Tracking the Concentrations of Oxygenated Blood, Deoxygenated Blood and Autoregulatory States in the Visual Cortex with fDOT

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INTRODUCTION

- Near infrared spectroscopic (NIRS) imaging was used to monitor vascular changes in the visual cortex, before and during application of a visual-system stimulus protocol (i.e., brief flashes of light, presented intermittently at randomized time intervals).
- Data obtained from a similar study were previously examined using a standard NIRS data analysis procedure.
  - Volumes of brain tissue most strongly involved were not identical for all study participants, but all had a region of intersection within the primary visual cortex.
  - For pixels within the common region, group-mean time series of oxygenated and deoxygenated hemoglobin (Hb_{oxy} and Hb_{deoxy}, respectively) are similar to a conventional BOLD response seen in fMRI studies.
- Here we have expanded on the capabilities of the NIRS imaging system, by also employing a novel data analysis strategy to extract additional dynamic features from the optical data.
  - As indicated in Figure 1, the principle of this method is a set of simple relational operations applied to the Hb_{oxy} and Hb_{deoxy} levels, that correspond to different states in a vascular autoregulation cycle.

Hb State	State 1	State 2	State 3	State 4	State 5	State 6
Hb_{oxy}	-	-	-	+	+	+
Hb_{deoxy}	-	+	+	+	-	-
Hb_{total}	-	-	+	+	+	-
Figure 1	Balanced	Uncompensated O_2 debt	Compensated O_2 debt	Balanced	Uncompensated O_2 excess	Compensated O_2 excess

METHODS

- Participants
  - 10 Right-Handed Healthy Adults
  - Age: 30.7 (11.3) years
  - Education: 15.9 (2.7) years
  - Free of substance abuse and major psychiatric disorders
  - No history of neurological disease or trauma
- Visual stimulation task (Figure 2)
  - A 16.3 mm², white square was presented for 2 sec, with a 10-20 sec inter-trial-interval
  - 120 stimuli were presented
  - Subjects were required to maintain fixation
- Apparatus
  - Multi-channel continuous wave near infrared imager (NIRx Medical Technologies; see Figure 3)
  - 30 source and 30 detector optodes (900 channels)
  - Two wavelengths of near infrared light (760 nm and 830 nm)
  - Optodes placed over occipital cortex, using the inion as a landmark
  - A 10x3 cm rectangle configuration was used
- Data Acquisition
  - 5 minute baseline
  - 40 min of stimulation
- Data Analysis
  - Optical data low-pass filtered and normalized to a resting-baseline mean value.
  - Images of ΔHb_{oxy} and ΔHb_{deoxy} concentrations computed by using a first-order perturbation algorithm.
    - $\Delta Hb_{oxy} = Hb_{oxy} - Hb_{oxy}^{baseline}$, $\Delta Hb_{deoxy} = Hb_{deoxy} - Hb_{deoxy}^{baseline}$.
  - Six vascular autoregulatory states are defined, as shown in Figure 1, according to the algebraic signs of ΔHb_{oxy}, ΔHb_{deoxy}, and their sum $\Delta Hb_{total} = \Delta Hb_{oxy} + \Delta Hb_{deoxy}$.
  - Each relational category reasonably corresponds to a different underlying state of oxygen supply/demand balance or imbalance.
  - Time fraction analysis:
    - Autoregulatory state calculation (Figure 1) allows us to compute not only the state-dependent ΔHb_{oxy} and ΔHb_{deoxy} concentrations, but also:
      - The percentage of image pixels that are in each state, at any time frame.
      - The percentage of overall time that each pixel spends in any of the six states.

Figure 2

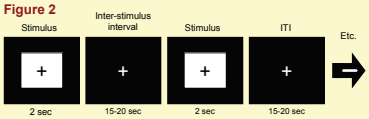


Figure 3

RESULTS

- For each participant, ΔHb_{oxy}, ΔHb_{deoxy} images were averaged across the 120 stimulus epochs, to produce average ΔHb_{oxy} and ΔHb_{deoxy} response curves for every image pixel.
- A GLM algorithm was subsequently used, to determine which image pixels have image time series most closely resembling the model hemodynamic impulse response function.
  - The red-colored brain tissue region (Figure 4), which lies within the primary visual cortex, is the volume that showed the most consistent statistically significant response, according to the GLM analysis.
  - Figure 5 shows the group-mean block-averaged ΔHb_{oxy} and ΔHb_{deoxy} response curves, for the image pixel at the intersection of the green cross-hairs in Fig. 4.
- Autoregulatory states (AS) results:
  - Preliminary testing [218 M-PM, 219 M-AM, 222 M-PM] of this data analysis strategy suggested that it may be capable of producing high-quality information at the individual participant level.
  - Further evidence of this is seen in the results from the present study (Figure 6).
    - Here the quantity plotted as color values is the percentage of time that each image pixel spends in the indicated autoregulatory states (see column labels), for each of the two experimental conditions (i.e., baseline and visual stimulation).
      - Each 2D colormap is a different planar slice (axial view) through the 3D image volume.
    - It is seen that:
      - Visual activation produces an increase in the time fraction for which pixel are in the oxygen-excess states (5 and 6), at the expense of the balanced states (1 and 4)
        - This phenomenon is commonly seen in brain tissues experiencing increased levels of neural activation, and is consistent with the known tight coupling between activity and blood supply.
      - The effect is spatially heterogeneous, with most of the increased states 5+6 residence time occurring in the middle portion of the image volume.
        - Anatomically, this agrees with the known location of the primary visual cortex.
  - Co-registration of functional and anatomical images:
    - Volume used for image reconstruction was derived from a 3D structural MRI of an adult human head. Thus it is straightforward to overlay any optical image parameter onto the anatomy, without any need for a warping algorithm.
    - Image co-registration facilitates interpretation of optical feature information.
      - Here (Figure 7), co-registration is used to indicate precisely which brain regions exhibit increased residence time in states 5+6, during the visual stimulation period of the measurement protocol.

Figure 4

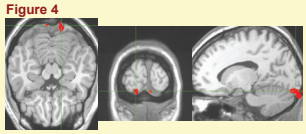


Figure 5

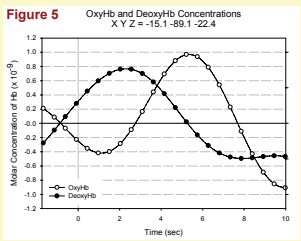


Figure 6

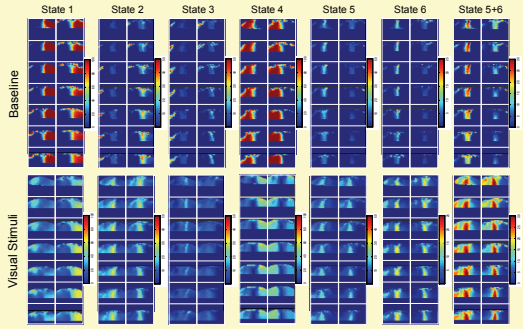
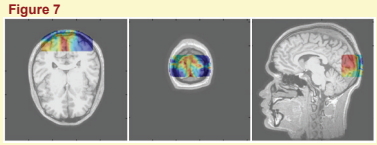
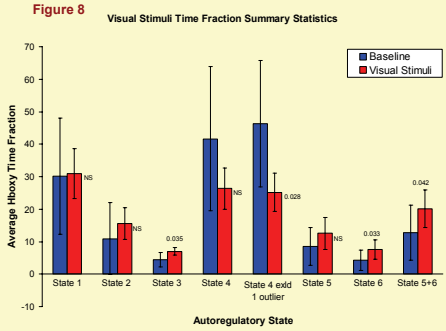


Figure 7



- Statistical analysis:
  - The preceding time fraction calculation was carried out for all 10 study participants.
  - Group means and standard deviations were computed, for each of the six autoregulatory states and for the baseline and visual stimulus time intervals.
  - Student t-tests were performed, to determine which states showed statistically significant group mean differences between the baseline and stimulus intervals.
    - F-test was conducted first, to determine which variety of t-test (equal- or unequal-variance) to perform.
  - Statistically significant differences were found for 3 of the 6 states, and for the union of states 5 and 6 (Figure 8).

Figure 8



CONCLUSIONS

- Results obtained for the present study reinforce findings obtained in frontal-lobe imaging studies [145 W-AM], in showing a consistent pattern of autoregulatory-state changes accompanying neural activation.
- These findings suggest that the technique described and demonstrated here may have considerable utility as a technique for monitoring normal and pathological brain function.

ACKNOWLEDGMENTS

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