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A validation study of the use of near-infrared spectroscopy imaging in primary and secondary motor areas of the human brain

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ABSTRACT

The electroencephalographically measured Bereitschafts (readiness)-potential in the supplementary motor area (SMA) serves as a signature of the preparation of motor activity. Using a multichannel, noninvasive near-infrared spectroscopy (NIRS) imager, we studied the vascular correlate of the readiness potential.

Sixteen healthy subjects performed a self-paced or externally triggered motor task in a single or repetitive pattern, while NIRS simultaneously recorded the task-related responses of deoxygenated hemoglobin (HbR) in the primary motor area (M1) and the SMA.

Right-hand movements in the repetitive sequence trial elicited a significantly greater HbR response in both the SMA and the left M1 compared to left-hand movements. During the single sequence condition, the HbR response in the SMA, but not in the M1, was significantly greater for self-paced than for externally cued movements. Nonetheless, an unequivocal temporal delay was not found between the SMA and M1.

Near-infrared spectroscopy is a promising, noninvasive bedside tool for the neuromonitoring of epileptic seizures or cortical spreading depolarizations (CSDs) in patients with epilepsy, stroke, or brain trauma because these pathological events are associated with typical spatial and temporal changes in HbR. Propagation is a characteristic feature of these events which importantly supports their identification and characterization in invasive recordings. Unfortunately, the present noninvasive study failed to show a temporal delay during self-paced movements between the SMA and M1 as a vascular correlate of the readiness potential. Although this result does not exclude, in principle, the possibility that scalp-NIRS can detect a temporal delay between different regions during epileptic seizures or CSDs, it strongly suggests that further technological development of NIRS should focus on both improved spatial and temporal resolution.

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1. Introduction

In 1965, Kornhuber and Deecke discovered a slow negative electro-encephalography (EEG) activity that preceded self-initiated movement

for up to 2 s [1]. This phenomenon was termed Bereitschaftspotential or readiness potential and is assumed to be the electrophysiological correlate of increased neural activity related to readiness, preparation, and execution of movement. In support of this hypothesis, the duration of the Bereitschaftspotential is reduced when the movement is externally cued [1,2]. The Bereitschaftspotential is subclassified into two components. The first component (Bereitschaftspotential 1, BP1, or readiness field 1) is recorded with maximum amplitude over the midline vertex area 2 s prior to movement onset and is assumed to originate from frontal medial wall areas including the supplementary motor area (SMA). Its amplitude correlates positively with movement complexity and bimanual synchronization [3–8]. About 500 ms prior to movement, the activity becomes lateralized contralateral to the movement, which

reflects activation of the primary motor cortex (M1). This lateralization is termed Bereitschaftspotential 2, BP2, or readiness field 2 [2,9–12]. The two components of the readiness potential demonstrate the hierarchy of the motor system, with the activation of the SMA prior to the activation of the M1, and indicate that the M1 is regulated by higher order motor areas. These EEG findings correspond with whole-scalp magnetoencephalographic observations [13].

Similarly, functional MRI (fMRI) studies demonstrated that changes of the blood-oxygen-level-dependent (BOLD) signal in the SMA precede BOLD changes in the M1 during voluntary finger movement. For instance, Wildgruber et al. [14] found a latency of 0.8 s of the SMA activity prior to the M1 activity. In another study, Weilke et al. [15] investigated the time course of the BOLD signal referring to the (rostral) pre-SMA, (caudal) SMA proper, as well as the M1 and demonstrated nearly constant temporal delays of 0.8 s between the SMA proper and M1, and 2.0 s between the pre-SMA and M1 at half-maximum activation during self-paced finger tapping. In a series of studies, Cunnington and colleagues showed that the BOLD response in the SMA preceded that in the M1 for both self-initiated and externally cued activation and demonstrated that the hemodynamic delay varied with the type of movements [16–18]. These findings were confirmed by a study using simultaneous measurements of fMRI and high-density EEG [11].

Anatomically, the SMA and M1 are partly located on the convexity of both cerebral hemispheres, which allows investigation of their hemodynamic responses with good temporal resolution using scalp-near-infrared spectroscopy (NIRS) [19–22]. Near-infrared spectroscopy, first described by Jöbsis in 1977, is an optically based technique which captures alterations of oxygenated (HbO) and deoxygenated (HbR) hemoglobin concentrations related to changes in regional cerebral blood flow (rCBF). Because near-infrared light penetrates human tissue rather well, NIRS allows us to investigate task-related local oxygenation changes in the human cortex through the intact skull [19,23,24]. Functional cerebral activation leads to a focal increase in total hemoglobin (Hb_{tot}) and HbO, a decrease in HbR in correlation with increased rCBF, and a disproportion between blood perfusion and metabolism in functionally activated, i.e., neurally engaged, brain areas [19,21,25–27]. Both the measured NIRS signal and the fMRI-BOLD signal depend largely on the HbR parameter and are therefore capable of indirectly detecting regions of changed neural activity.

The present study focused on the temporal pattern of hemodynamic responses in the M1 and SMA during different movement execution tasks (self-guided vs. externally triggered and single sequence vs. multiple sequences). The following hypotheses were tested by means of NIRS: (i) NIRS imaging is a suitable tool for identifying and differentiating the cortical areas of the primary and secondary motor systems involved in voluntary movements; (ii) compared to externally cued movements, self-paced movements lead to stronger hemodynamic responses in the M1 and SMA; and (iii) as a vascular correlate of the readiness potential, the onset of the hemodynamic response in the SMA precedes the response in the M1.

2. Material and method

2.1. Participants

Seven male and 9 female healthy volunteers aged 20–31 years (mean: 24.7 years, SD ± 2.96 years) participated in this study. Research consents were obtained. None of the subjects suffered from migraine or any other neurological or vascular disease, and none showed evidence of an idiopathic vascular disease in the family. All participants were strongly right-handed according to the Edinburgh handedness inventory [28]. Six of them were moderate smokers and were asked not to smoke at least 3 h before their scheduled arrival time at the laboratory. All research was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all participants, and the

study was approved by the Ethics Committee of the Charité, Universitätsmedizin Berlin.

2.2. Experimental setup and paradigm

The investigations were performed in a dark and quiet room. Participants were asked to lie comfortably in a supine position, to keep their eyes closed, to breathe smoothly, and to avoid any noninstructed movements. This procedure minimized fluctuations of systemic parameters like blood pressure, heart rate, respiration, and galvanic skin responses that might affect the NIRS signal [29]. In particular, participants were instructed to avoid head and jaw movements because these movements are generated in cortical subfields of the M1 close to the cortical subfield which generates movements of the upper limb. All experiments were carried out in one session without any changes in optode position, subject position, or experimental setup.

Each subject participated in four experiments, consisting of a sequential finger-to-thumb opposition task performed either in a singular or repetitive pattern and either in a self-paced or externally triggered manner. Externally triggered movements were cued by a 600-millisecond vibrotactile stimulus applied by a vibration device to the left lower leg. This position was chosen because the primary somatosensory representation area of the left lower leg is located outside of the cortical area where the NIRS signal was recorded.

In order to activate both primary and higher-order motor areas, participants performed a sequence of complex finger-to-thumb oppositions (2-3-2-4-2-5-2-4-2-5-2-4-2-3-2-4; 2 — index finger, 3 — middle finger, 4 — ring finger, 5 — little finger) either with one hand or, synchronously, with both hands. A complex sequence of finger-to-thumb oppositions was chosen because cortical motor areas are more active during complex finger movement than during simple finger movement tasks [7,8]. Prior to the experiment, participants practiced the finger tapping task until they were able to accomplish one cycle of the tapping sequence in 5 s. Each subject performed four experimental manipulations:

Experiment 1 *Externally triggered, single sequence, both hands synchronously*
In response to the external trigger, subjects had to execute the sequence of finger-to-thumb opposition movements simultaneously with both hands. This was repeated 80 times, interspersed with variable intertrial intervals (8–15 s) without movement.

Experiment 2 *Self-paced, single sequence, both hands synchronously*
Similar to experiment 1, the condition consisted of 80 repetitions of single finger-to-thumb opposition sequences. No external trigger was applied, forcing the participants to perform the task in a self-paced manner. Participants were requested to vary the intertrial interval in analogy to experiment 1.

Experiment 3 *Externally triggered, repetitive sequence vs. rest, right hand*
In this condition, participants alternated 23 times between a 20-second finger-to-thumb opposition sequence and a 20-second resting period with the right hand. The onset of the alterations was indicated by the vibration stimulus.

Experiment 4 *Externally triggered, repetitive sequence vs. rest, left hand*
Experiment 4 was identical to experiment 3, except that the movement was performed with the left hand.

2.3. Near-infrared spectrometer

A NIRS imaging system was developed comprising 16 laser diodes and 8 avalanche photon detector modules. To optimize light intensity, 16 laser drivers (based on a chip by IC-Haus GmbH, Bodenheim, Germany) allowed fast switching with rise and fall times of ≈3 µs. Eight laser diodes at 760 nm (RLT7605MG, Roithner Lasertechnik, 5 mW, Vienna, Austria) and 850 nm (RLT8505MG, Roithner Lasertechnik,