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## Human cortical perfusion and the arterial pulse: a near-infrared spectroscopy study

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### Abstract

**Background:** The pulsatile nature of the arterial pulse induces a pulsatile perfusion pattern which can be observed in human cerebral cortex with non-invasive near-infrared spectroscopy. The present study attempts to establish a quantitative relation between these two events, even in situations of very weak signal-to-noise ratio in the cortical perfusion signal. The arterial pulse pattern was extracted from the left middle finger by means of plethysmographic techniques. Changes in cortical perfusion were detected with a continuous-wave reflectance spectrophotometer on the scalp overlying the left prefrontal cortex. Cross-correlation analysis was performed to provide evidence for a causal relation between the arterial pulse and relative changes in cortical total hemoglobin. In addition, the determination of the statistical significance of this relation was established by the use of phase-randomized surrogates.

**Results:** The results showed statistically significant cross correlation between the arterial and perfusion signals.

**Conclusions:** The approach designed in the present study can be utilized for a quantitative and continuous assessment of the perfusion states of the cerebral cortex in experimental and clinical settings even in situations of extremely low signal-to-noise ratio.

### Background

A number of observations in recent near-infrared spectroscopy (NIRS) studies have shown the presence of rhythmic changes in total hemoglobin in cerebral perfusion in the neighborhood of the cardiac frequency. In an earlier non-invasive spectroscopy study in the prefrontal cortex of humans during cognitive tasks, spectral analysis of changes in cortical perfusion revealed a spectral peak at the heart rate frequency [1]. In a second study of oscillations in cerebral hemodynamics, a cardiac peak was also observed when changes in oxyhemoglobin were analyzed [2]. More recently, in noninvasive optical monitoring of

the newborn piglet brain under general anesthesia, a spectral component related to the arterial pulse was observed, which disappeared when the piglet died, an observation in confirmation of its cardiac origin [3]. However, one of the difficulties in using spectral analysis to study the relation between cerebral perfusion and the arterial pulse is that during the period of data collection, there is, in general, substantial heart rate variability. This would introduce spectral spreads in the spectra of both the heart rate and perfusion signals. The variability also complicates the statistical assessment of the causal relationship between pulse and changes in cortical perfusion. A second related

difficulty with spectral estimations is the reliance on a clear signal with high signal-to-noise ratio for quantitative assessment of the perfusion state.

In the present study, we sought to develop a more direct and quantitative method to examine the relations between the arterial pulse and changes in cerebral perfusion, even in the presence of weak signal-to-noise ratio, as may occur for example when cerebral perfusion is compromised by an increase in intracranial pressure. Our approach incorporated the analysis of the cross-correlation function between the cerebral perfusion signal and the arterial pulse. The cross-correlation approach has the advantage of being sensitive and robust in the presence of noise. As well, we developed a statistical measure of significance of the dependence between these two signals for each subject by the generation and analysis of surrogate data sets.

## Results

A stretch of 8 second raw data is shown in Figure 1 from one subject. The upper trace shows the optical signal representing changes in total hemoglobin in the prefrontal cortex, and the corresponding arterial pulse signals recorded at the left middle finger is shown below. Note that in this experimental setting, there is no evident oscillatory response in the optical data at the cortical level associated with each of the arterial pulses. This indicates that the response was weak, a conclusion corroborated by a weak Fourier component at the heart rate frequencies observed in the optical signal (Figure 3).

During the period of recording, there was a sizable heart rate variability which contributed to a broad peak in the Fourier spectrum of the arterial pulse signal around 1.3 Hz, with a harmonic around 2.6 Hz (Figure 2). This variability might have contributed to this spectral smearing observed in the cortical signal (Figure 3).

Cross-correlation analysis, however, demonstrated a clear linear dependence of the total hemoglobin perfusion signal on the arterial pulse (Figure 4). The cross-correlation function (green trace) is superimposed on a background (yellow) of cross-correlation functions computed from phase-randomized surrogates. Highly significant correlation peaks exceeding the boundaries of  $\pm 3$  standard deviations can be seen around zero delay, suggesting a causal relationship between the two signals. Significant cross-correlations were observed in 6 of the 7 subjects. The lack of significant correlation in the one subject might have been due to excessive artifacts in the prefrontal optical signal. This abnormally low signal-to-noise ratio might have contributed to the failure of detection of significant correlation.

## Discussion

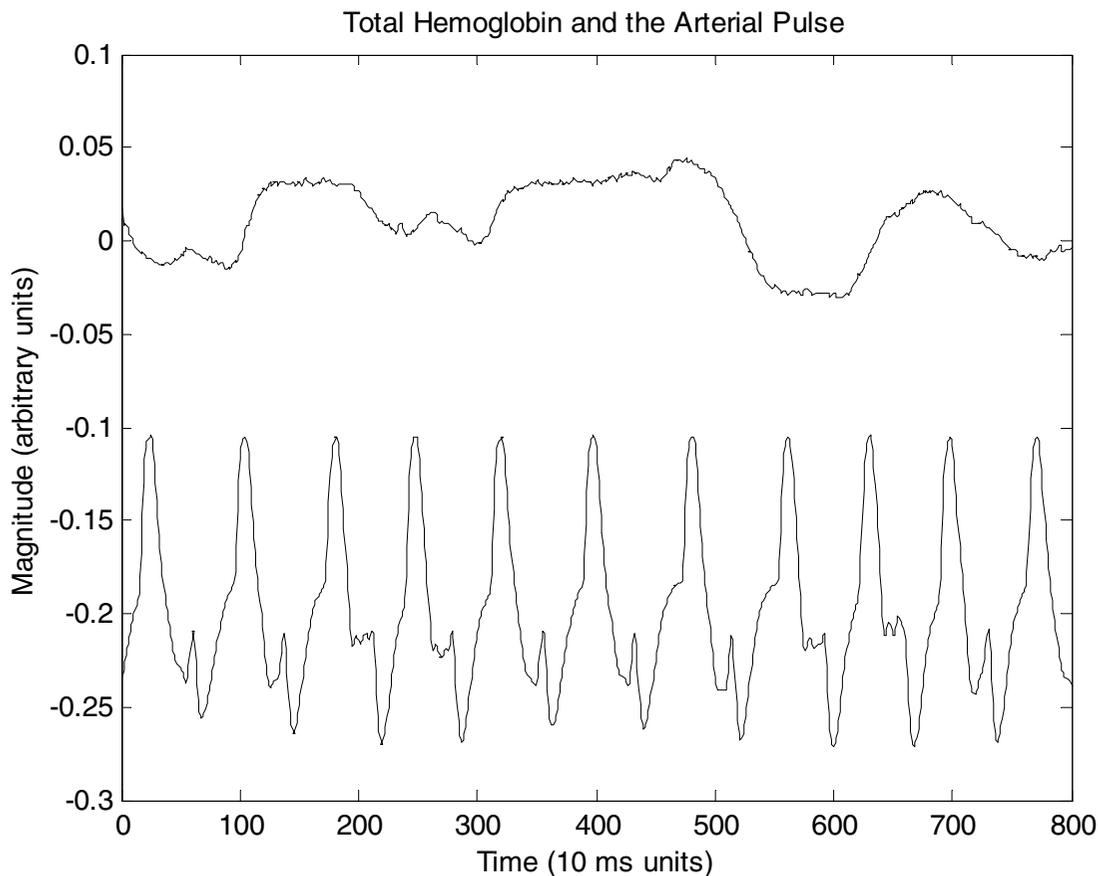
Changes in cortical perfusion bearing a constant phase or delay with respect to the arterial pulse will appear in the cross-correlation function as peaks in the neighborhood of that delay. The presence of statistically significant peaks around zero delay in the cross correlation function (Figure 4) strongly suggests a causal relationship between cortical perfusion and the arterial pulse. The time of occurrence of the correlation peak depends on the difference in the velocities of propagation of the arterial pulse wave from the aorta to the left middle finger on the one hand, and from the aorta to the prefrontal cortex on the other. The velocity of propagation of the pulse wave in the arteries has been estimated to be in the range of 8–10 m/s [4,5]. Given the fact that the difference in propagation distances from the heart-to-finger and heart-to-cortex is in the order of 500 cm, we should anticipate an approximately delay of 50 milliseconds. This delay is in agreement with the observation of correlation peaks in the neighborhood zero delay (Figure 4).

Although Fourier analysis alone [1-3] can provide evidence for relations between cardiac and brain events, the inevitable heart rate variability during the period of recording makes statistical evaluation of the spectral peaks (Figures 2 and 3) difficult. Computation of coherence, an approach based on spectral analysis, may be helpful in this regard [6,7].

The low cross-correlation ( $\sim 0.04$ , Figure 4) indicates a low signal-to-noise ratio of the cardiac related cortical perfusion signal (see Figure 1). In the present experimental setting, the signal-to-noise ratio can be improved by the incorporation of improved frequency response of the spectrophotometer in the range of 1 to 2 Hz, the dominant spectral characteristic of the arterial pulse signal, and appropriate filtering to further enhance the ratio.

## Conclusion

We have observed a detectable and statistically significant relation between cortical perfusion and the arterial pulse. In the context of our experimental design, we have permitted the arterial pulse to serve as a natural test signal to interrogate the state of perfusion of the cerebral cortex, or the patency of the cerebral vasculature under observation. In contrast to functional NIRS studies in which cardiac-related oscillations in optical signals [see e.g. [8]] often lead to an erosion of signal-to-noise ratio, our study focuses on the quantification of this optical response. The use of cross-correlation analysis and the generation of control surrogate data sets by phase randomization allow us, even in the presence of very low signal-to-noise ratio, to extract the linear component of the relation between the cardiac and brain perfusion signals and to provide a quantitative measure of the significance of this relation.



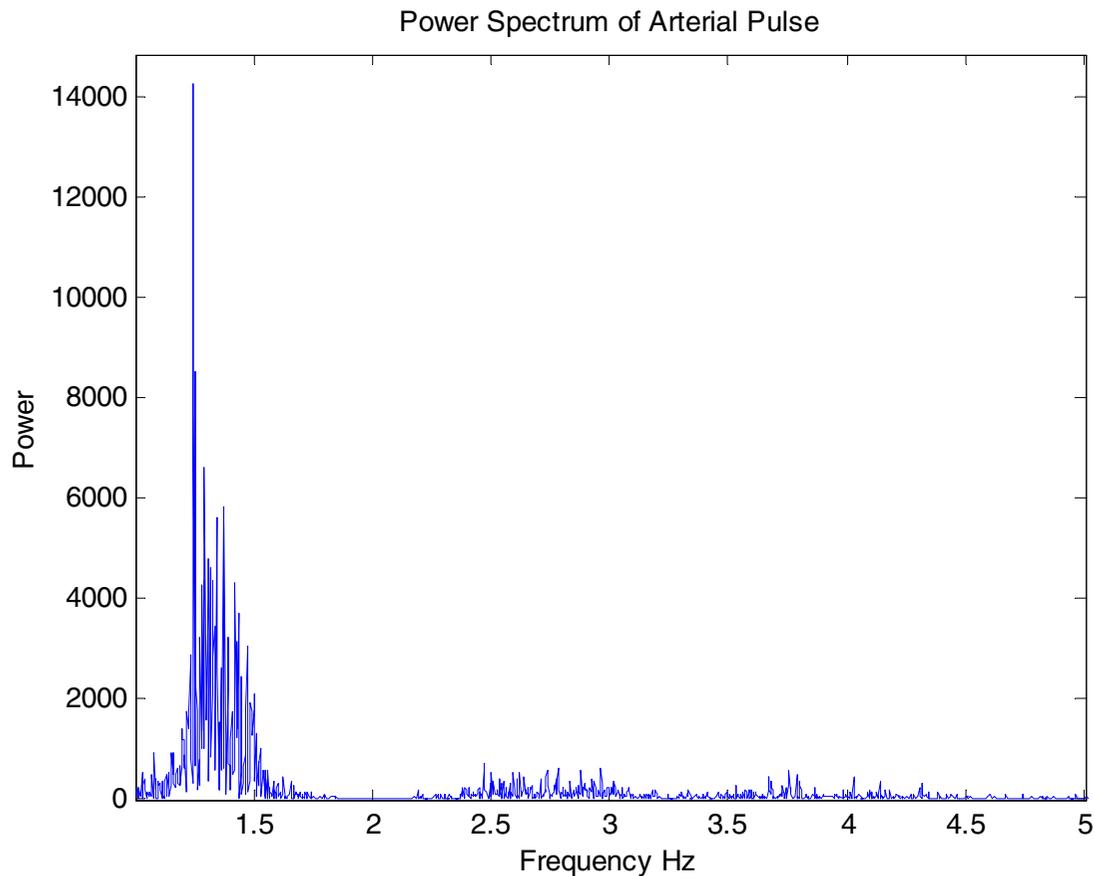
**Figure 1**  
 An example of the optical signal representing relative change in cortical total hemoglobin (upper trace) and the corresponding arterial pulses recorded over an eight second period from the left middle finger.

Since the optical probe can be readily miniaturized, this approach opens up the possibility of quantitative and long-term non-invasive monitoring of changes in total hemoglobin concentration, or cortical perfusion states time-locked to the arterial pulse in both experimental and clinical settings. These may include assessments of cortical vascular response to physiological or pharmacological activation, and reduction in cortical perfusion during conditions associated with an increase in intracranial pressure. By monitoring the decrease in cerebral diastolic blood flow that accompanies increased intracranial pressure, transcranial doppler testing is presently used as an

indirect, noninvasive measure of increased intracranial pressure [9]. The recording of the changes in pulsatile cortical perfusion associated with increased intracranial pressure by NIRS thus potentially represents a far simpler noninvasive measure that would have a wider field of application in the clinical sciences.

**Methods**  
**Instrumentation**

Photoplethysmographic recording of the arterial pulse was performed with a matched silicon emitter (900 nm) and detector pair spaced at approximately 4 mm apart and

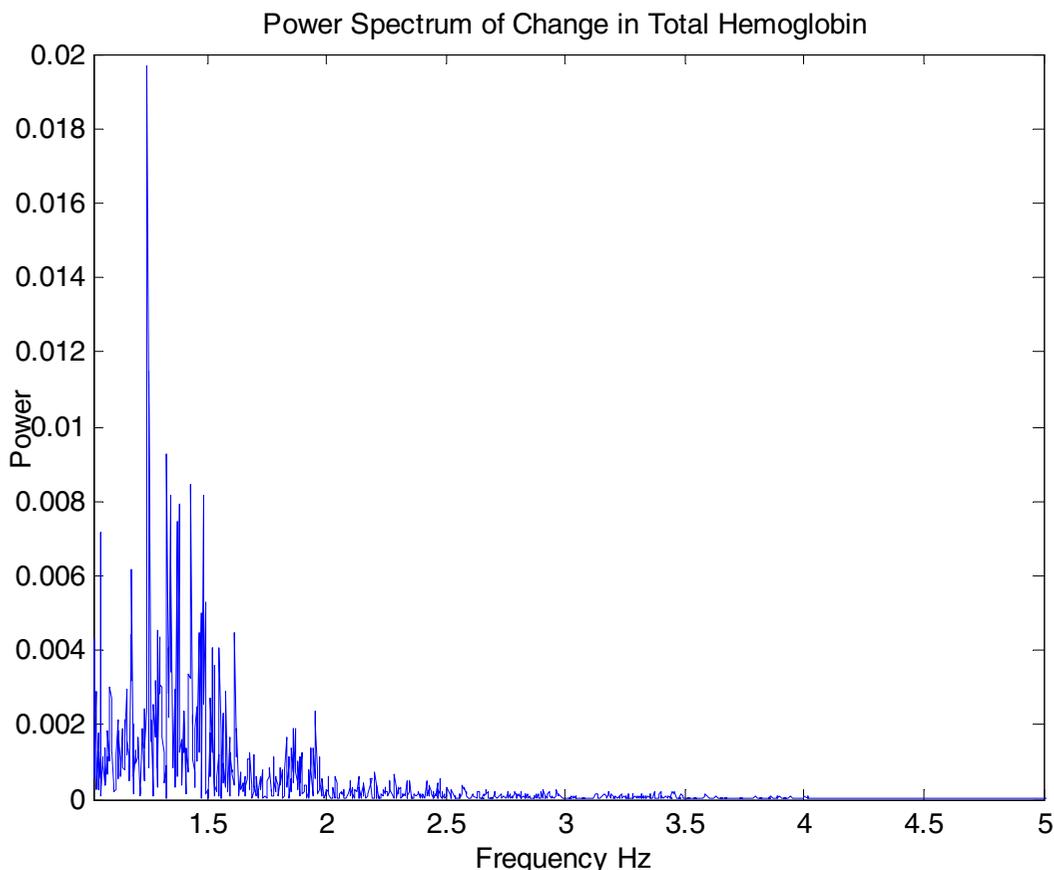
**Figure 2**

Power spectrum of the arterial pulse computed from plethysmographic recording (lower trace of Figure 1) at the left middle finger. Power in arbitrary units.

placed over the ventral surface of the distal phalanx of the left middle finger. This assembly was secured with a foam-padded bandage. The arterial pulse was indirectly inferred from a change in the absorption due to a change in finger blood volume upon arrival of the arterial pressure wave. This arterial pulse signal was amplified and filtered (bandwidth 1–10 Hz) (see Figure 1 lower trace). Both the arterial pulse and the spectrometer (see below) signals were sampled at 100 Hz.

A dual wavelength continuous-wave reflectance spectrophotometer (RunMan, NIM Inc., Philadelphia) with an

optical probe was used for non-invasive monitoring of the change in total hemoglobin perfusion signal of the cortex. The optical probe has an emitter-sensor spacing of 4 cm. The emitter is a small incandescent tungsten light source. There are two silicon sensors each equipped with an interference filter (10 nm-wide band) respectively at 760 nm and 850 nm. The geometrical arrangement of the assembly allows interrogation of approximately 5 ml volume of cortex 2 cm below the probe. Detailed description of the instrumentation has been published [1].



**Figure 3**  
Power spectrum of change in total hemoglobin (upper trace of Figure 1). Power in arbitrary units.

In order to ascertain that the spectrophotometer had a rise time sufficiently fast to respond to the arterial pulse wave, we applied a step input to a phantom to examine the transient response of the system. The total hemoglobin channel responded with a time constant of 280 milliseconds, which is approximately equal to a 3 dB cutoff frequency of approximately 0.5 Hz. This frequency response would introduce some attenuations of the prefrontal total hemoglobin response within the anticipated frequency range of 1 to 2 Hz, viz. the heart rate frequency.

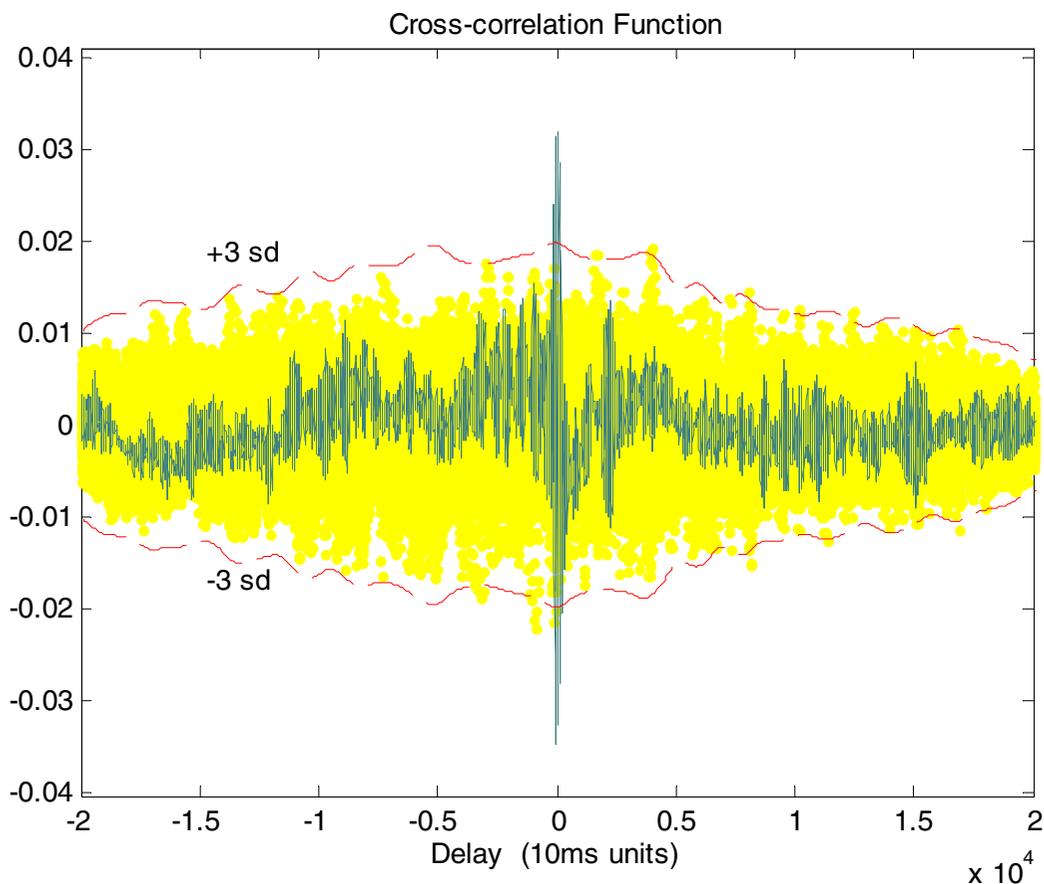
#### **Experimental procedure**

Subjects were seated comfortably in a normally lit quiet room with eyes closed. The probe was placed on the fore-

head over the left prefrontal cortex 1 cm lateral to Fp1 of the 10–20 International System, and secured with a wide soft elastic bandage around the head. The subject was instructed to be as motionless as possible for the duration of the recording, which lasted approximately five minutes. Three five-minute recordings were made for each of the 7 subjects (4 F, 3 M, ages 18 to 28 years, mean 20 years). The experimental protocol was approved by the Review Committee on Human Experimentation at the University of Toronto. All subjects gave their informed consents.

#### **Data analysis**

To examine the spectral characteristics of the signals, fast Fourier transform was applied to both the arterial pulse



**Figure 4**  
 Cross correlation function of the perfusion signal with reference to the arterial pulse (green trace) superimposed on a background (yellow) of 16 surrogate cross correlation functions computed from phase-randomization. The upper and lower red dash lines demarcate the boundaries of  $\pm 3$  standard deviations of the surrogates.

and prefrontal optical signals. The similarities and dependence between the two signals were examined by cross-correlation analysis [10]. Briefly, we computed the correlation function at different time delays or lags between the signals. At the delay in question, a value of 1 indicates maximum similarity between the signals, 0 no similarity, and -1 indicates that one signal is exactly the mirror image, or negative, of the other.

To ascertain statistical significance of correlation, we first generated from the original optical signal a set of surrogate data by randomizing the phase spectrum while preserving the magnitude spectral distribution of the original data [11]. Since in these randomized surrogates, the temporal relations between the arterial pulse and the optical signal would be lost, the corresponding surrogate cross-correlation functions formed a control set from which standard deviations were computed. Correlation peaks

were deemed statistically significant when they exceeded three times the standard deviation ( $p < 0.01$ ) of this surrogate set.

### Authors' contributions

HCK conceived and coordinated the study, and performed data analysis. He was also the writer of the article. AC and RL participated in data collection and contributed to the design of the experiment protocol. DSB conceived the study, contributed to the interpretation of data and writing of the article. All authors read and approved the final manuscript.

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