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ORIGINAL PAPER

Single-trial classification of antagonistic oxyhemoglobin responses during mental arithmetic

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Abstract Near-infrared spectroscopy (NIRS) is a non-invasive optical technique that can be used for brain–computer interfaces (BCIs) systems. A common challenge for BCIs is a stable and reliable classification of single-trial data, especially for cognitive (mental) tasks. With antagonistic activation pattern, recently found for mental arithmetic (MA) tasks, an improved online classification for optical BCIs using MA should become possible. For this investigation, we used the data of a previous study where we found antagonistic activation patterns (focal bilateral increase of [oxy-Hb] in the dorsolateral prefrontal cortex in parallel with a [oxy-Hb] decrease in the medial area of the anterior prefrontal cortex) in eight subjects. We used the [oxy-Hb] responses to search for the best antagonistic feature combination and compared it to individual features from the same regions. In addition, we investigated the use of antagonistic [deoxy-Hb], total hemoglobin [Hbtot] and pairs of [oxy-Hb] and [deoxy-Hb] features as well as the existence of a group-related feature set. Our results indicate that the use of the antagonistic [oxy-Hb] features significantly increases the classification accuracy from 63.3 to 79.7%. These results support the hypothesis that antagonistic hemodynamic response patterns are a suitable control strategy for optical BCI, and that only two prefrontal NIRS channels are needed for good performance.

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1 Introduction

Near-infrared spectroscopy (NIRS) is a non-invasive optical technique for the assessment of functional brain activity during cognitive, visual, visuo-motor, and motor tasks (e.g., [5, 7, 8, 10, 17, 25]). Resulting task-specific changes in the metabolic response, i.e., concentration changes of oxy- and deoxyhemoglobin ([oxy-Hb], [deoxy-Hb]), can be used alternatively to [2, 15, 22] or in combination with EEG [16] for brain–computer interfaces systems (optical and hybrid BCIs). The temporal resolution of the hemodynamic response—in the range of several seconds—limits the information transfer rates achievable for BCI-based communication. This can be seen as the major drawback of NIRS-based BCIs. There are, however, several advantages when using NIRS as input signal for non-invasive BCIs compared to the use of the electroencephalogram (EEG). These include no conductive gel required, no influence of electrooculographic artifacts, and most important the sensor placement is more practical and user-friendly and thus better suited for daily applications [3].

The robust single-trial detection of brain activity is one relevant issue for all types of BCIs that are based on classification. The identification of brain patterns that naïve user can reliably generate and that are stable over time may significantly contribute to more accurate discrimination. Previously we investigated changes of [oxy-Hb] and [deoxy-Hb] during a mental arithmetic (MA) task [17]. We found antagonistic activation patterns in eight out of ten

subjects, i.e., a focal bilateral increase of [oxy-Hb] in the dorsolateral prefrontal cortex (DLPFC) and simultaneously a [oxy-Hb] decrease in the medial area of the anterior prefrontal cortex (APFC). A Bonferroni post-test showed that the mean (over all eight subjects) [oxy-Hb] responses in left DLPFC and APFC displayed a statistically significant difference compared to a baseline period prior to the task; the mean response in the right DLPFC was not significant (for more details see [17]) but a few individuals showed additionally strong responses in this area (e.g., Fig. 3 in [17]). These findings are in line with results from fMRI and EEG studies where such antagonistic activation patterns ("focal activation/surround deactivation") have been already described (e.g., [4, 19]) during the performance of motor tasks. Given the results, we hypothesized that the focal antagonistic hemodynamic response pattern during MA may be reliably detected by recording only two NIRS channels over the prefrontal cortex.

In this article, we evaluate the above hypothesis by means of cue-based BCI off-line simulations using the data of eight subjects of a previous study [17] and show for the first time that antagonistic [oxy-Hb] responses from left or right DLPFC in combination with APFC significantly increase the discrimination of MA from rest compared to the standard way of using individual features only from one single region (e.g., [15]). One can certainly expect that the use of two features results in an increase of the discriminatory power. Our results, based on eight subjects, however, may be relevant for practical BCI systems because sensor location and instructions for subjects are known a-priori and well defined.

2 Materials and methods

2.1 Subjects, experimental paradigm, and data collection

In [17], the investigations were carried out on a group of Ten paid University students (five males and five females, all right-handed aged 26.1 ± 2.7 years. The study was approved by the Medical University of Graz Institutional Review Board. Subjects were without medical conditions, compensated for participation, and gave written informed consent after the aim of the study was explained to them. For the investigations presented in this article, we used the data of eight subjects (three male, five female, aged 26.0 ± 2.8 years) which showed a relative focal bilateral increase of [oxy-Hb] in the DLPFC in parallel with a decrease in the medial area of the APFC. Participants were asked to perform cue-guided mental subtraction. More precisely, prior each task a 10-s baseline interval was recorded. During the task, they had to sequentially subtract a one-digit number from a two-digit number (e.g., $97 - 4 = 93$, $93 - 4 = 89$, ...; the initial subtraction was presented visually on a monitor) as quickly as possible for 12 s, afterward a 28-s resting period was given. Subjects performed 3 or 4 runs (six trials per class and run) resulting in 18 or 24 trials per class, respectively.

A continuous wave system (ETG-4000, Hitachi Medical Co., Japan) was used to record brain oxygenation. The multi-channel system measures the change of [oxy-Hb] and [deoxy-Hb] in the unit of millimolar millimeter (mM $\times$ mm) and consists of 16 photo-detectors and 17 light emitters (3×11 grid), resulting in a total of 52 channels (Fig. 1a). The lowest line of channels was arranged along the FP1-FP2 line according to the international EEG 10-20 system. For further details on the channel placement, see [17].

2.2 Data analysis

After removing baseline drifts by using a 0.01 Hz high pass filter, the task-related concentration changes of [oxy-Hb] referred to a 10-s baseline interval prior to the task (seconds -10 to 0) were calculated (For further details see [1] and [17]). To capture the antagonistic [oxy-Hb] patterns, we defined three regions of interest (ROI): ROI_1 consisted of channels 46, 47, and 48 over APFC, ROI_2 of channels 18, 28, and 29 over left DLPFC and ROI_3 of channels 13, 23, and 24 over right DLPFC (Fig. 1a).

For classification, Fisher's linear discriminant analysis (LDA) classifier was used. To evaluate the LDA generalization, data recorded from each subject was split into a training and evaluation set. The former, consisting of 10 or 16 trials respectively, was used to train and test the discriminative power of [oxy- Hb] feature combinations selected from the different ROIs. The best performing features were selected and used to train the LDA. The evaluation set, composed of the last eight trials, was then used to assess the performance of the trained LDA.

Concentration changes of the [oxy-Hb] response at second $tm_j = 10, 11, 12, 13$, and 14 (± 2 s around the end of the MA task, to cover also delayed task-related parts of the response) were labeled as class MA. Samples at second $tr_k = 26, 27, 28, 29$, and 30 (lying in between two MA tasks) were labeled as class REST. Features consist of an individual [oxy-Hb] value of one channel at a fixed time (tm or tr). In Tables 1 and 2, the positions of the channels (channel number as well as underlying Brodmann and anatomical areas) and the corresponding time points are indicated. For each subject, independent LDAs were trained and validated (leave-one-out cross validation) with individual [oxy-Hb] responses for each possible

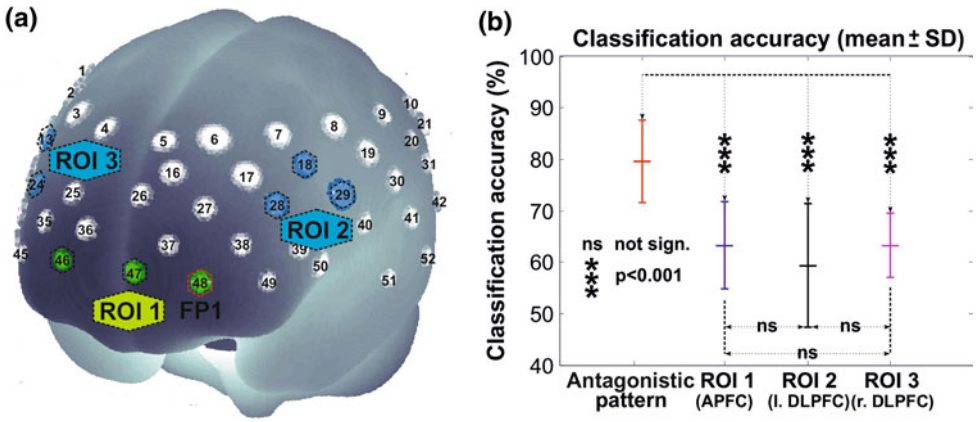

Fig. 1 **a** Projections of the 52 NIRS channel positions (3 × 11 grid) on the cortical surface. Positions are overlaid on a MNI-152 compatible canonical brain which is optimized for NIRS analysis [21]. Also indicated are the ROI. **b** Significant contrasts of the classification accuracy between the antagonistic and individual features

combination (ROI_i, tm_j, tr_k) with $i = 1,2,3$; $j = 1,2, \ldots, 5$, $k = 1, 2, \ldots, 5$. Exhaustive Search, i.e., all possible feature combinations were evaluated, was used in the above procedure to identify the best performing antagonistic feature combination (ROI_1, ROI_2, tm_j, tr_k) or (ROI_1, ROI_3, tm_j, tr_k) with $j = 1,2, \ldots, 5$ and $k = 1,2, \ldots, 5$.

The same procedure was applied also to the antagonistic [deoxy-Hb], antagonistic total hemoglobin [Hbtot] = [oxy-HB] + [deoxy-Hb] and to tuples of ([oxy-Hb], [deoxy-Hb]) concentrations. In addition, antagonistic [oxy-Hb] changes that perform best over all subjects were researched (group-related [oxy-Hb] pattern). In the latter, we identified the most commonly selected features over all subjects at the averaged time points of tm and tr.

3 Results

3.1 Off-line simulation

We used the best performing classifiers calculated from the training set and computed an off-line simulation with the evaluation set (eight trials per class, summarized in Tables 1, 2). Six out of the eight subjects (75%) performed better than the chance level (71.9% ($\alpha = 0.05$) for eight trials [14]) when antagonistic patterns are used (Table 1). Only one subject performed better than random when using individual features from ROI_1, ROI_2, or ROI_3, respectively (see Table 2). An analysis of variance (ANOVA) and a Newman–Keuls post-test revealed that antagonistic

Table 1 Classification accuracies (Acc.; bold numbers indicate classification accuracies above the chance level (71.9% for eight trials)) and used features (Pos.$_i$, indicating the underlying Brodmann and anatomical areas; tm and tr, corresponding time points) for the antagonistic [oxy-Hb] patterns for all subjects

Sub.	Antagonistic [oxy-Hb] pattern								
	Acc. (%)	Pos.$_1$			Pos.$_2$			tm (s)	tr (s)
		Ch.	BA	Anat.	Ch.	BA	Anat.		
S1	68.75	46[a]	10	SFG	24[b]	46	MFG	10	29
S2	**87.50**	47[a]	10	MeFG	24[b]	46	MFG	13	30
S3	**75.00**	48[a]	10	MFG	29[c]	9	IFG	12	29
S4	**87.50**	48[a]	10	MFG	29[c]	9	IFG	14	28
S5	**81.25**	47[a]	10	MeFG	28[c]	46	MFG	13	26
S6	68.75	46[a]	10	SFG	28[c]	46	MFG	10	26
S7	**87.50**	47[a]	10	MeFG	18[c]	9	MFG	10	29
S8	**81.25**	47[a]	10	MeFG	28[c]	46	MFG	12	26
Mean	79.69							11.75	27.88
SD	8.01							1.58	1.64

[a] APFC, [b] r. DLPFC, [c] l. DLPFC

BA Brodmann area, *SFG* superior frontal gyrus, *MFG* middle frontal gyrus, *IFG* inferior frontal gyrus, *MeFG* medial frontal gyrus

Table 2 Classification accuracies (in %) for individual [oxy-Hb] features for all subjects

Sub.	ROI_1 [oxy-Hb]						ROI_2 [oxy-Hb]						ROI_3 [oxy-Hb]					
	Acc. (%)	Pos.			tm (s)	tr (s)	Acc. (%)	Pos.			tm (s)	tr (s)	Acc. (%)	Pos.			tm (s)	tr (s)
		Ch.	BA	Anat.				Ch.	BA	Anat.				Ch.	BA	Anat.		
S1	62.50	46[a]	10	SFG	11	29	56.25	18[c]	9	MFG	10	26	56.25	24[b]	46	MFG	10	30
S2	62.50	47[a]	10	MeFG	10	26	50.00	28[c]	46	MFG	11	30	62.50	24[b]	46	MFG	14	26
S3	62.50	46[a]	10	SFG	11	27	50.00	29[c]	9	IFG	11	26	68.75	24[b]	46	MFG	12	27
S4	**81.25**	48[a]	10	MFG	13	29	50.00	29[c]	9	IFG	10	27	62.50	24[b]	46	MFG	13	26
S5	50.00	47[a]	10	MeFG	12	26	68.75	28[c]	46	MFG	11	27	56.25	24[b]	46	MFG	11	30
S6	62.50	46[a]	10	SFG	10	26	50.00	28[c]	46	MFG	10	26	62.50	24[b]	46	MFG	10	26
S7	62.50	46[a]	10	SFG	13	28	**81.25**	18[c]	9	MFG	10	29	62.50	23[b]	46	MFG	12	28
S8	62.50	48[a]	10	MFG	10	26	68.75	28[c]	46	MFG	12	26	**75.00**	23[b]	46	MFG	14	27
Mean	63.28				11.25	27.13	59.38				10.63	27.13	63.28				12.00	27.50
SD	8.48				1.28	1.36	12.05				0.74	1.55	6.19				1.6	1.69

Bold numbers indicate classification accuracies above the chance level of 71.9%

[a] APFC, [b] r. DLPFC, [c] l. DLPFC

BA Brodmann area, *SFG* superior frontal gyrus, *MFG* middle frontal gyrus, *IFG* inferior frontal gyrus, *MeFG* medial frontal gyrus

features perform significantly better than individual features ($F_{(3/21)} = 8.74$; $p < 0.001$; Fig. 1b). Figure 1b depicts the significant contrasts of the classification accuracy between the antagonistic and individual features. The *Y*-axis indicates the mean classification accuracy over all subjects for the use of antagonistic feature combinations and individual features from ROI_1, ROI_2, or ROI_3 (see also Tables 1, 2).

3.2 Comparison of antagonistic [oxy-Hb], [deoxy-Hb], [Hbtot], and ([oxy-Hb], [deoxy-Hb]) features

We computed an off-line simulation with the evaluation set using the best performing antagonistic [deoxy-Hb], [Hbtot], and ([oxy-Hb], [deoxy-Hb]) features (Table 3). By using antagonistic [deoxy-Hb], only two subjects performed better than random. An ANOVA and a Newman–Keuls post-test revealed that antagonistic [oxy-Hb] features perform significantly better than antagonistic [deoxy-Hb] features ($F_{(4/28)} = 2.81$; $p < 0.05$). No significant differences between antagonistic [oxy-Hb], antagonistic [Hbtot] as well as ([oxy-Hb], [deoxy-Hb]) tuples were found. In the case of [Hbtot] four and in the case of ([oxy-Hb], [deoxy-Hb]) three out of the eight subjects, respectively, performed significantly better than random.

3.3 Stability of antagonistic [oxy-Hb] features

According to the findings of the feature selection and off-line simulation, we used the most commonly selected features of all subjects (Ch. 47, APFC and Ch. 28, l. DLPFC at the averaged time points of tm and tr (tm = 12 s, tr = 28 s; Table 1)). The group-related [oxy-Hb] features set achieved in average a classification accuracy of 70.3% over all subjects (Table 3). No significant differences were found between the use of subject-specific antagonistic features and the above group-related feature set. Four out of the eight subjects performed better than the chance level (mean 78.1%).

4 Discussion

The aim of the study was to investigate the usefulness of antagonistic [oxy-Hb] patterns in the context of single-trial classification for brain-computer interfacing. The results show that two NIRS channels placed over predefined brain areas, i.e., left or right DLPFC and APFC, respectively, may significantly increase the performance of optical BCIs compared to the more common approach to use only one channel (e.g., [15, 20]).

In the feature selection process, we looked for best performing antagonistic and individual features, respectively. To account for the low number of trials available for evaluating the performance, we adapted the chance level of classification to guarantee the correct comparison [14]. By using the best antagonistic [oxy-Hb] features performing an off-line simulation mean classification accuracy (%) of 79.69 ± 8.01 (mean $\pm$ SD, Table 1) was computed. Individual features performed worse (classification accuracies (%) of 63.28 ± 8.48 (ROI_1), 59.38 ± 12.05 (ROI_2), and 63.28 ± 6.19 (ROI_3), Table 2). In each case, only one

Table 3 Classification accuracies (in %) for antagonistic [deoxy-Hb], [Hbtot], and tuples of [oxy-Hb] and [deoxy-Hb] features for all subjects

In addition, the classification accuracies (bold numbers indicate accuracies above the chance level of 71.9%) using a group-related set of antagonistic [oxy-Hb] features are shown

Subj.	Antagonistic pattern				
	[oxy-Hb]	[deoxy-Hb]	[Hbtot]	[deoxy-Hb] and [oxy-Hb]	Group-related
S1	68.75	68.75	50.00	68.75	68.75
S2	**87.50**	62.50	**81.25**	68.75	**75.00**
S3	**75.00**	62.50	56.30	**75.00**	68.75
S4	**87.50**	**81.25**	**93.75**	**81.25**	**87.50**
S5	**81.25**	50.00	68.75	68.75	62.50
S6	68.75	56.25	56.25	62.50	50.00
S7	**87.50**	62.25	**93.75**	68.75	**75.00**
S8	**81.25**	**87.50**	**81.25**	**93.75**	**75.00**
Mean	79.69	66.38	72.66	73.44	70.31
SD	8.01	12.48	17.33	9.88	10.95

subject reached accuracies above the chance level. In contrast, with the antagonistic features 6 of the eight subjects (75%) performed accuracies (mean 83.3%) above the chance level. So the use of antagonistic [oxy-Hb] features, compared to individual [oxy-Hb] features from ROI_1, ROI_2, and ROI_3, significantly increased the classification accuracy (Tables 1 and 2; Fig. 1b).

In addition, we compared antagonistic [oxy-Hb] with antagonistic [deoxy-Hb], [Hbtot], and ([oxy-Hb], [deoxy-Hb]) tuples features. [deoxy-Hb], [Hbtot], and [(de)oxy-Hb] performed worse (classification accuracies (%) of 63.38 ± 12.48 ([deoxy-Hb]), 72.66 ± 17.33 ([Hbtot]), and 73.44 ± 9.88 ([oxy-Hb] and [deoxy-Hb]), Table 3) whereby only [deoxy-Hb] exhibits significant difference to the use of [oxy-Hb]. These lower classification accuracies may be simply explained by the fact that [deoxy-Hb] changes are smaller in amplitude, usually by a factor two or more (e.g., [9, 13]), and higher in variance than [oxy-Hb] changes, more susceptible by noise and therefore less suitable as feature for single-trial classification.

The performance comparison between the use of subject-specific versus group-related features surprisingly revealed no significant differences. This supports the hypothesis that MA generates focal and rather well defined metabolic response patterns. For the realization of optical BCIs, this means that the considered features are spatially focused, task-related and valid for several users. Antagonistic activation patterns known as "focal activation/surround deactivation" have been described in different studies. So, e.g., "focal ERD / surround ERS" was reported during hand and foot movement execution or imagination in EEG [19, 23] and "positive BOLD/negative BOLD" in fMRI ([4, 11]. The usability of this phenomenon for classification in motor imagery based BCI systems (ERD/ERS) is well documented [18]. Novel is however that this phenomenon is also present in NIRS data [17], and in this study, we showed the first time the usefulness of this phenomenon for NIRS data classification. Although the study revealed significant results, some limitations should also be mentioned. First of all, the number of subjects is low. However, concerning the significant increase of the classification accuracy using antagonistic [oxy-Hb] changes instead of individual features only from one single region, our findings suggest that the use of antagonistic patterns may be a suitable control strategy for optical BCIs. However, to clarify this in more detail, especially in an online study, a bigger sample is needed. Another limitation is the temporal resolution of the hemodynamic response—in the range of several seconds—which limits the information transfer rates achievable for BCI-based communication. In [17], we found a delay of the onset and a peak latency of the hemodynamic responses in the order of 2–3 s. With the paradigm, classification approach and analysis windows used for this study in mind, around 12 s (MA) to 16 s (REST) (Table 1) would be needed to classify the task reasonable well. By shortening the baseline interval prior to the task to 5 s, this might lead to a maximal achievable information transfer rate of around 3–3.5 bits/min (comparable with results in [2]). To increase this transfer rate further basic research is necessary, e.g., investigating the use of fast optical signals [6, 12, 24].

In summary, this study suggests that the use of antagonistic [oxy-Hb] features may significantly increase the classification accuracy. The off-line simulation results confirmed our hypothesis that two prefrontal NIRS channels can capture antagonistic hemodynamic patterns during a MA task that can be detected reasonably well without the need of time consuming user-adaptation. In combination with the self paced paradigm, the use of antagonistic pattern may be an important contribution for simple and cheap optical BCI systems which are currently in development.

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