BuzsákiLab

Whole brain mapping of transcranial electrical stimulation-induced effects by BOLD-fMRI in rats

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* Contributed equally

Transcranial electrical stimulation (TES)

- Non-invasive brain stimulation method
- Effects depend on
  - Neuronal orientation/morphology[1]
  - Magnitude of electric field[2]

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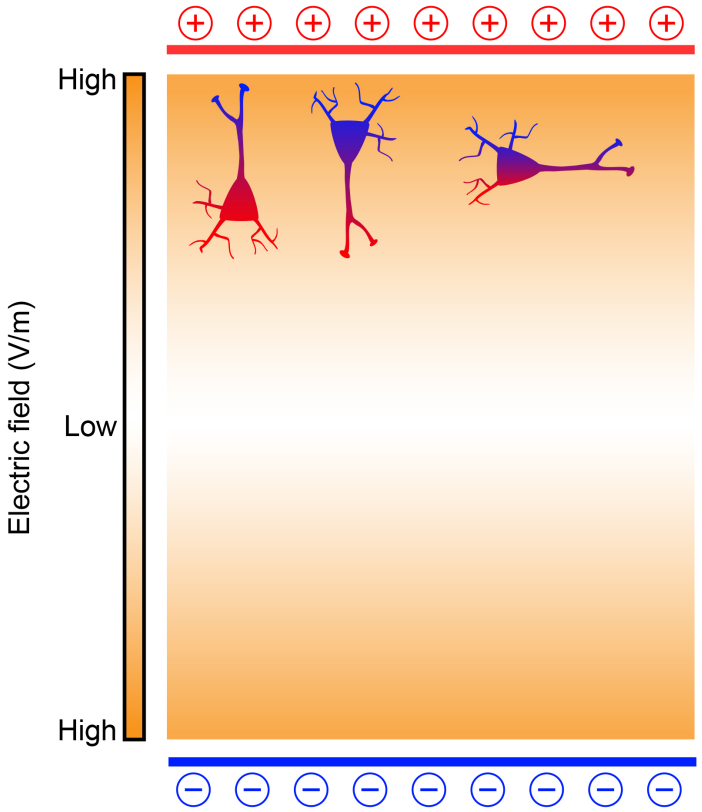
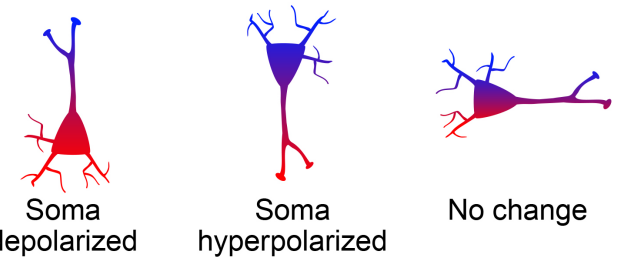


Orientation / morphology of neuron



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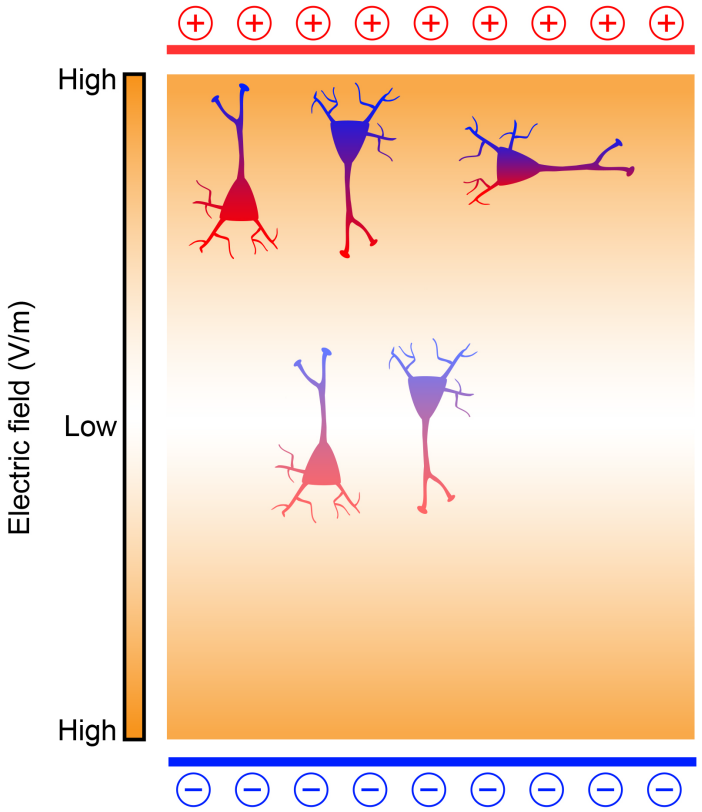

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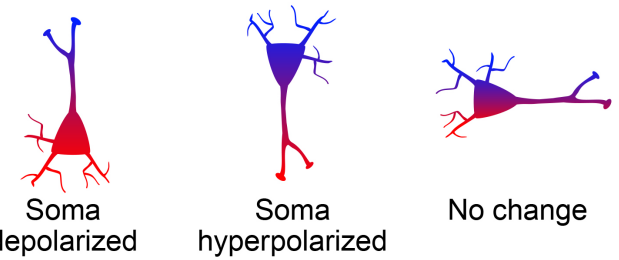
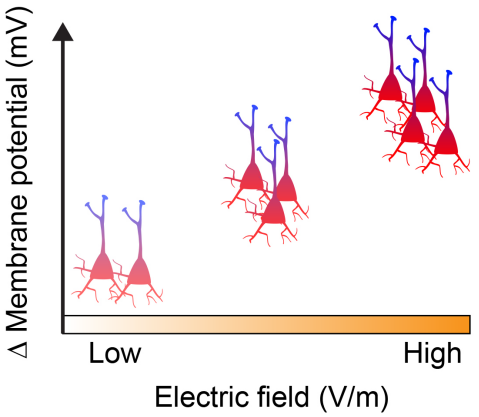


Effect of electric field strength



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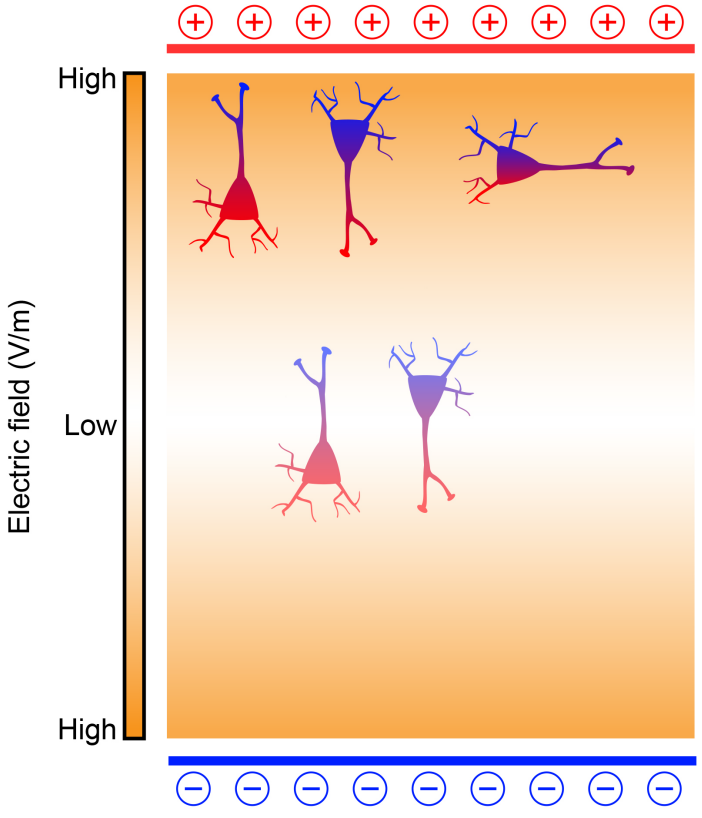
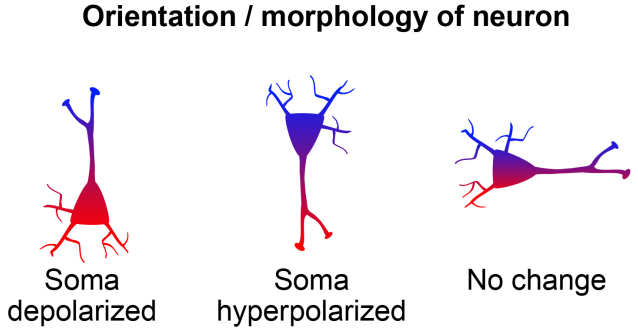
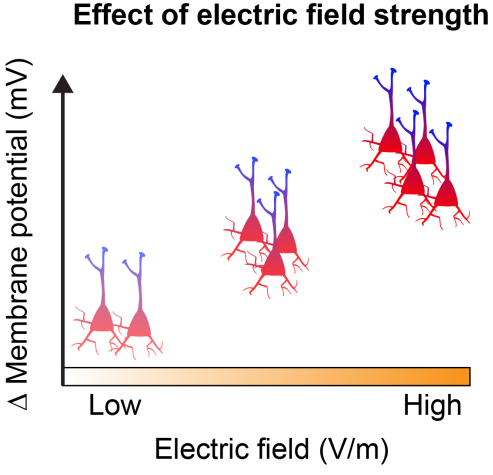
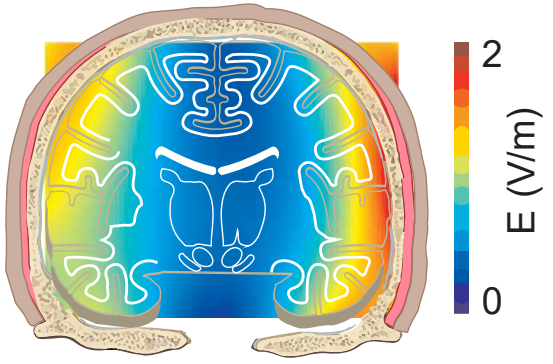


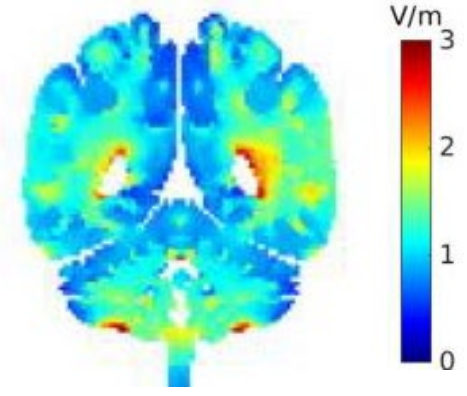




- Poor spatial resolution
  - *Electric field* (*E*) is highest in cortex[3]



- Modeling predictions[4]
  - Cerebrospinal fluid can serve as a conduit.



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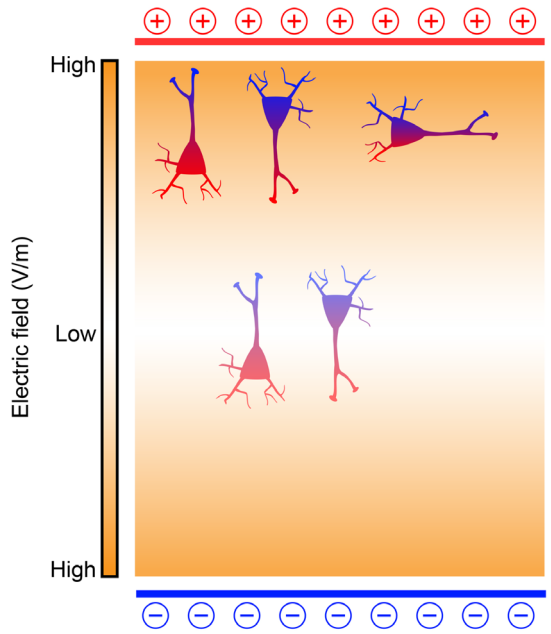
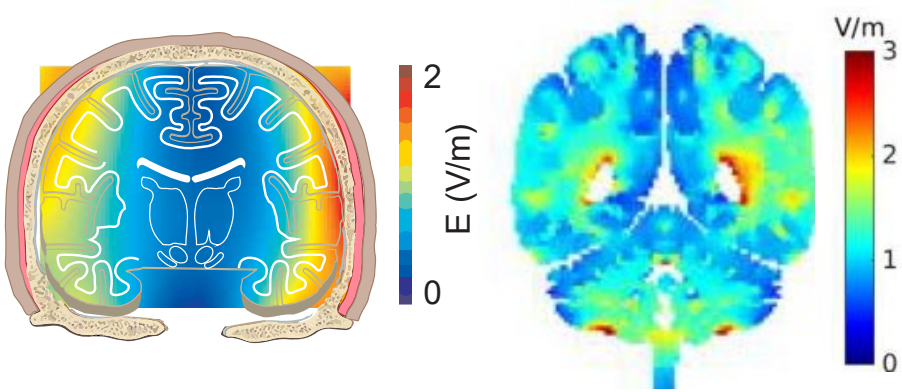
What is the extent and strength of TES on brain structures?





What is the extent and strength of TES on brain structures with:

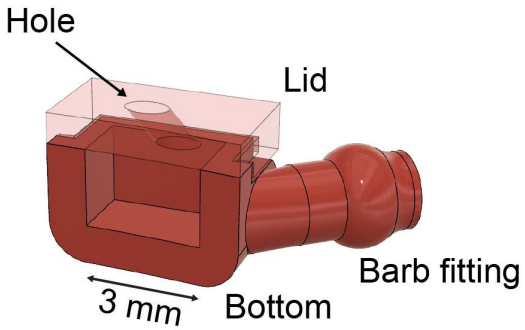
1. Different orientation?
2. Different distance from the stimulation electrodes?
3. Around the ventricles?

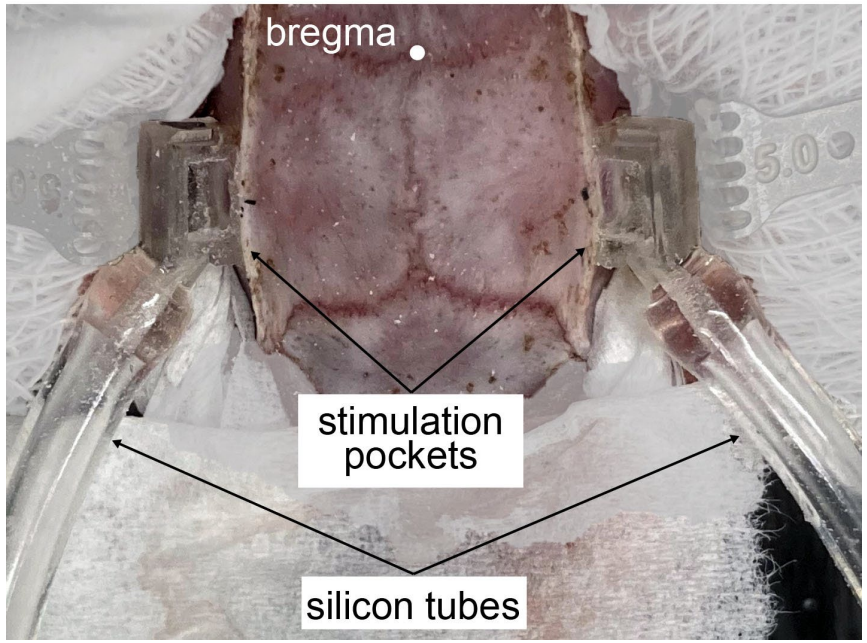
How to measure these effects?

- Electrophysiology
  - Limited number of brain structures to record from.
- c-FOS staining
  - Animals should be sacrificed after manipulation.
- **Whole brain imaging with resting state fMRI**

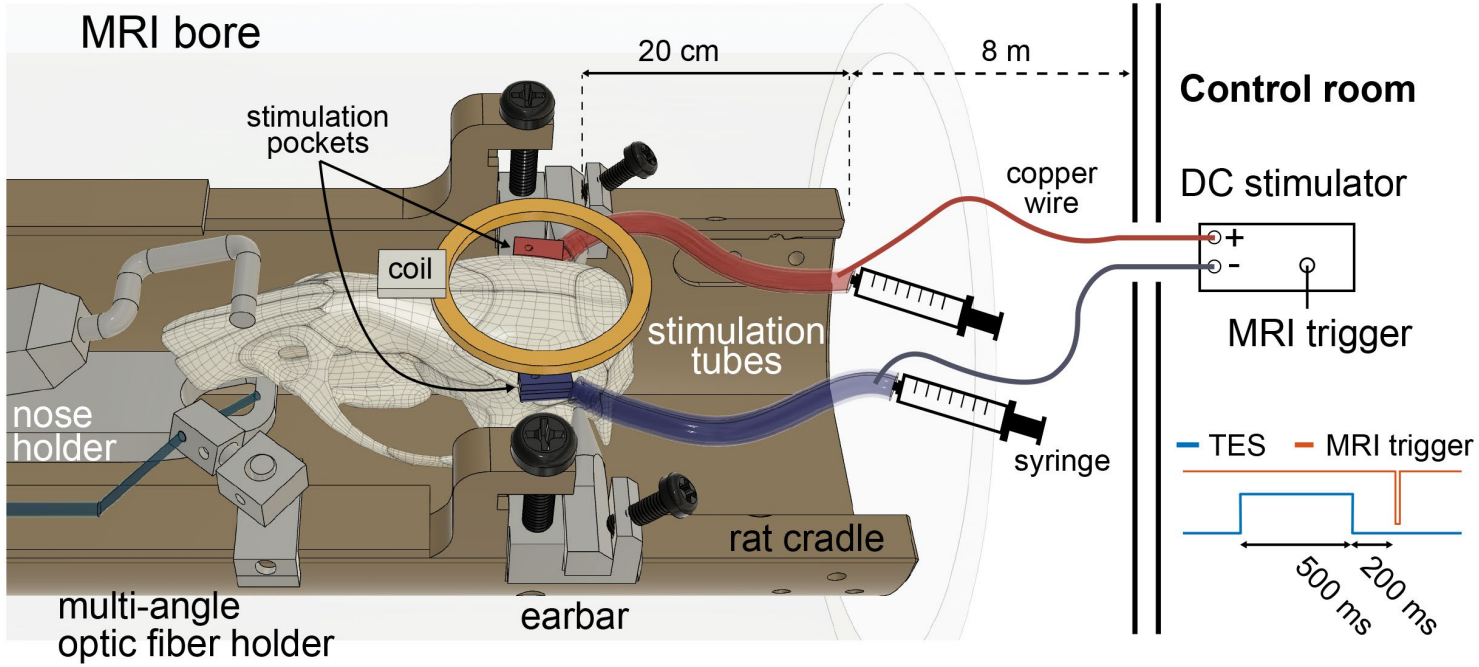
MR-compatible, deuterium-based TES system

Stimulation pocket



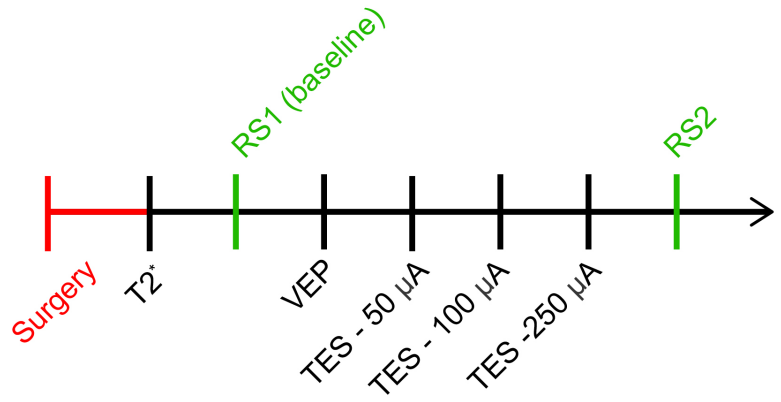


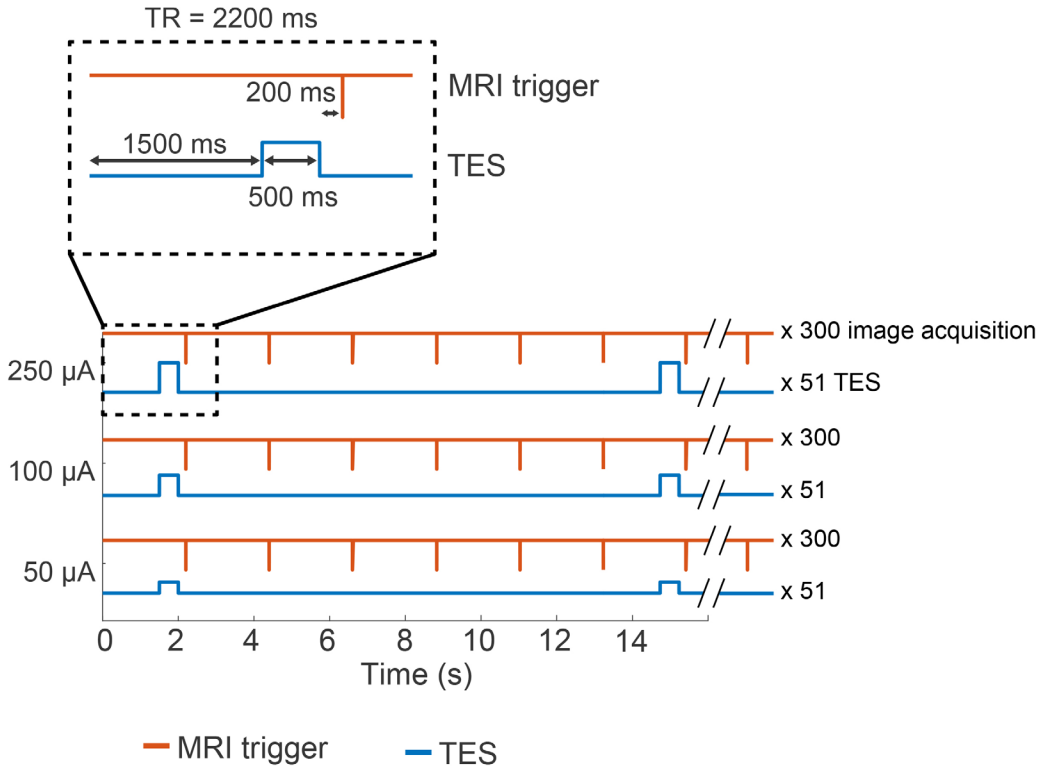
Head-fixation setup



1. Adjustable ear bars, nose and optic fiber holder (3D-printed).
2. Stimulation tubes are filled with 5% NaCl deuterium solution.
3. Metal wires are 20 cm away from the animal's head.

MRI scanning sessions, TES paradigm

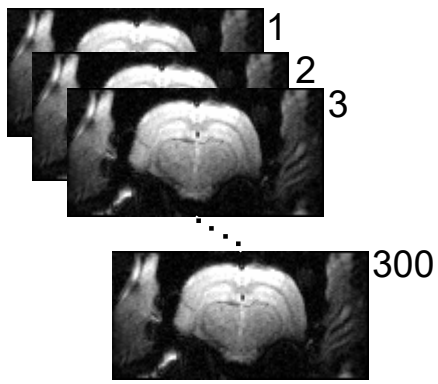


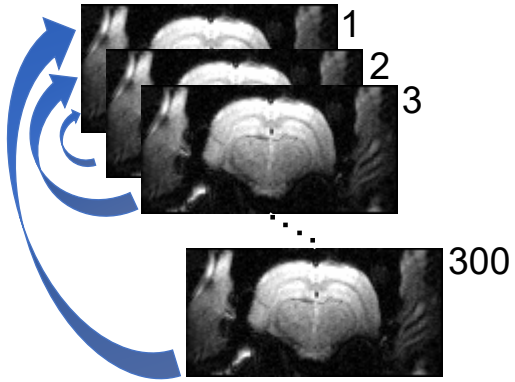


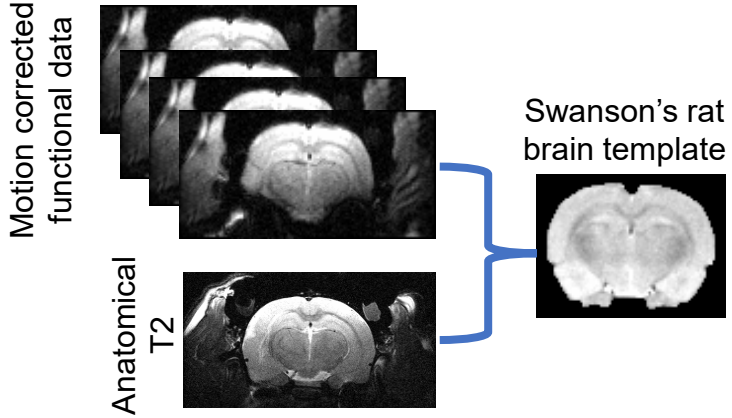
- Animal subjects
  - n = 10 Long-Evans rats (urethane anesthesia)
  - n = 3 rats were euthanized inside the scanner to evaluate TES-induced artifacts
- TES timing was shuffled for each subject
  - Control for dose-dependent long-lasting effects
- Functional MRI (fMRI) and resting state MRI (rs-fMRI)
  - Bruker 7T, blood oxygenation level dependent (BOLD) resting state functional MRI
- Physiological monitoring during MRI
  - Rectal temperature
  - Respiratory rate
  - Oxygen saturation
- Visual-evoked potential
  - Block design
- Electrophysiology after the fMRI experiments
  - n = 4 rats
  - 128-channel silicone probe

Data processing

fMRI raw data → **Motion correction** → **Normalization** → **Smoothing**







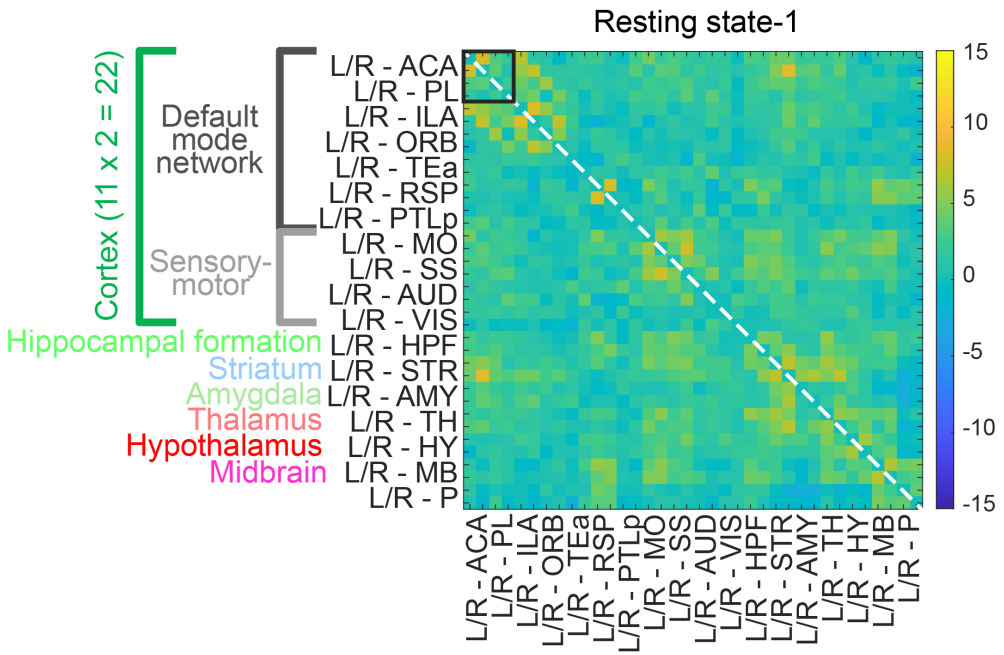
Gaussian kernel with FWHM of 0.7 X 0.7 X 0.7 mm³

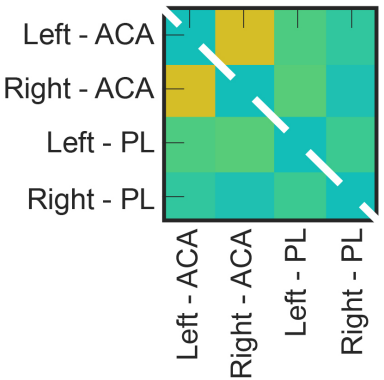
Segmentation

Swanson's modified rat atlas:
36 brain structures (18/hemisphere)

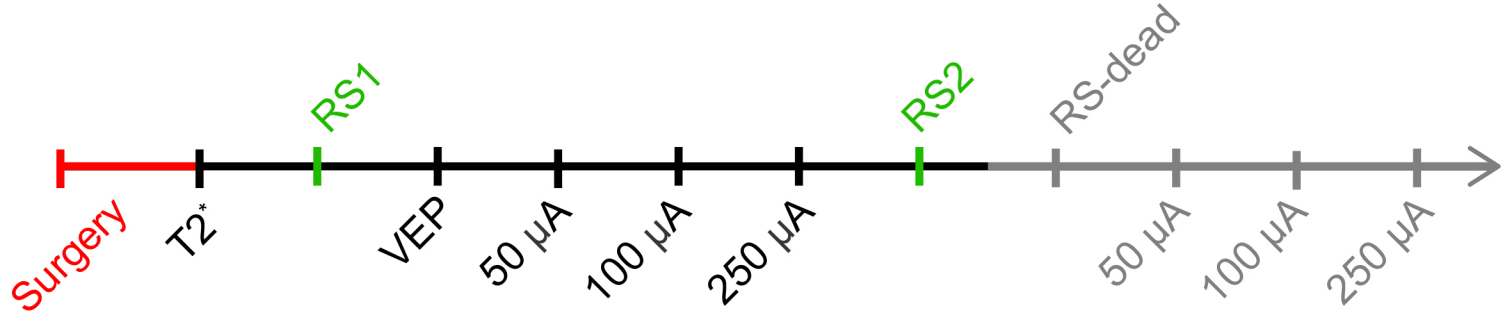
Functional connectivity mapping

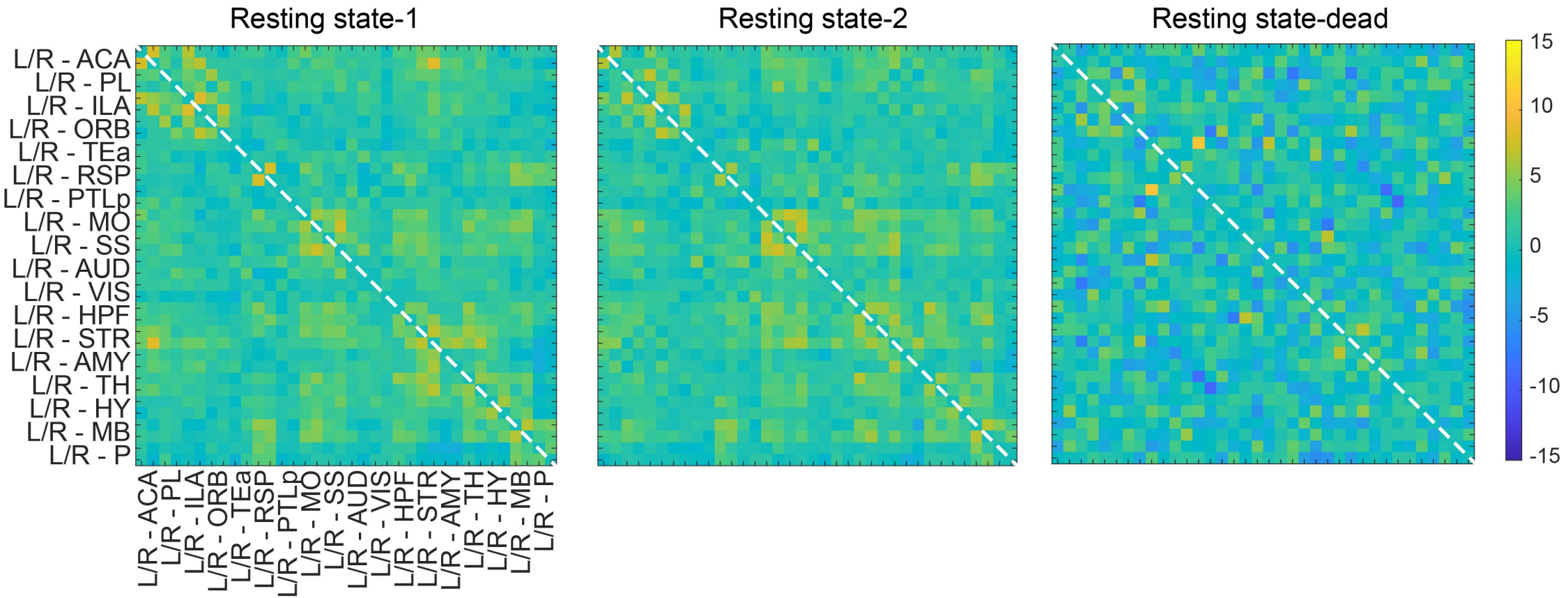
- Only the resting state data were temporally band-pass filtered:
  - 0.01 – 0.1 Hz (LFFs).
- Temporal drifts were removed by linear detrending.
- Pearson's correlation coefficient for each connection was calculated in subject's space and normalized to a z-score using Fisher's r-to-z transformation.



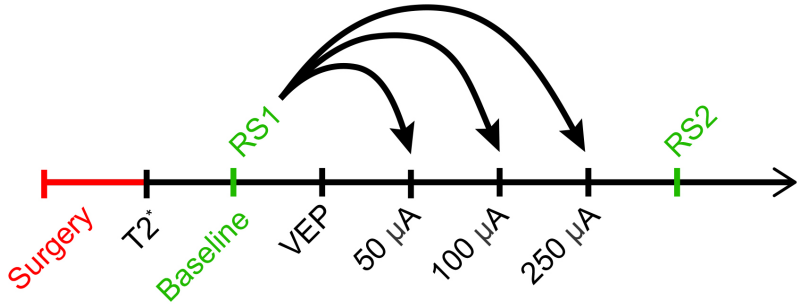


Artifact-free TES-fMRI

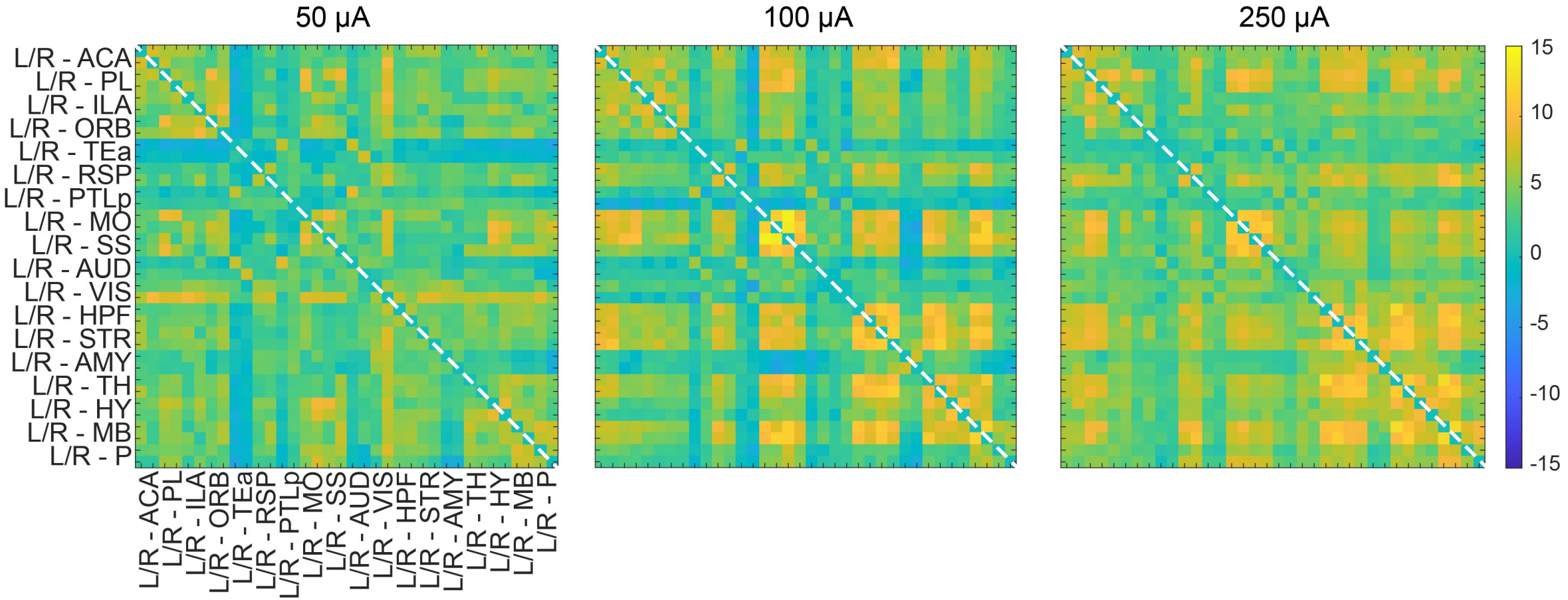




TES-dose dependent BOLD activation pattern



- **Resting-state 1** is used as baseline.
- TES conditions were shuffled across animals.



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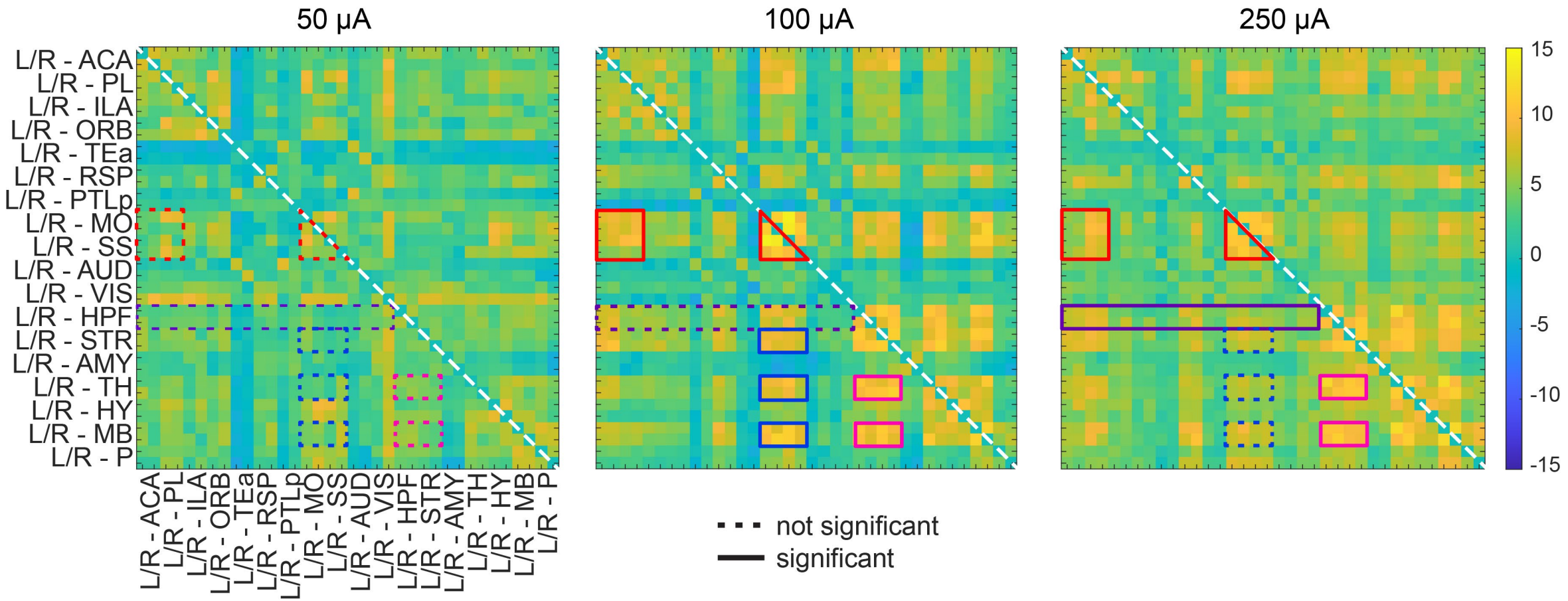

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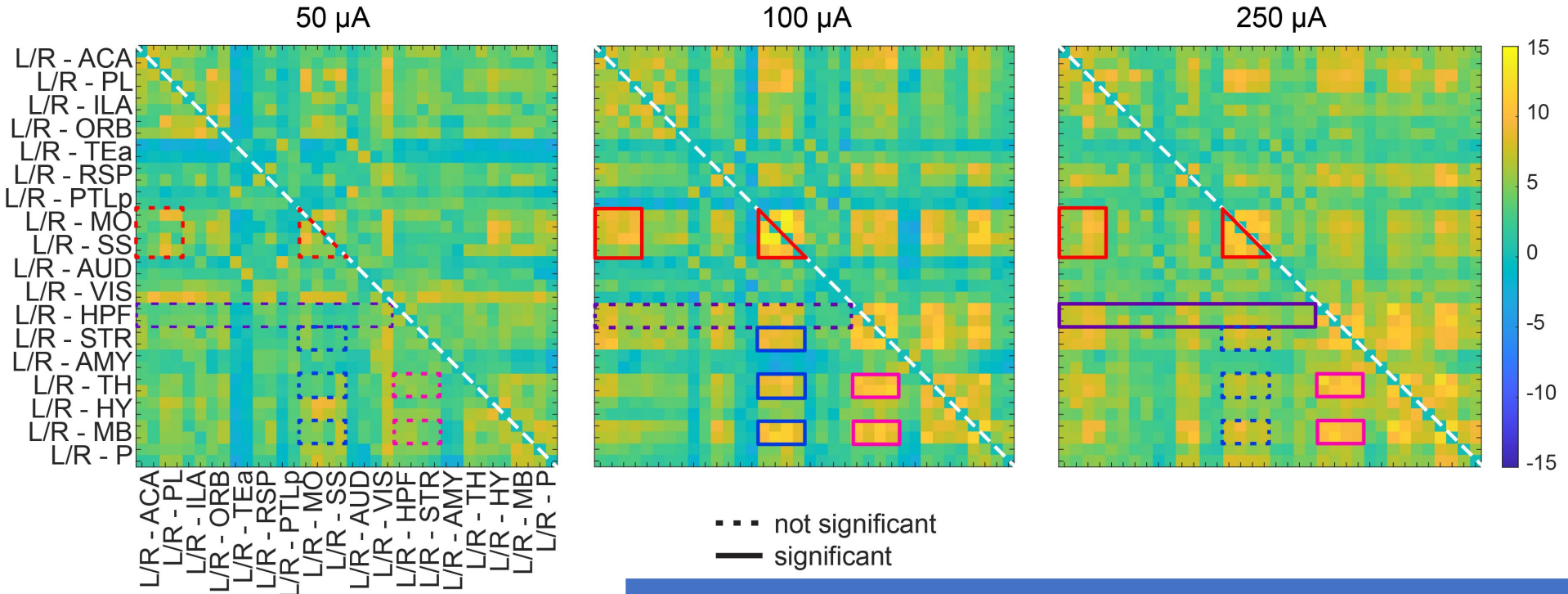
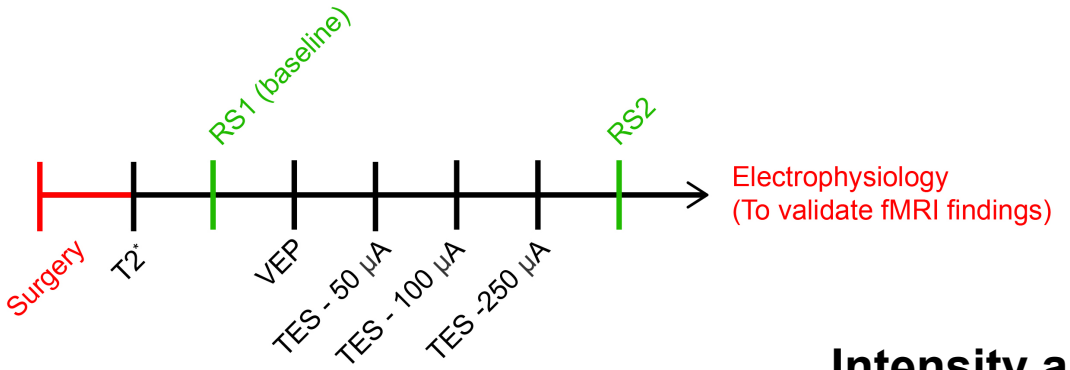


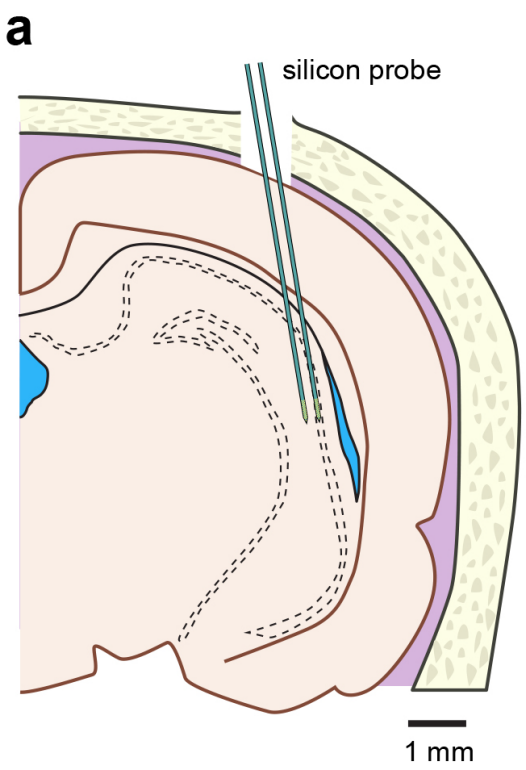
MODULATED BRAIN NETWORKS		
50 µA	**100 µA**	**250 µA**
-	Somato-motor	Somato-motor
-	Somato-motor-prefrontal	Somato-motor-prefrontal
-	-	Cortico-hippocampal
-	Hippocampal-striatal-thalamic/midbrain	Hippocampal-striatal-thalamic/midbrain
-	Somato-motor-striatal/thalamic/midbrain	-

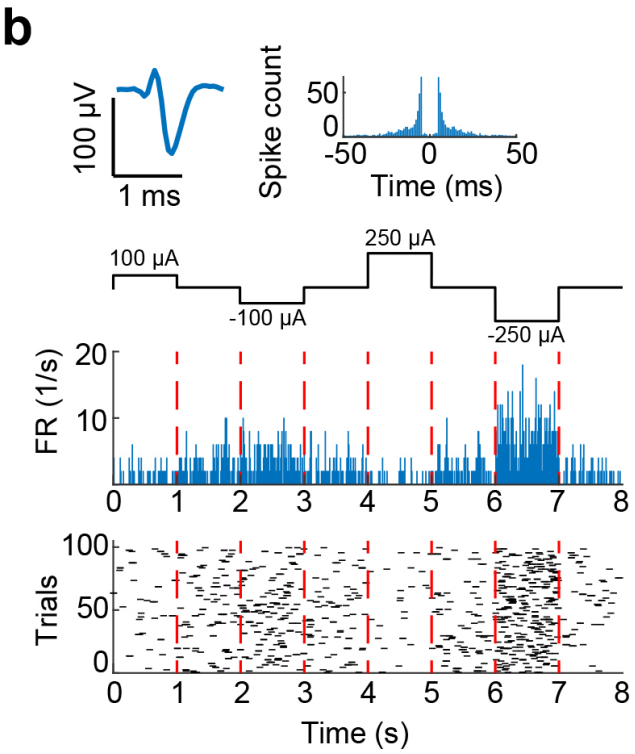
Electrophysiology validation of TES-fMRI

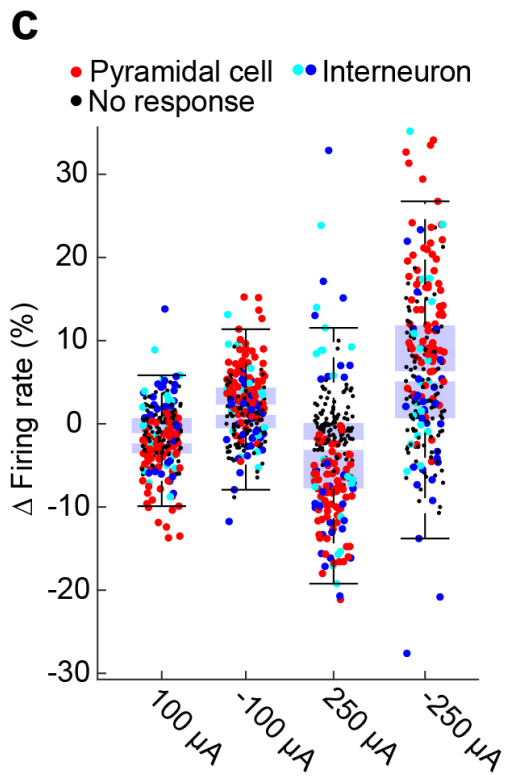


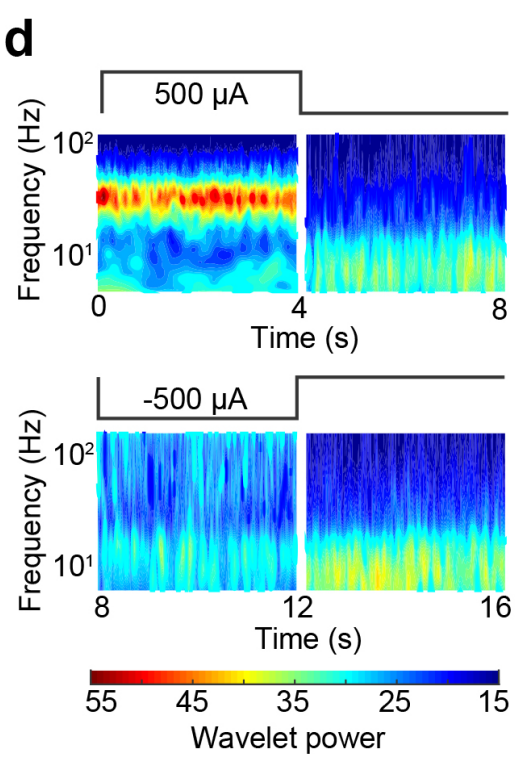
- Electrophysiology after fMRI scans using 128-ch silicon probe
- 2 different intensities and polarities were used

Intensity and polarity dependent single-unit and network effects.









Summary

1. We developed an MR-compatible, deuterium-based, concurrent TES-fMRI stimulation system for rats.

2. TES can affect connectivity within cortical and cortico-subcortical networks.

3. We found stimulation intensity-dependent changes in:
    - Somato – motor network
    - Somato – motor – prefrontal network
    - Cortico – hippocampal network
    - Somato – motor – striatal / thalamic / midbrain networks

4. Using electrophysiology, we confirmed the functionality of our TES system.

5. We found large discrepancies between activation sites by fMRI and electrophysiologically measured activity.

Acknowledgements

Equal contribution with **Tanzil Mahmud Arefin** from NYU Radiology Department.

Buzsaki lab

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Preclinical imaging facility at NYU

- Zaki Gironda
- Youssef Zaim Wadghiri

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