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Exploring the capability of wireless near infrared spectroscopy as a portable seizure detection device for epilepsy patients

Jesper Jeppesen [a,*], Sándor Beniczky [a,b], Peter Johansen [c], Per Sidenius [d], Anders Fuglsang-Frederiksen [a]

[a] Department of Neurophysiology, Aarhus University Hospital, Nørrebrogade 44, 8000 Aarhus C, Denmark
[b] Department of Clinical Neurophysiology, Danish Epilepsy Centre, Visby Álle 5, 4293 Dianalund, Denmark
[c] Department of Engineering, Aarhus University, Finlandsgade 22, 8200 Aarhus N, Denmark
[d] Department of Neurology, Aarhus University Hospital, Nørrebrogade 44, 8000 Aarhus C, Denmark

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ABSTRACT

Purpose: Near infrared spectroscopy (NIRS) has proved useful in measuring significant hemodynamic changes in the brain during epileptic seizures. The advance of NIRS-technology into wireless and portable devices raises the possibility of using the NIRS-technology for portable seizure detection.
Methods: This study used NIRS to measure changes in oxygenated (HbO), deoxygenated (HbR), and total hemoglobin (HbT) at left and right side of the frontal lobe in 33 patients with epilepsy undergoing long-term video-EEG monitoring. Fifteen patients had 34 focal seizures (20 temporal-, 11 frontal-, 2 parietal-lobe, one unspecific) recorded and analyzed with NIRS. Twelve parameters consisting of maximum increase and decrease changes of HbO, HbR and HbT during seizures (1 min before- to 3 min after seizure-onset) for left and right side, were compared with the patients' own non-seizure periods (a 2-h period and a 30-min exercise-period). In both non-seizure periods a 4 min moving windows with maximum overlapping were applied to find non-seizure maxima of the 12 parameters. Detection was defined as positive when seizure maximum change exceeded non-seizure maximum change.
Results: When analyzing the 12 parameters separately the positive seizure detection was in the range of 6–24%. The increase in hemodynamics was in general better at detecting seizures (15–24%) than the decrease in hemodynamics (6–18%) ($P = 0.02$).
Conclusion: NIRS did not seem to be a suitable technology for generic seizure detection given the device, settings, and methods used in this study. There are still several challenges to overcome before the NIRS-technology can be used as a home-monitoring seizure detection device.

1. Introduction

Near infrared spectroscopy (NIRS) is an evolving technology for continuous, non-invasive monitoring of hemodynamic changes in the brain [1,2]. Although the NIRS technology holds a disadvantage over BOLD-fMRI in spatial resolution and depths of measurement, NIRS is still superior to fMRI in temporal resolution and, importantly, gives the opportunity to measure the long-term hemodynamics in the brain even when patients are in motion [1]. Already in the beginning of the millennium NIRS proved to be a useful aid for lateralizing the seizure onset. Oxygenated hemoglobin (HbO) and saturation of the regional cerebral blood volume (rCBV) measured with NIRS, was shown to increase significantly in the seizure onset zone [3,4]. Recent research with NIRS furthermore revealed that the local hemodynamic changes during focal seizures quickly spread both extratemporal and contralateral in the brain [5,6]. Nguyen et al. reported significant changes of both oxy- and deoxygenated hemoglobin (HbO and HbR) in the frontal lobe both ipsi- and contralateral for temporal lobe seizures [5].

Prior research using NIRS in epilepsy have mainly focused on hemodynamic changes during seizures in regards to localizing focus, distinguishing seizure types, and spread of hemodynamic changes [3–7]. However, suggestions of using NIRS to predict or detect epileptic seizures have as of lately been proposed and also studied in a few cases [8–10]. Recently NIRS-devices with wireless connection have been introduced, which furthermore realize the

* Corresponding author. Tel.: +45 7846 9909.
E-mail addresses: jespjepp@rm.dk (J. Jeppesen), Sandor.Beniczky@aarhus.rm.dk (S. Beniczky), pj@eng.au.dk (P. Johansen), Per.Sidenius@aarhus.rm.dk (P. Sidenius), Anders.Fuglsang@aarhus.rm.dk (A. Fuglsang-Frederiksen).

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possibility of using the technology as a portable home-monitoring epilepsy seizure detection or prediction device [11,12]. However, it still remains uncertain if the NIRS-measured hemodynamic changes seen during seizures are greater than (and thereby can be distinguished from) the hemodynamic changes that happens during other daily non-seizure periods including random movement and exercise, which is also known to alter the oxygenation in the prefrontal cortex [2].

The aim of this study was to test if standardized quantitative NIRS-measurement of the changes of oxygenated- (HbO), deoxygenated- (HbR) and total-hemoglobin (HbT) that occur in the frontal lobe of the brain during seizures could be used as a biomarker for seizure detection. In order to test this we compared the hemodynamic changes during seizures from each patient with selected control non-seizure periods of both exercise and non-exercise periods from the same patient.

2. Methods

2.1. Patients

Thirty-three patients enrolled in long term video-EEG monitoring (LTM) at the epilepsy monitoring unit (EMU) in either Aarhus University Hospital or Danish Epilepsy Center in Dianalund for diagnostic or surgical evaluation of epilepsy were recruited to participate in the study. Fifteen (age: 20–58, med: 39) of the 33 patients had one or more epileptic seizures with frontal NIRS-recording during the period of hospitalization. If a patient had more than six NIRS-recorded seizures, only the first six seizures were chosen. A total of 34 focal seizures (31 complex partial, three simple partial) were recorded and analyzed with NIRS. All patients were instructed to perform an exercise-bike session with stepwise pulse increase of 110 beats/min for 2 min, 140 beats/min for 2 min and all-out maximum for 3 min. This was used as one of the sample control periods. One patient did not complete the test because of knee-injuries (Patient 15).

2.2. Equipment

Two PortaLite wireless near infrared spectroscopy devices (Artinis Medical Systems B.V., PW Elst, Holland) were used for all recordings. The devices were placed on each site of the forehead just below the hairline. On the left side this was between the Fp1 and F7 EEG-electrode and on the right side between the Fp2 and F8 EEG-electrode in the 10–20 EEG electrode placement system. Black cloths were attached on top of the EEG-cap to ensure that no external light from other than the NIRS-device would interfere with the NIRS signal (see Fig. 1). Each device has three light source emitting diodes at 30, 35 and 40 mm from the detector. The diodes emit near infrared light at wavelengths of 760 and 850 nm to continuously measure the hemoglobin changes using the modified Lambert–Beer Law method [13]. To derive quantitative concentration changes from measurements of light attenuation, the optical path length has to be known. This is obtained by multiplying the source/detector separation by a laboratory measured differential path length factor (DPF) which accounts for the increased distance the light travels due to scattering. As DPF increases with age a specific DPF was calculated for each patient using the formula: DPF = 4.99 + 0.067 (age^0.814), (if age $>$ 50 the age was set to 50) [14]. Oxy-, deoxy- and total hemoglobin concentration changes in units of micromoles pr. liter was computed with a sampling frequency of 10 Hz for each of the three diodes. The recorded data were transmitted online via Bluetooth from the battery-driven PortaLite device to a PC-laptop and obtained in the OxySoft program (versions 2.1.6 or 3.0.53). From both devices the mean value of the three estimates (one from each diode) of HbO, HbR and HbT was computed for further analyses. Timestamps was manually inserted during the recordings in the OxySoft program to synchronize timing with the video-EEG recordings. The batteries of the wireless NIRS-device could hold 8–10 h thus had to be changed three times every day.

2.3. Signal analyses

In order to even out the heart pulse-effect of the hemodynamic readings and even out short sudden artifacts of the measurements the sample frequency of 10 Hz was down-sampled to 0.25 Hz using simple moving average method. We found it reliable to down-sample the recordings to 0.25 Hz, as the physiological interpretation of the signal was unaffected because the seizures with hemodynamic responses generally showed sequences from nadir to peak and vice versa of at least 20 s, which also is in alignment with other NIRS-studies of epileptic seizures [3,4].

In order to quantify and compute the changes during seizures and test if they could be used as a possible seizure detection biomarker, we developed a custom made program to find maximum increases and decreases of HbO, HbR and HbT during seizures and non-seizure periods. A 4 min window from 1 min before seizure-onset to 3 min after seizure-onset was selected for all seizures and the maximum increases and decreases of HbO, HbR and HbT from both recording sides were computed. Each patient had these maxima compared with two non-seizure periods of (1) 30 min period in which the patient performed a bike exercise-test, (2) 2-h non-seizure period recorded from 3 to 1 h before the first analyzed seizure of the patient. If the 2-h non-seizure period contained the bike-exercise test or any notable artifacts caused by movement of the NIRS device or battery change of the wireless NIRS-device, the first previous 2-h period with none of the above artifacts was chosen instead. For both of the non-seizure periods a 4 min rectangular moving window with maximum overlapping

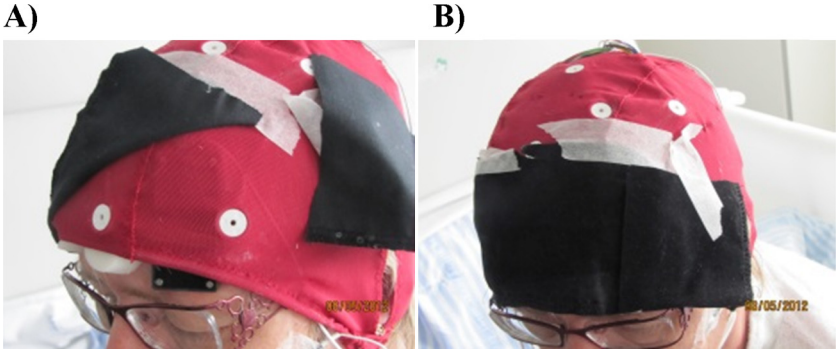

Fig. 1. (A) Left NIRS-device was placed between EEG-electrode F1 and F7. (B) Black cloths covered the NIRS and surrounding area from external light.

(moving one sample, 4 s = 98.3% overlapping) was applied and the maximum increases and decreases of HbO, HbR and HbT for all recordings computed to compare with that of the seizures from the patient.

2.4. Data analyses and statistics

The NIRS-data were analyzed using 12 parameters (increase/decrease of the HbO/HbR/HbT on the left/right side ($2 \times 3 \times 2$)). Positive seizure detection was defined for each parameter as when the maximum increase/decrease during the seizure exceeded that of the maximum during any 4-min window of the non-seizure periods from the patient. For example, the maximum increase of left-side HbO during the window of seizure was compared with the maximum increase of left-side HbO of the 4-min windows with the highest maximum of left-site HbO from the non-seizure periods of the patient. If the maximum seizure-value divided by the maximum non-seizure-value exceeded 1, positive seizure prediction using left-side HbO was regarded (see Table 1).

The same test for seizure detection was also done by comparing the seizure maxima with only the 2-h non-exercise maxima.

For statistical analysis we used the two-sided *students t-test* to compare the sensitivity of numbers of seizure detection between the (1) increases vs. decreases parameters and (2) ipsilateral vs. contralateral parameters for TLE seizures. For all 12 parameters we used two-sided *Fishers exact test* for evaluation of group differences in sensitivity of seizure detections between frontal and non-frontal lobe seizures. $P < 0.05$ was considered significant.

3. Results

The 12 parameters analyzed separately detected two to eight of the 34 seizures (6–24%) (Tables 1 and 2). The increase parameters were in general better for seizure detection (15–24%, Table 1) than the decrease parameters (6–18%, Table 2) ($P = 0.02$). No difference could be established in seizure detection sensitivity of ipsilateral vs. contralateral parameters for temporal lobe seizures ($P = 0.77$). The difference of seizure detection probability between frontal

Table 1
Increases of HbO, HbR and HbT: ratio of seizure maximum vs. non-seizure maximum.

Patient nr.	Lobe	Type	HbO left	HbO right	HbR left	HbR right	HbT left	HbT right
1	Temp. (right)	CPS	1.02	0.70	0.29	0.12	0.93	0.40
	Temp. (right)	CPS	1.59	0.81	0.47	0.43	1.51	0.58
2	Temp. (right)	CPS	0.47	0.87	0.37	0.33	0.44	0.74
	Temp. (right)	CPS	0.83	1.30	0.42	0.37	0.75	1.10
3	Temp. (right)	CPS	0.57	0.74	0.93	0.95	0.66	0.79
4	Temp. (right)	CPS	0.68	0.63	3.69	3.03	0.79	0.73
5	Temp. (left)	CPS	0.75	0.56	0.31	0.23	0.64	0.48
	Temp. (left)	CPS	0.93	0.71	0.28	0.20	0.66	0.43
	Temp. (left)	CPS	0.41	0.53	0.85	0.51	0.47	0.43
	Temp. (left)	CPS	0.47	0.69	0.58	0.64	0.58	0.76
6	Temp. (left)	SPS	0.36	0.63	0.09	0.21	0.28	0.55
	Temp. (left)	SPS	0.48	0.62	0.41	0.35	0.34	0.49
	Temp. (left)	SPS	0.56	0.88	0.50	0.51	0.41	0.72
7	Temp. (left)	CPS	0.56	0.40	0.86	0.91	0.75	0.48
8	Temp. (left)	CPS	0.79	0.91	0.55	0.60	0.69	0.82
	Temp. (left)	CPS	0.85	0.88	0.64	0.79	0.82	0.84
9	Temp. (left)	CPS	0.61	0.81	0.40	0.62	0.83	0.90
	Temp. (left)	CPS	1.00	1.01	0.40	0.68	1.18	1.12
10	Temp. (left)	CPS	0.44	0.51	0.44	0.69	0.46	0.57
	Temp. (left)	CPS	0.34	0.61	0.84	0.78	0.32	0.56
11	Paterio (right)	CPS	1.24	1.67	1.18	1.51	1.13	1.94
	Paterio (right)	CPS	0.76	1.26	1.14	1.20	0.92	1.42
12	Unspecified	CPS	0.62	0.87	0.63	0.95	0.55	0.64
13	Frontal	CPS	0.30	0.56	1.37	0.77	0.37	0.82
	Frontal	CPS	0.98	0.74	1.37	1.05	0.97	1.06
	Frontal	CPS	0.68	0.56	1.59	1.92	0.44	1.20
14	Frontal	CPS	1.15	1.16	0.32	0.46	0.95	1.17
	Frontal	CPS	1.16	1.20	0.82	0.51	1.03	1.13
	Frontal	CPS	0.89	0.50	0.98	0.41	0.92	0.53
	Frontal	CPS	0.83	0.67	0.75	0.52	0.92	0.70
	Frontal	CPS	0.86	0.50	0.57	0.39	0.83	0.50
	Frontal	CPS	0.95	0.53	1.54	0.60	1.06	0.54
15	Frontal	CPS	0.62	0.81	1.00	0.77	0.62	0.80
	Frontal	CPS	0.43	0.51	0.37	0.17	0.48	0.39
	Number of detection (frontal only)		2	2	4	2	2	4
	Detections in % (frontal only)		18%	18%	36%	18%	18%	36%
	Number of detection (non-frontal only)		3	4	3	3	3	4
	Detections in % (non-frontal only)		13%	17%	13%	13%	13%	17%
	Fischer exact test (frontal vs. non-frontal)		1	1	0.178	1	1	0.388
	Number of detections (total)		5	6	7	5	5	8
	Detections in % (total)		15%	18%	21%	15%	15%	24%

Colored spaces show positive seizure detection (seizure maximum > non-seizure maximum).
Abbreviations: Temp., temporal lobe; CPS, complex partial seizure; SPS, simple partial seizure.

Table 2
Decreases of HbO, HbR and HbT: ratio of seizure maximum vs. non-seizure maximum.

Patient nr.	Lobe	Type	HbO left	HbO right	HbR left	HbR right	HbT left	HbT right
1	Temp. (right)	CPS	0.07	0.03	0.67	0.74	1.22	0.59
	Temp. (right)	CPS	0.32	0.05	0.56	0.57	0.59	0.74
2	Temp. (right)	CPS	0.31	0.75	0.42	0.26	0.27	0.58
	Temp. (right)	CPS	0.64	0.76	0.40	0.48	0.55	0.56
3	Temp. (right)	CPS	0.43	0.44	0.43	0.46	0.45	0.43
4	Temp. (right)	CPS	0.72	0.51	0.29	0.13	0.15	0.17
5	Temp. (left)	CPS	0.04	0.07	0.43	0.36	0.06	0.10
	Temp. (left)	CPS	0.40	0.00	1.01	0.59	0.33	0.00
	Temp. (left)	CPS	1.07	0.99	0.46	0.56	0.95	0.70
	Temp. (left)	CPS	0.68	0.69	0.74	0.47	0.64	0.55
6	Temp. (left)	SPS	0.41	0.92	0.33	0.47	0.38	0.76
	Temp. (left)	SPS	0.20	0.68	0.56	0.64	0.22	0.64
	Temp. (left)	SPS	0.09	0.24	0.60	0.45	0.50	0.23
7	Temp. (left)	CPS	0.86	0.47	0.92	0.44	0.90	0.40
8	Temp. (left)	CPS	0.05	0.16	0.40	0.48	0.04	0.13
	Temp. (left)	CPS	0.17	0.25	0.48	0.84	0.76	0.84
9	Temp. (left)	CPS	0.09	0.86	0.15	0.31	0.15	0.30
	Temp. (left)	CPS	0.21	0.34	0.22	0.24	0.22	0.37
10	Temp. (left)	CPS	0.59	0.76	0.67	1.00	0.63	0.93
	Temp. (left)	CPS	0.56	0.68	0.52	0.67	0.54	0.66
11	Paterio (right)	CPS	0.90	0.91	0.08	0.33	0.76	0.67
	Paterio (right)	CPS	0.23	0.31	0.33	0.19	0.23	0.26
12	Unspecified	CPS	0.99	0.81	0.78	0.95	0.87	0.71
13	Frontal	CPS	0.41	0.05	0.28	0.12	0.21	0.08
	Frontal	CPS	0.01	0.73	0.21	0.57	0.02	0.69
	Frontal	CPS	0.78	0.45	0.51	0.33	0.35	0.39
14	Frontal	CPS	0.30	0.03	0.93	1.18	1.12	1.31
	Frontal	CPS	1.44	1.42	1.67	1.36	1.30	1.51
	Frontal	CPS	1.08	0.69	1.00	0.73	1.11	0.75
	Frontal	CPS	1.29	1.14	0.98	0.64	1.28	1.15
	Frontal	CPS	1.37	0.80	0.77	0.75	1.32	0.80
	Frontal	CPS	0.23	0.84	0.33	0.61	0.27	0.78
15	Frontal	CPS	0.98	0.13	1.36	0.03	0.72	0.10
	Frontal	CPS	0.52	0.31	0.20	0.16	0.45	0.27
	Number detection (frontal only)		4	2	2	2	5	3
	Detections in % (frontal only)		36%	18%	18%	18%	45%	27%
	Number detection (non-frontal only)		1	0	1	0	1	0
	Detections in % (non-frontal only)		4%	0%	4%	0%	4%	0%
	Fischer exact test (frontal vs. non-frontal)		0.029	0.098	0.239	0.098	0.008	0.028
	Number detections (total)		5	2	3	2	6	3
	Detections in % (total)		15%	6%	9%	6%	18%	9%

Colored spaces show positive seizure detection (seizure maximum > non-seizure maximum).
Abbreviations: Temp., temporal lobe; CPS, complex partial seizure; SPS, simple partial seizure.

lobe seizures and non-frontal lobe seizures was significant for 3 of the 12 parameters: left HbO decrease, left HbT decrease and right HbT decrease (Tables 1 and 2).

When comparing the seizures maxima with only the 2-h non-exercise control sample period maxima the 12 parameters separately detected 12–35% of the seizures (data not shown).

Initial qualitative analysis of NIRS-data from the seizures revealed most hemodynamic changes to occur just before or in the first minutes after seizure onsets in accordance with previous NIRS studies [3,6]. We did not find any trend of changes in the pre-ictal periods, which in general exceeded the ictal-periods of the seizures.

4. Discussion

The aim of our study was to compare changes of regional frontal lobe hemodynamic blood content of HbO, HbR and HbT seen in partial seizures with changes occurring in non-seizure periods in order to evaluate if the wireless-NIRS technology in the current state is suitable as an online seizure detection device.

The results of the study suggest that the quantified maximum NIRS-measured hemodynamic changes in the frontal lobe during seizures exceeded only in a small number of seizures the maximum hemodynamic changes during other non-seizure periods. Even when comparing the hemodynamic changes with only one non-exercise, non-seizure period of 2-h the positive detection rate was still surprisingly low (<35% for any of the analyzed parameter). Although seizure detection was poor for all parameters the increase rather than the decrease of HbO, HbR and HbT seemed to be overall better detectors of seizure. This is in alignment with most NIRS-studies mainly having reported increases of hemodynamic parameters during seizure [3,5,11,15,16].

We were not able to establish a trend for better detection of ipsi- vs. contralateral side NIRS-measurements for temporal lobe seizures. Generally we also did not see any notable systematic difference between probability of seizure detection in the left and the right side of the NIRS-recordings. We believe this is very likely to be due to the rapid contralateral spreading of the hemodynamic changes which has also been reported in other studies [5,6]. The EEG only showed bilateral propagation to the contralateral side of

the epileptic focus in one of the six seizures with positive seizure detection in at least one contralateral parameter. Although relatively more seizure detections were evident for frontal vs. non-frontal lobe seizures for some hemodynamic parameters, no single parameter had positive seizure detection of more than 45% of the frontal lobe seizures (left-side HbT decrease).

Peng et al. recently reported large inter-patient variability, when estimating the ability of fNIRS to detect hemodynamic responses of inter-ictal spikes in epilepsy patients [17]. One of the greatest challenges of using NIRS for seizure detection lies in the individual differences of hemodynamic responses seen among the patients [6,15]. The diversity of the amplitude and direction of hemodynamic change between patients makes it extremely difficult to develop a generic seizure detection algorithm. Fig. 2A and B depicts an example of this diversity for two different patients with temporal lobe seizures. The seizure depicted in Fig. 2A exposed an HbR increase in both left and right side that was more than threefold higher than in any control period. Yet, this seem to be a standalone case for this particular patient and seizure in this study, as no other patient or seizure had this extend of relative hemodynamic change when compared to control periods. However, Fig. 2B depicts an example of a seizure which would be extremely difficult to detect. Thus, we find it unlikely that generic seizure detection with frontal lobe NIRS-sensors is feasible. In spite of this, it still cannot be ruled out that individual patient tailored seizure detection algorithms could be applicable for some patients.

Supraventricular tachycardia has been reported not to cause notable changes in NIRS measured hemodynamics in the brain [18]. We found seizure induced pulse increase of at least 20 beats/min in all 34 seizure analyzed and such could not find any relation between the NIRS changes during seizures and the seizure induced tachycardia.

Two studies using forehead recordings with NIRS of a few epilepsy patients have suggested that pre-ictal increases of regional hemoglobin saturation arise several minutes before the seizure [8,9], in contrast another pilot-study showed a decrease of metabolic demand ipsilateral to the focus in the same period [10]. When qualitatively estimating the pre-ictal periods of our data, we could in general not find any changes in HbO, HbR or HbT that exceeded the changes in the 1-min before seizure-onset to 3-min after seizure-onset period we chose for quantitative analyses. Thus we are most hesitant when considering if a general prediction of seizures could be possible for the patients (and with the NIRS-measurements) presented in this study. We consider the difference in NIRS-equipment together with differences in methods when choosing the non-seizure periods (or baseline values) and the lengths of the non-seizure periods to be the main reasons for the controversies of the pre-ictal findings between our study and the pilot-studies [8–10].

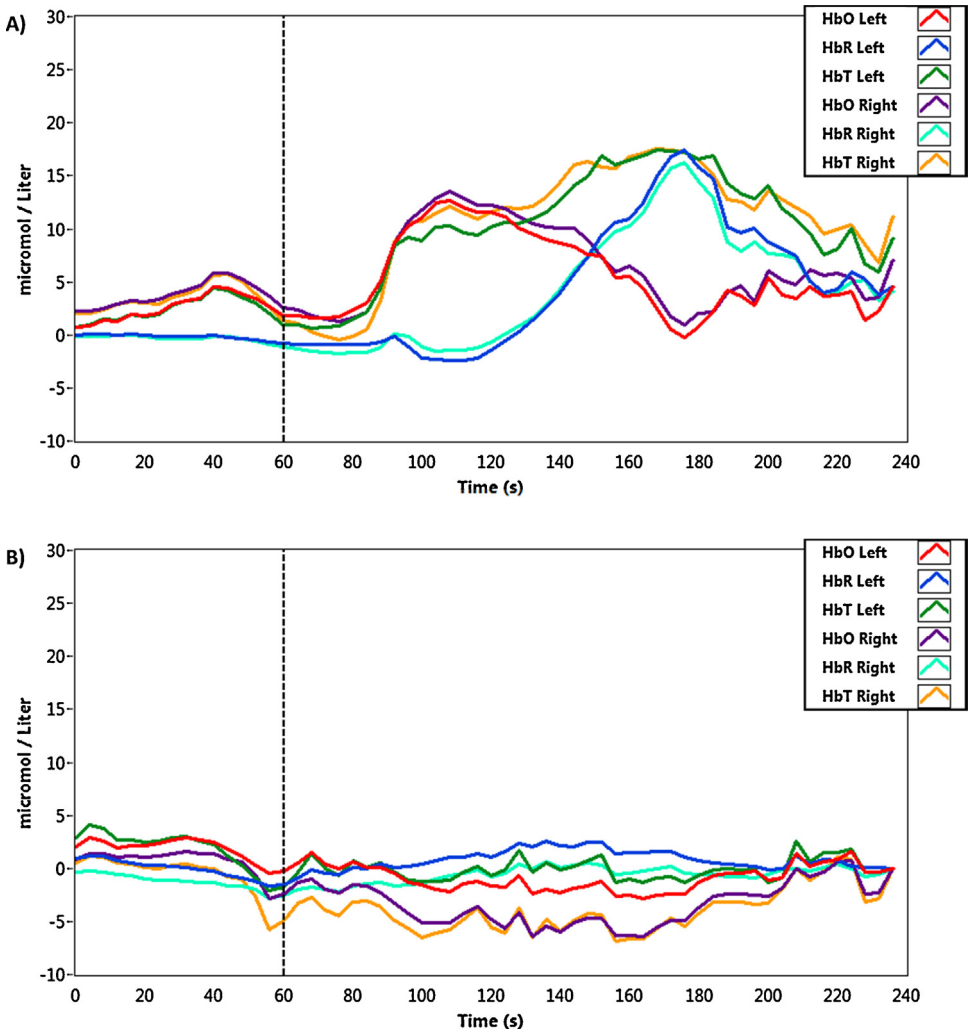

Fig. 2. Two examples of the diversity of hemodynamic changes in NIRS-recordings during seizures (1 min before to 3 min after seizure onset), dotted line resembles seizure-onset time. (A) Patient 4, 1st seizure. (B) Patient 10, 2nd seizure.

Motion artifacts and other physiological mediated artifacts in non-sedentary patients have been reported to be one of the greatest issues when doing brain NIRS-measurement [11,19]. Any movement of the body mobilizes the head directly or indirectly and therefore also the optical fibers, which temporarily modifies the contact between the skin and optode [20]. Wrinkling the forehead causes the emitter-detector angle to change and thereby alter the area of measurement, which is likely to alter the changes of HbO, HbR and HbT recorded. These types of artifacts could have had an influence on the poor seizure detection results we have presented here. However, the exact same artifacts would be very much likely to occur if the wireless-NIRS system should be employed in a home-monitoring seizure alarm system, although some filtering and attends of different fixation might help the signal to noise ratio (SNR) for better NIRS-recordings [20]. In term of the long-term forehead NIRS-measurements of patients we additionally experienced a general discomfort with wearing the device for several days, which resulted in patients touching and scratching the device and in some cases asked to have it removed.

A potential limitation of this study is the unknown influence of extra-cerebral tissue on cerebral NIRS signal. Theoretically, the NIRS signal is considered to originate from a banana-shaped volume from both the superficial layers (skin and extra-cranial tissue) and the deeper cortical layers [5]. Therefore, contributions from the superficial layers cannot be ruled out with the NIRS-equipment we used in this study, as it did not possess the ability to subtract the possible contamination from the superficial extra-cranial tissue. However this problem is also a known issue in other commercial NIRS-devices [21]. The manual timestamp method we used is another potential limitation, as we did experience timely drift between the video-EEG system (Nicolet-One) and the NIRS-laptop system (Oxysoft). However, when using the relatively long-time seizure window of 4 min, we do not consider this to have any influence on the results.

5. Conclusion

We believe there are still some challenges to overcome both practically and technically before the NIRS-technology can be used as a home-monitoring seizure detection device. The quantified hemodynamic changes in the frontal lobe during seizures only in 6–24% of the seizures exceeded the same changes during 2½-h non-seizure periods from the same patient. A generic algorithm for seizure detection with NIRS does not seem probable. However, individual patient tailored algorithms using NIRS-measurements may in the future be considered for some eligible patients.

Conflict of interest

We have no conflicts of interest or financial support with regards to the authorship or publication of this article.

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