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TMS: A navigator for NIRS of the primary motor cortex?

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ABSTRACT

Near-infrared spectroscopy (NIRS) is a non-invasive optical imaging technique, which is increasingly used to measure hemodynamic responses in the motor cortex. The location at which the NIRS optodes are placed on the skull is a major factor in measuring the hemodynamic responses optimally. In this study, the validity of using transcranial magnetic stimulation (TMS) in combination with a 3D motion analysis system to relocate the TMS derived position was tested. In addition, the main goal was to quantify the advantage of using TMS to locate the optimal position in relation to the most commonly used EEG C3 position. Markers were placed on the TMS coil and on the head of the subject. In eleven subjects, a TMS measurement was performed to determine the individual motor-evoked potential center-of-gravity (MEP-CoG). This procedure was repeated in nine subjects to test the validity. Subsequently, hemodynamic responses were measured at the MEP-CoG position and at the C3 position during a thumb abduction and adduction task. On average, the MEP-CoG location was located 19.2 mm away from the C3 position. The reproducibility study on the MEP-CoG relocation procedure revealed no systematic relocations. No differences in early and delayed hemodynamic responses were found between the C3 and MEP-CoG position. These results indicate that using TMS for NIRS optodes positioning on the motor cortex does not result in higher hemodynamic response amplitudes. This could be explained if NIRS and TMS assess slightly different functions.

1. Introduction

Near-infrared spectroscopy (NIRS) is a non-invasive optical imaging method, relatively new in neuroscience studies compared to fMRI, PET, and EEG. Using light in the near-infrared range, it measures local hemodynamic changes in oxy-hemoglobin (OHb) and deoxy-hemoglobin (HHb) (Cope and Delpy, 1988) and thereby indirectly the local neural activity (Villringer and Dirnagl, 1995). The advantage of NIRS being portable, non-invasive, and less expensive compared to fMRI and PET makes NIRS an interesting neuro-imaging technique in, for example, the field of brain computer interfacing (BCI). In addition, NIRS does not require stringent motion restrictions and the subject preparation time can be much smaller compared to EEG.

During the last decades, several studies have performed near-infrared spectroscopy measurements on the prefrontal cortex (Hoshi and Tamura, 1997; Herrmann et al., 2005; Hatakenaka et al., 2007), the visual cortex (Colier et al., 1999b; Wolf et al., 2002; Herrmann et al., 2008), and the motor cortex (Obrig et al., 1996; Jasdzewski et al., 2003; Holper et al., 2009). Most studies revealed the typical hemodynamic response, an increase in OHb and a decrease in HHb, while performing cognitive, visual, or motor tasks. However, the results are not always consistent and some studies revealed opposite changes in OHb and HHb in one or more subjects. For example, a study by Hoshi et al. (1994) revealed decreases in both the HHb and OHb responses in nine of 33 subjects over frontal regions during a mental arithmetic task. Quaresima et al. (2005) found the typical activation response in four of eight subjects, whereas various unexpected patterns of activation were found in the other four subjects (lack of HHb decrease or even an HHb increase). A study by Bauernfeind et al. (2008) revealed opposite hemodynamic changes for the prefrontal cortex during mental arithmetic tasks in 11 of 12 subjects, and the other subject revealed decreases in both HHb and OHb. Similarly, a study by Sato et al. (2005) revealed that the motor cortex also shows substantial intersubject variability of the hemodynamic responses. The typical OHb increase was seen in 90% of the cases; however, the decrease in HHb was noted in only 76% of the cases. Although most studies found the typical hemodynamic response of an increase in OHb and a

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decrease in HHb, the studies described above indicate that optical imaging could result in unexpected observations.

The positioning of the optodes is difficult and might be a reason for the unexpected observations found in hemodynamic responses. Most studies use the international 10/20 system for EEG recordings (and skull surface landmarks) to localize the target cortex and position the NIRS optodes. Subsequently, functional oxygenation was controlled by executing a simple task to reveal hemodynamic responses. If no hemodynamic changes were detected, the optodes were moved several millimeters and the task was executed again. This was repeated until a consistent hemodynamic response was found (Colier et al., 1999a; Mackert et al., 2008; Shibuya et al., 2008). Other studies focused on decreases in HHb to ensure the correct location of the channel (Kleinschmidt et al., 1996). Although these methods roughly estimate anatomical positions, essential signals could be easily overlooked and there is no guarantee that the best response was measured. A study by Strangman et al. (2003) using Monte Carlo simulations on a realistic head model reported that NIRS signal levels drop substantially when off target by more than 10 mm in either the longitudinal or transverse direction. They also showed that errors in the NIRS data increase when the NIRS optodes are positioned further away from the location of hemodynamic change. Especially for the application of NIRS in BCI's, the most accurate signal is needed in order to obtain good classification scores. Hence, there is a need for a reproducible procedure revealing more accurate results without underestimations of the real changes in OHb en HHb.

To increase the spatial specificity in NIRS imaging, a combination with transcranial magnetic stimulation (TMS) is suggested to map the functional cortex. TMS has been widely used as a tool for functional brain mapping because of its accurate detection of activation sites from the surface of the scalp (Barker et al., 1985; Rothwell, 1997; Boroojerdi et al., 1999). In a study by Neggers et al. (2004) TMS results were also compared to fMRI data of the same subjects. They found that the distance between the center of gravity (CoG) of the motor evoked potential (MEP) responses and the location marked on the scalp overlying maximum fMRI activation was on average less than 5 mm. Since the spatial resolution of NIRS is worse compared to fMRI, the 5 mm difference between the TMS position and the position fMRI revealed is negligible using NIRS. Therefore, combining TMS with NIRS could, in principle, result in functional NIRS imaging with a better positioning of the optodes.

A previous study by Akiyama et al. (2006) combined these techniques. Hemodynamic responses were measured at seven channels during repeated hand grasping. The center channel covered the optimal position that a TMS procedure revealed. Considering the typical hemodynamic response, no differences were found in the increase in OHb and decrease in HHb between the channel that covered the TMS location and the surrounding channels. However, in the period between 1 and 3 s after task initiation a significant increase in HHb was found only at the TMS location. This indicates a period of early oxygen consumption, called the early response phase. Therefore, the authors concluded that they found the most optimal NIRS position. However, a simultaneously significant decrease in OHb during the early response phase was not found. The delayed response phase, previously mentioned as the typical response, did not reveal differences in amplitude between the TMS location and the surrounding channels. Furthermore, no other previous NIRS studies with motor tasks revealed an early response phase, making it questionable whether TMS has additional value. In addition, no comparison was made with results from the conventional position, using the 10–20 EEG electrode positioning system.

In order to quantify the advantages of using TMS for the localization of the NIRS optodes, the present study compares the hemodynamic responses measured at the TMS location and at the most commonly used C3 position from the EEG 10–20 system. First, a TMS measurement was performed in each subject to determine the optimal TMS location (Boroojerdi et al., 1999). Secondly, hemodynamic responses were measured with NIRS during thumb adduction and abduction tasks. The hemodynamic response amplitudes of the channel covering the TMS recommended position and the channel covering the C3 position were compared. In addition to the main goal, we examined the reproducibility of the TMS procedure that we used in this study by repeating the TMS procedure in the majority of the participants of the present study.

2. Materials and methods

2.1. Study subjects

Twelve healthy right handed subjects (7 males and 5 females, mean (SD) age of 26.1 (4.3) years) participated in the study. All subjects gave their written informed consent after explanation of the protocol and risks and the study was in accordance with the Declaration of Helsinki.

During the study, two positions on the head were determined for the localization of the NIRS channels. One for the TMS defined position and one for the conventional location. A TMS measurement was performed in order to determine the position that covers the motor cortex of the right hand, the so-called center of gravity of the motor-evoked potentials (MEP-CoG) (Boroojerdi et al., 1999; Akiyama et al., 2006). To determine the reproducibility of the TMS procedure used in this study, in nine subjects a second TMS procedure was performed. Approximately one week later, after analysis of the TMS data, NIRS recordings were performed. Hemodynamic responses were measured during hand movement tasks at the MEP-CoG position and at the C3 position of the 10–20 EEG electrode positioning system, the conventional location.

2.2. TMS procedure

Focal TMS was delivered by an experienced investigator (M.M.) using a figure of eight shaped coil with loops of 7 cm in outer diameter. The coil was connected to a single pulse stimulator, the Magstim 200 (The Magstim Company Ltd., UK). During stimulations, the handle of the coil was pointing backwards and approximately 45 degrees lateral from the mid-line following the procedure described by Kaneko et al. (1996). EMG recordings were measured at the relaxed right abductor pollicis brevis (APB) muscle, because this muscle was involved in the task that was used in this experiment (thumb abduction and adduction). Ag/AgCl surface electrodes (Kendall ARBO H124SG, Tyco Healthcare Ltd., Neustadt Donau, Germany) were used and wireless EMG signals were recorded with ZeroWire (Aurion, Italy). An eight-camera 3D motion analysis system (Vicon Motion Systems Ltd., Oxford, UK) was used to determine the position of the TMS-coil and the position of the head in all trials. Three markers were placed at anatomical landmarks of the head (the two pre-auricular points and the frontal bone between the eyebrows) and another three markers were placed at the coil. Hence, the exact position on the skull at which the pulse was applied could be calculated from the position of the three markers on the coil related to the three markers on the head.

In order to determine the location of the MEP-CoG, first the resting motor threshold was determined by searching for the minimum intensity necessary to induce a response of at least 50 μV in three out of five consecutive trials (location C3). Later TMS pulses were applied with an intensity of 120% of the resting motor threshold. A grid of 5×5 points, one cm apart, was marked on a tightly fitting swimming cap on the head with the center point located on C3. In consecutive order, each of the 25 points was stimulated twice