

The object of this work is to study the relationship between electrical and hemodynamic responses relating to neuronal activation. Diffuse optical imaging (DOI) and electroencephalography (EEG) were recorded simultaneously and non-invasively on the intact rat head during electrical forepaw stimulation. We used these two modalities to obtain information about neurovascular coupling at a macroscopic level in rats, which will translate to non-invasive human studies.

Measurement setup

DOI system

o 16 laser diode sources (690 & 830 nm) frequency encoded

o 16 parallel APD detectors
o Detector's output is digitized at ~40kHz on-line, individual source signals obtained off-line by infinite-impulse-response filters

o Acquisition time per image (16x18 channels) can be as short as 10ms!!!

o 8 auxiliary channels records the stimulation trigger, and physiological parameters as blood pressure, pulse oximeter SaO₂, heart rate, respiration and end tidal CO₂.

EEG system

o Up to 32 electrodes

o Continuous EEG recordings using LabVIEW-based acquisition software (National Instruments Inc.)

o Band-pass filter from 0.01Hz to 50Hz

o Trigger signals sent from the stimulation trigger to a DAQ board (PCI6052E - National Instruments Inc.) in the same computer

Animal prep

o Male Harlan Sprague-Dawley rats (weight 250-350 g)

o Anesthesia for surgery a gas mixture of 80% air, 20% oxygen, and 1-3% isoflurane administered via face mask

o Tracheotomy and cannulation of the femoral artery and vein

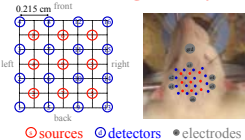
o Ventilation parameters are adjusted to maintain PaCO₂ between 35 and 45 mmHg, PaO₂ between 140 and 180 mmHg, and pH between 7.35 and 7.45.

o After surgery, isoflurane is discontinued and anesthesia is maintained with a 50 mg/kg intravenous bolus of alpha-chloralose followed by continuous intravenous infusion at 40 mg/kg/hr.

o Heating blanket circulating warm water maintains core temperature at 37-38°C

o Stimulation experiments is delayed by at least 1 hr to allow the anesthetic transition

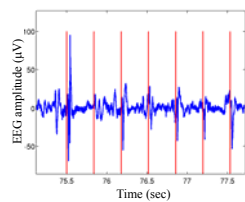
Probe geometry



Paradigms

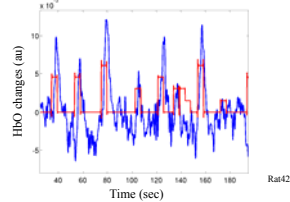
- o left and right electrical forepaw stimulation
- o 200 ms, 0-1-0.2 mA 2-8 Hz trains electrical stimuli, 1-4 s trains
- o 12-6 min runs on each paw, alternatively
- o 4 conditions randomized in sequence and delay between trains (average ISA 12s)
- o We changed stimulus duration (1, 2, 3, and 4 sec) (4 animals), amplitude (0.5 MT, 0.75 MT, motor threshold (MT), 1.25 MT) (6 animals), and frequency (2,3,4, and 8 Hz) (4 animals).

EEG raw data



EEG responses to a 3 Hz train of 1.35MT stimuli

DOI raw data



DOI HbO₂ raw data corresponding to trains of stimuli of different amplitude

DOI image reconstruction

oxy-hemoglobin changes during activation (a.u.)



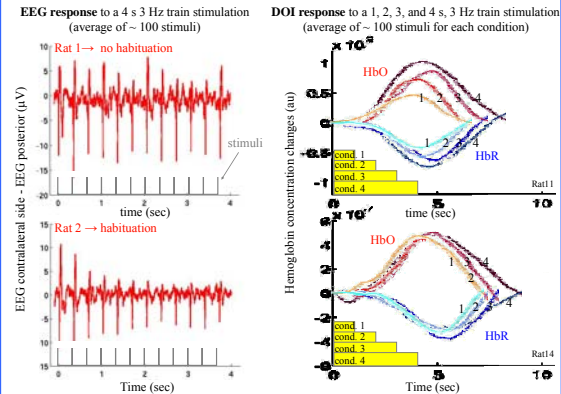
deoxy-hemoglobin changes during activation (a.u.)



Maps of the hemodynamic evoked response on a rat during right and left forepaw stimulation (200 ms, 0.2 mA, 3 Hz repetition and 4 sec train duration, average of 12.6 min runs)

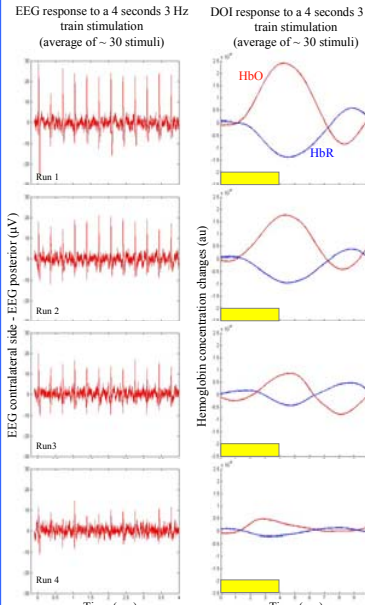
Correlation between EEG and optical signals

Habituation within a train of stimuli: the EEG response to a train of stimuli is different in different animals. In some rats the response is the same for each stimulus pulse, in others there is a large response to the first pulse which decreases in amplitude in the following pulses in the same train



In the first rat, the EEG response is constant during the train, the amplitude of the hemoglobin response (both HbO and HbR) increases with stimulus duration. In the second rat, the EEG response decreases in the train, the amplitude of the hemoglobin response doesn't increase with stimulus duration.

"Habituation" with repeated runs:



The EEG signal in our rats decreases in amplitude if we stimulate them in the same paw for 6-min runs without breaks between runs.

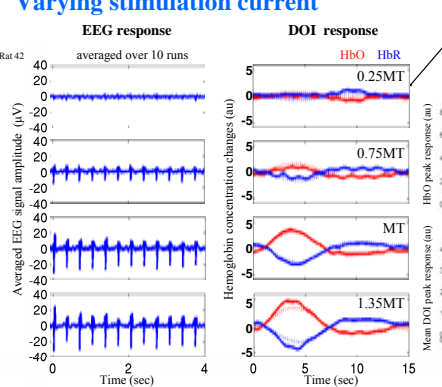
The hemodynamic response follows the EEG. HbO and HbR amplitudes decrease with runs.

If we alternate left and right forepaw runs this "habituation" is reduced

Acknowledgments

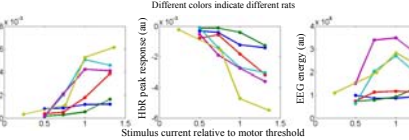
The authors would like to thank Dr. Sol Diamond for his invaluable contributions in statistics and the deconvolution method

Varying stimulation current Results



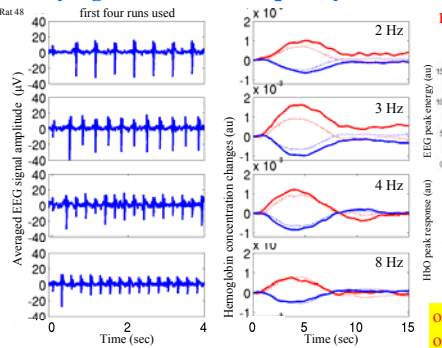
Solid line = DOI response obtained deconvolving the optical data with the train onsets
Dotted line = DOI response predicted based on the EEG response by assuming a linear model between the EEG power and DOI

Dependency of the HbO and HbR peak amplitude and EEG response energy on the stimulus intensity in six rats

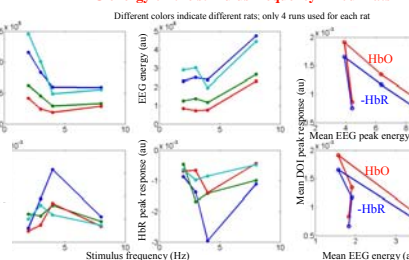


- o EEG response saturates in most rats near MT
- o DOI response continues to grow beyond MT
- o Predicting HbR and HbO responses from known EEG using a linear model leads to underestimation of hemoglobin responses at high stimulus intensities and overestimation at low stimulus intensities. **This may be a result of systemic hemoglobin responses at higher currents.**

Varying stimulation frequency

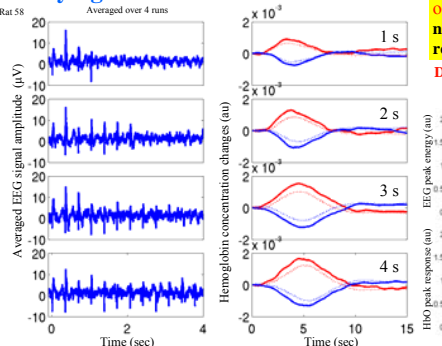


Dependency of the HbO and HbR peak amplitudes, EEG peak energy, and EEG energy on the stimulus frequency in four rats

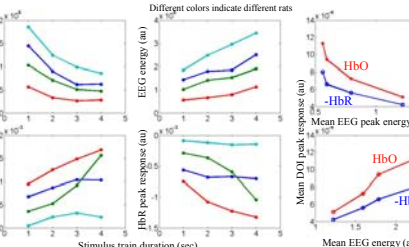


- o EEG response energy (per train) is largest at 8 Hz
- o EEG response amplitude per peak declines at higher frequencies
- o HbO and HbR responses peak around 3-4 Hz
- o **The dissociation between EEG and DOI suggests that other neuronal parameters are required for predicting the hemodynamic response during inhibition of the EEG response.**

Varying stimulus train duration



Dependency of the HbO and HbR peak amplitudes & time to peak, EEG peak response energy on the stimulus train duration in four rats



- o Time-to-peak of response increases progressively as train duration increases
- o Typically, longer trains create larger hemodynamic responses
- o **Strong correlation between EEG and DOI with increasing stimulus train duration.**

Funded by NIH R01-EB001954, P41RR14075, the MIND Institute, and the Athinoula A. Martinos Center for Biomedical Imaging

