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Spectrally resolved neurophotonics: the optical BOLD effect and vascular components in the mammalian brain.

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Abstract: We developed a broad band spectral technique that is independent of the light transport modality to separate optical changes in scattering and absorption in the cat's brain due to the hemodynamic signal following visual stimulation.
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1. Introduction

We examine the visual cortex of the cat using a spectral technique that allows non-invasive measurements through the skull. Specifically, we determine spectral changes due to changes in concentrations of tissue chromophores and scattering during visual stimulation. This is the first study to employ a spectral technique to separate contributions from different tissue components with high temporal (in the ms time scale) and spatial resolution (in the millimeter range) for the determination of neuronal activity. We show that different spectral components associated with known tissue chromophores can be identified and that the time course of the changes in spectral components can also be obtained. Control measurements were done to validate that the observed effects result from the external visual stimulation. In particular, we performed control trials without visual stimulation, with other conditions remaining the same. Brain regions outside the cat's visual cortex were examined, during visual stimulation, to determine if the changes observed were localized to a specific region of the brain or were due to systemic changes in blood flow. The framework for the interpretation of the hemodynamic changes observed is based on the well-established BOLD effect (Blood Oxygenation Level Dependence response) from the fMRI literature. The BOLD effect is primarily due to neurovascular coupling between the part of the brain that is activated by a given task and the corresponding local increase in blood flow, following stimulation. This increase in flow causes a local decrease in the deoxy-hemoglobin (HHb) content which is visible both in the MRI experiments and in the optical counterpart. In addition to the changes in concentration of the deoxy-hemoglobin (HHb), the spectral method provides concomitant changes in concentration of other tissue chromophores such as oxy-hemoglobin (O2Hb) and water, thereby complementing the information obtained with the fMRI methodology. Furthermore, the spectral approach that we developed provided the changes in the scattering spectrum during brain activation. Our results confirm the general model of neurovascular coupling, and provide new information in regard to changes in the scattering spectrum and apparent changes in the local water concentration that require a new interpretation model.

2. Method and Data Analysis

The preparation of the cat [1, 2] and spectral method is described in Tanner et al [3]. For this experiment there were two types of trials, one in which the cat was visually stimulated (VS trial), and one where there was no visual stimulation (NVS). The trials were done where the NVS trials were performed first (in blocks of 100) followed immediately by the VS trials The tip of each fiber was placed in contact with the acrylic which was roughly 1-2 mm above the cat's skull . Spectral measurements were performed using an Ocean Optics (830 Douglas Avenue, Dunedin, FL 34698, USA) detector system consisting of a S2000 spectrometer sensitive in the NIR window of 650-990nm, an ADC2000 PCI card and a tungsten lamp as the white light source. We apply the spectral approach to the differential spectrum obtained by subtracting the average spectrum during the baseline period from the stimulation period. Data acquisition and analysis

were performed by the Elantest software (This program is available at ftp://www.lfd.uiuc.edu/lfd/egratton/elantest/). Synchronization of the data acquisition with the visual stimulation was achieved by an external Stanford Research (1290-D Reamwood Avenue, Sunnyvale, CA 94089, USA) pulse generator (model DS345). The spectrometer acquired spectra every 5 ms as triggered by the generator that was triggered by the external system that generates the visual stimulation. Data were collected for the first 8 seconds of each trial. All analysis was done with respect to an initial reference spectrum. We performed a folding routine on the collected spectra as a function of number of trials to see if there were any differences in the signals observed due to physiological changes occurring across trials. We performed spectral deconvolution and principal component analysis (PCA) on the raw, but folded data. From the PCA, it was determined that the minimum number of basis components required to correctly fit the differential spectrum was four: scattering, water, HHb and O2Hb. The spectrum was then separated into the weighted contributions of these individual species and their changes observed as a function of time.

3. Results

Maps displaying the raw data matrix of S-D pair over the visual cortex, areas 17 and 18 show a significant change in the shorter wavelengths for the first 3 seconds of the visual stimulation. (Figure 1a) Similar maps over the frontal lobes show that there are no significant changes as expected. For both regions during NVS trials, the changes in wavelengths as a function of time were also minimal. (Figure 1b, c, d) Spectral deconvolution into O2Hb, HHb, water and scattering show that there is an optical BOLD effect seen in the visual cortex only during visual stimulation, where the O2Hb increases ~ 2 seconds after the onset of visual stimulation with a quasi-simultaneous decrease in HHb. For the visual cortex, a maximum decrease in scattering is seen at roughly the same time as the O2Hb reaches a maximum in the optical BOLD effect during VS trials. The water component is seen to decrease at the onset of stimulation and tracks the HHb changes with some time delay. (Figure 2a). Control experiments (Figure 2b, c, d) show that there are no major changes in the O2Hb and HHb (BOLD effect) that track with the visual stimuli for the frontal lobes. In the frontal lobes, the signals due to the changes in water and scattering are on the same order of magnitude but they don't appear to be correlated to visual stimulation.

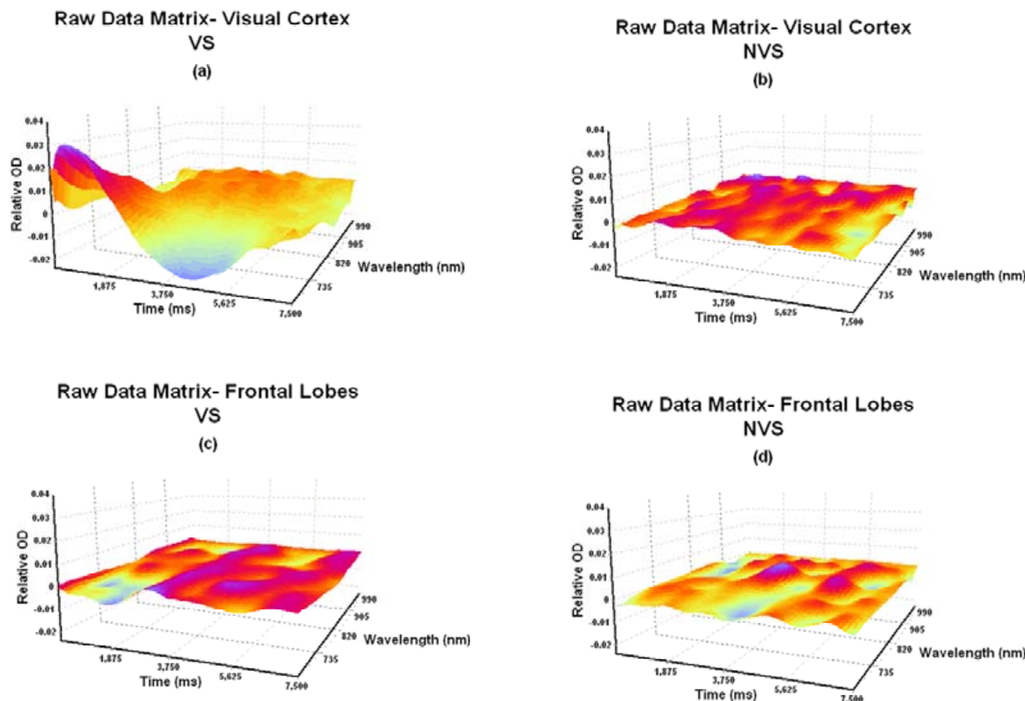

Fig 1. Raw data matrix indicating location in the brain and trial type: (a) Visual Cortex VS, (b) Visual Cortex NVS, (c) Frontal Lobes VS, (d) Frontal Lobes NVS

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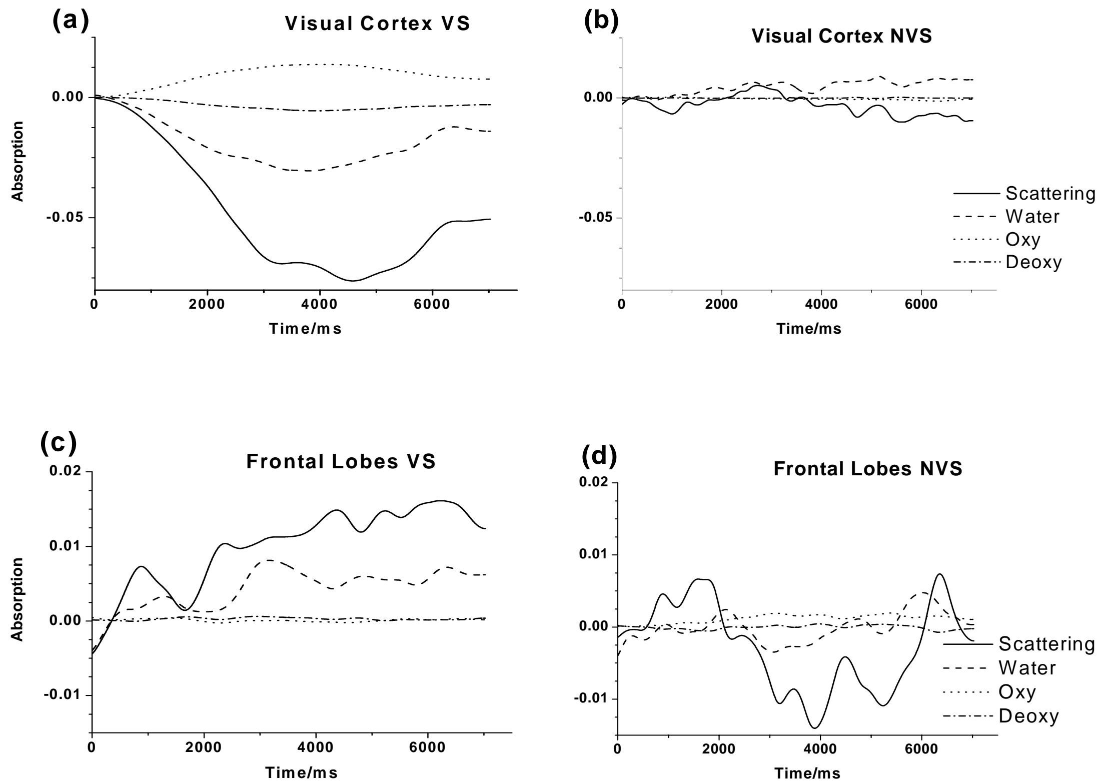

Fig 2. Spectral deconvolution, O2Hb and HHb. (a) Visual Cortex VS (b), Visual Cortex NVS, (c) Frontal Lobes VS, (d)Frontal Lobes NVS

4. Discussion and Conclusions

In summary, we have developed a technique based on spectral analysis, that is independent of the light modality (diffusive or non-diffusive), where a broad-band spectral approach is used to determine the individual NIR spectrum of tissue components. For the application in a mammalian brain, we have examined the behavior of the scattering, O2Hb and HHB (optical BOLD effect) simultaneously with other tissue components such as water content. The changes in the water component are quite surprising since we expect no net change of the tissue water content during the short time of visual stimulation. We propose that this is an optical effect due to the dilation of blood vessels upon stimulation.

5. Acknowledgements

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6. References

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