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P18

ADC-fMRI of excitatory and inhibitory responses to visual stimulation in the rat brain

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BACKGROUND

Blood Oxygen Level Dependent (BOLD) response to stimulation :

- (+) Positive → Excitatory neuronal firing vs (-) Negative → Neuronal inhibition[1]
- Vascular origin → poor spatial and temporal specificity and reduced sensitivity in white matter

Apparent Diffusion Coefficient (ADC) fMRI :

- Neuromorphological coupling altering the diffusion properties upon neuronal firing[2].
- (+) Positive → ? vs (-) Negative → ?
- Isotropic diffusion-encoding[3] to avoid sensitivity to fiber orientations[4]
- ADC + high b-values + cross terms compensation[5] → ~~Vascular contribution~~

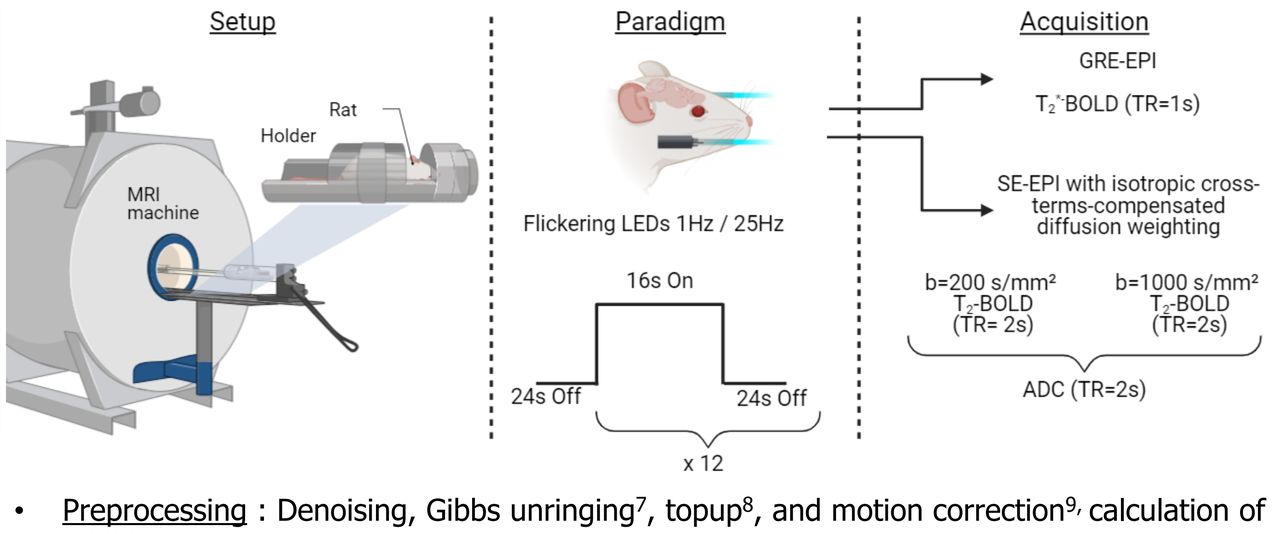
METHODS

Acquisition: Ten female rats (200-250g) under medetomidine perfusion.

- 14T Bruker MRI system with volume TX/surface RX coils
- **T_2-weighted** (TurboRARE, TR/TE=2500/6ms, 0.125x0.125x0.5 mm^3),
- **BOLD-fMRI** (GRE-EPI, TR/TE =1000/14ms, 0.38x0.38x1.5 mm^3) and
- **ADC-fMRI** (SE-EPI, TR/TE=1000/41ms, b-values=200/1000 s/mm²).

Stimulation:

- Bilateral visual stimulation 16s of flashing light at the frequency of 1Hz (excitatory for V1) or 25Hz (inhibitory for V1) followed by 24s of rest, repeated 12 times.
- Two runs per frequency and contrast were acquired for each rat.



- Preprocessing : Denoising, Gibbs unringing[7], topup[8], and motion correction[9], calculation of ADC time series.
- Segmentation : Multivariate template from all animals[10]. Waxholm Space Atlas ROIs registration to subject space (**SC**: Superior Colliculus, **V1/V2** : Primary/Secondary visual Cortex, **DLGn**: Dorsolateral geniculate nucleus)
- Statistics: First-level GLM per contrast and run in subject space with cluster-correction (Z>2.3).
- Group-level GLM in template space with cluster correction Z>3.1, Z>2.3 and Z>1.5 for BOLD, b200, and ADC respectively.

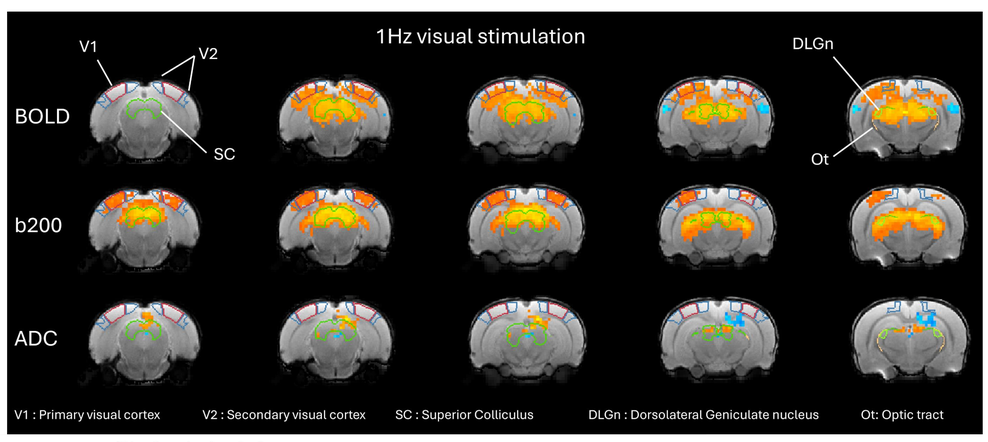
RESULTS

1Hz stimulation:

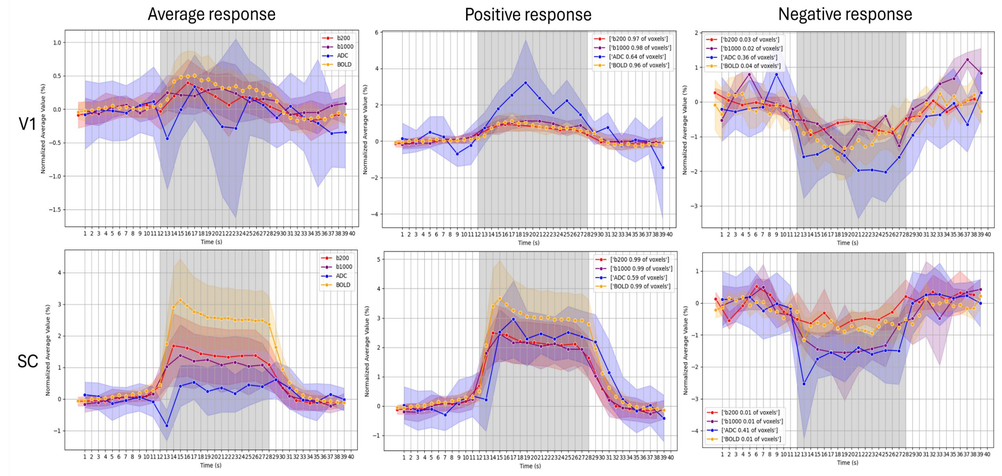
+ BOLD-fMRI in SC, V1, V2 and DLGn.

+ ADC-fMRI in DLGn, SC, and V1,

- ADC-fMRI in SC, V1, and white matter.



1Hz visual stimulation response



SC and V1 response:

+ BOLD-fMRI in 96-99% of significant voxels

- ADC-fMRI in 36-41% of significant voxels.

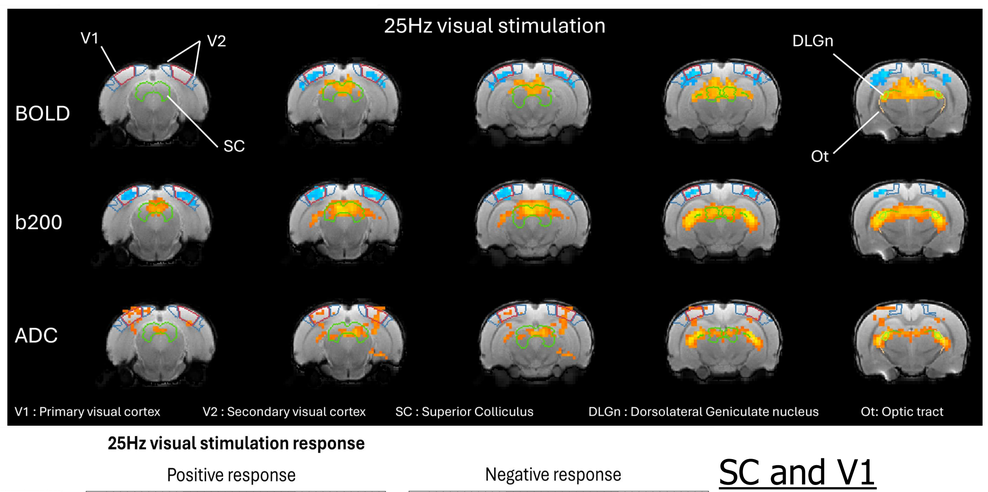
- Rapid drop → Initial dip in average response

25Hz stimulation:

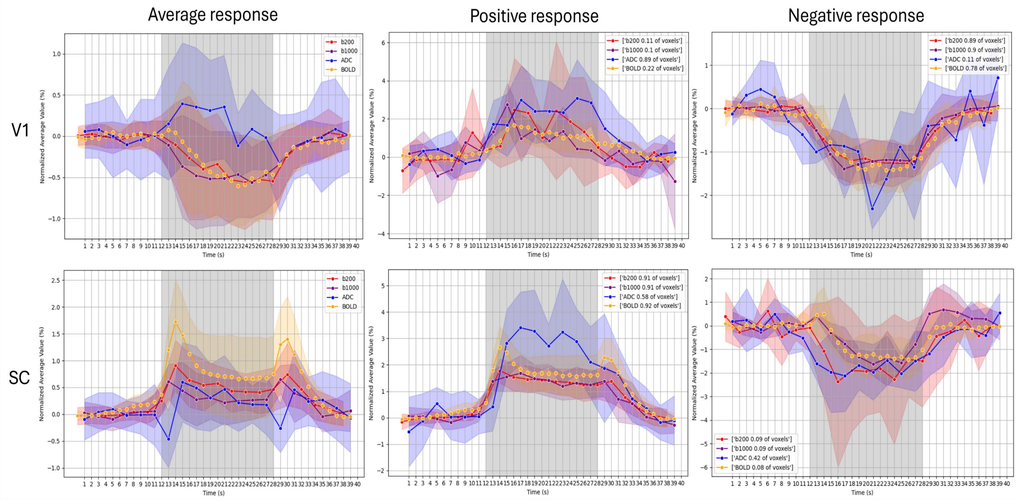
+ BOLD-fMRI in SC and DLGn

- BOLD-fMRI in V1 and V2

+ ADC-fMRI in SC, DLGn, V1, and between SC and V1.



25Hz visual stimulation response



SC and V1 response:

+ BOLD-fMRI in 90% of significant voxels in SC

- BOLD-fMRI in 78% of significant voxels in V1

+ ADC-fMRI in 89% of significant voxels in V1

+ ADC-fMRI in 58% of significant voxels in SC

DISCUSSION

Excitatory vs inhibitory response to 1Hz and 25Hz stimulation:

- Vast positive BOLD and b200 response to 1Hz stimulation in **SC** and **V1** → Excitatory activity
- Negative BOLD and b200 responses to 25Hz stimulation in **V1** consistent with previous work[11] → Inhibitory activity. Concomitant positive BOLD response in **SC** → Active inhibition of V1 from SC

Interpretation of positive and negative ADC-fMRI:

- Negative BOLD ↔ positive ADC in **V1** in 90% of voxels → positive ADC sensitivity to inhibition.
- Positive BOLD ≠ negative ADC (90% vs 40% of voxels in V1 at 1 Hz) → concomitant inhibitory response or contamination from positive BOLD ?

Vascular contribution to ADC-fMRI:

- Negative ADC response faster than positive BOLD response → minimal contribution of vascular response to ADC[3,12].
- Positive ADC in SC at 25Hz > Positive ADC in SC at 1Hz, while Positive BOLD in SC at 25Hz < Positive BOLD in SC at 1Hz → No BOLD contamination
- Positive and Negative ADC between SC and V1 → Projections representing active excitation/inhibition ? White matter = reduced vascular contribution

1.Devor, A. *et al.* Suppressed Neuronal Activity and Concurrent Arteriolar Vasoconstriction May Explain Negative Blood Oxygenation Level-Dependent Signal. *J Neurosci* 27, 4452–4459 (2007). **2.**Nunes, D., Gil, R. & Shemesh, N. A rapid-onset diffusion functional MRI signal reflects neuromorphological coupling dynamics. *Neuroimage* 231, 117862 (2021). **3.**Eriksson, S., Lasic, S. & Topgaard, D. Isotropic diffusion weighting in PGSE NMR by magic-angle spinning of the q-vector. *Journal of Magnetic Resonance* 226, 13–18 (2013). **4.**Nunes, D., Ianus, A. & Shemesh, N. Layer-specific connectivity revealed by diffusion-weighted functional MRI in the rat thalamocortical pathway. *NeuroImage* 184, 646–657 (2019). **5.**Nguyen-Duc, J. *et al.* Mapping activity and functional organisation of the motor and visual pathways using ADC-fMRI in the human brain. 2024.07.17.603726 Preprint at https://doi.org/10.1101/2024.07.17.603726 (2024). **6.**Veraart, J., Fieremans, E. & Novikov, D. S. Diffusion MRI noise mapping using random matrix theory. *Magnetic Resonance in Medicine* 76, 1582–1593 (2016). **7.**Kellner, E., Dhital, B., Kiselev, V. G. & Reisert, M. Gibbs-ringing artifact removal based on local subvoxel-shifts. *Magn Reson Med* 76, 1574–1581 (2016). **8.**Jenkinson, M., Beckmann, C. F., Behrens, T. E. J., Woolrich, M. W. & Smith, S. M. FSL. *Neuroimage* 62, 782–790 (2012). **9**.Avants, B. B., Epstein, C. L., Grossman, M. & Gee, J. C. Symmetric diffeomorphic image registration with cross-correlation: evaluating automated labeling of elderly and neurodegenerative brain. *Med Image Anal* 12, 26–41 (2008). **10.**Avants, B. *et al.* Multivariate analysis of structural and diffusion imaging in traumatic brain injury. *Acad Radiol* 15, 1360–1375 (2008). **11**.Gil, R., Valente, M. & Shemesh, N. Rat superior colliculus encodes the transition between static and dynamic vision modes. *Nat Commun* 15, 849 (2024). **12.**Szczepankiewicz, F. & Sjölund, J. Cross-term-compensated gradient waveform design for tensor-valued diffusion MRI. *J Magn Reson* 328, 106991 (2021).

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