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Temporal analysis of fluctuations in cerebral hemodynamics revealed by near-infrared spectroscopy

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ABSTRACT

We have non-invasively studied the motor cortex hemodynamics in human subjects under rest and motor stimulation conditions using a multichannel near-infrared tissue spectrometer. We obtained optical maps of oxy- and deoxy-hemoglobin concentration changes in terms of amplitudes of folding average, power spectrum and coherence at the stimulation repetition frequency, and the phase synchronization index. Under periodic motor stimulation conditions, we observed coherence and phase synchronization of the local hemodynamic changes with stimulation.

1. INTRODUCTION

The advantages of near-infrared spectroscopy (NIRS), such as non-invasiveness, high temporal resolution and relatively low cost, make it an effective method for studying the dynamics of physiological processes, particularly brain hemodynamics¹. Recent near-infrared measurements of brain activity following visual and motor stimulations confirmed the positron emission tomography and functional magnetic resonance imaging observations of a significant hemodynamic response at the activated brain area. Several important features of cerebral hemodynamics were discovered. For instance, it was found that while the oxy- and deoxy- hemoglobin concentrations exhibit irregular fluctuations at rest, during stimulation the statistical average change of deoxy-hemoglobin concentration in activated brain area is negative, and the corresponding oxy-hemoglobin change is positive. The dependence of the hemodynamic response on the duration of the relaxation phase preceding a motor stimulation was demonstrated.

In this article we discuss temporal and spatial patterns of brain hemodynamics under rest and motor stimulation conditions obtained by fast (160 ms per image) multi-site NIRS measurements in the motor cortex area. Particularly, we study the relationship between the underlying hemodynamic fluctuations and responses to stimulation.

2. INSTRUMENTATION

We use a two-wavelength instrument for near-infrared probing of tissues in which light emitted by laser diodes (758 and 830 nm, ~2 mW average power) is guided to the tissue through multi-mode silica optical fibers (400 μ m core diameter). Sixteen laser diodes (eight per each wavelength) operate in a sequential multiplexing mode with 10 ms on-time for each diode. Two glass fiber bundles (3.2 mm internal diameter) collect the scattered light and conduct it to the photomultiplier tube (PMT) detectors. The sixteen sources and two detectors provide thirty two source-detector channels. The output signals from the PMT's are applied to the inputs of an interface card for an IBM-PC computer, where data processing is performed. To obtain cerebral optical maps, we designed a headset consisting of the fiber-optic probe and a frame securing the probe on the head. Two detector fibers are securely fixed in the central part of the probe. The paired (758 and 830 nm wavelength) source optodes are attached to the probe pad at 8 positions. The range of source-detector distances (0.5-4.0 cm) allows us to distinguish processes occurring at different tissue depths. For brain mapping we use six equidistant 2.8 cm source - detector channels.

In addition to the optical signals probing the brain hemodynamics, we acquire the heart rate, and the arterial saturation by means of a pulse oximeter N-200 (Nellcor) with the sensor attached to the left hand index finger, and the respiratory signal with the monitoring system Resp-EZ (Sleepmate/Newlife Technologies). All these physiological signals are acquired by the

PC computer simultaneously with the near-infrared signals.

3. MEASUREMENT PROTOCOL

We performed measurements on 5 subjects, right-handed males of age ranging from 30 to 65 years. A written informed consent was obtained from each subject before measurements. The probe was positioned above the left primary motor cortex.

During measurements the subjects were comfortably supine and instructed not to speak or to make unnecessary movements. Each measurement consisted of the rest epoch (10 min) and three exercise epochs. During the rest epoch the baseline data were acquired. During the exercise epoch, subjects were asked to begin or stop performing a finger-motion (a light palm squeezing) exercise by the right hand. The squeezing rhythm (1.5 Hz) was maintained by means of a metronome. Exercise epochs E1, E2, and E3 differed by the duration of the stimulation/relaxation period: 20/60 s, 20/20 s, 10/17 s, respectively, and consisted of 5, 10 and 10 periods, respectively.

Mathematically each exercise epoch can be associated with a rectangular stimulation wave, whose magnitude is zero during relaxation phases and one during stimulation phases. We used such stimulation rectangular waves in the analysis of coherence and phase synchronization between the stimulation and hemoglobin signals.

4. RESULTS

4.1 Spontaneous fluctuations under rest conditions

Optical signals acquired on the head under rest conditions exhibit fluctuations. A typical $[\text{HbO}_2]$ power spectrum includes the structures towering around the average respiration frequency and some frequency lower than the respiratory one. The phase of the complex spectrum of coherence between $[\text{Hb}]$ and $[\text{HbO}_2]$ indicates that the oscillations at this frequency range are about 180° out of phase. If one assumes that these oscillations are related to blood flow variations, the opposite changes of $[\text{Hb}]$ and $[\text{HbO}_2]$ may be due to the oxy-hemoglobin accumulation and deoxy-hemoglobin washout when the flow increases. Hemodynamic fluctuations in different zones of motor cortex at rest conditions are not identical (compare Figs. 4(a) and 5(a), showing rest hemodynamics in the precentral and postcentral areas of motor cortex, respectively, as simultaneously acquired by NIRS). However, their coherence magnitude in the frequency band below 0.3 Hz is high (not shown in figures) and their fluctuation power spectra in this band have similar shapes and magnitudes.

4.2 Temporal and spectral patterns of hemoglobin fluctuations during exercises

Figure 1 shows $[\text{Hb}]$ and $[\text{HbO}_2]$ time traces observed in a typical experiment performed according to the protocol described above during three exercise epochs E1, E2, and E3 differing in the duration of stimulation/relaxation phases (20/60 s, 20/20 s and 10/17 s, respectively). The order of Figs. corresponds to the order of the epoch sequence. The stimulation periods are indicated by the shaded areas.

One can see that the $[\text{Hb}]$ signal, (supposedly at the precentral area of the motor cortex) during E3 (10/17 s stimulation/relaxation period) is the most regular and synchronous with the stimulation. The dynamic pattern of hemoglobin concentration change during E3 is in agreement with the one obtained by other researchers. Namely, during the stimulation $[\text{HbO}_2]$ increases and $[\text{Hb}]$ decreases, and during the relaxation there is a recovery toward the baseline level. Unlike epoch E3, $[\text{Hb}]$ does not manifest a significant correlation with the stimulation sequence during epoch E1. At epoch E2 the character of the $[\text{Hb}]$ trace is intermediate between the ones corresponding to the epochs E1 and E3. One can recognize a pattern which correlates with the stimulation sequence, but its periodicity is less regular than in the case of the epoch E3. Meanwhile, $[\text{HbO}_2]$ exhibits a quite regular oscillatory pattern.

4.3 Phase synchronization analysis

We estimated the phase synchronization strength between the stimulation rectangular wave and the oxy- and deoxy-hemoglobin signals. Recently, phase synchronization was understood as a specific relationship between two signals of arbitrary nature, including non-periodic and noisy signals². This interpretation required a generalization of the concept of phase and of the mathematical condition restricting the relative phase change of two signals.

The power spectrum analysis reveals frequency locking of the [Hb] and [HbO₂] time series with stimulation. Since the frequency locking may be an indication of phase synchronization, we calculated the entropy phase synchronization index (PSI) which was proposed in ² to quantify the strength of the (*n*/*m*) phase synchronization state. One can see that during epochs E2 and E3 some zones exhibit (1:1) phase synchronization in [HbO₂], [Hb], or in both signals. Unlike E2 and E3, during epoch E1 some zones exhibit (2:1) synchronization in [HbO₂], which is in agreement with Fig.6(a), showing two maxima of oxy-hemoglobin change during the stimulation/relaxation period, and with Fig. 3(b) displaying the highest [HbO₂] power spectrum peak at the second harmonic of stimulation repetition frequency. However, during E1 none of the zones shows significant phase synchronization in the [Hb] signal.

Figure 1.

5. CONCLUSION

Using multichannel near-infrared cerebral spectroscopy we have found that the hemoglobin changes in the motor cortex under periodic motor stimulation can be highly regular or irregular depending on the duration of stimulation/relaxation period. We found that the oxy-hemoglobin concentration changes are significant and phase-synchronous with the stimulation at most of the exercise conditions. The deoxy-hemoglobin response to stimulations depends on the stimulation and relaxation timing, partially due to the interference with the background fluctuations, and partially due to the possible stimulation-response phase synchronism. Using the power spectrum, coherence and phase synchronization analysis, we have shown that functional stimulation can cause local frequency- and phase- synchronization of cerebral hemodynamic fluctuations.

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