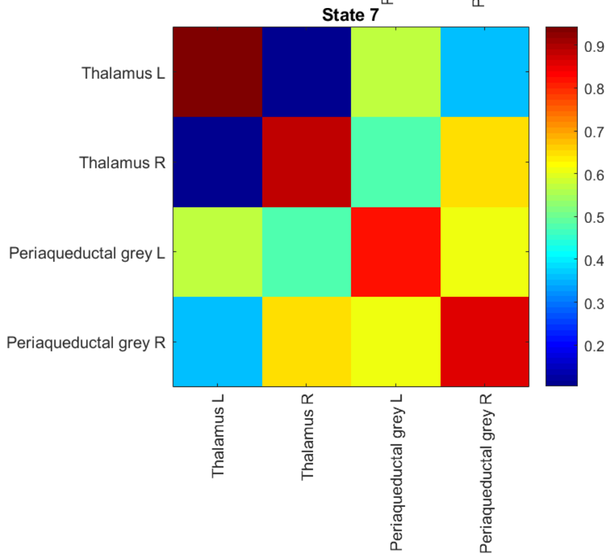


Project results – effect of capsaicin

Interpretation

1. **State 2**
    - related with disconnection between L TH and both PAG
    - Observed increase in mean time of stay in state 2 in WT group explains pain sensitivity in this group
2. **State 7**
    - the most frequent in all mice; each mouse spent 22.4 ± 3.9 % of time in this state.
    - probably represents part of resting state network
    - characterized with decreased connectivity between left and right TH
    - Observed decrease of occurrence of this state in KO group after capsaicin injection reflects disruption of resting state with activity related to pain perception





Conclusions

- *Resting state functional imaging can be used to determine differences in pain processing in KO vs WT mice (with sparse information on brain states)*

- *Dynamic analysis of fMRI data is greatly adding to our understanding about brain processing as a whole (described as brain states)*

- *We plan to use established processing pipelines for future studies involving brain function*