

## Task complexity relates to activation of cortical motor areas during uni- and bimanual performance: A functional NIRS study

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### ABSTRACT

Hand motor tasks are frequently used to assess impaired motor function in neurology and neurorehabilitation. Assessments can be varied by means of hand laterality, i.e. unimanual or bimanual performance, as well as by means of task complexity, i.e. different degrees ranging from simple to complex sequence tasks. The resulting functional activation in human primary motor cortex (M1) has been studied intensively by traditional neuroimaging methods.

Previous studies using functional near-infrared spectroscopy (fNIRS) investigated simple hand motor tasks. However, it is unknown whether fNIRS can also detect changes in response to increasing task complexity. Our hypothesis was to show that fNIRS could detect activation changes in relation to task complexity in uni- and bimanual tasks.

Sixteen healthy right-handed subjects performed five finger-tapping tasks: unimanual left and right, simple and complex tasks as well as bimanual complex tasks. We found significant differences in oxy-hemoglobin (O<sub>2</sub>Hb) and deoxy-hemoglobin (HHb) concentration in the right hemisphere over M1. Largest O<sub>2</sub>Hb concentration changes were found during complex (0.351 ± 0.051 μmol/l) and simple (0.275 ± 0.054 μmol/l) right hand tasks followed by bimanual (0.249 ± 0.047 μmol/l), complex (0.154 ± 0.034 μmol/l) and simple (0.110 ± 0.034 μmol/l) left hand tasks. Largest HHb concentration changes were found during bimanual (−0.138 ± 0.006 μmol/l) tasks, followed by simple right hand (−0.12 ± 0.016 μmol/l), complex left (−0.0875 ± 0.007 μmol/l), complex right (−0.0863 ± 0.005 μmol/l) and simple left (−0.0674 ± 0.005 μmol/l) hand tasks.

We report for the first time that fNIRS detects oxygenation changes in relation to task complexity during finger-tapping. The study aims to contribute to the establishment of fNIRS as a neuroimaging method to assess hand motor function in clinical settings where traditional neuroimaging methods cannot be applied.

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### Introduction

Hand motor tasks are frequently used to train and assess impaired motor function in neurology and neurorehabilitation. Traditional neuroimaging methods such as functional magnetic resonance imaging (fMRI) (Mansfield and Maudsley, 1977; Lauterbur, 1986; Jäncke et al., 2006; Horenstein et al., 2009), positron emission tomography (PET) (Phelps et al., 1975; van Mier et al., 1998), electroencephalography (EEG) (Gerloff and Andres, 2002), and magneto encephalography (MEG) (Waldert et al., 2007) have therefore been used intensively to study hand motor tasks.

Examples of sequential hand motor tasks using finger-tapping are single finger or thumb tapping, abduction of index finger, thumb to digit opposition, and tapping of the thumb against single fingers. Task conditions can thereby be varied both by means of laterality, i.e. unimanual or bimanual performance, as well as by means of task

complexity, i.e. different degrees of sequence difficulty. Both laterality and complexity appear to strongly affect associated functional changes in the primary motor cortex (M1, ipsilateral and contralateral) and the broader cortical and subcortical networks engaged in motor output, such as supplementary motor area (SMA) and premotor area (PMA).

In unimanual tasks, fMRI and PET studies show hemispheric asymmetry with predominant activation of the contralateral hemisphere controlling the tapping hand (Colebatch et al., 1991; Rao et al., 1993; Pulvermuller et al., 1995; Solodkin et al., 2001). Ipsilateral activation is found in M1 and additionally shifted laterally, ventrally, and anteriorly with respect to that observed during contralateral hand movements (Hess et al., 1986; Tinazzi and Zanette, 1998; Cramer et al., 1999; Muellbacher et al., 2000; Verstynen et al., 2005; Shibuya and Kuboyama, 2007). This may indicate stronger and broader activation of primary and secondary motor cortices (Witt et al., 2008).

In complex finger-tapping tasks, hemispheric asymmetry decreases, possibly due to additional recruitment of the ipsilateral hemisphere (Rao et al., 1993; Solodkin et al., 2001). Likewise ipsilateral activation results in a signal shifted laterally, ventrally, and anteriorly (Cramer et al.,

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1999; Verstynen et al., 2005). As tested in control measurements, the stronger activation in M1 seems to be specific to complex tasks and does not depend on the number of required muscles, i.e. the number of fingers used in a certain task (Verstynen et al., 2005).

A third factor influencing hemodynamic changes in hand motor task is hand-dominance. The signal appears to be stronger when tapping is performed with the non-dominant hand which may reflect a lateralization effect (Cramer et al., 1999; Verstynen et al., 2005; Park et al., 2008). Summarized, traditional neuroimaging data show that tasks with higher sequence complexity elicit stronger and less asymmetric activation pattern in motor areas.

Functional near-infrared spectroscopy (fNIRS) is a comparably young neuroimaging method. fNIRS utilizes the tight coupling between neuronal activity and regional cerebral blood flow (Villringer and Dirnagl, 1995) to measure regional hemodynamic changes in the brain's oxygenation state of oxy-hemoglobin (O<sub>2</sub>Hb) and deoxy-hemoglobin (HHb) (Jöbsis, 1977). Direct comparison between data based on NIR and traditional methods is difficult unless these methods are applied simultaneously. Therefore, single fNIRS results need to be carefully considered as preliminary with potential further relevance. A major potential of NIR based techniques is that they could facilitate assessments of motor function by offering the following advantages: NIR techniques 1) are noninvasive, 2) require low constraints of body movements, 3) are relatively low cost and 4) provide small, flexible and portable instrumentation for user-friendly applications in pre- and post-treatment monitoring, in ambulatory settings and even at the bedside (Wolf et al., 2007).

Previous studies using fNIRS confirmed results from traditional methods demonstrating functional oxygenation changes in response to simple motor activation tasks (Kleinschmidt et al., 1996; Maki et al., 1996; Obrig et al., 1996; Franceschini et al., 2003; Koenke et al., 2004; Li et al., 2005; Sato et al., 2007; Grefkes et al., 2008; Mackert et al., 2008; Shibuya et al., 2008). It is unknown, however, whether fNIRS can also detect changes in response to tasks with increasing complexity. Therefore, the aim of the present study was to provide data from healthy subjects showing that fNIRS can be used to assess not only activation in ipsi- and contralateral M1 in response to uni- and bimanual tasks, but also in relation to increasing task complexity. We expected to detect changes in blood oxygenation at different complexity levels ranging from highest changes in complex sequence tasks compared to lower changes in simple tasks.

The new insight revealed by this study is relevant for the diagnostic evaluation of neurological hand motor assessments which commonly include different degrees of task complexity. As the assessment of tasks with different complexity is widely used in neurology and neurorehabilitation (Umphred and Carlson, 2006), it remains an important issue to establish a reliable neuroimaging method. Such a method could be used to examine the cortical activation during the assessment and at the same time monitor treatment progress. This is currently not possible with traditional neuroimaging methods which are usually time- and resources-consuming, costly, and not applicable in certain patient populations, e.g. critical care patients or children. They require strict movement constraints and are not portable which renders them unsuitable for ambulatory settings and even more so for bedside use. In contrast, NIR based techniques promise a faster evaluation of motor function and less strenuous procedures. Especially patients requiring frequent ambulatory assessments following brain injury and children who cannot be assessed using traditional neuroimaging methods would benefit from NIR based techniques.

## Materials and methods

### Subjects

Eighteen healthy subjects participated in the study. Informed consent after explanation of risks and benefits was obtained from all

subjects prior to enrollment. The ethical committee of the canton of Zurich approved the study.

### Protocol

Experiments were conducted in a quiet and darkened room at the University Hospital Zurich. Each subject was measured once in one session. Subjects were asked to sit at a table, place their hands on the table and face a computer screen.

The fNIRS sensor was placed on the subject's head covering C3 according to the international 10–20 system (Jaspers, 1958), considering there currently being no other recommended method for positioning fNIRS sensors. Therefore, the international 10–20 system is commonly used for placement with good reproducibility even if it can only provide an approximation of the correct cortical location.

With the compact sensor of 3.75 mm length and 25 mm width, we assumed covering the cortical areas including M1, comprising the hand knob, as well as part of PMA. The subject's head was covered with a custom-made cap to adjust and fixate the sensor. Hairs under the sensor were carefully brushed away to avoid problems with signal detracting.

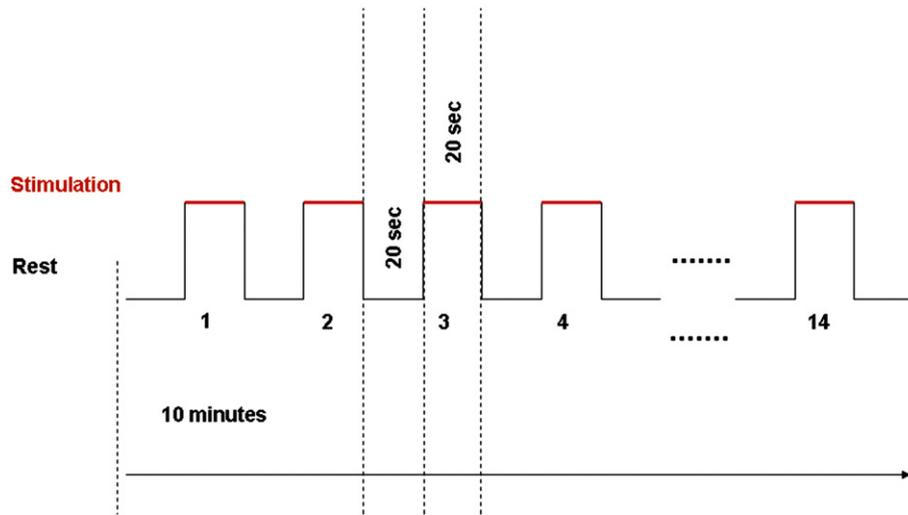
The experimental design comprised five conditions of finger-tapping conducted in a block paradigm (Table 1, Fig. 1). The order of the block paradigms was pseudo-randomized to avoid ordering effects. Each condition started with an instruction signal (1 s) after which stimulation periods (20 s) alternated with rest periods (20 s). Each condition lasted approx. 10 min, resulting in 14 stimulation and rest periods. Total measurement length for the five conditions was approx. 50 min. Between conditions, subjects were encouraged to take short breaks to prevent fatigue during finger-tapping.

All finger-tapping tasks were self-paced, however subjects were asked to perform finger-tapping with frequencies of approx. 3 Hz. Subjects were instructed to perform all tasks as precise and as fast as possible while avoiding errors. During all periods, subjects were reminded to avoid any movements not associated with the required tasks. Each subject performed finger-tapping tasks with increasing complexity as employed by previous studies (Hausmann et al., 2004; Lissek et al., 2007): two 'simple' unimanual (condition 1 and 2) and two 'complex' unimanual (condition 3 and 4) sequence finger-tapping tasks each first using the right and then the left hand. Each subject also performed one 'complex' bimanual (condition 5) sequence finger-tapping task using both hands.

In the unimanual 'simple' motor tasks, subjects were asked to press one button on a keyboard repetitively using their thumb over the whole stimulation period; first with their right hand (condition 1) and with their left hand (condition 2). In the unimanual 'complex' motor tasks, subjects were asked to press five buttons on the keyboard using all fingers in a predefined sequence; again, first with their right (condition 3) and then their left hand (condition 4): thumb, middle, pinky, index, ring finger, i.e. "1–3–5–2–4". This task is similar to that used in various fMRI studies of stroke and stroke recovery (Chollet et al., 1991; Weiller et al., 1993; Cao et al., 1998; Seitz et al., 1998). In the 'complex' bimanual motor task, subjects were asked to press eight buttons alternating with their right and left hand (condition 5): thumb, middle, index, ring finger, i.e. "1–3–2–4".

**Table 1**  
Five conditions of uni- and bimanual, simple, complex, finger-tapping tasks.

Condition	Hand side	Task complexity
1 (SR)	Unimanual simple right	Single: thumb (1)
2 (SL)	Unimanual simple left	Single: thumb (1)
3 (CR)	Unimanual complex right	Sequence: thumb, middle, pinky, index, ring finger (1–3–5–2–4)
4 (CL)	Unimanual complex left	Sequence: thumb, middle, pinky, index, ring finger (1–3–5–2–4)
5 (B)	Bimanual complex both	Sequence, alternating: thumb, middle, index, ring finger (1–3–2–4)



**Fig. 1.** Experimental design. Each condition consisted of 14 stimulation (20 s) alternating with rest periods (20 s). Duration of each condition was 10 min.

All tasks were carried out using a wireless numerical keyboard (Logitech® Cordless Number Pad) which allows measurement of finger-tapping using all five fingers. However, the bimanual task did not include the fifth finger, since tapping would have otherwise required a too large dislocation of the whole arm in relation to the keyboard. Subjects were trained for 5–10 min prior to measurements. All keystrokes were recorded and transferred to PC via USB and stored for further analysis.

Previous results demonstrated that the application of visual pacing stimuli results in a higher motor activation related to finger-tapping tasks than without pacing stimuli (Witt et al., 2008). In this study, all conditions were paced by visual stimuli generated by the software Presentation® and presented on a screen facing the subject. The visual stimulus ‘GO’ requested subjects to start finger-tapping at the beginning of the stimulation period, the visual stimulus ‘STOP’ requested subjects to stop finger-tapping at the beginning of the rest period.

*Behavioral measures*

Prior to the experiment, all subjects completed the Edinburgh Inventory (EHI) (Oldfield, 1971). During each condition, behavioral performances of the correct order of tapped sequences (target keys) were recorded and stored in the log files of Presentation® for further analysis.

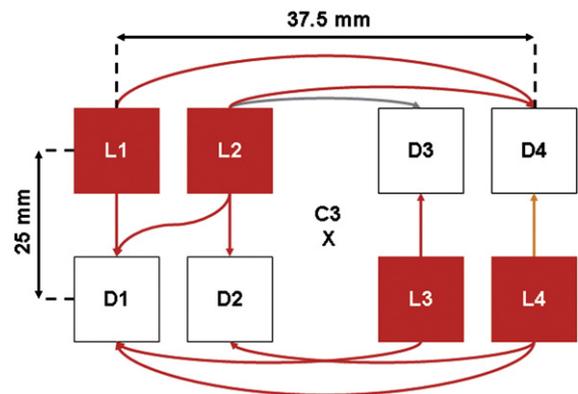
*Instrumentation*

A multi-channel continuous-wave (CW) fNIRS instrument, the MCP-II, developed by the Biomedical Optics Research Laboratory (BORL) was used (Haensse et al., 2005). In general, current available commercial and custom-built fNIRS differ with respect to their use and engineering, in particular regarding light sources, detectors, and instrument electronics. Three distinct types of fNIRS systems, each with its own strengths and limitations, have been developed: time-resolved, frequency-domain, and CW systems – the latter type being used in the present study. CW systems apply continuous or slow-pulse light to tissue and measure the amplitude attenuation of the incident light (Strangman et al., 2002a; Hoshi, 2003; Obrig and Villringer, 2003). Although CW instruments have certain limitations, such as providing less information than time-resolved or frequency-domain systems, they offer two advantages compared to time-resolved and frequency-domain systems that are beneficial for use in clinical and research settings: 1) the manufacturing is less expensive, and 2) the size of the sensor can be very small. We benefited from both advantages in the development of our fNIRS system. (For review and discussion over

existing methods and systems, see Strangman et al., 2002a; Hoshi, 2003; Obrig and Villringer, 2003; Boas et al., 2004; Wolf et al., 2007).

The CW system used in this study, described in detail by Haensse et al. (2005), consists of a sensor and a data acquisition unit. The sensor incorporates emission and detection of NIR light using four light sources and four detectors covering an area of 25 mm by 37.5 mm (Fig. 2). Each light source comprises light emitting diodes (LED) with wavelengths of 750 nm, 800 nm and 875 nm. The light sources are time multiplexed; i.e. only one source is on at a time. Detectors consisting of silicon PIN photodiodes detect the light. Two detectors can measure the light of each LED simultaneously, allowing the measurement of O<sub>2</sub>Hb and HHb concentration changes in up to 16 different locations simultaneously. For the current study, the 11 light paths shown in Fig. 2 were considered. One of these channels was measured twice (Fig. 2: L4–D4) (which is a consequence of the instrumentation’s configuration) and one was used to remove systemic physiological signals by reducing the effect of superficial layers (Fig. 2: L2–D3). Ten channels were considered for analysis after the subtraction procedure.

The light sources and detectors are mounted onto a rigid-flexible printed circuit board (PCB) which is cast in a highly flexible cover made of medical grade silicone rubber. The flexibility of the sensor allows it to be aligned to curved body surfaces such as the head. Even though the source-detector distance is fixed, the flexibility of the sensor may imply that the exact source-detector distance varies within several



**Fig. 2.** Arrangement of light sources (L1, L2, L3, and L4) and detectors (D1, D2, D3, and D4) on the sensor. The centre of the sensor was positioned over C3. Ten channels were considered for analysis (red, one was measured twice (orange)), one was used to remove systemic physiological signals (grey).

millimetres. The sensor is connected to the data acquisition unit, which transfers data to a laptop to store for further analysis.

The data acquisition unit of the MCP-II allows the simultaneous measurement of up to 48 channels with a sampling rate of 100 Hz and low noise. According to the *in vitro* studies of Haensse et al. (2005), for the current protocol the instrumental detection limit for a change in  $\mu\text{a}$  is  $<0.00002$  [1/cm], which corresponds to a concentration change of  $0.005 \mu\text{M}$ . A notebook computer was used to record and display the data. The stimulation software Presentation<sup>®</sup> was used to present the visual stimuli to the subjects and synchronize them to the data acquisition unit.

## Data analysis

### Behavioral data

Behavioral performance was analyzed using SPSS<sup>®</sup> (Version 16.0) as described previously (Horenstein et al., 2009). Number of finger taps, error rate, and left/right asymmetry during the bimanual task were calculated for each individual subject by counting incorrect sequences. An error was defined as any finger taps occurring outside the one of the prescribed sequences and the error rate was defined as the (total number of errors)/(total number of finger taps). The asymmetry score, defined as the absolute value of  $((1 - \text{error rate left hand}) - (1 - \text{error rate right hand})) / ((1 - \text{error rate left hand}) + (1 - \text{error rate right hand}))$ , was calculated based on the error rates from the bimanual finger-tapping task.

### fNIRS data

Albeit the room was dark itself, the monitors required by the tasks and by the instrumentation illuminate the room, indirectly. To account both for light intensity changes caused by monitors and to be able to observe the noise generated by the detectors, background measurements are performed.

fNIRS raw data contain the relative intensities of NIR light for all light-source/detector/wavelength combinations in use, intensities of background light and event markers. With the intensity information of different NIR wavelengths at a particular location, it is possible to determine changes in concentration of O<sub>2</sub>Hb and HHb, representing the dominant chromophores in human tissue at the range of NIR light. This is feasible for O<sub>2</sub>Hb and HHb as their absorption coefficients in dependence of wavelength are known (Wray et al., 1988). The transformation from changes in light intensity to changes in concentration is accomplished by application of the modified Beer-Lambert law (MBLL) which furthermore accounts for scattering properties of tissue (Delpy et al., 1988).

A customized code implemented in MATLAB<sup>®</sup> (Version 2008a) performed the signal processing and the transformation of the raw data into changes in concentration of O<sub>2</sub>Hb and HHb as follows:

Signal processing began with subtracting the background light and calculating the logarithm. The next step in data processing was dedicated to remove systemic physiological signals. Changes in concentrations of chromophores (HHb and O<sub>2</sub>Hb) in superficial tissue layers superimpose on the signals of the brain tissue. To reduce the effect of superficial layers, data of the light-source/detector pair (DLSDP) with shortest source-detector separation (2 cm) were used as reference and subtracted from each DLSDP according to Saager and Berger (2005). The reference channel for the superficial layer (channel with minimum source-detector distance) was fitted to each channel. The fitted results was then subtracted from the channel. To exclude intervals of extreme intensity changes from further analysis, each channel was then broken into 1.5 s long segments, temporarily. The variance within each segment of a channel was determined for the purpose of calculating the median value (MV) over the given variances. All segments that led to a greater variance as the MV multiplied by 5,

could be marked as artifacts, safely. This way each reassembled channel was freed from extreme changes in light intensities.

Before changes of O<sub>2</sub>Hb and HHb (differential path length factor (DPF) 6.46) (Kohl et al., 1998) were determined using DLSDP, the preprocessed raw data were low pass filtered (windowed linear-phase finite impulse response filter, order: 160, fc: 0.4 Hz). Finally, the traces of concentrations were smoothed by a Savitzky-Golay filter (order: 1, window-length: 5 s).

Data were then transferred to SPSS<sup>®</sup> (Version 16.0). From the resulting signals, the O<sub>2</sub>Hb and HHb concentrations during the last 10 s of each artifact free stimulation period were averaged and compared to the concentrations during the last 10 s of each rest period. For each condition and channel, the average change in O<sub>2</sub>Hb and HHb concentrations was calculated. Within each subject, the statistical significance of the O<sub>2</sub>Hb and HHb differences between the stimulation and the rest periods were assessed using the paired Wilcoxon sign rank test. Within each subject and between all subjects, the statistical significance of the O<sub>2</sub>Hb and HHb differences between the five conditions were further assessed using one-way ANOVA. Significance alpha-value was set to 0.05, and the Bonferroni correction was used for ANOVA.

## Results

### Subjects

Data of 16 subjects (5 male, 11 female, ages ranged from 21 to 58 years) were included for statistical analysis. Two further subjects were excluded from analysis due to missing signal detection. After sensor positioning, the raw signal strength was examined on-line. If the signal strength was low, positioning was repeated. After the first two conditions the signal was averaged on-line using MATLAB<sup>®</sup> to provide an impression of a detectable signal. The criterion for a detectable signal was the relative value between stimulation and baseline, i.e. increase in O<sub>2</sub>Hb and decrease in HHb. If at this point no signal could be detected, the subject was disqualified from data analysis. Reasons for the observed failure to obtain sufficient signal may be hair color as well as dark skin pigmentation in one of the subjects. It is further known that there are still unsolved inter-individual anatomical and/or physiological differences occurring in NIRS which may lead to failure of sufficient signal (Hiroki et al., 2005; Wassenaar and Van den Brand, 2005).

### Behavioral data

All 16 subjects were right-handed according to the Edinburgh Handedness Inventory (EHI) with a mean EHI of 77 (range 26–100). All subjects had finger-tapping frequencies of approx. 3 Hz. There were no significant differences in the error rates between left and right hands (significance level  $p < 0.05$ ). Behavioral data of all subjects are shown in Table 2: total number of finger taps varied little between the five conditions without significant difference. During right hand tasks (SR, CR), subjects performed slightly more finger taps, i.e. were slightly faster, and showed slightly lower mean error rates compared to left hand (SL, CL) and bimanual (B) tasks. Slightly more errors occurred with the left hand during the bimanual task, indicated by

**Table 2**  
Behavioral data of all subjects.

Condition	Mean total taps	Mean error rates	Mean asymmetry score
Simple right	1009 ± 194	0.000	
Simple left	893 ± 393	0.000	
Complex right	956 ± 290	0.02 ± 0.02	
Complex left	902 ± 267	0.03 ± 0.04	
Bimanual	897 ± 239	0.02 ± 0.02	−0.003 ± 0.006

negative value of mean asymmetry score. During unimanual tasks, the experimenter documented no detectable movements of the contralateral hand.

#### fNIRS data

In all subjects and conditions, significant increases in O<sub>2</sub>Hb and significant decreases in HHb were found in one or more channels over M1. During simple unimanual right and left motor tasks, significant differences of O<sub>2</sub>Hb and HHb concentration changes between stimulation and rest periods were found in both contra- and ipsilateral M1 within and between subjects. O<sub>2</sub>Hb concentration changes during ipsilateral (left hand) hand motor tasks were significantly smaller than those observed during contralateral (right hand) unimanual motor tasks. A similar distribution was found in HHb concentration changes, where right hand tasks resulted in significant greater decrease of HHb than left hand tasks.

In complex tasks, we found significant differences of O<sub>2</sub>Hb and HHb concentration changes with increasing complexity of the sequence task within and between subjects. Both during right and left hand tasks, complex tasks elicited significant larger O<sub>2</sub>Hb changes than simple tasks. Whereas HHb concentration changes showed a correlation during simple tasks, the corresponding distribution could not be found during complex tasks. Overall, bimanual tasks showed lower M1 activation than unimanual right hand tasks, but greater activation than left hand tasks.

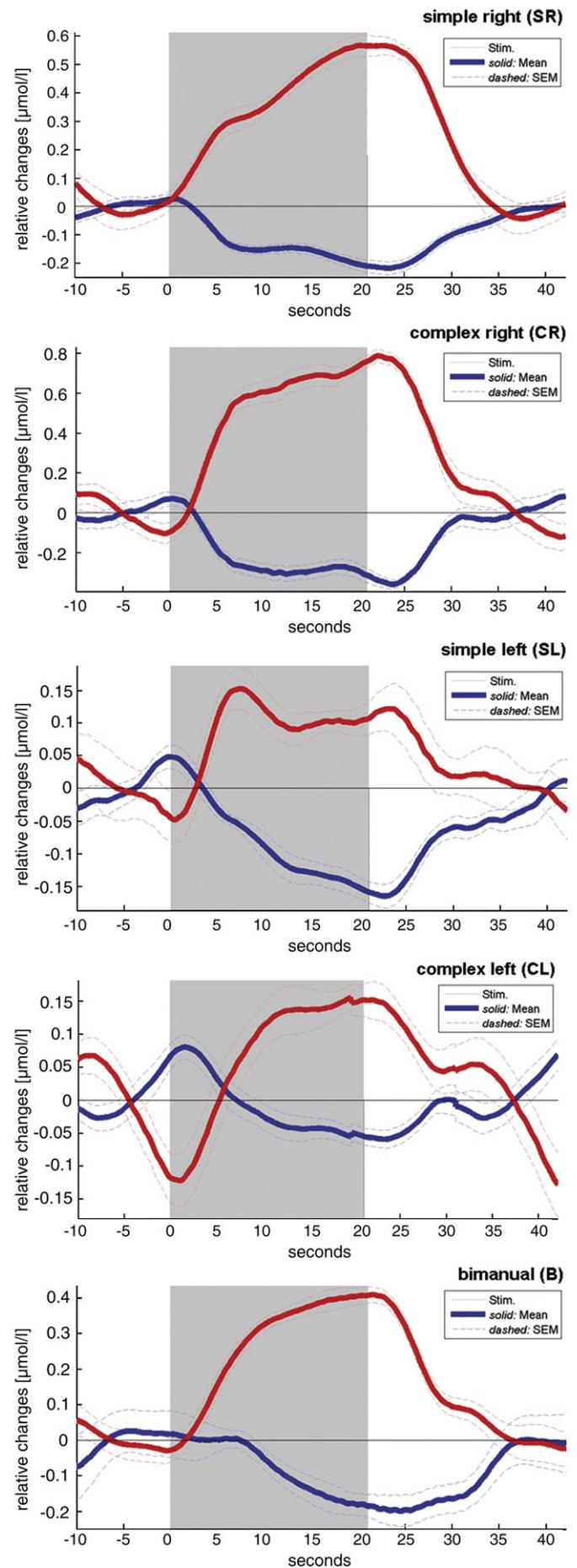
Fig. 3 shows examples of O<sub>2</sub>Hb and HHb changes during the five conditions taken from one subject representing all others.

Changes in O<sub>2</sub>Hb and HHb concentration during motor stimulation are shown in Table 3 for each subject. The last two rows of Table 3 show that the average increase of O<sub>2</sub>Hb of all significant responses among all channels and subjects were largest during complex right task, followed by simple right, bimanual, complex and simple left task. The decrease of HHb was largest during bimanual, followed by simple right, complex right, complex and simple left tasks.

Table 4 summarizes the number of changes in O<sub>2</sub>Hb and HHb concentration between stimulation and rest period for each subject during each of the five conditions. Varying in number, significant differences of O<sub>2</sub>Hb and HHb were found between all five conditions. The significance level was  $p < 0.05$ .

Fig. 4 shows the mean significant differences in O<sub>2</sub>Hb and HHb concentration over all subjects during each of the five conditions. The significance level for the paired Wilcoxon sign rank test was  $p < 0.05$ ; error bars indicate standard deviation (SD). Average increase of O<sub>2</sub>Hb (Fig. 4, top) of all significant responses among all channels and subjects was largest during complex right task, followed by simple right, bimanual, complex and simple left task. The decrease of HHb (Fig. 4, bottom) was largest during bimanual, followed by simple right, complex right, complex and simple left tasks.

Signal variability of O<sub>2</sub>Hb and HHb concentration changes were found in five (approx. 30%) subjects. This signal variability can best be described as an inversion of the typical oxygenation signal. Inversion in this context means that the values of the O<sub>2</sub>Hb and HHb concentration changes are inverted i.e. decrease of O<sub>2</sub>Hb and increase of HHb concentration changes, as compared to the typical activation pattern i.e. increase in O<sub>2</sub>Hb and decrease in HHb. Similar signal discrepancies have previously described as partial volume effect (Boas et al., 2001). Consequently, our results for the characterization of the signal variability however show an overall decrease of O<sub>2</sub>Hb after



**Fig. 3.** Examples of the five conditions (1 = simple right (SR) taken from subject ID = 6, 2 = complex right (CR), 3 = simple left (SL), 4 = complex left (CL), 5 = bimanual (B)) from one subject. Relative changes (μmol/l) of HHb = deoxy-hemoglobin (blue curve), O<sub>2</sub>Hb = oxy-hemoglobin (red curve), Stim = stimulation period (including instruction signal (1 s)) alternating with rest periods, averaged over 10 min.

**Table 3**  
Mean changes ( $\mu\text{mol/l}$ ) and number of channels with significant differences in  $\text{O}_2\text{Hb}$  and HHb concentration in response to motor stimulation for each subject (subject identification number (ID)) in the five conditions (1 = simple right (SR), 2 = simple left (SL), 3 = complex right (CR), 4 = complex left (CL), 5 = bimanual (B)), only given for significant ( $p < 0.05$ ) changes in  $\text{O}_2\text{Hb}$  and HHb assessed using paired Wilcoxon sign rank test ( $p < 0.05$ ).

ID	Sex	Age	Simple task		Complex task		Bimanual
			Contralateral (1)	Ipsilateral (2)	Contralateral (3)	Ipsilateral (4)	Bimanual (5)
1	f	25	9	4	8	9	6
2	f	23	10	8	4	2	9
3	f	25	6	5	8	9	9
4	f	30	10	2	10	4	10
5	f	26	7	7	7	5	4
6	f	28	9	10	8	8	10
7	m	32	10	6	10	4	10
8	m	21	7	1	5	1	7
9	m	28	2	3	8	2	2
10	f	21	4	2	8	3	2
11	f	24	9	7	9	8	6
12	m	31	8	6	8	4	9
13	f	58	6	7	9	7	5
14	m	26	6	5	10	3	5
15	f	24	9	2	10	4	10
16	f	29	10	2	10	4	10
Significant channels			122 (86.25%)	77 (48.125%)	137 (82.35%)	77 (48.125%)	114 (71.25%)
Mean changes $\text{O}_2\text{Hb}$ ( $\mu\text{mol/l}$ )			$0.275 \pm 0.054$	$0.110 \pm 0.034$	$0.351 \pm 0.051$	$0.154 \pm 0.034$	$0.249 \pm 0.047$
Mean changes HHb ( $\mu\text{mol/l}$ )			$-0.12 \pm 0.016$	$-0.0674 \pm 0.005$	$-0.0863 \pm 0.005$	$-0.0875 \pm 0.007$	$-0.138 \pm 0.006$

Numbers were rounded to three decimal digits.

stimulus onset followed by increase after stimulus offset averaged over the whole time course of 10 min. HHb concentration increases or decreases after stimulus onset.

## Discussion

### Behavioral data

Analog to a previous fMRI study, our motor task required subjects to repeatedly tap simple (thumb only) and complex sequences (thumb–middle–pinky–index–ring finger) with separate hands and by alternating the right and the left hand (Horenstein et al., 2009). Our results are consistent with previous findings demonstrating that behavioral hand performance generally shows a low asymmetry, i.e. a slight superiority of the dominant hand (Borod et al., 1984; Provin and Magliaro, 1993; Bryden, 2000).

### Simple task

The well-known lateralization to contralateral M1 during unimanual simple tasks was confirmed showing smaller  $\text{O}_2\text{Hb}$  changes for ipsi- compared to contralateral movements. Overall, although our study applied analog finger-tapping tasks as used in fMRI (Horenstein et al., 2009), results can generally only partially be compared to MRI findings.

Using traditional imaging methods, it has been shown that simple motor tasks involving repetitive finger movements such as flexion–extension (Rao et al., 1993; Cramer et al., 1999; Verstynen et al., 2005) or abduction–adduction (Kobayashi et al., 2003) require less effort in motor execution and may therefore result in reduced ipsilateral activation. The ipsilateral activation cannot be detected in all subjects (Rao et al., 1993; Kobayashi et al., 2003) and is more prominent following movements performed by the non-dominant hand (Kim et al., 1993; Kobayashi et al., 2003; Hanakawa et al., 2005). Overall, the observed significant concentration changes of  $\text{O}_2\text{Hb}$  and HHb during unimanual motor tasks in our study show the expected activation of ipsi- and contralateral M1 (Horenstein et al., 2009).

### Complex task

Motor tasks in our study were varied by means of increasing task complexity. It is generally unresolved whether activation changes in

motor areas observed during complex tasks are related to increased task complexity or to the use of additional fingers, covering broader cortical areas that could account for stronger signals. However, as tested in control measurements, it has been suggested that the stronger activation in M1 is specific to complex movements and does not depend on the number of required muscles, i.e. the number of fingers used in a certain task (Verstynen et al., 2005).

Overall, our findings are consistent with fMRI showing greater M1 activation as a result of increasing task complexity. This result contrasts a previous fNIRS study that showed no task-related changes in oxy-hemoglobin (Kleinschmidt et al., 1996).

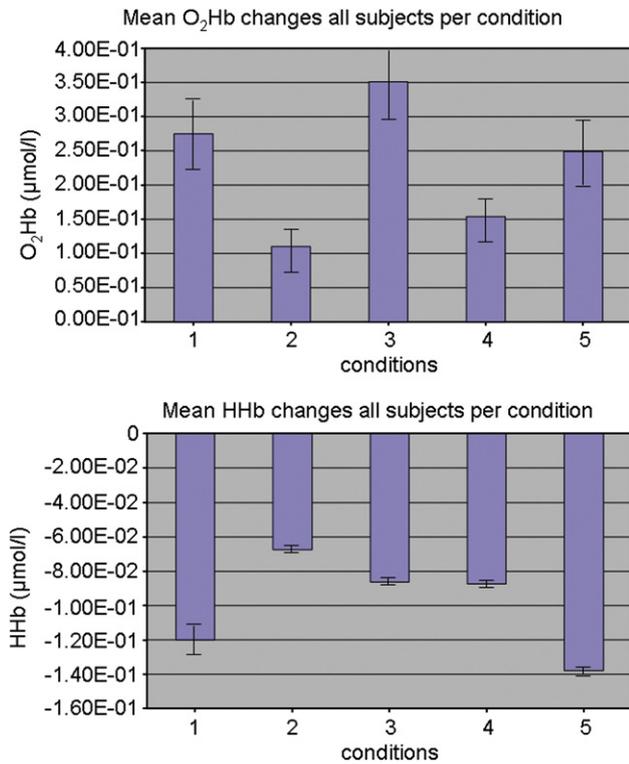
The number of finger transitions in a sequence, i.e. moving one finger and then another, was found to be positively correlated with increased activation, in accordance with a previous study (Harrington et al., 2000). As in our study, it has been described that tapping of sequences results in greater activation than tapping of chords, where multiple fingers are moved simultaneously. Also, both of these tasks produce greater activation than simple finger-tapping (Verstynen et al., 2005; Witt et al., 2008).

### Bimanual task

We found significant lower oxygenation changes in M1 during bimanual compared to unimanual tasks that are in line with activation patterns described in traditional imaging studies. The phenomenon of lower bimanual activation has been suggested to be a consequence of inter-hemispheric inhibition, hemispheric asymmetry and task-dependence of motor activation (Taniguchi et al., 2001; Ghacibeh et al., 2007). Our bimanual tasks required subjects to move fingers in

**Table 4**  
Number of significant differences between the five conditions over all subjects, given for significant ( $p < 0.05$ ) changes in  $\text{O}_2\text{Hb}$  (red) and HHb (blue) assessed using ANOVA, Bonferroni correction.

Condition	$\text{O}_2\text{Hb}$				
	1	2	3	4	5
HHb	1	12	15	12	11
	2	14	13	7	10
	3	14	13	15	14
	4	15	16	15	12
	5	15	14	14	15



**Fig. 4.** Mean significant differences (mmol/l) in O<sub>2</sub>Hb (top) and HHb (bottom) concentration for all subjects (ID 1–16) in five conditions (1 = simple right (122 channels), 2 = simple left (77 channels), 3 = complex right (137 channels), 4 = complex left (77 channels), 5 = bimanual (114 channels)). Significant ( $p < 0.05$ ) changes in O<sub>2</sub>Hb and HHb assessed using paired Wilcoxon sign rank test ( $p < 0.05$ ) are represented. Error bars indicate standard deviation (SD).

alternating sequences. Consistent with our results, this kind of bimanual coordination task, i.e. in which homologous muscles are alternately engaged, has been shown to result in lower M1 activation compared to those in which homologous muscles are active simultaneously (Swinnen et al., 1997; Aramaki et al., 2006). This may be attributable to stronger involvement of the dominant motor cortex in ipsilateral hand movements via interaction with the non-dominant motor system, known as neural crosstalk. The concept of inter-manual crosstalk (Marteniuk and MacKenzie, 1980) assumes two independent motor plans where a fraction of the motor command sent to one hand is dispatched as a mirror image to the other hand (Cattaert et al., 1999). This phenomenon may have contributed to our findings of lower M1 activation during bimanual motor tasks.

#### Partial volume effect

In approx. 30% of subjects signal variability of O<sub>2</sub>Hb and HHb concentration changes were found. This signal variability can best be described as an inversion of the typical oxygenation signal by means of inverted values of the O<sub>2</sub>Hb and HHb concentration changes. Typical oxygenation signals show an increase in O<sub>2</sub>Hb and decrease in HHb. The characterization of the signal variability however can be described as an overall decrease of O<sub>2</sub>Hb after stimulus onset followed by an increase after stimulus offset averaged over the whole time course of 10 min. HHb concentration increases or decreases after stimulus onset.

Similar discrepancies have been described further as partial volume effect (Boas et al., 2001; Strangman et al., 2002b; Huppert et al., 2006; Xu et al., 2007). Partial volume effect is the effect wherein insufficient image resolution leads to a mixing of different tissue types. This effect has been explained as a partial volume error arising from source-detector positions relative to activation site, depth of

activation, scalp and skull thickness, and baseline optical properties that can all potentially cause discrepancy in the NIRS estimate of hemoglobin concentration changes among subjects. A partial volume error in a NIRS measurement can result in an underestimate of the amplitude of the hemodynamic response (Okada et al., 1997; Boas et al., 2001). Further, spectral differences in the partial volume effect can cause crosstalk in the estimated hemoglobin changes (Boas et al., 2001; Uludag et al., 2002), i.e. changes in O<sub>2</sub>Hb can appear as HHb changes and vice versa. Consequently accurate statements about the relative magnitudes of the O<sub>2</sub>Hb and HHb changes cannot always be made.

#### Study limitations

The main limitation of this study is that the NIRS data cannot be directly compared with another neuroimaging technique, e.g. fMRI. Although our study applied the same finger-tapping tasks as used in a previous fMRI study (Horenstein et al., 2009), comparing our current data with published fMRI studies is problematic due to differences in spatial resolution and statistical approaches used to study the motor system.

Individual subjects showed a variable activation pattern during finger-tapping which may be obscured during analysis at the group level. Inter-individuality has been described in previous fNIRS studies of inter-subject (Hiroki et al., 2005; Sato et al., 2005) and inter-session reliability (Plichta et al., 2006; Strangman et al., 2006; Plichta et al., 2007). Subjects in our study were measured only once. Therefore, we could not test reproducibility. Possible causes for variability or insufficient signal detection may be inter-individual differences in physiological baseline properties, task performance, attention, motivation, and task difficulty. Additional work is needed to investigate the origin of inter-individual variability.

We only included right-handed subjects who were measured over the left hemisphere. This approach was chosen according to the finding that ipsilateral M1 appears to be strongly activated during performance with the non-dominant hand (Cramer et al., 1999; Verstynen et al., 2005; Park et al., 2008). This possible effect of hand-dominance may result in different findings when investigating the other hemisphere of left-handed subjects.

#### Conclusion

We present the first fNIRS study measuring finger-tapping in relation to increasing task complexity. We found significant differences in O<sub>2</sub>Hb and HHb concentration changes between all conditions of simple, complex and bimanual tasks. We report largest oxygenation changes during right hand tasks, followed by bimanual and left hand tasks. Additionally, we observed signal variability in M1 activation pattern as it has been previously described by means of the partial volume effect. Our observations are in accordance with traditional neuroimaging studies. The new insight revealed by this study is relevant for the diagnostic evaluation of neurological hand motor assessments which commonly include different degrees of task complexity. The results reflect new knowledge on the capabilities of NIRS in clinical diagnosis demonstrating that NIRS is able to measure differences in oxygenation changes, which could be directly used within the clinical assessment of hand motor function. fNIRS as a neuroimaging method could facilitate the assessment and the monitoring of treatment progress of the human motor system in patient populations and clinical settings where traditional neuroimaging methods cannot be applied.

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.neuroimage.2009.03.027.

## References

- Aramaki, Y., Honda, M., Sadato, N., 2006. Suppression of the non-dominant motor cortex during bimanual symmetric finger movement: a functional magnetic resonance imaging study. *Neuroscience* 141, 2147–2153.
- Boas, D.A., Gaudette, T., Strangman, G., Cheng, X., Marota, J.J.A., Mandeville, J.B., 2001. The accuracy of near infrared spectroscopy and imaging during focal changes in cerebral hemodynamics. *NeuroImage* 13, 76–90.
- Boas, D.A., Dale, A.M., Franceschini, M.A., 2004. Diffuse optical imaging of brain activation: approaches to optimizing image sensitivity, resolution, and accuracy. *NeuroImage* 23, S275–S288.
- Borod, J., Caron, H., Koff, E., 1984. Left-handers and right-handers compared on performance and preference measures of lateral dominance. *Br. J. Psychol.* 75, 177–186.
- Bryden, P., 2000. Lateral preferences, skilled behavior and task complexity: hand and foot. In: Mandal, M., et al. (Ed.), *Side Bias: a Neuropsychological Perspective*. Kluwer Academic Publishers, Dordrecht, pp. 225–248.
- Cao, Y., D'Ohaberrigau, L., Vikingstad, E.M., Levine, S.R., Welch, K.M.A., 1998. Pilot study of functional MRI to assess cerebral activation of motor function after poststroke hemiparesis. *Stroke* 29, 112–122.
- Cattaert, D., Semjen, A., Summers, J., 1999. Simulating a neural cross-talk model for between-hand interference during bimanual circle drawing. *Biol. Cybern.* 81, 343–358.
- Chollet, F., DiPiero, V., Wise, R., Brooks, D., Dolan, R., Frackowiak, R., 1991. The functional anatomy of motor recovery after stroke in humans: a study with positron emission tomography. *Ann. Neurol.* 29, 63–71.
- Colebatch, J.G., Deiber, M.P., Passingham, R.E., Friston, K.J., Frackowiak, R.S., 1991. Regional cerebral blood flow during voluntary arm and hand movements in human subjects. *J. Neurophysiol.* 65, 1392–1401.
- Cramer, S.C., Finklestein, S.P., Schaechter, J.D., Bush, G., Rosen, B.R., 1999. Activation of distinct motor cortex regions during ipsilateral and contralateral finger movements. *J. Neurophysiol.* 81, 383–387.
- Delpy, D., Cope, M., van der Zee, P., Arridge, S., Wray, S., Wyatt, J., 1988. Estimation of optical path length through tissue from direct time of flight measurements. *Phys. Med. Biol.* 33, 1433–1442.
- Franceschini, M., Fantini, S., Thompson, J., Culver, J., Boas, D., 2003. Hemodynamic evoked response of the sensorimotor cortex measured noninvasively with near-infrared optical imaging. *Psychophysiology* 40, 548–560.
- Gerloff, C., Andres, F., 2002. Bimanual coordination and interhemispheric interaction. *Acta Psychol. (Amst.)* 110, 161–186.
- Ghacibeh, G.A., Mirpuri, R., Drago, V., Jeong, Y., Heilman, K.M., Triggs, W.J., 2007. Ipsilateral motor activation during unimanual and bimanual motor tasks. *Clin. Neurophysiol.* 118, 325–332.
- Grefkes, C., Eickhoff, S.B., Nowak, D.A., Dafotakis, M., Fink, G.R., 2008. Dynamic intra- and interhemispheric interactions during unilateral and bilateral hand movements assessed with fMRI and DCM. *NeuroImage* 41, 1382–1394.
- Haense, D., Szabo, P., Brown, D., Fauchère, J., Niederer, P., Bucher, H., Wolf, M., 2005. New multichannel near infrared spectrophotometry system for functional studies of the brain in adults and neonates. *Optics Express* 13, 4525–4538.
- Hanakawa, T., Parikh, S., Bruno, M.K., Hallett, M., 2005. Finger and face representations in the ipsilateral precentral motor areas in humans. *J. Neurophysiol.* 93, 2950–2958.
- Harrington, D., Rao, S., Haaland, K., Bobholz, J., Mayer, A., Binder, J., Cox, R., 2000. Specialized neural systems underlying representations of sequential movements. *J. Cogn. Neurosci.* 12, 56–77.
- Hausmann, M., Kirk, I., Corballis, M., 2004. Influence of task complexity on manual asymmetries. *Cortex* 40, 103–110.
- Hess, C.W., Mills, K.R., Murray, N.M.F., 1986. Magnetic stimulation of the human brain: facilitation of motor responses by voluntary contraction of ipsilateral and contralateral muscles with additional observations on an amputee. *Neurosci. Lett.* 71, 235–240.
- Hiroki, S., Yutaka, F., Masashi, K., Takusige, K., Atsushi, M., Takeshi, Y., Hideaki, K., 2005. Intersubject variability of near-infrared spectroscopy signals during sensorimotor cortex activation. *J. Biomed. Opt.* 10, 044001.
- Horenstein, C., Lowe, M., Koenig, K., Phillips, M., 2009. Comparison of unilateral and bilateral complex finger tapping-related activation in premotor and primary motor cortex. *Hum. Brain Mapp.* 30 (4), 1397–1412.
- Hoshi, Y., 2003. Functional near-infrared optical imaging: utility and limitations in human brain mapping. *Psychophysiology* 40, 511–520.
- Huppert, T.J., Hoge, R.D., Diamond, S.G., Franceschini, M.A., Boas, D.A., 2006. A temporal comparison of BOLD, ASL, and NIRS hemodynamic responses to motor stimuli in adult humans. *NeuroImage* 29, 368–382.
- Jäncke, L., Lutz, K., Koeneke, S., Neuper, C. and Wolfgang, K., 2006. Converging evidence of ERD/ERS and BOLD responses in motor control research. *Progress in Brain Res.*, vol. 159. Elsevier, pp. 261–271.
- Jaspers, H., 1958. The ten–twenty electrode system of the International Federation. *Electroencephalogr. Clin. Neurophysiol. Electroencephalography and Clinical Neurophysiology*, 10, pp. 371–375.
- Jöbsis, F., 1977. Noninvasive infrared monitoring of cerebral and myocardial oxygen sufficiency and circulatory parameters. *Science* 198, 1264–1267.
- Kim, S., Ashe, J., Georgopoulos, A., Merkle, H., Ellerman, J., Menon, R., Ogawa, S., Ugurbil, K., 1993. Functional imaging of human motor cortex at high magnetic field. *J. Neurophys.* 69, 297–302.
- Kleinschmidt, A., Obrig, H., Requardt, M., Merboldt, K.-D., Dirnagl, U., Villringer, A., Frahm, J., 1996. Simultaneous recording of cerebral blood oxygenation changes during human brain activation by magnetic resonance imaging and near-infrared spectroscopy. *J. Cereb. Blood Flow Metab.* 16, 817–826.
- Kobayashi, M., Hutchinson, S., Schlaug, G., Pascual-Leone, A., 2003. Ipsilateral motor cortex activation on functional magnetic resonance imaging during unilateral hand movements is related to interhemispheric interactions. *NeuroImage* 20, 2259–2270.
- Koeneke, S., Lutz, K., Wüstenberg, T., Jäncke, L., 2004. Bimanual versus unimanual coordination: what makes the difference? *NeuroImage* 22, 1336–1350.
- Kohl, M., Nolte, C., Heekeren, H., Horst, S., Scholz, U., Obrig, H., Villringer, A., 1998. Determination of the wavelength dependence of the differential pathlength factor from near-infrared pulse signals. *Phys. Med. Biol.* 43, 1771–1782.
- Lauterbur, P., 1986. NMR imaging in biomedicine. *Cell Biophys.* 9, 211–214.
- Li, J., Dietsche, G., Iftime, D., Skipetrov, S., Maret, G., Elbert, T., Rockstroh, B., Gisler, T., 2005. Noninvasive detection of functional brain activity with near-infrared diffusing-wave spectroscopy. *J. Biomed. Opt.* 10, 44002.
- Lissek, S., Hausmann, M., Knossalla, F., Peters, S., Nicolas, V., Güntürkün, O., Tegenthoff, M., 2007. Sex differences in cortical and subcortical recruitment during simple and complex motor control: an fMRI study. *NeuroImage* 37, 912–926.
- Mackert, B.-M., Leistner, S., Sander, T., Liebert, A., Wabnitz, H., Burghoff, M., Trahms, L., Macdonald, R., Curio, G., 2008. Dynamics of cortical neurovascular coupling analyzed by simultaneous DC-magnetoencephalography and time-resolved near-infrared spectroscopy. *NeuroImage* 39, 979–986.
- Maki, A., Yamashita, Y., Watanabe, E., Koizumi, H., 1996. Visualizing human motor activity by using non-invasive optical topography. *Front. Med. Biol. Eng.* 7, 285–297.
- Mansfield, P., Maudsley, A., 1977. Medical imaging by NMR. *Br. J. Radiol.* 50, 188–194.
- Marteniuk, R., MacKenzie, C., 1980. Information processing in movement organization and execution. In: Nickerson, R. (Ed.), *Attention and Performance VIII*. Erlbaum, Hillsdale, pp. 29–57.
- Muellbacher, W., Facchini, S., Borojerdi, B., Hallett, M., 2000. Changes in motor cortex excitability during ipsilateral hand muscle activation in humans. *Clin. Neurophysiol.* 111, 344–349.
- Obrig, H., Hirth, C., Junge-Hulsing, J.G., Doge, C., Wolf, T., Dirnagl, U., Villringer, A., 1996. Cerebral oxygenation changes in response to motor stimulation. *J. Appl. Physiol.* 81, 1174–1183.
- Obrig, H., Villringer, A., 2003. Beyond the visible—imaging the human brain with light. *J. Cereb. Blood Flow Metab.* 23, 1–18.
- Okada, E., Firbank, M., Schweiger, M., Arridge, S., Cope, M., Delpy, D., 1997. Theoretical and experimental investigation of near-infrared light propagation in a model of the adult head. *Appl. Opt.* 36, 21–31.
- Oldfield, R., 1971. The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 9, 97–113.
- Park, J., Kwon, Y., Lee, M., Bai, D., Nam, K., Cho, Y., Lee, C., Jang, S., 2008. Brain activation pattern according to exercise complexity: a functional MRI study. *NeuroRehabilitation* 23, 283–288.
- Phelps, M., Hoffman, E., Mullani, N., Ter-Pogossian, M., 1975. Application of annihilation coincidence detection to transaxial reconstruction tomography. *J. Nucl. Med.* 16, 210–224.
- Plichta, M.M., Herrmann, M.J., Baehne, C.G., Ehlis, A.C., Richter, M.M., Pauli, P., Fallgatter, A.J., 2006. Event-related functional near-infrared spectroscopy (fNIRS): are the measurements reliable? *NeuroImage* 31, 116–124.
- Plichta, M., Herrmann, M., Baehne, C., Ehlis, A., Richter, M., Pauli, P., Fallgatter, A., 2007. Event-related functional near-infrared spectroscopy (fNIRS) based on cranio-cerebral correlations: reproducibility of activation? *Hum. Brain Mapp.* 28, 733–741.
- Provins, K.A., Magliaro, J., 1993. The measurement of handedness by preference and performance tests. *Brain Cogn.* 22, 171–181.
- Pulvermüller, F., Lutzenberger, W., Preiszl, H., Birbaumer, N., 1995. Motor programming in both hemispheres: an EEG study of the human brain. *Neurosci. Lett.* 190, 5–8.
- Rao, S.M., Binder, J.R., Bandettini, P.A., Hammeke, T.A., Yetkin, F.Z., Jesmanowicz, A., Lisk, L.M., Morris, G.L., Mueller, W.M., Estkowski, L.D., Wong, E.C., Haughton, V.M., Hyde, J.S., 1993. Functional magnetic resonance imaging of complex human movements. *Neurology* 43, 2311.
- Saager, R., Berger, A., 2005. Direct characterization and removal of interfering absorption trends in two-layer turbid media. *J. Opt. Soc. Am. A Opt. Image Sci. Vis.* 22, 1874–1882.
- Sato, H., Fuchino, Y., Kiguchi, M., Katura, T., Maki, A., Yoro, T., Koizumi, H., 2005. Intersubject variability of near-infrared spectroscopy signals during sensorimotor cortex activation. *J. Biomed. Opt.* 10, 44001.
- Sato, T., Ito, M., Suto, T., Kameyama, M., Suda, M., Yamagishi, Y., Ohshima, A., Uehara, T., Fukuda, M., Mikuni, M., 2007. Time courses of brain activation and their implications for function: a multichannel near-infrared spectroscopy study during finger tapping. *Neurosci. Res.* 58, 297–304.
- Seitz, R.J., Hoffich, P., Binkofski, F., Tellmann, L., Herzog, H., Freund, H.-J., 1998. Role of the premotor cortex in recovery from middle cerebral artery infarction. *Arch. Neurol.* 55, 1081–1088.

- Shibuya, K., Kuboyama, N., 2007. Human motor cortex oxygenation during exhaustive pinching task. *Brain Res.* 1156, 120–124.
- Shibuya, K., Sadamoto, T., Sato, K., Moriyama, M., Iwamoto, M., 2008. Quantification of delayed oxygenation in ipsilateral primary motor cortex compared with contralateral side during a unimanual dominant-hand motor task using near-infrared spectroscopy. *Brain Res.* 1210, 142–147.
- Solodkin, A., Hlustik, P., Noll, D.C., Small, S.L., 2001. Lateralization of motor circuits and handedness during finger movements. *Eur. J. Neurol.* 8, 425–434.
- Strangman, G., Boas, D.A., Sutton, J.P., 2002a. Non-invasive neuroimaging using near-infrared light. *Biol. Psychiatry* 52, 679–693.
- Strangman, G., Culver, J.P., Thompson, J.H., Boas, D.A., 2002b. A quantitative comparison of simultaneous BOLD fMRI and NIRS recordings during functional brain activation. *NeuroImage* 17, 719–731.
- Strangman, G., Goldstein, R., Rauch, S.L., Stein, J., 2006. Near-infrared spectroscopy and imaging for investigating stroke rehabilitation: test–retest reliability and review of the literature. *Arch. Phys. Med. Rehabil.* 87, 12–19.
- Swinnen, S., Jardin, K., Meulenbroek, R., Dounskaia, N., Hofkens-Van Den Brandt, M., 1997. Egocentric and allocentric constraints in the expression of patterns of interlimb coordination. *J. Cogn. Neurosci.* 9, 348–377.
- Taniguchi, Y., Burle, B., Vidal, F., Bonnet, M., 2001. Deficit in motor cortical activity for simultaneous bimanual responses. *Exp. Brain Res.* 137, 259–268.
- Tinazzi, M., Zanette, G., 1998. Modulation of ipsilateral motor cortex in man during unimanual finger movements of different complexities. *Neurosci. Lett.* 244, 121–124.
- Uludag, K., Kohl, M., Steinbrink, J., Obrig, H., Villringer, A., 2002. Cross talk in the Lambert–Beer calculation for near-infrared wavelengths estimated by Monte Carlo simulations. *J. Biomed. Opt.* 7, 51–59.
- Umphred, D. and Carlson, C., 2006. *Neurorehabilitation for the Physical Therapist Assistant*. Slack Inc.
- van Mier, H., Tempel, L.W., Perlmutter, J.S., Raichle, M.E., Petersen, S.E., 1998. Changes in brain activity during motor learning measured with PET: effects of hand of performance and practice. *J. Neurophysiol.* 80, 2177–2199.
- Verstynen, T., Diedrichsen, J., Albert, N., Aparicio, P., Ivry, R.B., 2005. Ipsilateral motor cortex activity during unimanual hand movements relates to task complexity. *J. Neurophysiol.* 93, 1209–1222.
- Villringer, A., Dirnagl, U., 1995. Coupling of brain activity and cerebral blood flow: basis of functional neuroimaging. *Cerebrovasc Brain Metab Rev.* 7, 240–276.
- Waldert, S., Braun, C., Preissl, H., Birbaumer, N., Aertsen, A. and Mehring, C., 2007. Decoding performance for hand movements: EEG vs. MEG. Proceedings of the 29th Annual International Conference of the IEEE. Engineering in Medicine and Biology Society, pp. 5346–5348.
- Wassenaar, E., Van den Brand, J., 2005. Reliability of near-infrared spectroscopy in people with dark skin pigmentation. *J. Vclin. Monit. Comput.* 19, 195–199.
- Weiller, C., Ramsay, S., Wise, R., Friston, K., Frackowiak, R., 1993. Individual patterns of functional reorganization in the human cerebral cortex after capsular infarction. *Ann. Neurol.* 33, 181–189.
- Witt, S.T., Laird, A.R., Meyerand, M.E., 2008. Functional neuroimaging correlates of finger-tapping task variations: an ALE meta-analysis. *NeuroImage* 42, 343–356.
- Wolf, M., Ferrari, M., Quaresima, V., 2007. Progress of near-infrared spectroscopy and topography for brain and muscle clinical applications. *J. Biomed. Opt.* 12, 062104.
- Wray, S., Cope, M., Delpy, D.T., Wyatt, J.S., Reynolds, E.O.R., 1988. Characterization of the near infrared absorption spectra of cytochrome aa3 and haemoglobin for the non-invasive monitoring of cerebral oxygenation. *Biochim. Biophys. Acta (BBA) - Bioenergetics* 933, 184–192.
- Xu, M., Takata, H., G., S. Hayami, T., Yamasaki, T., Tobimatsu, S. and Iramina, K., 2007. NIRS measurement of hemodynamic evoked responses in the primary sensorimotor cortex. Proceedings of the 29th Annual International Conference of the IEEE. Conf. Proc. IEEE Eng. Med. Biol. Soc. pp. 2492.