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Non-invasive brain cortex hemodynamic monitoring: A step towards motor disorder assessment via TD fNIRS

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Summary. — The state of the art in diagnosing motor impairments involves looking for anomalies as the patient performs particular movements. However, subjectivity of perception, which is influenced by the operator's experience, has an impact on this procedure. A more rigorous approach involves monitoring cerebral response to motor stimuli by functional Magnetic Resonance Imaging (fMRI). However, given the bulkiness of current fMRI devices, this solution forces the subject to maintain a static condition, limiting the range of response. Moreover, the temporal resolution of such acquisition is often sub-optimal in following fast hemodynamic variations in short motor tasks. In this framework, time-domain functional near-infrared spectroscopy (TD fNIRS) that exploits the diffusion of picosecond laser pulses in cerebral tissue allows for quantitative and non-invasive acquisition of brain functional activity. Given the latest hardware development, it is now possible to exploit compact and wearable TD-fNIRS devices allowing for real time brain monitoring of unconstrained moving subjects. To assess the potential of the TD fNIRS technique in the field of motor disorders, we studied motor cortex hemodynamic response functions on healthy subjects performing standard physiotherapy protocols and simple motor tasks including goal-oriented and non-goal-oriented activities.

1. – Introduction

Motor disorders are a diverse group of conditions that affect the ability to control movements and posture in humans. Several aspects of the human body are impacted by physical impairments, including the loss of coordination, limb movement issues, and more generally compromised muscular functions. Nowadays, motor dysfunction's diagnosis is ascertained by a medical doctor, and it is mainly performed through meticulous observation of the patients executing basic and standardized movements to evaluate their motor

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coordination status and the efficiency of their motor activity. However, these procedures are highly dependent on the medical doctor's or physiotherapist's expertise, may lack objectivity, and require substantial training to be effectively applied [1]. Since the nervous system plays a critical role in controlling movement and posture, damage or dysfunction to any part of the cerebral motor cortex can lead to motor disabilities. Brain imaging examinations such as function magnetic resonance imaging (fMRI) may be used to evaluate the structures and function of the brain in order to assess the extension and type of lesion. This technique carries the drawback of severely restricting patient's motions mainly due to constraints caused by the design of the equipment and being prone to motion artifacts. To address these limitations, time domain near-infrared spectroscopy (TD-NIRS) has been proposed as a novel promising approach to non-invasively investigate on specific brain activities. TD-NIRS is a branch of NIRS technique, which exploits the property that the information about the depth reached by a detected photon is encoded in its arrival time. TD-NIRS is able to discriminate between deep and superficial layers of the brain and determine the absolute concentrations of the chromophores. Recent technological advancements have led to the development of compact TD-NIRS devices that can be worn like a backpack, overtaking historical limitation related to bulkiness and expensiveness of such devices and technology, allowing for more convenient and portable use [2]. In this study, two TD-NIRS devices were used either in pairs or as stand-alone devices to monitor different brain regions. The measurements proposed in this article included common motor tasks which are also used in physiotherapy clinics for patient rehabilitation, such as forward/backward walking and arm raising with/without grasping, to quantify complex functional activation. The aim of the experiment was to provide evidence of the device capability to distinguish different motor exercises with varying cognitive demands.

2. – Materials and method

2·1. *Device*. – The TD-NIRS platform used in this study is a compact and battery-operated single channel dual wavelength device (NIRSBOX, PIONIRS s.r.l., Italy) [3], in which the reliability of device measurements was widely tested both on phantoms [4] and in-vivo [2]. It is equipped with two pulsed laser diodes operating at 685 nm and 830 nm, and a time-to-digital converter with a temporal resolution of 10 ps to record the Distribution Time of Flight (DToF). The Full Width at Half Maximum (FWHM) of the Instrument Response Function (IRF) is below 200 ps. The device is placed in contact with the tissue through the optical fibers and a custom probe (PIONIRS s.r.l., Milan, Italy), with a source-detector distance of 3 cm.

2·2. *Protocol*. – The measurement settings were configured with a single channel, probing a specific area, associated with the motor activation for upper and lower limbs. Specifically, C3 position, as defined by the 10/20 EEG system, was used to investigate upper limb activation, while the C1 position was used to investigate lower limb activation respectively for the two tasks. In the arm raising task, a second channel was added, placed on the prefrontal region to monitor any global systemic effect involved in the prefrontal cortex (Fp2) area during the tasks. The present study involved three healthy volunteers who performed a protocol consisting of two exercises: forward/backward walking and arm raising with/without grasping, repeated 10 times each. Each exercise was divided into two phases. During the first phase of the forward/backward walking task, participants were instructed to walk in a straight line for 20 s. In the second phase, they were asked to walk backward for the same duration. During the 1st phase of the arm raising task, the participants were asked to return directly to the resting position, while in the other phase, they were instructed to grasp an object before returning to the resting position. The arm raising task consisted in moving the hand longitudinally from a resting position to the height of the eyes while keeping the arm straight (before returning to the resting position) within a time limit of 5 s.

2˙3. *Analysis and results*. – The convolved photon path-length approach was used to analyze the raw DToF, for separating information of deep and superficial layers [5]. Figure 1 reports the hemodynamic responses of the deep layers (cerebral tissue), averaged across the subjects. The hemodynamic response function (HRF) for O_2Hb and HHb activations for both protocols was obtained by an adaptive fitting technique that was motivated by the approach suggested by Uga *et al.* [6]. The HRF is the result of a linear combination of three gamma functions: one positive for main activation, and two negative for initial dip (before the main activation peak) and undershoot (relaxation after the main activation peak). An initial guess of the HRF is obtained by convolving the curve with a boxcar function matching task length. The Levenberg-Marquardt algorithm is then applied to minimize the error between the theoretical and measured HRFs for both oxygenated and deoxygenated hemoglobin; the amplitude and peak delays of the three gamma functions are set as fitting parameters. Forward/backward walking exercises were performed to detect motor cortex activity associated to lower limb movements, while arm raising and grasping were performed to measure cerebral efforts during goal-oriented and

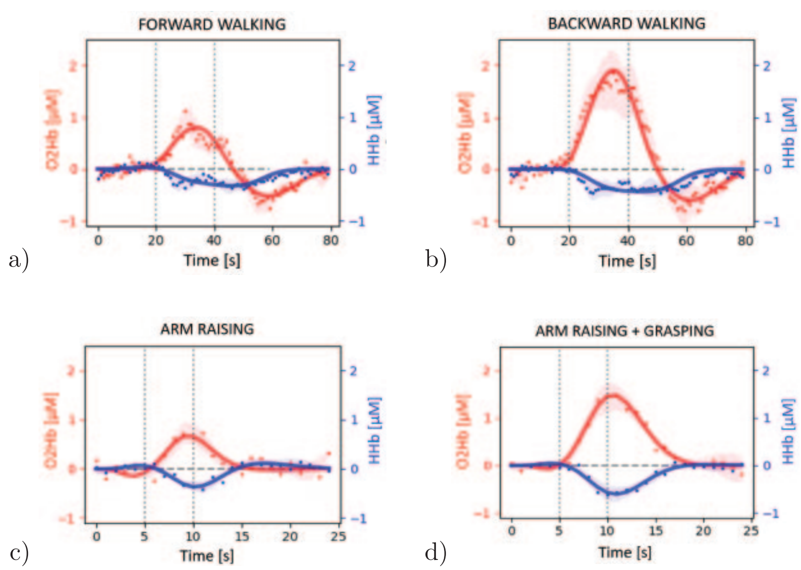

Fig. 1. – The outcomes related to participants' performances during the tasks of forward/backward walking are displayed in (a) and (b), while (c) and (d) exhibit the results related to arm raising with/without grasping. Analyzed data for the concentrations of O_2Hb (red) and HHb (blue) are shown as round dots, while thicker lines and shaded areas show the fitted HRF (sect. **2**˙3) and standard deviations within the average, where each concentration value shown on the timeline of the graphs is the result of averaging across three subjects and the ten repetitions, normalized to the baseline.

non-goal-oriented tasks. The data collected from the probe placed on the motor area reveal a substantial difference between the neuro-functional engagement needed for both tasks. One can observe that the absence of visual assistance during backward walking requires the brain to concentrate more on the task, resulting in increased cognitive effort. On the other hand, when a subject is required to grasp an object, the coordination and complexity of the movement increases the demand for oxygen to the brain, leading to greater cognitive demand. In the second probe, placed in the prefrontal site, the results (not shown) did not highlight any systemic activation, indicating that the observed hemodynamic responses are related to the brain effort induced by motor activity.

3. – Conclusion

The results of this pilot study demonstrated the effectiveness of the technique in detecting changes in brain activation patterns associated with different motor tasks. Specifically, the instrument was able to accurately detect differences in motor cortex involvement between forward/backward walking exercises, as well as distinguish between arm movements goal-oriented/non-goal-oriented. This technique can be considered as a promising alternative to the traditional methods of diagnosis and treatment for people with motor difficulties through the use of a portable, battery-operated TD-NIRS device that can monitor brain activity in real time. This can be useful in clinical settings, where the ongoing observation of cerebral effort associated with motor activity is crucial for patient's care and rehabilitation, providing physiotherapists and hospital staff with a helpful tool allowing the objective measurement of cerebral motor cortex activations. Moreover, this technology may support in designing more accurate and customized treatment plans, offering a solution to quantitatively assess the effectiveness of physiotherapy treatment on motor disorder injury. The low number of subjects enrolled in this study strongly limits its statistical significance, and therefore the reliability and reproducibility of the results. This emphasizes the requirement for additional study to support the application of this technology in a hospital ward. Future studies will aim to establish benchmarks in motor performance assessment across a larger number of healthy subjects to be compared in future therapeutic applications in pathological patients. Additionally, in this work, the hemodynamic response was acquired using a single detection channel, thereby limiting the analysis to a restricted cerebral region. In order to attain a more exhaustive comprehension of the neural mechanisms associated with the motor tasks, it would be necessary to increase the number of detection channels and extend the investigated region.

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