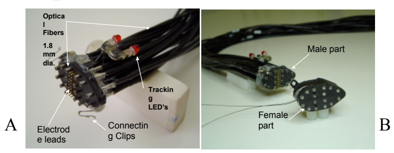
4-D Functional Imaging in Freely Moving Rats.

R.L. Barbour, C.H. Schmitz, Y. Pei, R. Ansari, M.B. Holzer, B. Rivard, J. Barry, R.U. Muller, S. Schwartz-Giblin., Department of Pathology and Department of Physiology, SUNY Downstate Medical Center, Brooklyn, NY 11203

Introduction

We have developed a system for doing Diffuse Optical Tomography (DOT) imaging in freely moving rats. In short, this system promises to make possible many of the measurements currently made with functional MRI, PET and similar methods without the need to anesthetize or otherwise immobilize the animal subject and at much lower cost. The system has high spatial and temporal (~17 Hz) resolution and can record continuously for long intervals. In this initial stage of development, we have combined DOT methods with EEG recordings, allowing us to classify optically detected hemodynamic signals according to the electrical state of the rat's brain. We report that time-variant DOT signals averaged over the whole head differ greatly according to the state of the hippocampal EEG. Moreover, we detect clear spatial variations of hemodynamic signals depending on the hippocampal EEG state. It is our intention to look for functional hemodynamic changes in different brain regions depending on the behavioral demands of a learning task, following the triple dissociation experiment of McDonald and White (1993, Behavioral Neuroscience, 107, 3 - 22).

Optical + EEG Connections

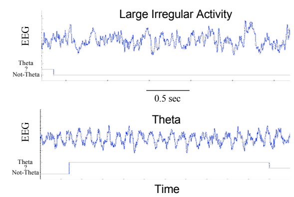


A) 16 fiber optic bundles inserted in retainer; all bundles are sensors and 4 serve as light sources. The upper ends of the bundles are inserted into the tomography device. Note double row of electrical contacts for EEG recordings. B) The two parts of the entire assembly. The female part is surgically implanted on the rat's skull; the male part is inserted at the start of each recording session.

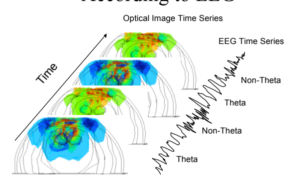
Recording System in Place

The dental cement used to anchor the implanted side of the connectoron the skull is visible as a white band. The weight of the fiber optic bundles is supported by an elastic band, permitting the rat to move freely. With this arrangement, hungry rats will walk around the recording chamber for periods of 15 min or more.

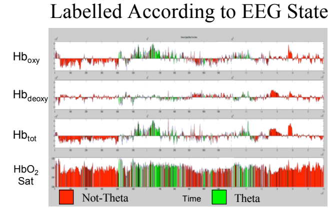
EEG Recordings for Classifying Optical Recordings



Selection of Optical Data According to EEG



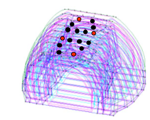
Time Series of Whole Brain Hemoglobin Response Labelled According to EEG State



Whole brain Hb Signals are Distinct in the Theta and Non-Theta States of the Hippocampal EEG

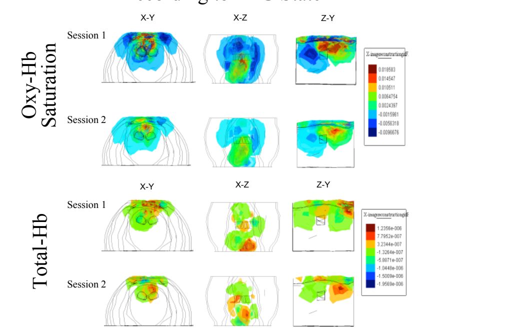
Hemoglobin State	EEG classification	Mean (M)	Standard deviation	Number of time frames	t-statistic (df)	p-value
Hb_{oxy}	Non-Theta	-6.18e-9	1.46e-8	7976	-25.27 (935.92)	2.39e-104
	Theta	1.06e-8	1.86e-8	828		
Hb_{deoxy}	Non-Theta	1.93e-9	9.38e-9	7976	16.80 (1056.43)	2.57e-56
	Theta	-3.25e-9	8.34e-9	828		
Hb_{tot}	Non-Theta	-4.25e-9	1.55e-8	7976	-15.98 (929.08)	5.93e-51
	Theta	7.37e-9	2.03e-8	828		
HbO_2 Sat	Non-Theta	0.68787	0.00029	7976	-29.37 (1026.08)	4.29e-138
	Theta	0.68817	0.00028	828		

Three-D Model of Rat Head Obtained from CT Scan



The limited resolution model recognizes the existence of 7 anatomical compartments. Its use permits the spatial origin of DOT signals to be determined. Also shown as filled circles are the skull locations of light detectors (black) and combined sources and sinks (red).

Spatial Distributions of Hb Signal differences According to EEG State



Each stacked 3-D map shows the color coded spatial distribution of the EEG-selected difference in a signal seen from coronal (X-Y), horizontal (X-Z) and sagittal (Z-Y) views. The two key points are the distinct variations of both the example signals and the reproducibility of the signals from session 1 to session 2.

Conclusions

Simultaneous DOT and EEG recordings allow us to see that several well-accepted hemodynamic signals derived from absorption of infra-red light by oxy and deoxy hemoglobin covary strongly with the state of the hippocampal EEG. Early tests of this combined measurement system suggest that the strength of this covariation is very great. Thus, differences between space-averaged hemodynamic signals classified according to EEG state are evident by inspection of colored figures; these impressions are fully corroborated by statistical testing. In addition, we see positional variations in hemodynamic signals as a function of EEG state. The ability to look at a fundamental aspect of function (activity-dependent blood supply regulation) everywhere in the brain at the same time encourages us to believe that we may be able to find regional differences according to the progress of learning of different food-motivated tasks that are known to engage different brain structures.