ELSEVIER

NeuroImage

www.elsevier.com/locate/ynimg
NeuroImage 42 (2008) 49–59

Dynamics of oxygen delivery and consumption during evoked neural stimulation using a compartment model and CBF and tissue P_{O2} measurements

Alberto L. Vazquez,[a,*] Kazuto Masamoto,[b] and Seong-Gi Kim[a]

[a]*Department of Radiology, University of Pittsburgh, Pittsburgh, PA, USA*
[b]*Molecular Imaging Center, National Institute of Radiological Sciences, Chiba, Japan*

Received 8 December 2007; revised 7 March 2008; accepted 5 April 2008
Available online 16 April 2008

The dynamics of blood oxygen delivery and tissue consumption produced by evoked stimulation of the rat somato-sensory cortex were investigated. Tissue oxygen tension (P_{O2}) and laser Doppler flowmetry (LDF) measurements were recorded under two experimental conditions: normal, which represented both oxygen delivery and consumption, and suppressed CBF (achieved using a vasodilator), which only represented tissue oxygen consumption. Forepaw stimulation for 10 s produced increases of 27.7% and 48.8% in tissue P_{O2} and LDF signal under normal conditions, respectively. The tissue P_{O2} response peaked 9.8 s after stimulation onset and did not show any early transient decreases indicating that measurable oxygen deficits are not required to increase the delivery of oxygen by blood flow. Under suppressed CBF conditions, the LDF signal was mostly suppressed while the tissue P_{O2} decreased by 11.7% and reached a minimum 10.8 s after stimulation onset. These data were analyzed using a dynamic model that described the transport of oxygen from blood to tissue. In order to explain the differences between the model prediction of the tissue P_{O2} changes and the experimental data, several hypothetical scenarios were considered, such as changes in the vascular volume, permeability–surface area or arterial oxygenation. The increase in tissue P_{O2} was found to probably require the recruitment of upstream oxygen from larger arteries as well as increases in the vascular volume at the oxygen exchange sites. The amplitude of the estimated tissue tension of oxygen delivered was about 2.7x larger than the estimated consumption under normal conditions (45.7% vs. 17.1%, respectively).
© 2008 Elsevier Inc. All rights reserved.

Keywords: CBF; CMRO2; Oxygen Delivery; Brain; Oxygen transport; Microcirculation; fMRI

Introduction

Brain function relies on the delivery of oxygen from blood for its metabolism in tissue. Under normal resting physiologic conditions, arterial blood carries sufficient oxygen to satisfy the demand of tissue while also maintaining a relatively high venous blood oxygenation. Moreover, during evoked neural activity both the cerebral blood flow (CBF) and the cerebral metabolic rate of oxygen (CMR_{O2}) increase (Fox et al., 1988; Davis et al., 1998; Kim et al., 1999; Shulman et al., 2001). It has also been observed that the suppression of the stimulation-evoked CBF response achieved using a vasodilator does not alter cortical electrical activity and that the decrease in tissue oxygen tension due to the metabolic increase does not decrease below hypoxic levels (Fukuda et al., 2006; Masamoto et al., 2007, 2008). Therefore, the increase in CBF appears to be unnecessary because, not only does it exceed the demand of tissue (Weiss et al., 1983), the baseline supply of oxygen in blood is sufficient to satisfy the functional demands of tissue. Therefore, the role of the evoked hemodynamic response due to changes in function has not been clearly understood. It is possible that a dynamic mismatch between blood oxygen delivery and tissue oxygen consumption plays an important role, but these temporal changes have yet to be carefully investigated. In particular, investigating the properties of oxygen supply is not trivial since it is difficult to generate sudden changes in blood flow alone without changes in oxygen consumption. Any information on the properties of these processes may help understand the dynamic role of oxygen delivery and consumption in functional neurophysiology.

Oxygen sensors have been reliably used to measure the absolute concentration of dissolved oxygen in living tissues, including the brain, and blood vessels (Vovenko 1999; Ances et al., 2001; Thompson et al., 2003; Masamoto et al., 2003). Oxygen sensors are generally sensitive to a volume that spans about 10 times the electrode diameter (Fatt, 1976). Additionally, these sensors can have sufficient temporal sensitivity to detect transient decreases in signal due to oxygen consumption and also transient increases in signal due to an increased delivery of oxygen by increases in blood flow (Masamoto et al., 2003). The changes in CBF can be measured using numerous techniques,

* Corresponding author.
E-mail address: alv15@pitt.edu (A.L. Vazquez).
Available online on ScienceDirect (www.sciencedirect.com).

1053-8119/$ - see front matter © 2008 Elsevier Inc. All rights reserved.
doi:10.1016/j.neuroimage.2008.04.024

including laser Doppler flowmetry (LDF). This technique relies on the scatter of light by moving cells in blood that generates a Doppler shift that is indicative of the blood flow. LDF has a sub-millimeter spatial sensitivity and fast temporal sensitivity (Arbit and DiResta, 1996), and can be easily incorporated with oxygen sensor measurements.

The objective of this work was to investigate the dynamics of the blood oxygen delivery and its consumption in tissue produced by the evoked changes in CBF and tissue CMR_{O2} due to the stimulation of the rat somato-sensory cortex. For this purpose, two conditions (control and suppressed CBF) were established in all the animals tested whereby LDF and tissue oxygen tension (P_{O2}) signals were measured. These data were analyzed using a model that described the transport of oxygen from blood to tissue. The tissue P_{O2} data obtained under control conditions (also referred to as normal conditions) was used to represent both oxygen delivery and consumption, while the tissue P_{O2} data under suppressed CBF conditions was used to determine the tissue oxygen consumption. The changes in oxygen delivery were inferred from the changes in CBF and tissue P_{O2} under control conditions considering the tissue oxygen consumption determined from the suppressed CBF condition data. The following specific questions were investigated using these data and the oxygen transport model: (1) How does the delivery of oxygen change due to the evoked hemodynamic response in order to satisfy the changes in tissue oxygen represented in the data? (2) What are the possible mechanisms responsible for the changes in blood oxygen delivery? The results provided by the model were investigated over physiological ranges for the arterial oxygen concentration and tissue oxygen consumption rate as well as other model parameters. The validity of the assumptions made was also investigated and a preliminary model that describes the behavior observed in the data is proposed.

Methods

Experimental design and data collection

The data used in this work was obtained by our group and is described in detail in the following reference (Masamoto et al., 2007, 2008). A summary of the important details regarding the animal preparation, experimental details and data collection follows.

Five male Sprague–Dawley rats (400 to 560 g) were used under an experimental protocol approved by the University of Pittsburgh Institutional Animal Care and Use Committee. The animals were initially anesthetized using isoflurane (5%), nitrous oxide (50 to 65%) and oxygen (30 to 50%) for intubation and placement of catheters in the femoral artery and femoral vein. The respiration rate and volume were controlled using a ventilator. After intubation, the animals were placed in a stereotaxic frame and the skull was exposed and thinned over the somato-sensory area. The anesthesia and breathing mixture were then changed to isoflurane (1.5%), oxygen (25 to 30%) and air (70 to 75%). The arterial blood pressure, respiration rate, heart rate, rectal temperature, expired CO_2 tension and isoflurane level were monitored and recorded using a polygraph data acquisition software.

Two needle electrodes were placed in the right forepaw of the animals for electrical stimulation. A short stimulation experiment was performed to locate the activation area using optical imaging (Masamoto et al., 2007, 2008). A small hole was then made over the activation area and the oxygen sensor was placed 0.3 mm under the cortical surface to record tissue P_{O2}. The LDF probe was also placed over the activation area just over the thin skull preparation and less than 0.5 mm from the oxygen sensor location. The LDF sensitivity area spanned about 450 μm while the tissue P_{O2} sensitivity spanned at most 300 μm. Evoked stimulation of the somato-sensory cortex was then performed while recording LDF and P_{O2} under two different conditions. The stimulation consisted of 60 electrical stimulation pulses (1.2 mA and 1.0 ms in duration) delivered at a frequency of 6 Hz every 80 s for 1210 s. These stimulation parameters were previously optimized for isoflurane anesthesia (Masamoto et al., 2007).

Experimental conditions

Two experimental conditions were used: a control condition and a suppressed CBF condition. The control condition was the default condition established as described above. The changes in tissue P_{O2} measured during this condition result from both oxygen delivery (i.e. the oxygen supplied by the blood as a function of the CBF response) and oxygen consumption (i.e. the oxygen metabolism in brain tissue). The suppressed CBF condition required the administration of the vasodilatory agent, sodium nitroprusside (sNP). This agent dilates blood vessels and as a result suppresses the CBF response during evoked stimulation without altering neural activity (Nagaoka et al., 2006; Fukuda et al., 2006). The infusion of the agent was adjusted to maintain a mean arterial blood pressure between 40 and 45 mmHg over the course of the evoked stimulation experiment. The infusion of the agent was terminated after approximately 25 min and all the animals were re-tested after the control condition was re-established (after about 1 h) to verify the functional response was the same as that prior to sNP administration. The neural response was also verified to be the similar between control and sNP conditions using a platinum electrode embedded in the oxygen sensor (Masamoto et al., 2007, 2008). In the suppressed CBF condition, the changes tissue P_{O2} are mostly due to oxygen consumption.

Oxygen exchange model

An overview of the model used to describe the dynamics of the transport of oxygen from blood to tissue with evoked neural stimulation follows. For a detailed description of the model please refer to (Valabregue et al., 2003). Two compartments were considered: a capillary blood compartment and a tissue compartment. The capillary compartment consisted of a homogenous suspension of blood where oxygen is bound to hemoglobin and also dissolved in plasma (C_p). The amount of capillary oxygen (C_c) depends on the delivery of oxygen from upstream arteries (C_a) and the amount transported to tissue (last term in Eq. (1)). The transport of oxygen to tissue (last term in Eq. (1)) was assumed to depend on the concentration difference between plasma and tissue oxygen concentration (C_t) as well as the capillary oxygen permeability (P) and surface area of exchange (S_c). In Eq. (1), the gradient of oxygen along the direction of the vessel was assumed to be approximately linear, such that the capillary concentration of oxygen (C_c) was represented by its average concentration. The Hill equation was used to relate the dissolved oxygen in plasma to that bound to hemoglobin and the kinetics of this association and dissociation were considered to be instantaneous (Popel 1989). The average concentration of tissue oxygen (C_t) depends on the amount of oxygen transported from the vessel and the consumption in tissue (CMR_{O2}). The relative volumes of these compart-

Download English Version:

https://daneshyari.com/en/article/3073011

Download Persian Version:

https://daneshyari.com/article/3073011

Daneshyari.com