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Measuring Respiration-Driven Perturbations of Intra- and Extra- cerebral Hemodynamics During Slow Breathing: a TD-NIRS Study

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Abstract: We investigated the impact of slow breathing on the cerebral hemodynamics of 16 subjects using TD-NIRS. Results show increased respiratory-associated oscillations and suggest a possible change in strategy for vascular tone control at low frequencies.

1. Introduction

Cerebral hemodynamics are influenced by both local neurovascular mechanisms and systemic physiological factors, including respiration and cardiac activity. Time-Domain Near-Infrared Spectroscopy (TD-NIRS) is a powerful optical technique for investigating cerebral hemodynamics with depth sensitivity, allowing differentiation between intra- and extracerebral contributions. In this study, we investigated the impact of respiratory modulation on cerebral oscillations by employing high sampling rate TD-NIRS measurements to measure oxygenated (OHB) and deoxygenated (HHB) hemoglobin concentration changes in both intra- and extracerebral layers. By analyzing the power spectral density (PSD) and wavelet coherence among the recorded signals, we aimed at quantifying how slow breathing influences hemodynamic oscillations in different frequency bands.

2. Material and methods

2.1. Protocol

Two TD-NIRS measurements of 15 minutes each were performed on the right forehead of 16 adult subjects, who voluntarily took part in this study. The study was approved by the Ethical Committee of Politecnico di Milano and was conducted in compliance with the Declaration of Helsinki. A high throughput TD NIRS device presented in Re et al. [1] was used, with a source-detector distance of 4 cm and a sampling frequency of 20 Hz [2]. During the acquisitions, the subjects were lying on a 30◦ tilted backrest bed with closed eyes. Two acquisitions were performed in series, without any probe repositioning. The first acquisition was a resting-state measurement (Rest), while during the second one (Slow Breathing, SB), the subjects were instructed to reduce their breathing rate down to 5 breaths per minute (0.083 Hz) by following the sound of a metronome. This task was selected to induce a modulation of cerebral hemodynamics by an increased respiration volume with respect to normal ventilation. A blood volume pulse (BVP) sensor on the left hand fingertip and a strain belt around the chest were also used to measure systemic physiology and respiration rate, respectively.

2.2. Data analysis

TD-NIRS data were analyzed to extract the time series of concentration of OHB and HHB hemoglobin using the Mean Partial Pathlength method proposed by Zucchelli et al. [3], assuming a bilayer model with a 1 cm-thick extracortical layer. The signals were then detrended using a third-order polynomial and their PSD was derived with a custom Matlab script. Six frequency regions of interest were identified within the available frequency spectrum, based on the origin of the associated hemodynamic activity [4]. First, the average PSD value measured in the 6-10 Hz frequency range was subtracted from the PSD to account for different noise level of signals derived from the intra- (DW layer) and extra- (UP layer) cerebral compartments. Then, the relative power measured in each band, computed as the integral within the band, divided by the integral over the whole available range (0-10 Hz) and expressed in percentage, was compared among different measurement conditions. Differences between the distribution of values were evaluated using non-parametric Wilcoxon Signed-Rank tests and the resulting p-values were corrected for multiple comparisons using the false discovery rate correction by Benjamini & Hochberg [6].

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Table 1 describes the considered frequency bands. Bands I and II were adapted from literature [4] based on the signal recorded by the additional sensors. Band II was modified as indicated in brackets in the SB case to include the imposed respiration frequency while maintaining the same width. Band III was excluded from the analysis due to superimposition with band II. The wavelet transform coherence (WTC) among the hemoglobin concentrations and between each hemoglobin and systemic physiology signal were also calculated using the wavelet-coherence Matlab toolbox proposed by Grinsted et al. [5] to quantify linear correlations in the time-frequency space.

Table 1. Details of each considered frequency band.

ID	Origin	Lower frequency limit (Hz)	Higher frequency limit (Hz)
VI	Endothelial	0.005	0.0095
V	Nitric oxide (NO) -related endothelial	0.0095	0.021
IV	Neurogenic	0.021	0.052
III	Myogenic	0.052	0.145
II	Respiratory	0.1 (0.05)	0.4 (0.35)
I	Cardiac	0.6	1.6

3. Results

Figure 1 reports the average relative power measured for each frequency band, hemoglobin species, and intra- (UP) and extra- (DW) cerebral compartments, compared between the two measurement conditions. In band II, a significant increase in relative power is observed for all the species for the SB case, while in bands IV and V, lower values were measured, especially for OHB. No significant differences were found in bands I and VI. These results suggest that during the slow breathing task, a strong modulation of the hemodynamics occurs in both intra- and extracortical compartments at the frequency of breathing, while the activity in the frequency bands related to NO-mediated endothelial function and neurogenic control over the vascular tone is partially reduced.

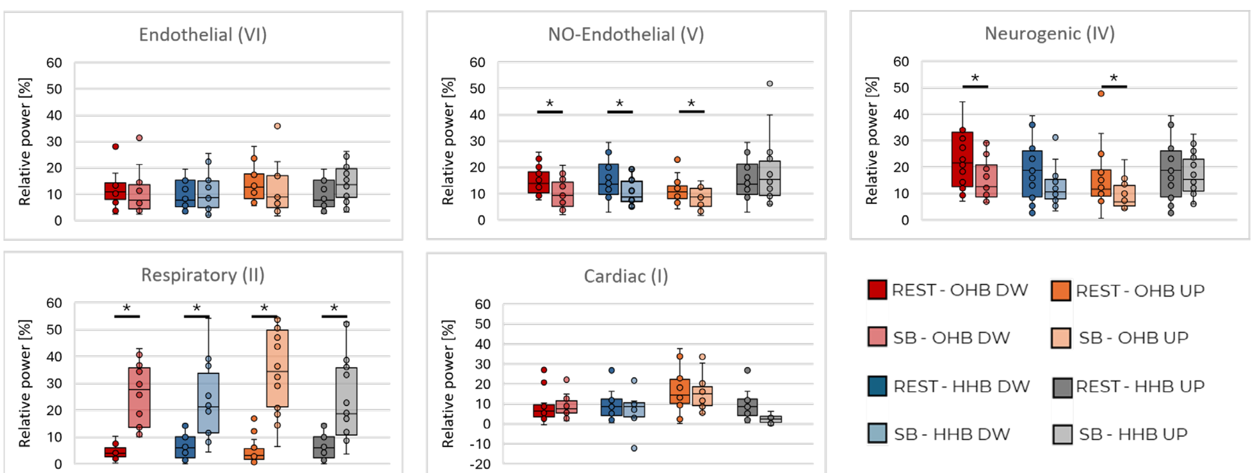

Fig. 1. Comparison between average relative power distributions for the two conditions: rest and Slow Breathing, SB.

Figure 2 reports the time-averaged wavelet coherence values measured between the BVP signal, representative of the peripheral skin hemodynamics, and each hemoglobin species, compared among conditions. The same statistical test as before was used to evaluate the significance of the observed differences. Similar trends can be observed, with increased coherence measured for all the species in band II during the SB acquisition. An overall decrease in coherence is also observed in bands IV, V and VI. Differently than before, an increase in coherence was also observed for all species in band I. The results indicate that during the task the coherence between the acquired signal and the peripheral hemodynamics increase in frequency bands mostly related to systemic phenomena such as respiration and heartbeat, while decreases in frequency regions related to phenomena controlling the local vascular tone. When comparing the time-averaged wavelet coherence measured among combinations of hemoglobin species (data not shown) we found a significant increase in coherence between OHB UP and HHB UP and between OHB UP and OHB DW in both bands I (cardiac) and II (respiratory) during SB, showing that the respiratory-driven modulations observed in the TD-NIRS signal during the slow breathing task is mostly affecting the hemodynamics in the extra-cortical compartment, and is also affecting OHB more than HHB in both compartments.

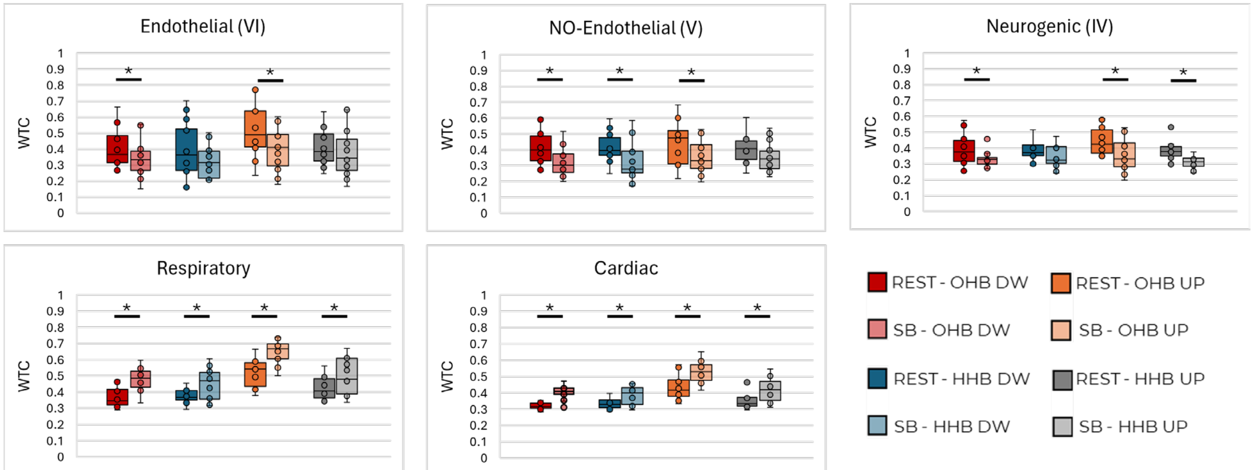

Fig. 2. Comparison between average wavelet coherence distributions for the two conditions: rest and Slow Breathing, SB.

4. Conclusion

This study investigated the effects of a slow breathing protocol on cerebral resting-state hemodynamics using high sampling rate TD-NIRS measurements. Our measurements show that significant changes in intra- and extra-cerebral hemodynamics can be induced by reducing the breathing rate, with increased respiratory-associated oscillations and a reduction of power in lower frequency ranges. Wavelet coherence analysis further revealed increased synchronization between cerebral hemoglobin signals and peripheral blood volume measurements, particularly in frequency regions associated with respiration and cardiac activity. This suggests a stronger coupling between systemic physiological oscillations and cerebral hemodynamics during slow breathing with respect to rest. A decrease in coherence at frequencies associated with endothelial and neurogenic function was also observed, potentially indicating a switch in strategy for vascular tone control during the task. Additionally, coherence in the respiratory and cardiac frequency ranges also increased between hemoglobin species in the extracerebral compartment and among OHB signals across both compartments, indicating that the respiratory-driven perturbations mainly affect the extracortical tissue and the concentration of oxygenated hemoglobin. These observations align with prior studies on physiological noise in functional NIRS and reinforce the importance of understanding the interplay between brain hemodynamics and systemic phenomena, supporting ongoing efforts to improve accuracy in discriminating intra- and extra- cerebral tissue contributions to NIRS signals.

3. References

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