

# Intra and cross-modal negative BOLD responses in grey matter regions and large draining veins under contrast-varying visual stimulation

Joao Jorge<sup>1,2</sup>, Patricia Figueiredo<sup>2</sup>, Rolf Gruetter<sup>1</sup>, and Wietske van der Zwaag<sup>1</sup>

<sup>1</sup>Center for Biomedical Imaging, University of Lausanne/Ecole Polytechnique Federale de Lausanne, Lausanne, Switzerland, <sup>2</sup>Institute for Systems and Robotics, Instituto Superior Tecnico, Universidade Tecnica de Lisboa, Lisbon, Portugal

**Target audience:** Neuroscientists and clinicians interested in the study of the negative BOLD response, regarding both its neurophysiological interpretation and analysis methodologies.

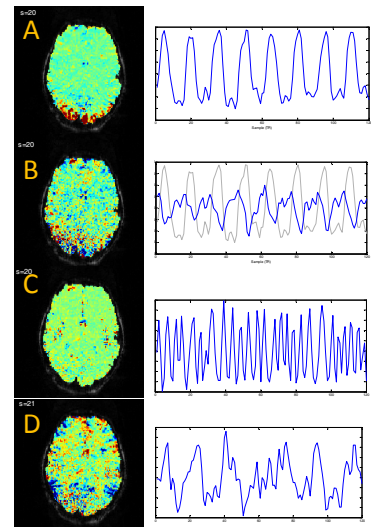
**Purpose:** During presentation of a stimulus, positive BOLD responses (PBR) are generally attributed to local increases in neuronal activity. Sustained negative BOLD responses (NBR) are also frequently observed, but their underlying neurovascular coupling mechanisms are less well understood. Here, we studied the NBR to contrast-varying visual stimuli. Both intra-modal<sup>1</sup> and cross-modal responses<sup>2</sup> were analyzed.

**Methods:** 10 healthy subjects were scanned at 7T with a multi-slice GE-EPI sequence (TR/TE=2000/25ms, 1.5×1.5×1.5mm<sup>3</sup> spatial resolution). During acquisition, subjects were presented with visual stimuli consisting of 10s 8Hz flashing checkerboard blocks alternated with 20s fixation blocks; checkerboards were presented at 4 different contrast levels (2%, 5%, 20% and 80%, counter-balanced, 8 repetitions per level), and at 20% for a separate functional localizer run. fMRI data were motion-corrected, brain-extracted and temporally de-trended. Physiological noise and motion-related confounds were identified with ICA (Fig. 1), and included in subsequent GLM analyses. Three ROIs were defined based on the functional localizer run: (a) occipital regions with significant PBR, (b) occipital regions with significant NBR, and (c) temporal lobe regions with significant NBR (Brodmann areas 41-42). Contributions from grey matter tissue and from large draining veins were analyzed separately for each region (Fig. 2).

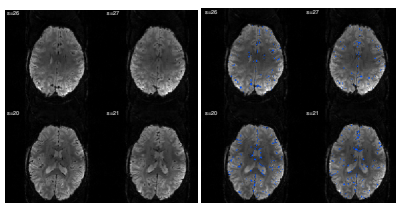
**Results:** as expected, the visual stimuli induced occipital PBR surrounded by NBR, and also NBR in typical auditory regions (example in Fig. 3). Significant PBRs were observed for all stimulus contrast levels, increasing with contrast level. In grey matter, NBR consistently decreased with increasing stimulus contrast in both visual and auditory regions. Responses in venous regions were stronger, but tended to be less contrast-dependent (Fig. 4).

**Conclusion:** under checkerboard-based stimulation, PBR and both intra-modal and cross-modal NBR become stronger with increasing contrast level, in grey matter. Although of larger amplitude, responses observed in draining veins tend to be less contrast-dependent, and can contaminate the average behavior observed in strictly grey matter tissues.

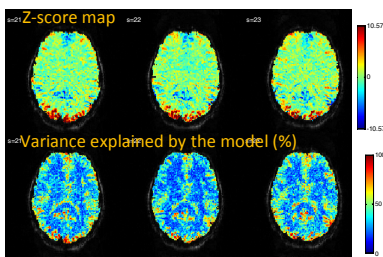
**References:** (1) Shmuel A, et al. Neuron 2002. (2) Laurienti P, et al. Journ. of Cogn. Neurosc. 2002.



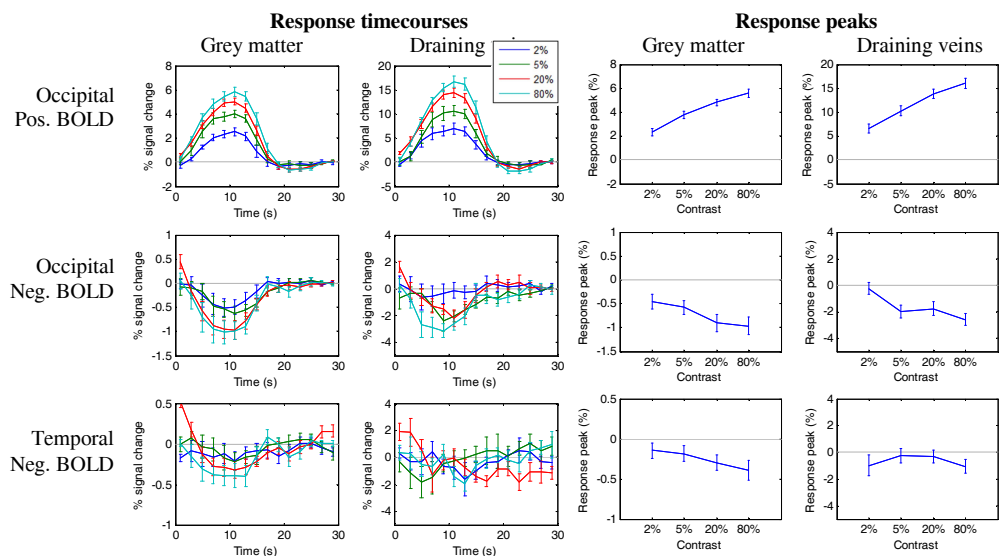
**Fig 1.** Event-related (A,B), artifactual (C), and spontaneous activity-related (D) sources identified by ICA decomposition, for a representative subject.



**Fig 2.** Identification of large draining veins (in blue, on the right) directly from the EPI images, in a representative subject.



**Fig 3.** GLM analysis results for the functional localizer run of a representative subject.



**Fig 4.** Average BOLD responses for each contrast level in each ROI, shown as response timecourses (left) and response peaks (right). Error bars represent the standard error across subjects.