454.9

A Spatial-Temporal Analysis of Neural-Vascular Coupling During Evoked Responses in Rat Somatosensory Cortex

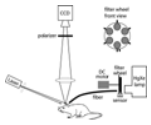
S.R. Jones, A. Devor, A.K. Dunn, E.M.C. Hillman, S. Narayanan, I. Ulbert, A.M. Dale, D.A. Boas

Abstract

We present a full-field analysis using multiple-wavelength optical imaging spectroscopy (OIS) and electrophysiology to investigate the spatiotemporal properties of the neurovascular coupling relationship during small, brief single-vibrissa stimulation. We find a spatially biphasic response in hemodynamic measures of oxy- (HbO), deoxy- (Hb), and total hemoglobin (HbT), consisting of regions of maximal activation surrounded by activation that is opposite in sign, *i.e.,* a "center-surround" activation pattern (Devor etal. 2003, 2005; Boas etal. Poster 454.2). It is possible that this center-surround activation pattern is mediated by neuronal activity consisting of center excitation and surround inhibition. However, we do not observe a similar biphasic spatial pattern in neuronal activity measured electrophysiologically as spiking multi-unit activity (MUA), extracellular local field potential activity (LFP), or using voltage-sensitive dyes (VSD) imaging.

Methods

OIS: Rats were anesthetized with urethane, and an area of skull overlying the primary somatosensory cortex was thinned to ~150 mm. The cortex was illuminated through a 6-position continuously rotating filter wheel and was coupled to a 12 mm fiber bundle that illuminated the cortex. The filters were 10 nm bandpass centered at wavelengths of 560, 570, 580, 590, 600 and 610 nm. Images were acquired by a cooled 12-bit CCD camera at 15 Hz. The spectral data were converted to percent change from baseline maps for HbO, Hb, and HbT using the modified Beer-Lambert law.



Stimulation: A single vibrissa was briefly deflected by a computer-controlled piezoelectric stimulator using randomized event-related stimulus presentation with a 1-second inter-stimulus interval. The stimulator deflected a vibrissa upward for a duration of 20ms and allowed a free return to the resting position. Results shown are derived from the average of three deflection amplitudes evenly spaced from 833 mm to 1200 mm vertical displacement.

Electrophysiologic recordings: MUA and LFP were collected simultaneously with OIS by inserting electrodes (2-4 M□) into small holes in the thinned skull. Electrodes were inserted at a depth of approximately 400-500 □m. The signals were amplified and filtered between 500-5000 Hz to record MUA, and between 0.1-500 Hz to record LFP. To collect VSD Images the skull removed, and the dura matter was dissected to expose the underlying cortical tissue. Immediately after the exposure the well was filled with a buffered saline containing 135 mM NaCl, 5 mM KCl, 5 mM Hepes, 1.8 mM $CaCl_2$, 1 mM $MgCl_2$. Commercially available voltage sensitive dye 1691 (Optical Imaging Ltd, Mountainside, NJ) was dissolved in the buffered saline described above, and the well was filled with 100-200 □l of the dye solution. The data were acquired using a commercial CCD-based VSD imaging system (Optical Imaging Ltd, Mountainside, NJ).

Center-Surround Hemodyanmic Activation Patterns

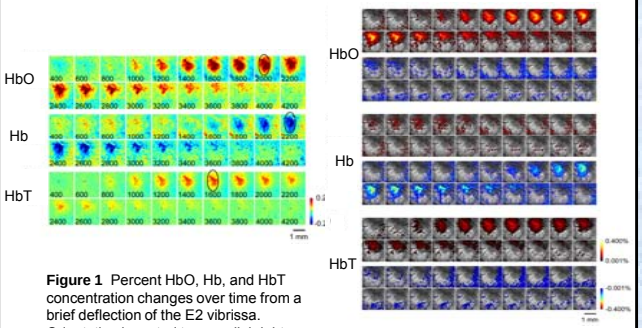
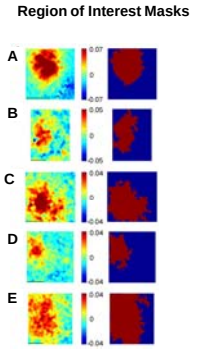


Figure 1 Percent HbO, Hb, and HbT concentration changes over time from a brief deflection of the E2 vibrissa. Orientation is rostral top, medial right. Ellipses in each panel outline a 1x2mm region of interest at the time of peak activation (2000ms HbO, 2200ms Hb, and 1600ms HbT) to be compared with ellipse of the same scale in Figure 6A.

Figure 2 Corresponding percent concentration changes showing positive and negative activation separately, statistically thresholded at 3X the level of prestimulus variance.



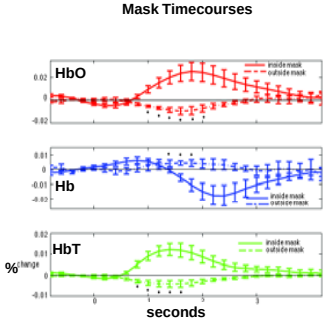


Figure 3 Left panels: HbT concentrations at time of peak activation (1600ms) for five different animals (A-E). Right panels: Corresponding masks used to calculated time courses inside and outside of the masks in Figure 4.

Figure 4 Percent concentration changes over time for HbO, Hb, and HbT.. Solid (dotted) lines show percent changes inside (outside) of the masked region defined at the time of peak activation for each measure (e.g. see Figure 3). Traces are the average over animals (n=5) and error bars represent standard error (* indicates p<0.05).

Surround Inhibition is Not Observed with Electrophysiology

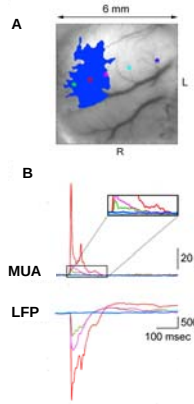


Figure 5 A) Colored asterisks mark five locations in which MUA and LFP were recorded. The blue mask represents peak positive HbT activation generated as in Figure 3. B) Corresponding color-coded MUA and LFP from marked locations in A. As the distance from the stimulated barrel increases, the level of MUA and LFP decreases. There is no net decrease from baseline in MUA or LFP in the region where surround negative hemodynamic (e.g. HbO) activity is observed.

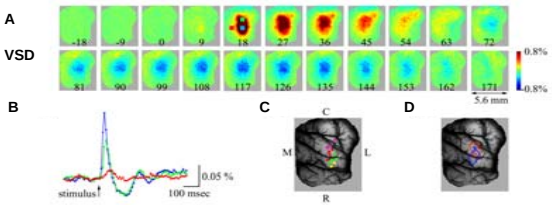


Figure 6 A) Full-field VSD imaging of the neuronal response to a single deflection of E1 whisker. Ellipse at 18ms outlines 1x2mm region of interest to be compared with ellipses of same scale in Figure 1. B) Timecourses from 500x500 □m ROI marked by squares in A (t=18). The response starts in the principal barrel column (blue trace) and propagates throughout the entire barrel cortex. A decrease in the depolarization amplitude towards the edge of the response is coupled to a decrease in the hyperpolarization. C) Barrel field mapping: δ, γ magenta; E1, D1 red; E2, D2 green, E3 yellow. D) 60% contour plots for stimulation of E1 (blue) and D1 (red) whiskers at18 ms following the stimulus onset.

Conclusions

- The surround "negative" hemodynamic activation pattern is mediated by vascular mechanics that induce transient flow decreases in local vessels rather than from an active vasoconstriction induced by neuronal inhibition. This conclusion is confirmed by a spatially distributed balloon model of the cerebral vascular response to brain activation in Boas etal. Poster 454.2.

- The spatial spread of center "positive" hemodynamic activity measured with OIS is roughly as large as neuronal activation as measured with VSD (compare ellipses in Fig 1 and Fig 6).