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ORIGINAL RESEARCH

# Near-infrared spectroscopy determined cerebral oxygenation with eliminated skin blood flow in young males

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**Abstract** We estimated cerebral oxygenation during handgrip exercise and a cognitive task using an algorithm that eliminates the influence of skin blood flow (SkBF) on the near-infrared spectroscopy (NIRS) signal. The algorithm involves a subtraction method to develop a correction factor for each subject. For twelve male volunteers (age 21 ± 1 yrs) +80 mmHg pressure was applied over the left temporal artery for 30 s by a custom-made headband cuff to calculate an individual correction factor. From the NIRS-determined ipsilateral cerebral oxyhemoglobin concentration ($O_2Hb$) at two source-detector distances (15 and 30 mm) with the algorithm using the individual correction factor, we expressed cerebral oxygenation without influence from scalp and scull blood flow. Validity of the estimated cerebral oxygenation was verified during cerebral neural activation (handgrip exercise and cognitive task). With the use of both source-detector distances, handgrip exercise and a cognitive task increased $O_2Hb$ ($P < 0.01$) but $O_2Hb$ was reduced when SkBF became eliminated by pressure on the temporal artery for 5 s. However, when the estimation of cerebral oxygenation was based on the algorithm developed when pressure was applied to the temporal artery, estimated $O_2Hb$ was not affected by elimination of SkBF during handgrip exercise ($P = 0.666$) or the cognitive task ($P = 0.105$). These findings suggest that the algorithm with the individual correction factor allows for evaluation of changes in an accurate cerebral oxygenation without influence of extracranial blood flow by NIRS applied to the forehead.

**Keywords** Headband inflation · Extracranial blood flow · Oxyhemoglobin · Temporal artery

## 1 Introduction

Near-infrared spectroscopy (NIRS) represents a non-invasive means to monitor cerebral oxygenation and is used, e.g. to detect cerebral activation and to direct critical care of the patients [1–10]. The brain is need for always enough oxygen to be supplied. However, tissue hypoxia occurs frequently in the perioperative setting. Therefore, always measuring and obtaining enough oxygen is important in clinical scenarios. The NIRS offers non-invasive method for in vivo real-time monitoring of tissue haemoglobin oxygenation in widely range of clinical scenarios [11]. The recent studies suggest that as determined by NIRS cerebral oxygenation is influenced by scalp and skull blood flow indexed by forehead skin blood flow (SkBF) because the near-infrared light transmit these tissues to reach the brain [12, 13]. Thus, a NIRS evaluation of cerebral oxygenation becomes problematic when scalp blood flow changes, e.g. during heat stress or infusion of vasopressors for which the NIRS-determined cerebral oxygenation seems to reflect changes in extra cranial blood flow rather than cerebral oxygenation [14–17]. Especially during critical care and in

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the operating room, it is very important for the patients to measurement an accurate cerebral oxygenation and the establishment of the methodology is needed.

To eliminate scalp and skull influence on the NIRS-derived evaluation of cerebral oxygenation, continuous wave NIRS devices employ two or multiple source-detector distances. Thus, algorithms aim to eliminate the effect of scalp and scull circulation on the NIRS signal in so-called spatially resolved NIRS. In principle, spatially resolved NIRS subtracts the signal from a short source-detector distance from that of a long-distance [18–22]. It is considered that the short source-detector distance reflects photons returning from surface layers that by subtraction, should be eliminated from the profound signal. The penetration depth of the photons is proportional to the source-detector distance but SkBF equally affects NIRS with source-detector distances from 15 to 30 mm [23]. Therefore, an increase in the source-detector distance is required without attenuating the signal to noise ratio significantly [24] and the majority of NIRS devices employ a source-detector distance of 40 mm (e.g. INVOS, EQUANOX, and NIRO) or 50 mm (FORESIGHT). And yet even with the use of a large source-detector distance, influence from scalp and scull blood flow, as indicated by SkBF, to the NIRS signal is not eliminated [25].

Several other attempts are made to eliminate scalp and scull influence on the NIRS signal including signal discrimination using principal component analysis [26, 27] and temporal independent component analysis in phantoms models [28–32]. However, studies in homogeneous phantom models do not allow for direct comparison to humans due to the heterogeneity of interrogated tissue (scalp, scull and brain). Therefore, we constructed an algorithm to express the NIRS-determined cerebral oxygenation based on suppressed scalp and scull blood flow as indexed by SkBF. Validity of the algorithm was also verified during cerebral activation by handgrip exercise and a cognitive task.

## 2 Materials and methods

Twelve healthy young males participated in the study (21 ± 1 yrs.; mean ± SD) after written informed consent was obtained from each subject. The study was approved by the Institutional Review Boards of the Faculty of Science Engineering, Toyo University (IRB # 2012-R-01) and performed in accordance to the Declaration of Helsinki.

### 2.1 Measurements

Throughout the experiment, changes in oxyhemoglobin concentration ($O_2Hb$) (milli mol per liter × millimeter; mM mm) were determined by an optical topography system (ETG-7100 Optical Topography System; Hitachi Medical CO., Tokyo, Japan), that is particular sensitive to the cerebral microvasculature and enables for determination of $O_2Hb$ and has a high temporal resolution. The $O_2Hb$ was calculated using light at 695 and 830 nm in accordance with the modified Beer–Lambert law [33, 34]. An optode with two detector channel distances (15 and 30 mm) from the emitter was applied. The short source-detector distance was considered to reflect oxygenation of mainly scalp and scull while detection with a 30 mm source-detector distance was taken to reflect oxygenation also of intracranial layers. The light transmittance of the 15 mm channel is 1–2 orders of magnitude greater than that of the 30 mm channel. Thus, only for the 15 mm channel, an optical filter for attenuating detected light was used to prevent overflow. The light transmittance of the optical filter was 6.8 and 9.8 % for 695 and 830 nm light, respectively. All measurements are expressed as changes relative to baseline ($\Delta O_2Hb_{15mm}$ and $\Delta O_2Hb_{30mm}$) and the device was calibrated before each measurement. Data were sampled at 10 Hz and stored on the NIRS device until analyzed using the ETG-7100 software. The custom-made NIRS optode was placed on the left side of the forehead above the supraorbital edge and fasten by a rubber band (Fig. 1).

SkBF was measured at a depth of 1–2 mm next to the NIRS optode by a laser Doppler tissue blood flow meter (MoorLAB, Moor Instruments, Axminster, UK). Heart rate (HR) was obtained from an electrocardiogram (BMS-2401, NIHON KOHDEN, Tokyo, Japan) while mean arterial pressure (MAP) was recorded by finger photoplethysmography from the middle or index finger of the right hand (Finometer, Finapress Medical Systems BV, Amsterdam, Netherlands). SkBF, HR and MAP were sampled at 1 kHz

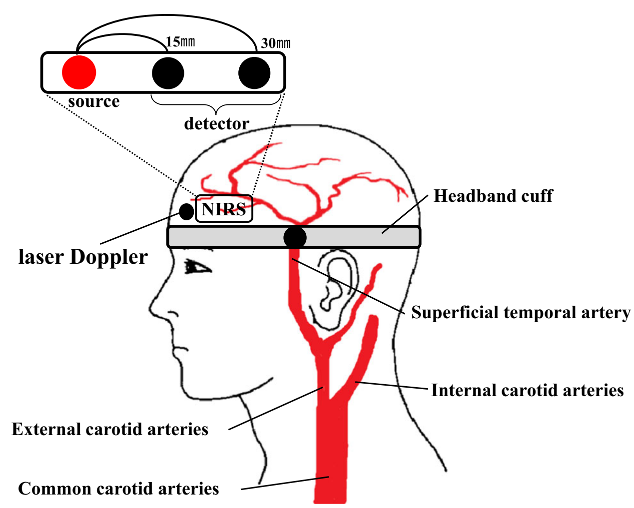


**Fig. 1** Placement of the headband, near-infrared spectroscopy (NIRS) and laser Doppler. The *left upper panel* presents location of the channels within the NIRS optode

using an analog to digital converter (PowerLab; ADInstruments, Milfored, MA, USA) interfaced with a computer.

## 2.2 Experimental design

### 2.2.1 *Experiment 1: determination of individual algorithms*

The algorithm used to suppress influence of scalp and scull blood flow to the NIRS signal was constructed from the correction factor for each subject during elimination of forehead SkBF by occlusion of the temporal artery. The subjects were in a semi-recumbent position and a custom-made pneumatic headband provided with a flat cap was placed circumferentially around the head (Fig. 1) [23]. The protuberance of the headband was positioned over the left temporal artery that bifurcates from the external carotid artery and supplies the main part of forehead. After a 180 s baseline period, an inflation–deflation protocol (+80 mmHg 30 s cuff inflation and 30 s cuff deflation) was repeated four times to determine an individual correction factor ($a_0$) to suppress the influence of the extracranial blood flow on the NIRS signal assuming that the cuff affects scalp and scull blood flow and not cerebral oxygenation. The cuff inflation of +80 mmHg is enough to manipulate extracranial blood flow and affect NIRS signal non-pharmacologically without haemodynamic change [23]. Therefore, we decided to use +80 mmHg cuff pressure for the occlusion of temporal artery to reduced extracranial blood flow and $O_2Hb$ surely. Moreover, the individual equation is $\Delta O_2Hb_{30mm}$ is expressed $a_0 \cdot \Delta O_2Hb_{15mm}$ where $a_0$ is determined by the least squares method.

### 2.2.2 *Experiment 2: cerebral oxygenation during exercise and the cognitive task*

To evaluate validity of the algorithm, NIRS was used at rest (control condition), during static handgrip exercise and a cognitive task with and without 5 s headband cuff inflation (Fig. 2). After a 180 s baseline period, the subjects performed 30 s isometric left-handgrip exercise at 60 % of the maximal voluntary contraction (MVC) and values were followed for a 30 s post-task period. Also the subjects performed a verbal fluency task [35]: after a 150 s baseline period and 30 s pre-task rest recording, the word fluency task was followed by a 30 s post-task period. During the word fluency task, subjects were requested to verbalize as many words as possible that began with a Japanese character emitted. The characters in the words included /a/,/ka/,/na/and/sa/ and the number of words generated was taken as a measure of performance. The subjects were instructed

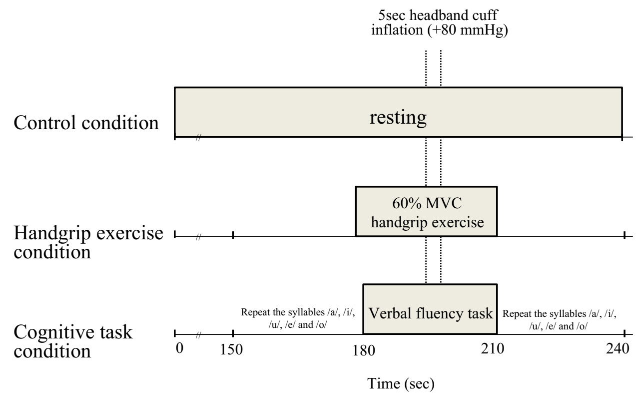


**Fig. 2** Experimental protocol. (1) control condition; (2) 60 % MVC handgrip exercise condition; (3) cogonitive task (verbal fluency task) condition. In all condition, 5 s headband cuff inflation (+80 mmHg)

to repeat the syllables /a/,/i/,/u/,/e/and/o/ during the pre- and post-task periods. In addition, variables were recorded for a 240 s control condition.

We determined $O_2Hb$ by integrating the individual correction factor into the equation:

$$\text{Estimated}\ \Delta O_2Hb = \Delta O_2Hb_{30\,mm} - a_0 \times \Delta O_2Hb_{15\,mm}$$

In order to verify the validity of the algorithm, forehead SkBF was reduced by 5 s headband inflation (+80 mmHg) during each of the experimental conditions (handgrip exercise, cognitive task, and control). It was considered that if the algorithm is valid, then the estimated $\Delta O_2Hb$ would not change by headband inflation because the mechanical head cuff would affect scalp and scull blood flow and not cerebral oxygenation.

## 2.3 Statistical analysis

The $O_2Hb$ and SkBF are presented as changes from baseline ($\Delta O_2Hb$ and $\Delta$SkBF) while MAP and HR are expressed as mean $\pm$ SD. Repeated measurements were evaluated using a one-way analysis of variance (ANOVA) followed by a Tukey–Kramer post hoc test (SPSS 22, IBM, Tokyo, Japan). Comparisons between baseline versus handgrip exercise and the cognitive task was compared by paired Student's *t* test. By 5 s headband inflation, comparisons between baseline versus SkBF and $O_2Hb$ were by paired Student's *t* test. A *P* value <0.05 was considered to indicate a statistically significant difference.

# 3 Results

HR and MAP were unaffected by 30 s headband cuff inflation to +80 mmHg, while decreases in SkBF and $O_2Hb$ were detected in both a source-detector distance of 15

**Table 1** Heart rate (HR), mean arterial pressure (MAP) and changes in skin blood flow ($\Delta$SkBF) and oxyhemoglobin ($\Delta O_2Hb$) at baseline and four times during headband inflation by +80 mmHg to temporal artery

| | Baseline | Cuff1 | Cuff2 | Cuff3 | Cuff4 |
|---|---|---|---|---|---|
| HR (bpm) | 55 ± 8 | 55 ± 8 | 55 ± 9 | 56 ± 8 | 56 ± 10 |
| MAP (mmHg) | 87 ± 10 | 88 ± 9 | 87 ± 9 | 87 ± 9 | 88 ± 9 |
| $\Delta$SkBF (AU) | | −158 ± 60* | −176 ± 82* | −170 ± 90* | −147 ± 85* |
| $\Delta O_2Hb_{15mm}$ (mM mm) | | −0.52 ± 0.26* | −0.75 ± 0.41* | −0.66 ± 0.48* | −0.61 ± 0.30* |
| $\Delta O_2Hb_{30mm}$ (mM mm) | | −0.73 ± 0.40* | −0.87 ± 0.43* | −0.75 ± 0.51* | −0.71 ± 0.32* |

Values are mean ± SD

* $P < 0.01$ different from the baseline

**Table 2** Individual correction factors ($a_0$) used to estimate cerebral oxygenation without influence from skin blood flow

| Subjects | $a_0$ |
|---|---|
| 1 | 0.898 |
| 2 | 1.936 |
| 3 | 2.083 |
| 4 | 1.221 |
| 5 | 1.310 |
| 6 | 1.432 |
| 7 | 1.573 |
| 8 | 1.310 |
| 9 | 1.490 |
| 10 | 1.546 |
| 11 | 1.386 |
| 12 | 1.157 |

and30 mm (Table 1). The individual correction factor ($a_0$) that was calculated from data sampled during four times 30 s headband cuff inflation ranged from 0.898 to 2.083 (Table 2).

During handgrip exercise, HR, MAP, SkBF and $O_2Hb$ all increased (+21 ± 14 bmp; $P < 0.001$, +8 ± 10 mmHg; $P = 0.006$, +161 ± 221 AU; $P = 0.046$ and +0.56 ± 0.60 mM mm; $P = 0.008$, respectively; Table 3). Similarly, the cognitive task increased HR, SkBF and $O_2Hb$ (+4 ± 11 bpm; $P = 0.001$, +69 ± 73 AU; $P = 0.008$ and +0.49 ± 0.40 mM mm; $P = 0.001$, respectively), while MAP remained stable.

Figure 3 shows the individual $\Delta$SkBF and $\Delta O_2Hb$ during the 5 s headband cuff inflation during handgrip exercise, the cognitive task and the control conditions from one representative individual. The 5 s headband cuff inflation reduced the NIRS-determined $O_2Hb$ during handgrip exercise ($P = 0.005$), the cognitive task ($P = 0.001$) and also in the control condition ($P < 0.001$) along with decrease in forehead SkBF (handgrip exercise, $P = 0.001$; the cognitive task, $P < 0.001$; control, $P < 0.001$; Fig. 4). In contrast, the algorithm-estimated $O_2Hb$ was not affected by headband cuff inflation under the three circumstances (handgrip exercise, $P = 0.666$; cognitive task, $P = 0.105$; control, $P = 0.062$).

## 4 Discussion

We constructed an algorithm to obtain an individual correction factor ($a_0$) during elimination of forehead SkBF to suppress the influence of scalp and scull blood flow on the NIRS signal. The individual correction factor varied widely in each subject (ranged from 0.898 to 2.083; CV = 23 %). Also, the validity of the algorithm was verified during handgrip exercise and a cognitive task. The forehead $O_2Hb$ increased during both handgrip exercise and the cognitive task, which is consistent with previous studies [2, 35, 36]. Also as expected, compression of the left temporal artery was reduced the NIRS-determined $O_2Hb$ along with decrease in forehead SkBF, however, by use of the algorithm the estimated $O_2Hb$ was unchanged significantly from the baseline value immediately before decrease in SkBF.

NIRS is a non-invasive technique for real time monitoring of tissue hemoglobin oxygenation and is widely used to assess regional cerebral activation in humans [5, 8]. However, evaluation of the NIRS-determined cerebral oxygen saturation is influenced by extracranial blood flow as exemplified by SkBF with administration of phenylephrine [16, 17, 37] or norepinephrine [15]. Moreover, the effect of mechanical manipulating SkBF on the NIRS signal without any systemic hemodynamic consequence is documented [23], which underlines that continuous wave NIRS methodology is limited in its ability to exclude an influence of scull and scalp oxygenation to the NIRS signal in humans. Thus, NIRS does not report an accurate estimate of cerebral oxygenation in situations where SkBF changes.

The algorithm assumed that photons returning from deep tissue layers, i.e. the grey matter, were not affected by compression of the temporal artery. Thus, the headband cuff induced changes in $O_2Hb$ is considered to be governed by changes in superficial tissue blood flow such as the skin, and not in cerebral blood flow or oxygenation. The headband cuff did not induce any systemic hemodynamic changes as expressed by MAP and HR, but it reduced SkBF (Table 1). These results are similar to findings in our previous study [23]. Importantly, we could identify the

**Table 3** Heart rate (HR), mean arterial pressure (MAP) and changes in skin blood flow (ΔSkBF) and oxyhemoglobin ($\Delta O_2Hb$) at rest, during handgrip exercise and a cognitive task

| | Handgrip exercise | | | Cognitive task | | |
|---|---|---|---|---|---|---|
| | Rest | During HG | *P* value | Rest | During cognition | *P* value |
| HR (bpm) | 58 ± 8 | 83 ± 14 | 0.000 | 61 ± 8 | 66 ± 11 | 0.001 |
| MAP (mmHg) | 95 ± 7 | 104 ± 10 | 0.006 | 94 ± 7 | 100 ± 17 | 0.149 |
| ΔSkBF (AU) | | 161 ± 221 | 0.046 | | 69 ± 73 | 0.008 |
| $\Delta O_2Hb_{30mm}$ (mM mm) | | 0.56 ± 0.60 | 0.008 | | 0.49 ± 0.40 | 0.001 |

Value are mean ± SD. *P* value are different from rest

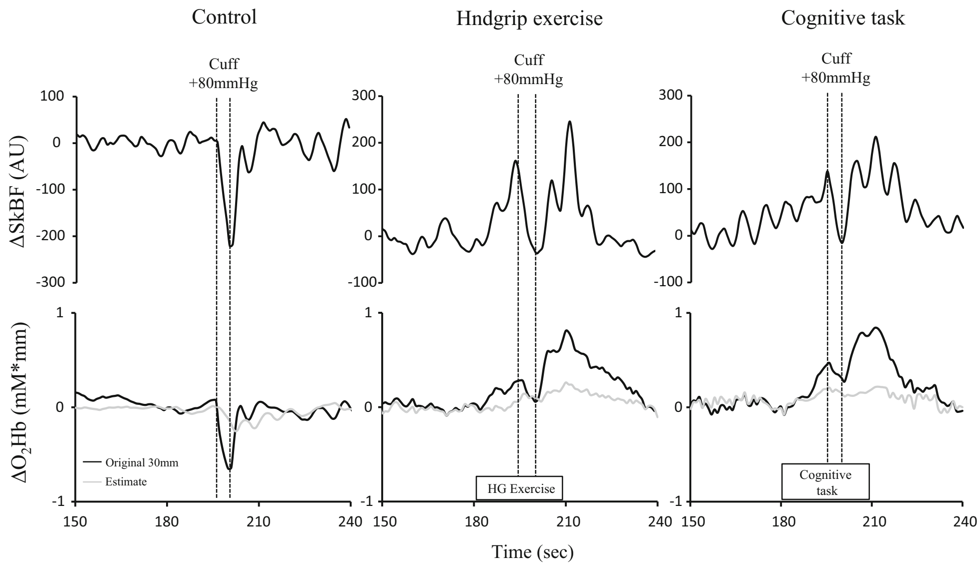


**Fig. 3** A typical example of changes in forehead skin blood flow (ΔSkBF) and oxyhemoglobin ($\Delta O_2Hb$) during control, 60 % maximal handgrip exercise (HG) and a cognitive task. In order to verify the validity of algorithm, forehead SkBF was reduced by 5 s headband inflation (+80 mmHg) during control, handgrip exercise and cognitive task

individual correction factor valid for inclusion in the algorithm by this mechanical manipulation of SkBF.

The some studies indicate that the optical paths length and the sensitivity to surface layer oxygenation are influenced by the source-detector distance [38, 39]. Kohri et al. [40] reported that the contribution of cerebral tissue to optical signals were related to the source-detector distance (20 mm; 33 %, 30 mm; 55 %, 40 mm; 69 %), indicating that increasing the detector distance increases effective optical path length within brain tissue. However, there is a large variation in individual correction factor (Table 2), indicating that the effect of the source-detector distance (15 vs. 30 mm) on the contribution of cerebral tissue to optical signals varied widely in each subject. This large vaiasion in individual correction factor may deppend on an individual different anatomy (different forehead skin vessel distribution or arterial and venous blood flow distribution etc.). These findings suggest that in order to exclude SkBF information from NIRS signal, an individual effect of extracranial blood flow on NIRS signal (individual correction factor) need to be identified. Indeed, our algorithm with individual correction factor determined cerebral oxygenation from NIRS signal was not affected by change in forehead SkBF statistically (Figs. 3, 4).

To eliminate the effect of surface-layer circulation on the NIRS-signal, the subtraction method using multiple distance optodes is applied [18–22]. Moreover, NIRS apparatus uses this subtraction method with difference source-detector distance from 15 to 30 mm [25]. Nevertheless, the NIRS signal with a subtraction algorithm is unable to isolate cerebral oxygenation from extra cranial tissues. Cerebral oxygenation measured by commercial cerebral oximetry apparatus (e.g. INVOS) is affected by changes in scalp and scull blood flow as indexed by SkBF [14, 15]. However, those previous studies did not consider influence of extracranial contamination include in the NIRS signal greatly varied in each subject. Since the commercial cerebral oximetry may have only one constant correction factor to exclude extracranial blood flow information from NIRS signal with multi light source-detector separation, it may be impossible for these devices to isolate an accurate cerebral oxygenation. This study provide an unprecedented way of algorithm for evaluating the accurate forehead cerebral oxygenation from NIRS measurement.

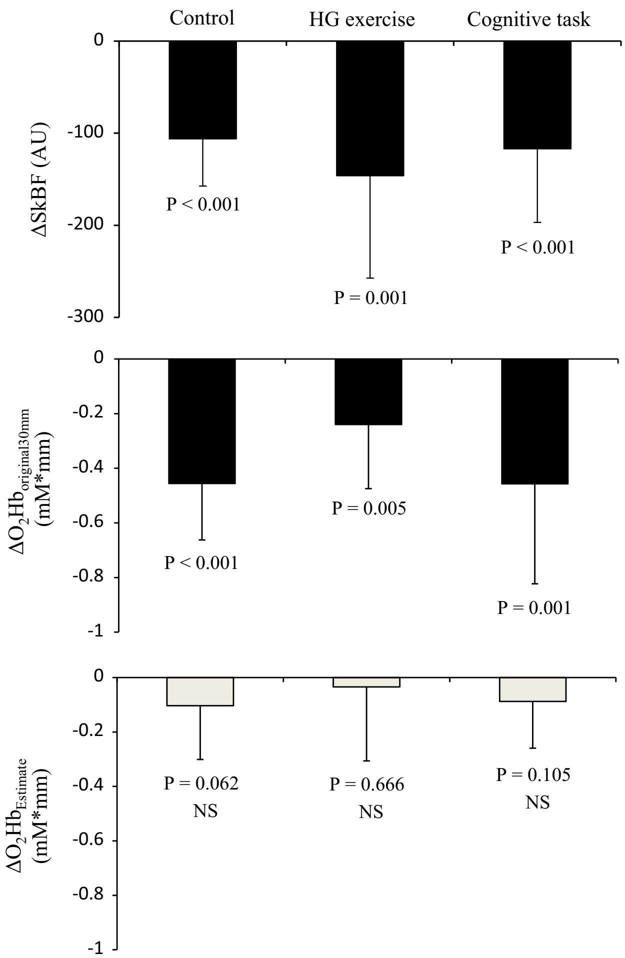


**Fig. 4** Changes in forehead skin blood flow (ΔSkBF; *upper panel*) and the original oxyhemoglobin with a source-detector distance of 30 mm ($\Delta O_2Hb_{original30mm}$; *middle panel*) and the algorithm-estimated oxyhemoglobin ($\Delta O_2Hb_{Estimate}$) by 5 s headband inflation (+80 mmHg). Values are mean ± SD

By employing an individual correction factor based on changes in SkBF, we here demonstrate that our algorithm eliminated influence from SkBF on the NIRS-signal during handgrip exercise, a cognitive task and a control condition.

### 4.1 Limitations

Some limitations to the study are to be mentioned. First, we did not identify forehead cerebral activity using, e.g. positron emission tomography or functional magnetic resonance imaging. However, regardless of changes in cerebral activity, the algorithm seems able to suppress influence of variation is SkBF on the NIRS-determined cerebral oxygenation. Secondly, the ratio between influence from skin and cerebral oxygenation to the NIRS signal remains debated. Over a broad range of interventions known to affect SkBF and/or cerebral oxygenation a 35 % contribution has been suggested [25]. However, the ratio may likely vary between interventions, thus, taking the present findings into account it seems that when SkBF is altered it is reflected in the NIRS-derived value for cerebral oxygenation. Finally, we did measure MAP by finger photoplethysmography. Central and peripheral arterial pressure are dissimilar due to interaction of incident and reflected waveforms. The peripheral arterial pressure method such as the finapres requires rigorous validation to understand its accurate and limitations. However, the accuracy of finger photoplethysmography such as the Finapres compared with inter-arterial reference pressure has now been assessed in many studies [41, 42]. Moreover, Friedman et al. [43] have made an evaluation of the mean arterial pressure recorded by finger photoplethysmography and invasively determination during head-up tilt induced hypertension and found excellent correlation. In fact, we revised peripheral aeterial pressure by Finometer with brachial artery blood pressure before all measurement.

## 5 Conclusion

In conclusion, a headband cuff inflation was used to develop an individual correction factor. The algorithm with this individual correction factor successfully eliminated SkBF on NIRS during handgrip exercise and cognitive task. Thus, we recommend that influence of different extracranial contamination in NIRS signal by each subject is determined when NIRS is applied for detailed investigations of, e.g. cerebral activation.

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**Conflict of interest** The authors have no conflicts of interest to disclose.

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