Kirlangic, Mehmet Eylem; Yeo, Yi Lin; Fiedler, Patrique; Haueisen, Jens

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Original published in:	Current directions in biomedical engineering. - Berlin : De Gruyter. - 8 (2022), 2, p. 125-128.
Original published:	2022-09-02
ISSN:	2364-5504
DOI:	10.1515/cdbme-2022-1033
[*Visited:*	2022-10-12]

Mehmet Eylem Kirlangic*, Yi Lin Yeo, Patrique Fiedler, Jens Haueisen

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https://doi.org/10.1515/cdbme-2022-1033

Abstract: DC potential shifts are the shifts observed in the EEG baseline which can last from seconds to minutes. The significance of these low-frequency components in healthy as well as pathological states of human physiology is getting more and more attention not only in scientific research but also in clinical applications. In this paper, we present our novel multimodal measurement setup for simultaneously investigating DC potential shifts in EEG (DC-EEG) and the changes in noninvasive transcutaneous pCO2 measurements. We present preliminary results of our measurements during hyperventilation and apnea, which are two commonly used activation methods for changes in pCO2.

Keywords: electroencephalography, apnea, hyperventilation, potential shift, carbon dioxide.

1 Introduction

The so-called DC potential shifts are the shifts observed in the EEG baseline which can last from seconds to minutes [1,2]. They are studied in various contexts under different provocation/activation methods and paradigms. Behavioural changes associated with the sleep-wake cycle [2], seizure activity [3], and deviations of gas pressures in blood and tissue [2] serve as experimental models for investigating them in the brain.

Currently, there is no consensus on the definition of these lower frequency components of EEG. Terms like DC potentials [1,2], slow cortical potentials [4,5], slow waves [6,7], infra-slow rhythm [8], ultra-low frequency [9], slow periodic activity [10] are used as synonyms in the related literature and refer to the frequency range below 1 Hz down to 0.05 Hz [11] or even down to 0.01 Hz [12]. Neither is there a consensus on the origin and generation mechanism of these potentials [2,3,13-15]. Nevertheless, they are reported to be fundamental in diverse states of the brain such as the sleep-wake cycle [2] and seizure activity [3] and are accepted to be indicators of cortical excitability [1,2,5]. These low frequency components can only be acquired with DC-EEG or DC-MEG measurements which require specific hardware. Additionally, they are vulnerable to technical and biological artefacts including movements and instabilities at the electrode-skin interface [16,17]. Apparently, these are the main reasons why these frequency components have been investigated less often.

According to Caspers [2], the cortical DC potential shift is an indicator of the cortical excitability changes with negative and positive shifts respectively indicating increased and decreased cortical excitability. At the neuronal level, these potentials are proposed to reflect changes in the depolarization of apical dendrites and regulate local thresholds of cortical cell assemblies. On the other hand, cortical DC-shifts are observed in association with the alterations of partial gas pressures, both pCO2 and pO2, in blood and tissue [2,14]. DC-shifts are reported to result from a rise in the inspiratory CO2 content, from a reduction of the ventilation rate (apnea), or from a respiratory arrest following a period of breathing pure oxygen (oxygenated apnea). These shifts are reported to be predominant at the vertex and midline electrodes [1,2,13,18].

Applying the aforementioned activation methods and using pCO2 as a control parameter, it is possible to observe and analyse the dynamics of the DC-shifts in EEG. We propose a setup for non-invasive simultaneous EEG and pCO2 measurements for this purpose and present the first proof-of-principle results.

2 Methods

2.1 Setup

The setup (Figure 1) comprises a DC-coupled EEG amplifier (eego™ EE-225, ANT Neuro B.V., Hengelo, The

***Corresponding author: Mehmet Eylem Kirlangic:** Technische Universität Ilmenau, Institute of Biomedical Engineering and Computer Science, Gustav-Kirchhoff Str. 2, Ilmenau, Germany, Mehmet.Kirlangic@tu-ilmenau.de
Yi Lin Yeo, Patrique Fiedler, Jens Haueisen: Technische Universität Ilmenau, Institute of Biomedical Engineering and Computer Science, Ilmenau, Germany

Netherlands) and a system for continuous non-invasive monitoring of transcutaneous pCO2 (SenTec Digital Monitoring System, SenTec AG, Therwil, Switzerland). The analogue outputs of the SenTec system are connected to the eego amplifier's auxiliary bipolar inputs. All inputs of the EEG amplifier including the auxiliary inputs are sampled at 1024 samples/second. At the analogue output of the SenTec system, the internally calculated values of SpO2, pulse rate (PR) and pCO2 are updated once per second, whereas the perfusion index (PLETH/PI) is updated once per 32 ms.

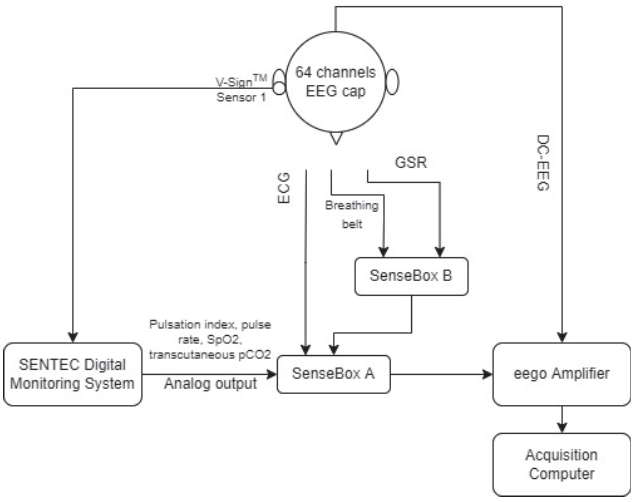

Figure 1: Setup constructed for simultaneous measurement of DC-EEG and transcutaneous pCO2. SenseBox A and B are cascadable auxiliary bipolar input channel units of the eego amplifier system.

In addition to the output signals of the pCO2 monitoring system, the multimodal measurement setup enables the acquisition of further biosignals such as ECG, respiration (via breathing belt), and galvanic skin response (GSR). A 64-channel gel-based equidistant EEG cap (waveguard original, ANT Neuro B.V., Hengelo, The Netherlands) is used for the EEG measurements. Reference and ground electrodes are placed at the right and left mastoids, respectively.

2.2 Measurement protocol

Hyper- and hypoventilation are two activation methods to experimentally cause and observe DC-shifts in EEG. We use hyperventilation and breath-holding (i.e. apnea) in our measurements (Figure 2) which are performed with eyes open on two volunteers.

Hyperventilation protocol: For a baseline measurement, we start with a recording of 3 minutes in a relaxed alert state. After 3 minutes, the volunteer is asked to breathe deeper in a constant rhythm that is close to his/her natural breathing. The volunteer is instructed to avoid head and eye movements. The

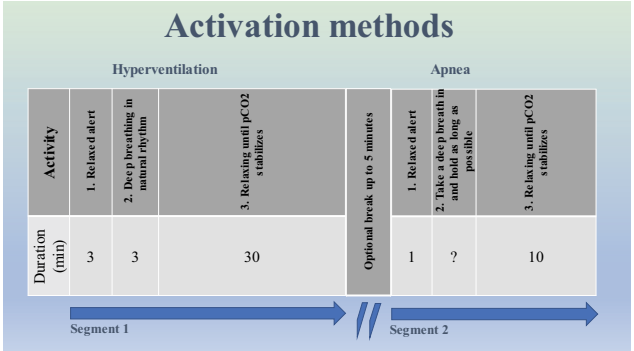

Figure 2: Time course of the activation methods, hyperventilation and apnea, during a complete measurement of two segments.

measurement is continued for another 30 minutes to observe the long-term changes in the DC-EEG.

Apnea protocol: For baseline measurement, we start with a recording of 1 minute in a relaxed alert state. After 1 minute, the volunteer is asked to take a deep breath and to hold the breath as long as possible. After the exhalation, the acquisition is continued for another 10 minutes. The volunteer is instructed to avoid head and eye movements during the complete recording.

Depending on the need of the volunteer, we pause between these two activation methods for up to 5 minutes.

2.3 Signal conditioning and processing

The raw signals are exported as CNT files by the eego software (ANT Neuro B.V., Hengelo, The Netherlands), which are then imported to MATLAB (The Mathworks Inc., Natick, USA). Signal conditioning and processing are performed using custom MATLAB scripts.

The EEG signals and the pCO2 signal are lowpass filtered by an FIR-filter with a cut-off frequency of 0.001 Hz. Because of this very low cut-off frequency, there is no need to specifically treat other possible artefacts, for example, ECG artefacts around 1 Hz.

In the hyperventilation segment, the global minimum of the pCO2 signal is determined. Correlation coefficients between the midline DC-EEG channels and the pCO2 signal are calculated for a moving window of 6 minutes (3 minutes activation and 3 minutes recovery) starting 10 seconds before the beginning of hyperventilation until 1.5 minutes thereafter (half the activation interval). The time step of the moving analysis window is 0.5 seconds.

For the apnea segment (segment 2) a local maximum is identified in the pCO2 signal as the first turning point within a window length of 2 minutes after the end of apnea. For correlation coefficient calculation, a window of 1 minute

length is moved from 10 seconds before the beginning of apnea to 0.5 minutes thereafter (half the approximate activation length for apnea). Here, the time step for the moving window is again 0.5 seconds.

The maximum correlation coefficient is considered and reported as the resulting correlation coefficient for each hyperventilation and apnea segment.

3 Results

In Figure 3, the results of the DC-EEG for the midline electrodes and the transcutaneous pCO2 channel monitoring are illustrated during hyperventilation and apnea for one volunteer.

The pCO2 level decreases during hyperventilation. A rise in pCO2 level can be observed with a time lag upon apnea. Simultaneous DC changes can be observed in the central EEG channels.

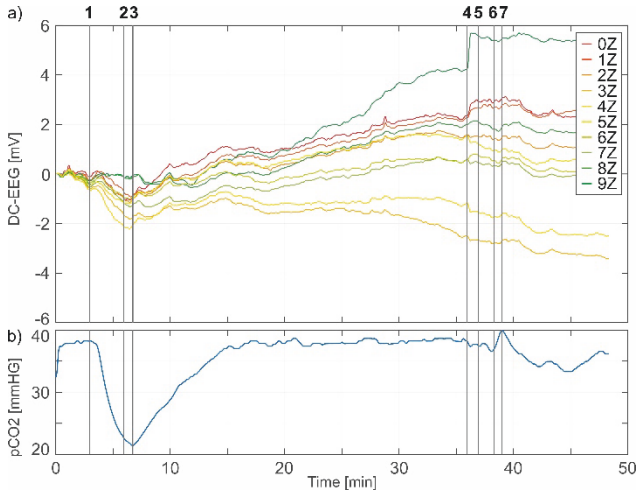

Figure 3: Example of a simultaneous DC-EEG and pCO2 measurement (Table 1: volunteer 1, measurement M1): (a) the midline DC-EEG channels and (b) the pCO2 channel. The event labels are indicating (1) start hyperventilation, (2) stop hyperventilation, (3) minimum pCO2 level upon hyperventilation, (4) beginning of segment 2, (5) start apnea, (6) stop apnea, (7) maximum pCO2 level upon apnea.

In Table 1, we present the preliminary results of our correlation calculations between the midline EEG channels and the pCO2 signal. For hyperventilation, the highest correlation is observed around the vertex (i.e., channels 3z, 4z, 5z, 6z). For apnea, this is similar in volunteer 1, whereas no considerable correlations are observed in volunteer 2. Apparently, correlation values differ for hyperventilation and apnea within a subject, as well. In a previous study [18], similar or inversely correlated shifts (e.g, at occipital electrodes) are reported for volunteers and epilepsy patients.

Table 1: Correlation coefficients between the DC-EEG channels and the pCO2 signal for the midline electrodes for two measurements (M1 and M2) and two volunteers. HV and AP respectively indicate hyperventilation and apnea activation.

EEG Chn.	Volunteer 1				Volunteer 2			
	M1		M2		M1		M2	
	HV	AP	HV	AP	HV	AP	HV	AP
0z	0.90	0.05	0.88	0.92	0.47	0.97	0.92	0.27
1z	0.93	0.23	0.79	0.97	0.75	0.86	0.68	0.20
2z	0.96	0.29	0.82	0.97	0.97	0.58	0.92	-0.20
3z	0.96	0.45	0.97	0.99	0.81	0.16	0.99	0.48
4z	0.98	0.95	0.91	0.99	0.99	0.03	0.99	0.57
5z	0.90	0.99	0.86	0.97	0.97	0.00	0.99	0.71
6z	0.95	0.83	0.95	-0.38	0.75	0.16	0.99	0.78
7z	0.91	0.70	0.60	-0.22	0.96	0.53	0.86	0.19
8z	-0.02	0.78	0.46	-0.40	0.96	0.42	0.45	0.81
9z	0,19	0.40	0.85	-0.41	0.74	0.02	0.91	0.84

4 Discussion

Using our multimodal measurement setup, we are able to simultaneously monitor changes in the DC-EEG and transcutaneous pCO2. During hyperventilation, the pCO2 level decreases and continues decreasing after the end of hyperventilation until recovery starts. The initial baseline level of pCO2 is attained approximately 10 minutes after returning to regular breathing. This recovery process is slower than the respective activation process.

On the other hand, the expected rise in the pCO2 level upon apnea is observed with an average time lag of 1 minute. Before this increase, there is an initial decrease in the pCO2 level (see Figure 3b). The initial decrease is related to the deeper breath taken at the beginning of apnea. The time lag reflects the metabolic response of the volunteer, which apparently varies inter-individually.

Conform to the literature [1,2,13,14,18], our preliminary results indicate a high correlation between negative DC shift in EEG and decreasing pCO2 level during hyperventilation, and between positive DC shift in EEG and increasing pCO2 level during recovery from hyperventilation and upon apnea. Strength of these correlations and the causality between the

observed changes will be the focus of our future research, including the topographical distribution of these correlations over the scalp utilizing all 64 EEG channels in an ensemble of a statistically well-defined number of volunteers. Optimal data processing and analysis, such as optimal filtering, eventual re-referencing, optimal window length and step size, as well as visualization options will be further investigated.

EEG preparation, mechanical and electrochemical stability of the EEG electrodes are crucial for reproducible DC-EEG measurements [16,17]. We are therefore investigating optimal preparation procedures and electrode-electrolyte combinations [19]. It is also very important that the volunteer is relaxed during the measurements. This is certainly a challenge for any volunteer for longer recording intervals after the activation. In order to counteract this problem, we introduced presenting pieces of neutral videos for the longer acquisition sections, which start 10 minutes after the end of hyperventilation and 5 minutes after the end of apnea.

Author Statement

Research funding: This research was supported in part by the Free State of Thuringia (2018 IZN 004), co-financed by the European Union under the European Regional. Conflict of interest: Authors state no conflict of interest. Informed consent: Informed consent has been obtained from all individuals included in this study. Ethical approval: The research related to human use complies with all the relevant national regulations, institutional policies and was performed in accordance with the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee.

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