NEURAL-METABOLIC COUPLING IN THE CENTRAL VISUAL PATHWAY

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INTRODUCTION

One of the most important current areas of neuroscience concerns the use of non-invasive imaging techniques. There are several different types of non-invasive approaches and arguably, the most interesting currently is functional magnetic resonance imaging (fMRI). This method relies on the monitoring of alterations of oxygen in the blood. It infers changes in levels of neural activity from variations of deoxyhemoglobin in the vasculature of the brain. This blood oxygen level dependent (BOLD) signal is the critical measurement from which inferences are made concerning neural function. In general, neural activity increases cause a decrease in deoxyhemoglobin, which is expressed as an increase in the BOLD signal. This positive BOLD response is utilized to assess changes in levels of neural activity. Although the process is straight-forward, there are assumptions and limitations that require consideration. In the case of the BOLD response, large draining veins relatively distant from activation regions are also involved. This places limits on the spatial resolution that can be achieved.

Because spatial resolution is of critical importance for the application of fMRI, some effort has been made to utilize all aspects of the BOLD response. In particular, the response consists of an initial negative component that is attributed to a rapid increase in deoxyhemoglobin. This negative response, referred to as the "initial dip", has been observed in fMRI measurements and is thought to occur because of a local increase in oxygen consumption by neurons that have been activated via a sensory pathway. This initial part of the BOLD signal, because it is thought to reflect activity of a relatively small volume of tissue, is a candidate for the monitoring of high resolution signals from limited numbers of neurons. Although the initial negative portion of the BOLD response has appealing features, it is not accepted in a rigorous manner. First, it is a relatively weak signal and not universally observed in fMRI procedures. Second, its detection by use of spectroscopy is not straight-forward. Specifically, this is because of the need to correct for the wavelength dependence of light scatter. In addition, interpretation of the initial dip is complicated because it could be caused by alterations in blood volume instead of oxygen consumption.

The relationships between neural and metabolic activities in relation to fMRI measurements have not been well studied. It is technically very challenging to simultaneously obtain recordings of neural impulse activity and fMRI signals. This has been accomplished in macaque visual cortex but the analysis was limited to the positive BOLD response. Since the stimuli used activated large volumes of visual cortex, it was not possible to analyze neural-metabolic coupling at high resolution. (Logothetis et. al. 2001).

We have used a unique approach to measure simultaneously single neuron activity and tissue oxygenation in co-localized regions of the visual cortex. The relevance of tissue oxygenation is that it is connected to deoxyhemoglobin via a local oxygen concentration gradient in tissue. Since it is also linked via the oxygen-hemoglobin dissociation curve, we assume that it reflects the hemodynamic alterations that are measured in fMRI procedures. Our findings demonstrate direct links between metabolic and neural factors. (Thompson et. al. 2003)

METHODS

Standard procedures are used to prepare animals for neurophysiological investigation. Adult cats are tranquilized, then anesthetized with isoflurine or pentothal or a combination of both. Veins are cannulated, a tracheostomy is performed, a tracheal cannula is positioned, a rectal thermometer is inserted, and contact lenses are placed on the eyes. The animal is paralyzed to prevent eye movements, placed in a stereotaxic holder, and positioned in front of a video monitor on which visual stimuli are presented to explore receptive field characteristics. A craniotomy is made, and the dura is excised so that microelectrodes may be lowered into the brain. Details of these procedures are given elsewhere (Li et. al. 2003).

A double barrel glass micropipette is used to construct a combined sensing device to measure simultaneously neural activity from single cells and changes in oxygen concentration in small volumes of tissue that surround the recorded neurons. The combined sensor is positioned in the primary visual cortex or the lateral geniculate body. Results in this report are limited to data from the primary visual cortex.

RESULTS AND DISCUSSSION

In the work reported here, simultaneous measurements were made of single-cell neural activity in the cat's primary visual cortex and of tissue oxygenation concentrations in the same region of cortex. We assume that tissue oxygenation is related to deoxyhemoglobin via a gradient in the tissue we measure. Because this gradient is reflected in the oxygen-hemoglobin dissociation curve, it is also assumed to represent the hemodynamic changes that are measured in fMRI procedures.

Neurons in the visual cortex are selective to the orientation of the stimulus. This is illustrated in Fig. 1A. In this case, the cell's maximum response occurs for a grating stimulus that is oriented vertically. Response falls off on either side of vertical so that only a range of orientations are effective in driving the cell. In the cartoon of Fig. 1B, oxygen response level changes are shown as a function of orientation. These changes are illustrated for the same measurement sequence as that shown for the neural response of Fig. 1A. In this case, the oxygen curve for a vertical grating presentation shows an initial negative response followed by a positive component. As the grating orientation is varied on either side of vertical, oxygen response curves change so that the initial negative component is reduced and the positive subsequent portion is increased.

A second major property of cells in the visual cortex is that they are mainly binocular. Signals from left and right eyes converge on neurons in the primary visual cortex. The degree to which a given eye influences a cortical cell varies and this is designated as ocular dominance. In the example shown in the cartoon of Fig. 1C, the neural response is stronger for the left eye (L) compared to the right (R). Correspondingly, the oxygen response is relatively large and has a prominent initial dip for stimulation through the left eye (Fig. 1D). Oxygen change for right eye stimulation is weaker and there is a minimal initial negative component.

We obtained overall relationships for a population of neurons recorded while we simultaneously measured changes in oxygen levels for different grating orientations. Tuning functions are illustrated in Fig. 1E. The top curve (solid line) is an average orientation tuning profile for a cortical cell. The bottom curve (dashed lines) conveys the changes in oxygen levels as orientation of the target is varied. A clear symmetry emerges in which the peak of the neural response function is inversely related to the change in oxygen. The highest neural response corresponds to the largest change in oxygen level. The oxygen curve is broader than the neural tuning function and this reflects the relatively wide volume of tissue that is sensed compared to that for neurons.

In Fig. 1F, histograms are illustrated that indicate the difference in response strength for left and right eye activation of a cortical cell and of the associated changes in oxygen levels. In this case, left eye responses are larger as are the associated changes in oxygen levels.

In summary, these results provide direct evidence of a close link between neural and metabolic activity in the cerebral cortex. The initial dip in the oxygen measurements suggests that high-resolution fMRI methods may be able to reliably show details of cerebral columns.

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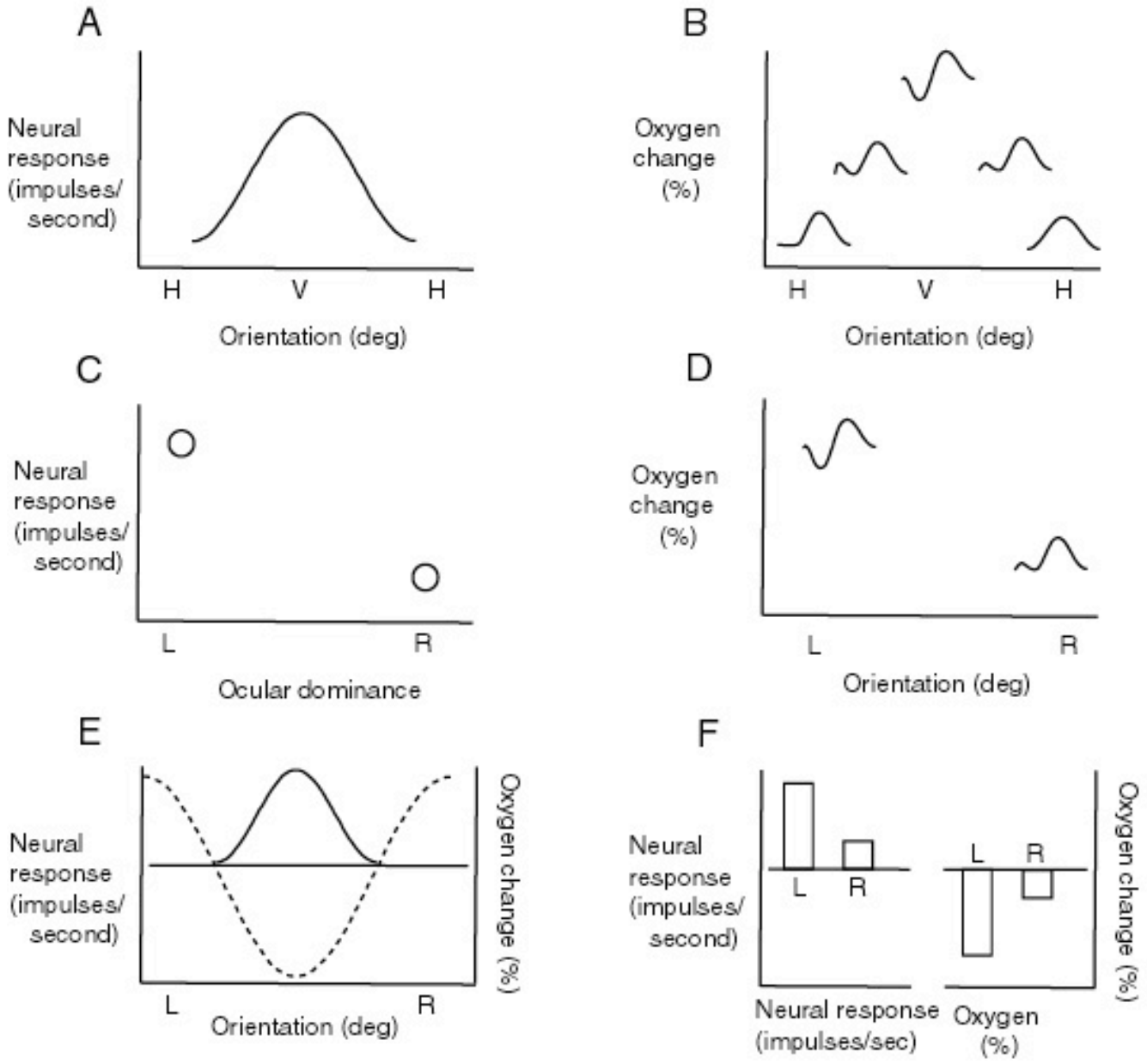

Figure 1

Representations are given for the data that are obtained by simultaneous measurements of neural impulse activity of cells in the visual cortex and oxygen concentration changes of tissue surrounding the neurons. In (A), an orientation tuning curve is illustrated and in (B) the associated oxygen response functions are shown. In (C) responses of a cell are depicted for separate stimulation through the left and right eyes. In (D) associated oxygen changes are illustrated for left and right eyes. Two tuning curves are represented in (E), the solid line for neural response and the dashed curve for oxygen change. Neural and oxygen responses are illustrated in (F) for left and right eye visual stimulation.