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Study of neurovascular and autonomic response in a divided attention test by means of EEG, ECG and NIRS signals

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Abstract — **We evaluated neurovascular and autonomic response to a Divided Attention task within a group of 16 healthy subjects, by means of Electroencephalography, Electrocardiography, functional Near Infrared Spectroscopy techniques, acquired simultaneously. We exctracted Alpha (8-13,5 Hz) and Beta (13,5-30 Hz) power rhythms with a spectral autoregressive residual model, and inter-beat-interval (RR series) and separated superficial (extracortical) and depth NIRS contribution. Cross Correlation Function at different time lags was then calculated between each signal and the task, modeled as a square wave and among couples of signals, in order to evaluate the sequence of activation of the different physiological districts involved and the common information shared. Results showed the presence of a cascade of responses and a strong influence by the block task on each signal, representative of the neurovascular coupling elicited by the cognitive cerebral activation.**

I. INTRODUCTION

Neurovascular coupling is a ticklish question, that has been faced by means of a multitude of methods and techniques during the last decades. Despite hemodynamic and electrical activities have been widely investigated individually, interesting physiological concerns could be clarified by considering them jointly. The considerable differences existing between hemodynamic and electrical signals, their different physiological nature and time dynamics, make it difficult to investigate neurovascular coupling as a whole.

In previous studies it has been demonstrated that the performance of a cognitive task involves the response of several physiological districts, such as Central Nervous System (CNS), Autonomic Nervous System (ANS) and Cerebro-Vascular System [1,2,3]. In this study, neurovascular coupling is induced by a bimodal audiovisual task of divided attention defined as the ability to divide the attentive resources among two or more information sources or stimuli [4]. As a consequence, divided attention tasks are particularly suitable whenever a saturation of attentive resources is needed. Given the two-faced nature of neurovascular coupling, instrumentation currently used for brain mapping exploit different physical principles, and can be roughly divided into electrophysiological and haemodynamic non-invasive techniques. Electrophysiological techniques are characterized by a high temporal and low spatial resolution in opposition to the haemodynamic ones, that establish their investigation of the neuronal activity on a coupling function representative of a complex and only partially understood vascular mechanism. The combined use of two or more techniques, usually defined "multimodal approach" complements the information acquired. In this study, we used Electroencephalography (EEG) and Near Infrared Spectroscopy (NIRS) techniques. This optical technique can detect the changes in concentration of the two blood cromophores oxy and deoxygenated-haemoglobin ([O_2Hb] and [HHb]) using two different wavelengths chosen in the near infrared spectrum where the absorption of water and lipids by the tissues is negligible [5]. The present work specifically aims at clarifying the time relationship between electroencephalographic and hemodynamic correlates of neurovascular coupling and quantifying the degree of information shared by EEG and NIRS [O_2Hb] and [HHb] signals during a divided attention task involving visual and auditory resources. In order to obtain further information about the hemodynamic response and to study the activation of ANS elicited by the execution of the cognitive task, an additional electrocardiographic (ECG) derivation was recorded.

II. MATERIALS AND METHODS

A. Subjects

Sixteen healthy volunteers (8 males, 8 females) took part in the present study. All subjects were right handed and declared normal vision and hearing. Mean age was 25,6 (SD 3,8 years). None of them had a life time or family history of neurological or psychiatric illness. Written informed consent was obtained from all volunteers after the examination and test procedure have been explained.

B. Divided Attention Test

The divided attention test (TDA) is a modification of the attention test described in [6] achieved in order to improve its difficulty. It was presented on a PC screen using the software Presentation (Neurobehavioural Systems Inc, Albany, CA) and it consists of a 86 seconds baseline rest period, followed by five blocks of task (165 seconds each) alternated with four 85 seconds rest periods. At the end of the test a 300 seconds recovery period is recorded.

Each block of task is composed by 60 couples of auditory

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and visual stimuli, 5 targets, and 55 non-targets. The auditory stimulus consists of two frequency tones (1000 or 1500 Hz), lasting 100 ms each. Target auditory stimulus is represented by two stimuli of different frequency. The subjects are asked to press a button with the middle finger of the right hand as quickly as possible when an auditory target stimulus was presented. The visual stimulus consists of 17 white crosses in a black background. The target stimulus occurs when a cross is replaced with a white circle (Figure 1). The subjects were asked to press a button with the right forefinger to recognize it. The visual stimulus was presented simultaneously with the second frequency tone and it lasted 1,5 s. The interstimulus interval was 1,05 s.

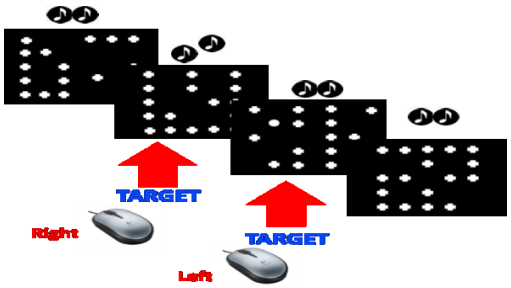


Figure 1. Schematic representation of the stimulation protocol.

C. *Acquisition setup*

A 19 channels EEG was recorded with Ag/AgCl electrodes (impedance below 5 KΩ, international 10/20 system), using common ground as reference. Two couple of bipolar electrodes were used to collect Electrooculogram and ECG signal. The recordings were performed by a 32-channel AC/DC amplifier (SAM-32, Micromed Italy, QuickBrain System). The A/D sampling rate was 256 Hz. A dual channel wavelength (690 and 829 nm) time domain NIRS system [7] was used for the acquisition of [O_2Hb] and [HHb] signals at 1 Hz sampling frequency. The two acquisition channels were positioned on the forehead of the subjects, on left and right side. The described instruments have been synchronized so that the recording of the signals started automatically with the beginning of the test and all the signals (NIRS, EEG and ECG) and the behavioural data recorded by Presentation were time realigned.

D. *EEG analysis*

Raw EEG data were digitally band pass filtered between 0,5 and 48 Hz, they underwent Laplacian Surface Operator and were cleaned by ocular and muscular artifacts by Independent Component Analysis (ICA) and downsampled at 128 Hz, using the free MatLab toolbox EEGlab (Schwartz Centre for Computational Neuroscience, University of California, San Diego, CA) for reducing the computational time of following processing steps. EEG frequency analysis was implemented through an autoregressive (AR) batch modeling, performed on the electrode Fz with time windows of 2 s, overlap 50%, in order to obtain a stationary signal with a frequency resolution of 1Hz. Then, by an automatic spectral decomposition, based on a residual integration algorithm [8], the main two EEG rhythms were obtained (8-13,5 Hz Alpha, 13,5-30 Hz Beta).

E. *RR series*

The RR series was extracted from the ECG derivation. They were resampled in order to obtain one value every second of activity, and to have the same sampling rate of EEG and NIRS signals.

F. *NIRS analysis.*

For each wavelength λ (690 and 829 nm) a time-resolved fNIRS reflectance curve (TRR) is acquired in time. Modeling the head as a two layered semi-infinite medium, with reduced scattering coefficient μ'_s equal in both layers, we separated the deep and superficial contributions to the [O_2Hb] and [HHb] signals. If a change in the absorption coefficient μ_a occurs, as a consequence of an haemodynamic activation, it is possible to estimate $\Delta\mu_a$ in the upper and the lower layer according to the method presented in [9]. Taking the assumption that O_2Hb and HHb are the main chromophores contributing to absorption, their concentration changes are then derived by Lambert-Beer law. We identified two main contributions in NIRS signals: one, in low frequency, due to the substained attention condition required by the whole test and another one, in higher frequency, due to the modulation caused by the switching between test and rest periods. We separated NIRS low and high frequency components (LF and HF): a low pass filter (Chebychev IIR filter, 6 coefficients, pass band 0,002 Hz and stopped-band 0,003 Hz, with 30 dB maximum ripple amplitude) allowed the isolation of LF contribution, which was then subtracted from the whole signal to obtain the HF contribution. An example is shown in Figure 2.

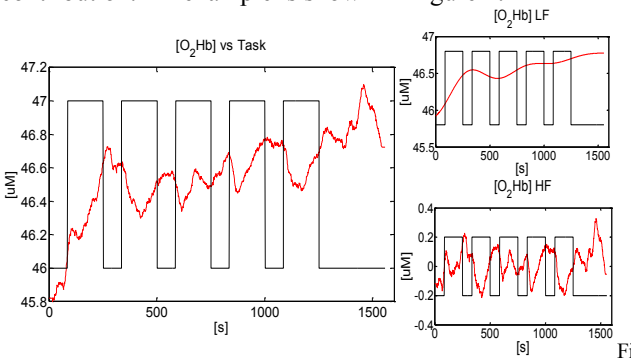


Figure 2. (left) Time course of the original O_2Hb depth signal, (right) after the separation of LHF (top) and HF (bottom) components. The square wave represents the time course of the blocks of task.

G. *Correlation*

After modeling the task as a square wave, "high" during the test blocks and "low" during the rest ones, we calculated the Cross Correlation Function (CCF) between it and Alpha and Beta power rhythms, RR series, HF component of depth and surface [O_2Hb] and [HHb] signals. We then evaluated CCF between couples of signals. Mean value was subtracted from all signals and they have been normalized by the standard deviation. We evaluated the temporal shift between each couple of signals for which the CCF had maximum absolute value and we extracted the corresponding CCF value and the p-value. Depending on the couple of analyzed signals we considered a maximum or minimum of correlation.

III. RESULTS

A. Behavioural results

The 16 subjects committed an average of 0,13±0,49 Visual Omission errors (0,13 missing answers on 15 visual target stimuli), 0,47±0,63 Auditory Omission errors (0,47 missing answers on 15 auditory target stimuli) and an average of 11,63±24,42 Commission errors (all kinds), corresponding to 11,63 wrong answers during all the divided attention test. Subjects answered to the visual target stimuli in 649,55±129,27 ms and to the auditory target stimuli in 698,14±141,30 ms.

B. CCF results

Figure 3 shows the Grand Average of signals (EEG Alpha and Beta rhythms, NIRS depth signals of Oxy and Deoxy haemoglobin, RR series) acquired from all the 16 subjects.

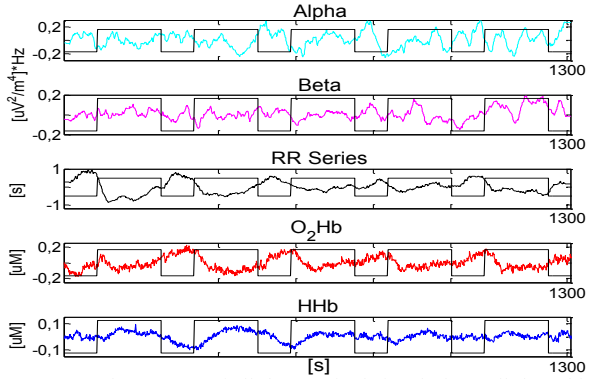


Figure 3. Grand Averages of all the acquired signals from all the subjects. From top: power of Alpha and Beta rhythm, RR series, concentration of O_2Hb and HHb depth signals.

The CCF between Alpha rhythm and the task was negative for 11 on 16 subjects (Alpha power increased during the resting periods, mean value -0,31±0,13, p<<0,001). The CCF between Beta rhythm and the task was positive for 10 subjects but the mean delay for which the CCF reached its maximum value (17,6±20,21 s) was considered too long to represent a neuronal response, so Beta rhythm was excluded from the following analysis. RR series showed a strong modulation by the square wave task. Correlation with the task was negative for all the subjects (that means that RR period decreased during test periods and increased in the resting periods), mean value -0,43±0,23, p<<0,001. The CCF with the task was calculated only for HF components of the NIRS depth and superficial signals. All the p-values resulted <<0,001. The correlation between [O_2Hb] depth signals and the square wave task was negative for 12/16 subjects. The mean value of CCF minima between the two pads was -0,41±0,6. The CCF of [HHb] depth signals and the task had a positive value for 11/16 subjects, mean value 0,43±0,17. LF NIRS depth signals showed a general increase of [O_2Hb], opposed to a decrease in [HHb]. The correlation for the surface signals showed a larger variability among the subjects and between the two pads of the same subject, with respect to the depth one. We identified a group of 8 subjects (50% of the investigated population, codes 1, 4, 5, 10, 14, 15, 16, 20) showing the same time course for all the CCF. We then evaluated the mean delay between each signal and the task, in order to identify the time of response of each physiological district (neuronal, systemic, haemodynamic) to the divided attention task. As explained above, Beta signal was excluded from the analysis. The mean delays among the 8 subjects and the correspondent values of CCF are shown in Figure 4 (left). Figure 4 (right) is representative of the temporal cascade of responses.

Signals	CCF	Delay [s]
Alpha - Task	-0,26 ± 0,09	0,63 ± 13,87
RR - Task	-0,48 ± 0,19	12,00 ± 6,93
O_2Hb - Task	-0,43 ± 0,17	21,06 ± 21,77
HHb - Task	0,36 ± 0,29	27,56 ± 28,93

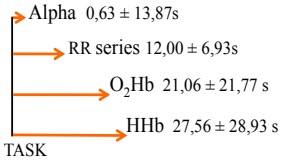
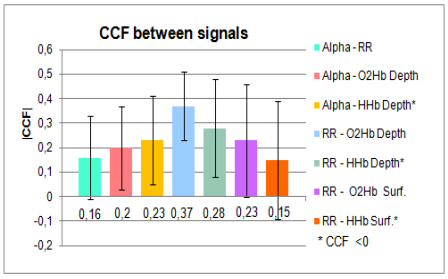


Figure 4. Left: table of CCF and mean delay between signals and task. In the first column the two signals are shown, for which the CCF was calculated (O_2Hb and HHb refer to depth contribution); 2nd column: mean value (±SD) of CCF. 3rd column: mean (±SD) temporal lag for which CCF presented a maximum, that represents the mean delay between the two signals. Right: delays of the subsequent responses (orange arrows) to the stimulation of the task. The mean time delay (±SD) of the CCF maxima (minima) among the 8 subjects are indicated.

Figure 5 shows the mean results of CCF (±SD) between couples of signals.



Signals	CCF
Alpha - RR	0,16±0,17
Alpha – O_2Hb D	0,20±0,17
Alpha - HHb D*	0,23±0,12
RR – O_2Hb D	0,37±0,14
RR - HHb D*	0,28±0,20
RR - O_2Hb S	0,23±0,23
RR - HHb S*	0,15±0,24

Figure 5. Mean values of CCF among couple of signals (left). Table representing the CCF mean value (right).

IV. DISCUSSION

Behavioural Results showed a higher number of errors in response to the Auditory stimuli rather to the Visual ones, and a longer response time concerning auditory stimuli. The two stimuli were always presented simultaneously, in order to enhance the duality of the task. The results concerning the response time are in opposition to previous studies that reported a longer time of response to Visual stimuli [10,11]. It could be due to a not perfect equalization in the stimuli difficulty. The results of CCF between each signal and the task showed that: the power of Alpha rhythm increased during the rest period, as found in previous literature [3], and the heart rate increased during test blocks, causing a negative correlation of RR series with the task [12]. The CCF of high frequency depth NIRS signals requires a more thorough analysis. The HF component appeared to be strictly modulated by the alternation of test and rest blocks and it mirrors the metabolic consumption of oxygen that takes place during test periods; in fact, when the subject is required to execute a cognitive task, there is an oxygen consumption, reflected in a decrease of O_2Hb concentration and an increase of HHb one. The LF component trend, confirming previous findings [13], is indeed representative

of the amount of oxygen supply that also takes places when carrying out a cognitive task. The subsequent evaluation of the time of activation of the different responses put into evidence the presence of a cascade of responses. Figure 3 shows an almost instantaneous response of CNS, represented by Alpha rhythm activation, followed by the response of ANS (RR series) and, at last, by the haemodynamic response, represented by changes in [O_2Hb] and [HHb]. The average response times are consistent with values previously reported [2,12]. These results lead to the hypothesis that [O_2Hb] is the pilot signal, whose trend is followed, in an opposite and delayed way, by [HHb]. Finally we considered the CCF between couple of signals, in order to evaluate the amount of shared information. The signs of the correlation values are consistent with the results of the correlation of each signal with the task. As shown in Figure 4, the highest correlation values are the ones between RR series and NIRS depth signals. It suggests that the signals of cardiovascular nature are the most influenced by the cognitive task. The presence of a correlation between RR series and [O_2Hb] surface could be representative of a common autonomic influence on the two signals. On the contrary we do not find any strong correlation between RR series and superficial [HHb]. It seems, then, that the RR series correlates only with [O_2Hb], probably due to the fact that changes in heart rate cause modulations in arterial compartement. [O_2Hb] results more affected by these changes, if compared to [HHb], as it is the most representative signal of the arterial compartment behavior [14]. The absence of a strong correlation between RR series and Alpha rhythm could be explained with the different origin of the two signals, respectively ANS and CNS. It seems, then, that there is no mirroring of cardiac activity in EEG. The time courses of Alpha rhythm and NIRS depth signals show the presence of a decrease in neuronal synchronization (reduction in Alpha power) and a reduction in O_2Hb concentration and increase in HHb one during test period. These results could mirror a metabolic economy: synchronized membrane oscillations could, in fact, be more energetically advantageous [3]. That could explain why there is an increase in synchronization in rest periods, coupled with metabolic consumption. The higher correlation of Alpha and HHb, compared to O_2Hb, is also reported in [3].

V. Conclusion

This study presents an investigation of the mechanisms of neurovascular and autonomic responses to a divided attention cognitive task, using a multimodal approach. The activation of a cascade of responses confirms the presence of the involvement of several systems, each one characterized by a different time delay: instantaneous neural electrical response, autonomic response and a slower haemodynamic response. The correlations between couple of signals show that the different responses to the task are not independent. In fact, considering Alpha rhythm, RR series and [O_2Hb]and [HHb], a desynchronization of Alpha rhythm, a reduction in [O_2Hb] and an increase in [HHb] and Heart Rate during test blocks are noticed. These phenomena somehow embed metabolic consumption information and show dynamics clearly different from what happens during rest phases. Considered these preliminary results, the proposed task seems to be a valuable tool for the investigation of brain activation during divided attention task. This cognitive function seems to be a valid candidate for studying neurovascular coupling, even if the big variability of physiological signals, mirrored in high standard errors, makes this aim really hard and prevents the research from finding the same trend in the whole studied group.

References

[1] Obrig H.,Israel H., Kohl-Bareis M., Uludag K., Wenzler R., Müller B., et al., (2002), Habituation of the visually evoked potential and its vascular response: implications for neurovascular coupling in the healthy adult, *Neuroimage*, 17(1): 1-18.

[2] Izzetoglu M, Bunce SC, Izzetoglu K, Onaral B, Pourrezaei K., (2007), Functional brain imaging using near-infrared technology., *IEEE Eng Med Biol,* 26(4):38-46.

[3] Moosmann P., Ritter P., Krastel I., Brink A., Thees S., Blankenburg F. et al., (2003), Correlates of alpha rhythm in functional magnetic resonance imaging and near infrared spectroscopy, *NeuroImage*, 20:145-158.

[4] Sarter M., Turchi J., (2002), Age and dementia –associated impairments in divided attention: psychological constructs. Animal models, and underlying neuronal mechanisms, Dementia and geriatric cognitive disorders, 13:46-58.

[5] Jöbsis F.F., (1977), Non invasive, infrared monitoring of cerebral and myocardial oxygen sufficiency and circulatory parameters, *Science,* 198: 1264.

[6] Zimmermann P., Fimm B., (1992), Handbuch der testbatterie sur Aufmerksamkeitsprüfung [Manual for the attention assessment test battery], Psytest, Herzogenrath.

[7] Re R., Contini D., Spinelli L., Caffini M., Cubeddu R., Torricelli A., (2010), A compact time-resolved system for near infrared spectroscopy based on wavelength space multiplexing. Review of Scientific Instruments 81, 113101.

[8] Baselli G., Cerutti S., Civardi S., Lombardi F., Malliani M., Merri M., Pagani M., Rizzo G., (1987), Heart rate variability signal processing: A quantitative approach as an aid to diagnosis in cardiovascular pathologies, *Int J of Bio-Medical Comp*, 20(1): 51-70

[9] Contini D., Torricelli A., Pifferi A., Spinelli L., Cubeddu R., (2007), Novel method for depth-resolved brain functional imaging by time-domain NIRS, In diffuse Otical Imaging of Tissue, Briaan W. Pogue, Rinaldo Cubeddu Editors, Proc. SPIE Vol. 6629,662908

[10] Hohnsbein J., Falkenstein M., Hoormann J., Blanke L.,(1991), Effects of crossmodal divided attention on late ERP components. I.Simple and choice reaction tasks, *Electroencephalography and Clinical Neurophysiology*, 78:438-446.

[11] Loose R., Kaufmann C., Auer D.P., Lange K.W., (2003), Human prefrontal and sensory cortical activity during divided attention tasks, *Human Brain Mapping,* 18:249-259.

[12] Moody M., Panerai R.B., Eames P.J., Potter J.F., (2005), Cerebral and systemic hemodynamic changes during cognitive and motor activation paradigms, *Am J Physiol Regulatory Integrative Comp Physiol,* 288:1581-1588.

[13] Schreppel T., Egetemeir J., Scheckelmann M., Plichta MM., Pauli P, Ellgring H. et al., (2008), Activation of the prefrontal cortex in working memory and interference resolution processes assessed with near-infrared spectroscopy, *Neuropsychobiology*, 57(4):188-193.

[14] Franceschini M.A., Fantini S., Thompson J.H., Culver J.P., Boas D.A., (2003), Hemodynamic evoked response of the sensorimotor cortex measured noninvasively with near-infrared optical imaging, *Psychophysiology*, 40:548-560.