ELSEVIER

Electroencephalography and clinical Neurophysiology 99 (1996) 90–97

Scalp-recorded direct current potential shifts induced by hypocapnia and hypercapnia in humans

Sayuri Tomita-Gotoh[a], Yoshiaki Hayashida[b,*]

[a]*Department of Physiology, Nara Medical University, Kashihara, Nara, 634, Japan*
[b]*Department of Systems Physiology, University of Occupational and Environmental Health, Yahatanishi, Kitakyushu, 807, Japan*

Accepted for publication: 25 March 1996

Abstract

Shifts in scalp-recorded direct current (DC) potential were studied in relation to the changes in end-tidal partial CO_2 ($PACO_2$) or O_2 (PAO_2) of the expired gas either during hyperventilation (HV), hypoventilation (HYPO) or inhalation of high CO_2 content air during HV or HYPO in 10 healthy subjects. The DC potential was obtained through a chopper stabilized type of DC amplifier from Cz referred to linked earlobes. Each session was comprised of 3 min control, 3 min experimental and 5 min recovery periods. HV induced a negative shift of the DC potential of 765.5 ± 203.0 μV (mean ± SEM). Inhalation of 6% CO_2 air during HYPO induced a positive shift of the DC potential of 280.6 ± 62.8 μV (mean ± SEM). The magnitude of the DC potential shifts was linearly dependent on the changes in the end-tidal $PACO_2$ ($r = 0.78$, $P < 0.0001$). There was no change in the cephalic inter-electrodes impedance during each experimental session. The results suggest that the scalp-recorded DC potentials reflect the changes in cortical excitability associated with the $PACO_2$ level.

Keywords: DC potential; Hyperventilation; Hypoventilation; End-tidal $PACO_2$; End-tidal PAO_2; Impedance

1. Introduction

Recently, there have been many studies on scalp-recorded DC potentials or slowly changing potentials in relation to cognitive information processing in human subjects (e.g. McCallum et al., 1988; Tomita et al., 1990; Lang et al., 1992; Uhl et al., 1994) as well as to the transition to sleep (Marshall et al., 1994).

In animal experiments, a negative cortical DC potential shift was associated with a depolarization of the cortical neurons during tonic-clonic convulsive seizure in a cat (Caspers et al., 1987; Caspers, 1993). Conversely, a positive shift of cortical DC potential was accompanied by a hyperpolarization of cortical neurons during hypercapnia in the cat (Caspers et al., 1987; Caspers, 1993). The cortical DC potential shifts were also associated with the changes in cortical excitability induced by the sleep-wakefulness cycle (Bechtereva, 1974; Caspers, 1993) and by various kinds of sensory stimulation (Gumnit, 1960; Goldring, 1974). These findings indicated that the cortical DC potential shift is an indicator of the cortical excitability changes (Caspers, 1993), with a negative shift showing an increased cortical excitability and a positive shift showing a decreased one.

The scalp-recorded DC potential shifts possibly reflect the cortical DC potential shifts (Cowen, 1974). A negative shift of the scalp-recorded DC potential has been observed in association with a seizure in humans (Cohn, 1964; Chatrian et al., 1968), indicating that scalp-recorded DC potential shifts also reflect the changes in cortical excitability. It has been suggested by animal experiments that an increase in $PACO_2$ decreases the cortical neuronal discharges (Caspers et al., 1987; Speckmann and Elger, 1987; Caspers, 1993). Hyperventilation (HV), which causes hypocapnia and, therefore, results in an increase in cortical excitability, causes a negative shift of scalp-recorded DC potential in healthy subjects (Picton et al., 1979; Bülow et al., 1989; Rockstroh, 1990). To the best of our knowledge, however, there has been no report as to the relationship between scalp-recorded positive DC

* Corresponding author. Tel.: +81 93 6917402; fax: +81 93 6922684.

PII S0921-884X(96)95170-3

EEG 95170

potential shift and changes in arterial gas tension using a genuine DC recording system. It is still difficult to obtain a stable DC recording from the scalp, for a long period of time, due to artifacts such as electrode drifts and skin potentials (Picton and Hillyard, 1972; Girton and Kamiya, 1974).

It was, therefore, our aim to establish the relationship between scalp-recorded DC potential shifts and the changes in arterial gas tension, particularly during positive DC potential shift, using a genuine DC recording system.

2. Methods and subjects

2.1. Subjects

Ten healthy volunteers (5 males, 5 females) ranging in age from 18 to 23 years (mean 19.8, SD 1.4) participated in the study after having the procedures explained to them, and consented to take part in the experiments.

2.2. Procedure

During the experiments, each subject sat in a reclining chair in an air-conditioned room at 25°C. The experiment started at the same time of the day for each subject.

The scalp-recorded DC potential changes were examined during HV and hypoventilation (HYPO), breathing either air or high CO_2 air in each experiment, thus making up 4 sessions; HV (HV with air), HV + 4% CO_2 (HV with air containing 4% CO_2), HYPO (HYPO with air), HYPO + 4% CO_2 or HYPO + 6% CO_2. Sessions were presented in random sequence with a pause of approximately 15 min between each session.

Each session consisted of 3 experimental periods. The first period was an approximately 3 min control period breathing normally. Thereafter, the subsequent 3 min HV (or HYPO) period was introduced by an experimenter. During HV (or HYPO) the subjects increased (or decreased) his or her breathing frequency paced to a rate indicated by a sound from a speaker (30/min or 5/min). The depth of breathing increased simultaneously by two times that of the control during HV and by 1.5 times that of the control during HYPO, respectively. The final period was a recovery period of 5 min after cessation of HV (or HYPO). In order to minimize eye movements that have artifactual influence on the DC potential and EEG recordings, subjects were instructed to fixate their eyes on a black circle (0.7 cm in diameter) which was located on a screen 1.5 m in front of them. Before the start of each experimental session, the subjects practiced for several minutes and familiarized themselves with the breathing method, that is, not touching the tip of the tongue to the roof of the mouth, because it may cause an artifactual negative shift of DC potential (Klass and Bickford, 1960).

2.3. DC potential recordings

Non-polarizable Ag/AgCl sintered disc-type electrodes (Nihonkohden, Japan) were used in this study. For at least 2 weeks before using the electrodes in the experiment, all of them were kept in a conducting paste (main ingredient NaCl) in a box and the lead wires of the electrodes were short-circuited altogether outside of the box, in order to stabilize the electrodes-electrolyte interface. Then, each pair of electrodes in the paste were directly connected to a chopper stabilized type of DC amplifier (AD611G, Nihonkohden, Japan) to check potential differences displayed. The pairs of electrodes with a potential of less than 15 μV/h were selected and kept in the same conducting paste before the experiment. The recording device was always turned on at least 2 h before the start of the experiment. The drift of this DC amplifier was checked repeatedly to make sure that it was less than 2 μV/h.

DC potentials were recorded from the vertex (Cz) with linked earlobes serving as references, and the forehead as a ground, using the selected pair of the electrodes mentioned above. The skin at the attachment sites of the electrodes was carefully cleaned with ethanol (99.5%), but was not abraded in order to avoid any influence of the injury potentials on the DC potentials (Goodman et al., 1985). After the conducting paste in which the electrodes had been kept was rubbed on the skin, the electrode was attached to the scalp through the conducting paste. Electrode impedance between the vertex and earlobes ranged from 0.7 to 3.3 kΩ (which was measured after the completion of the DC potential recording in order to avoid disturbing the electrode-electrolyte interface by passing a current through the electrodes). Scalp electrodes were securely fixed with collodion, and the earlobes-electrodes with ear clips. The DC potential was recorded by the same DC amplifier which was used to check the electrodes, with an input impedance of 2 MΩ, and a high-cut filter of 200 Hz. The DC potential level of 10 subjects ranged from +16.0 to −37.0 mV (mean ± SEM, −4.2 ± 6.2 mV) between Cz and linked earlobes. When necessary, the DC potential was brought to the zero level of the recorder by compensation voltage. The DC recording was restricted to one site, the vertex, because the compensation voltages interfered with each other, when more than two DC amplifiers were simultaneously used.

2.4. EOG recordings

The electro-oculogram (EOG) was recorded from the right supraorbital and outer canthal regions with a time constant of 10 s and a high frequency cutoff of 200 Hz. The gain of EOG was set to the same sensitivity as for DC potential recording. In the off-line analysis, if an EOG potential exceeding 100 μV was detected in one of the experimental periods, the data of that subject were rejected from the data analysis.

2.5. End-tidal gas and blood pressure monitoring

An air-tight mouth/face mask (model 7923, Hans Rudolph, USA) with two-way non-rebreathing valves was placed on the subject. In the HV + 4% CO_2 and HYPO + 4% CO_2 (or 6% CO_2) sessions, the subject breathed (41–53 l for 3 min) through the mouth/face mask which was tubed to a Douglas bag filled with 4% CO_2 or 6% CO_2 content air. Throughout the experiment, the end-tidal P_{ACO_2} and P_{AO_2} in the expired gas was monitored using an expired gas analyzer (1H26, Nihondenki-Sanei, Japan). The expired gas was sampled continuously at a flow rate of 20 ml/m via a side-tube (140 cm length) of the mouth/face mask.

Blood pressure (BP) was continuously monitored using a noninvasive instrument (Finapres, Ohmeda, USA) from the middle finger of the right hand. Heart rate (HR) was instantaneously calculated from BP waves.

2.6. Impedance monitoring

Electrode impedance between the scalp electrode and the linked earlobes, or between the other parts of skin electrodes, were measured in the following two experimental sessions: HV, and HYPO + 4% CO_2 (or 6% CO_2) to ascertain the possible origin of the DC potential shifts, because it has been reported that HV induced an increase in rectal temperature (Robinson and King, 1971) and that inhalation of CO_2 increased sweating (Bullard, 1964). The measurements were done using a LCR meter (4284A Precision LC meter, Hewlett Packard, USA) at 10 frequencies (20, 30, 40, 50, 60, 70, 80, 90, 100 and 120 Hz) with an application of 1 V across the electrodes. The digitized electrode impedance data were then stored on a hard disc.

2.7. Supplementary experiments

Supplementary experiments were done on 3 subjects on separate days to solve following particular points. (1) DC potential recordings from Fz, and Pz to examine regional differences in DC shifts. (2) The effect of breath-holding on the DC potential, end-tidal P_{ACO_2} and P_{AO_2}. (3) The effect of inhalation of pure oxygen during HV on the DC potential, end-tidal P_{ACO_2} and P_{AO_2}. (4) Electrode impedance measurements between the electrodes placed on the palmar surface and forearm, the usual recording sites for skin conductance responses (Simons, 1988).

2.8. Data reduction and analysis

Data of 3 subjects were rejected from the analysis according to the criterion of eye movement artifacts. Thus, the statistical analysis was carried out on the data of 7 subjects.

Signals of the DC potential, EOG, P_{ACO_2}, P_{AO_2}, BP and HR were displayed on-line, digitized and stored on a hard disc at a sampling rate of 10 Hz. The following parameters were calculated for each period in each session and each subject. (1) The maximal changes in DC potential during 3 min period of the modified ventilation rates referred to each control period. (2) The end-tidal P_{ACO_2}, P_{AO_2}, mean BP, HR and electrodes impedance for each experimental period in each session were calculated.

Differences between sessions and periods were statistically evaluated by the analysis of variance (ANOVA) with the within-subject factors, sessions (HV, HV + 4% CO_2, HYPO, HYPO + 4% CO_2, HYPO + 6% CO_2) and periods (control, during). Degrees of freedom were adjusted using the Greenhouse-Geisser correction. For each analysis initial degrees of freedom were reported. Where indicated by a significant F ratio ($P < 0.05$), post hoc analyses were performed using a Neuman-Keuls test. Correlations between DC potential shifts and end-tidal P_{ACO_2} values employed a product moment correlation procedure.

3. Results

3.1. Effects of hyperventilation

HV (3 min duration, 30 times/min) induced a marked negative DC shift in all the 7 subjects. Fig. 1 illustrates the grand average of the DC potential together with those of the end-tidal P_{ACO_2}, P_{AO_2} during control, HV, and recovery periods in 7 subjects. The negativity of the DC potential reached its maximum at the end of the 3 min HV period. Its amplitude between the baseline to the peak ranged between −1457.5 and −50.9 μV (mean ± SEM, −765.5 ± 203.0 μV). The two-way ANOVA for DC shifts revealed that there was a significant effect of session ($F(4, 24) = 13.3$, $P < 0.002$), period ($F(1, 6) = 7.6$, $P < 0.03$) and an interaction of session × period ($F(4, 24) = 13.3$, $P < 0.0001$). Post hoc analysis indicated that the DC shift induced by HV was significantly negative ($P < 0.0002$). Negative DC shifts were also obtained at Fz (40–80% of that at Cz) and Pz (20–50% of that at Cz) in the supplementary experiments, but the most enhanced negativity was obtained at Cz. After HV, the negativity of the DC potential showed a gradual returning towards the baseline level (Fig. 1).

As shown in Fig. 1, the end-tidal P_{ACO_2} decreased in all the 7 subjects at the start of HV and continued to decrease, reaching its maximum at the end of the 3 min HV. After HV, it gradually recovered to the control level. The time course of the change in the end-tidal P_{ACO_2} level coincided with the concomitant change in the DC potential (Fig. 1). The end-tidal P_{ACO_2} of 39.8 ± 1.3 mmHg (mean ± SEM) in the control decreased to 23.1 ± 1.5 mmHg during HV. The two-way ANOVA for the end-tidal P_{ACO_2} revealed that there was a significant effect of session ($F(4, 24) = 48.4$, $P < 0.0001$), and an in-

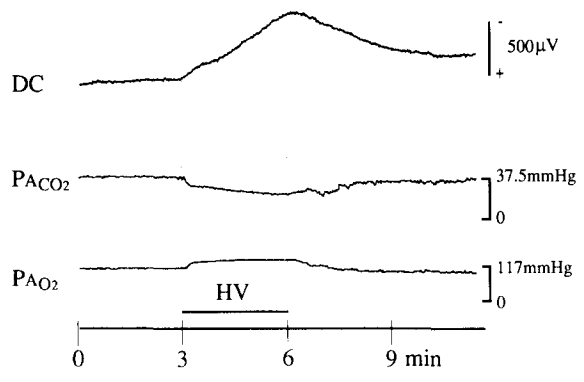

Fig. 1. Grand averages of the DC potential (top), end-tidal P_{ACO_2} (middle) and end-tidal P_{AO_2} (bottom) during control, HV and recovery periods. $n = 7$.

teraction of sessions × periods ($F(4, 24) = 98.7$, $P < 0.0001$). The post hoc analysis indicated that the end-tidal P_{ACO_2} during HV was significantly lower than that during the control period ($P < 0.0001$).

The end-tidal P_{AO_2} level of 106.0 ± 1.5 mmHg (mean ± SEM) in the control showed a gradual increase after the start of HV in all the 7 subjects and reached its maximum level of 136.9 ± 2.2 mmHg during HV, which level was maintained for about 15 s after the end of HV, then returned to the baseline level. The two-way ANOVA for the end-tidal P_{AO_2} revealed that there was a significant effect of session ($F(4, 24) = 18.4$, $P < 0.0003$), period ($F(1, 6) = 521.0$, $P < 0.0001$) and an interaction of sessions × periods ($F(4, 24) = 20.8$, $P < 0.0001$). The post hoc analysis indicated that the end-tidal P_{AO_2} level during HV was significantly higher than that during the control period ($P < 0.0002$).

There were no significant differences in the mean BP and HR between the control and HV periods.

All subjects reported numbness of the extremities and dizziness after 3 min HV.

3.2. *Effects of inhalation of high CO_2 content air during HV*

Inhalation of 4% CO_2 air during HV suppressed the negative shift of the DC potential in all the 7 subjects by 53% in average as compared to that of air during HV ($P < 0.002$). The negativity also reached its maximum at the end of the HV + 4% CO_2 period. The negative DC shifts were exhibited in 6 of 7 subjects and a positive shift was observed in 1 subject. The maximum DC shifts ranged from −998.0 to +50.3 μV (mean ± S.E.M.; −361.4 ± 131.1 μV) and were significantly negative ($P < 0.02$). After the end of HV + 4% CO_2, the DC level showed a gradual returning towards the control level.

The decrease in the end-tidal P_{ACO_2} level during HV +4% CO_2 was not pronounced in compared to that during HV; i.e. it changed from the control of 38.8 ± 0.8 mmHg to the peak magnitude of 35.8 ± 0.8 mmHg ($P = 0.14$, n.s.). The time course of the changes in the end-tidal P_{ACO_2} level coincided also with that of the changes in DC potential.

The changes in the end-tidal P_{AO_2} level were similar to those during HV. The end-tidal P_{AO_2} level significantly increased from the control of 106.7 ± 1.1 mmHg to 134.7 ± 1.6 mmHg ($P < 0.0001$).

There were no significant differences in the mean BP and HR between the control and HV + 4% CO_2 periods.

In the supplementary observations, the magnitude of the negative DC shifts were not altered by the inhalation of 100% O_2 during HV.

3.3. *Effects of hypoventilation*

The negative shift of the DC potential was less during HYPO in all the 7 subjects than during HV (average of 78% decrease as compared to that during HV; $P < 0.0002$). The negativity reached its maximum at the end of the HYPO period (Fig. 2). The negative DC shifts were observed in 5 of 7 subjects and the positive shifts were exhibited in two subjects. The maximum DC shift ranged from −414.3 to +85.8 μV (mean ± SEM, −168.1 ± 75.4 μV), and was not significant ($P = 0.46$, n.s.) as compared with the control period. After the end of HYPO, DC shifts gradually recovered to the control level in 3 min.

As shown in Fig. 2, during HYPO the end-tidal P_{ACO_2} level increased in all the 7 subjects during the initial 30 s by 6.5 mmHg, after which it continued to decrease. The end-tidal P_{ACO_2} level changed from the control of 38.8 ± 1.0 mmHg (mean ± SEM) to a maximal change of between 30.2 and 45.6 mmHg (mean ± SEM, 38.5 ± 2.1 mmHg; $P = 0.97$, n.s.).

The time course of the change in the DC potential did not coincide with that of the change in the end-tidal P_{ACO_2} level during the initial phase of 30 s.

The end-tidal P_{AO_2} level slightly increased in all the 7 subjects during HYPO from the baseline of 104.5 ± 1.5 mmHg (mean ± SEM) to the peak level of 114.8 ± 2.7 mmHg ($P < 0.0004$).

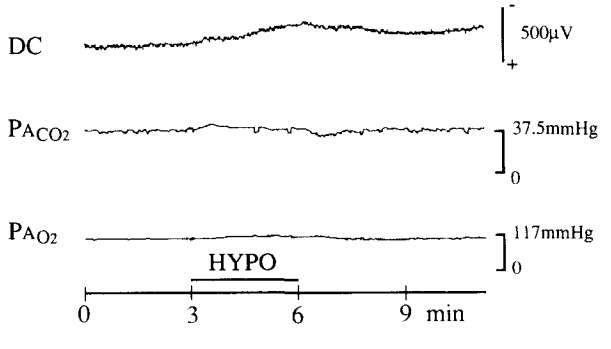

Fig. 2. Grand averages of the DC potential (top), end-tidal P_{ACO_2} (middle) and end-tidal P_{AO_2} (bottom) during control, HYPO and recovery periods. $n = 7$.

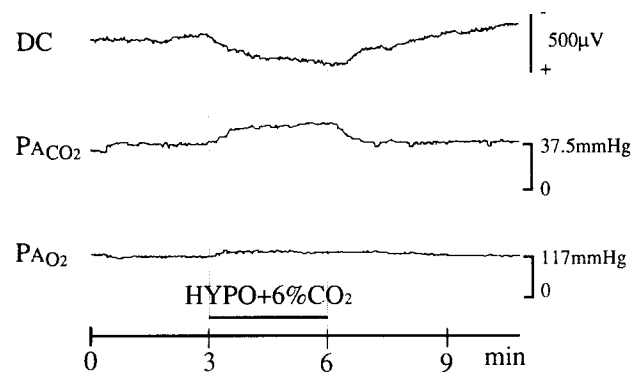

Fig. 3. Grand averages of the DC potential (top), end-tidal P_{ACO_2} (middle) and end-tidal P_{AO_2} (bottom) during control, HYPO + 6% CO_2 and recovery periods. $n = 7$.

There were no significant differences in HR between the control and HYPO periods. Mean BP slightly decreased during HYPO from the baseline of 84.7 mmHg to 81.8 mmHg. The two-way ANOVA for BP revealed that there was a significant interaction of session × period ($F(4, 24) = 4.12$, $P < 0.01$). The post hoc analysis indicated that BP during HYPO was lower than that during the control period ($P < 0.04$).

3.4. Effects of inhalation of high CO_2 content air during hypoventilation

A positive DC shift was observed in all the 7 subjects when a high CO_2 content air was inhaled during HYPO, as shown in the Fig. 3 during HYPO + 6% CO_2. The positive DC potential reached its peak at the end of HYPO period (i.e. HYPO + 4% CO_2 and HYPO + 6% CO_2), but inhalation of 6% CO_2 content air induced 120% more enhanced positivity than that of 4% CO_2 content air. During HYPO + 4% CO_2, maximum DC shifts ranged from 0 to +444.1 μV (mean ± SEM, +127.5 ± 60.5 μV), and were not significant ($P = 0.51$, n.s.). During HYPO + 6% CO_2, maximum DC shifts ranged from +18.3 to +491.4 μV (mean ± SEM, +280.6 ± 62.8 μV), and was significantly positive ($P < 0.05$). There were significant differences between the magnitudes in DC shifts during HV and during HYPO + 6% CO_2, and between those during HV and during HYPO + 4% CO_2 ($P < 0.0002$, respectively). After the cessation of HYPO + 4% CO_2 or HYPO + 6% CO_2 the positive DC shifts recovered to the control level in 3 min.

The end-tidal P_{ACO_2} level increased to maximum level within 2 min from the start of the inhalation of high CO_2 content air during HYPO in all the 7 subjects and was maintained to the end of the HYPO. After the cessation of HYPO + 4% CO_2 or HYPO + 6% CO_2 the end-tidal P_{ACO_2} recovered to the baseline level within 3 min. During HYPO + 4%, the end-tidal P_{ACO_2} level significantly increased from the baseline of 38.1 ± 0.8 mmHg (mean ± SEM) to the peak level of 47.8 ± 0.8 mmHg ($P < 0.0001$). During HYPO + 6%, it also significantly increased from the baseline of 37.3 ± 0.8 mmHg to the peak level of 52.8 ± 1.6 mmHg ($P < 0.0001$). The time course of the change in this end-tidal P_{ACO_2} level coincided with that of the change in the DC potential.

The end-tidal P_{AO_2} level increased within 30 s from the start of HYPO + 4% CO_2 or HYPO + 6% CO_2 in all the 7 subjects and this increased level was maintained 1.5 min after cessation of the HYPO, and then recovered to the baseline level. During HYPO + 4% CO_2, the end-tidal P_{AO_2} level significantly increased from the baseline of 108.2 ± 1.5 mmHg (mean ± SEM) to the peak level of 120.7 ± 1.5 mmHg ($P < 0.0001$). During HYPO + 6%, the end-tidal P_{AO_2} level significantly increased from the baseline of 107.5 ± 1.0 mmHg to the peak level of 120.7 ± 1.1 mmHg ($P < 0.0001$).

There were no significant differences in mean BP and HR between the control and HYPO + 4% CO_2 or 6% CO_2 periods.

There were also no subjective effects of HYPO + 4% CO_2 or 6% CO_2, except one subject complained of a headache after HYPO + 6% CO_2 period.

In the supplementary observations, a negative-positive DC displacement was observed by the breath-holding maneuver (duration of breath-holding ranged from 48 to 90 s). The DC potential shifts coincided with the changes in the end-tidal P_{ACO_2} level, with the positive shift being coincident with the increase in P_{ACO_2}.

3.5. DC shifts, end-tidal P_{ACO_2} and P_{AO_2} levels

The time courses of DC potential shifts and those of end-tidal P_{AO_2} level changes were independent in the present 4 experimental sessions. On the other hand, DC potential shifts and end-tidal P_{ACO_2} changes were mirror images through the 4 experimental sessions. A relationship between the DC potential and the end-tidal P_{ACO_2} was also observed during the recovery phases after the cessation of each experimental period (HV or HYPO). Fig. 4 illustrates the association of the magnitude of DC shifts in both polarities and end-tidal P_{ACO_2} levels. There was a linear relationship between them (correlation coefficient $r = 0.78$, $P < 0.0001$).

3.6. Electrode impedance measurements

There were no significant differences in impedance between the electrodes on the vertex and the linked earlobes across the experimental periods (control, HV, and recovery periods) and across the experimental periods (control, HYPO + 4% CO_2 or 6% CO_2 and recovery periods) as shown in Fig. 5.

In the supplementary experiment, the impedance between two electrodes on the palmar surface and forearm decreased during the HV (the decreased value ranged between 15 and 40 kΩ at 20 Hz) and increased during

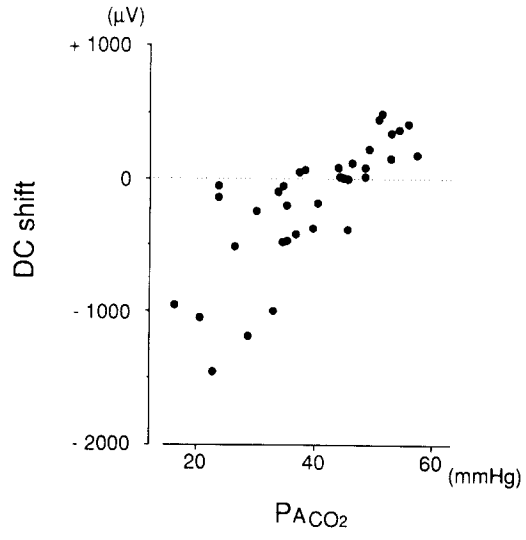

Fig. 4. The relation between the magnitude of DC shifts and end-tidal P_{ACO_2} level. Correlation coefficient, $r = 0.78$ ($P < 0.0001$).

HYPO + 4% CO_2 or HYPO + 6% CO_2 periods (the increased values ranged between 1 and 9 kΩ at 20 Hz) as compared to the control and the recovery periods.

4. Discussion

In the present study, HV induced negative shifts in scalp-recorded DC potentials and hypoventilation under inhalation of high CO_2 content air induced positive shifts. These shifts were related to changes in end-tidal P_{ACO_2} levels.

The following several points need consideration before interpreting these data. First, the DC shift might be induced by the drift of the amplifying system and/or electrodes. This is unlikely, however, because the resulting DC shifts in the present experiments ranged from ±several tens of μV to several mV, while the electrodes' drift displayed almost a linear trend in a range of ±15 μV/h in more than 20 investigations, that is, only ±4 μV within 15 min of each experimental session. Picton and Hillyard (1972) and Marshall et al. (1994) reported that a decrease in electrodes' impedance of more than 1 kΩ may occur within 15 min after electrodes had been affixed, and thereafter the impedance remained stable. In the present experiments, in which we started DC potential recordings 2 h after the completion of all electrodes attachments, the electrodes' impedance can be assumed to have been stable at the beginning of our DC recordings. Thus, the electrodes' drift in each experiment (including electrode-electrolyte interface) would be negligible. Secondly, one possible origin of scalp-recorded DC potential shift is electrodermal activity, since the skin of electrode sites was not abraded. In a series of impedance measurements, there were no changes in electrodes' impedance in each frequency between the vertex and the linked earlobes during HV and HYPO under an inhalation of high CO_2 content air as well as in the control and recovery periods. By contrast, impedance between the two electrodes on the palmar surface and on the forearm decreased during HV and increased during HYPO under an inhalation of high CO_2 content air. This result is consistent with the findings of Picton and Hillyard (1972) in which palmar skin potential changes were frequently observed in the absence of any cephalic deflections. Thus, it is suggested that scalp electrodermal activity does not play a significant role in DC potential shifts during HV or an inhalation of high CO_2 content air during HYPO. Thirdly, it is not likely that there might be any contribution of the motor activity of HV to the recorded negative DC shift, because HV + 4% CO_2 decreased the negative DC shift by 53% on average in this study, as suggested by Picton et al. (1979). Fourthly, it is not likely that eye movements produce the DC potential shifts, because artifact contaminated data were not included in the present analysis. Therefore, it may be concluded that scalp-recorded DC potential shifts during HV or an inhalation of high CO_2 content air during HYPO reflect brain neural activity.

In the present study, HV induced negative shifts in the scalp-recorded DC potential with a mean magnitude of −765.5 μV. Caspers and Speckmann (1974) and Caspers et al. (1987) have reported that HV induced negative DC shifts recorded on the rat cortex. Our results are also in line with the findings on the scalp-recorded slow potential during HV in humans (Picton et al., 1979; Bülow et al., 1989; Rockstroh, 1990; Marshall et al., 1994). The magnitude of the shifts reported by Picton et al. was of a

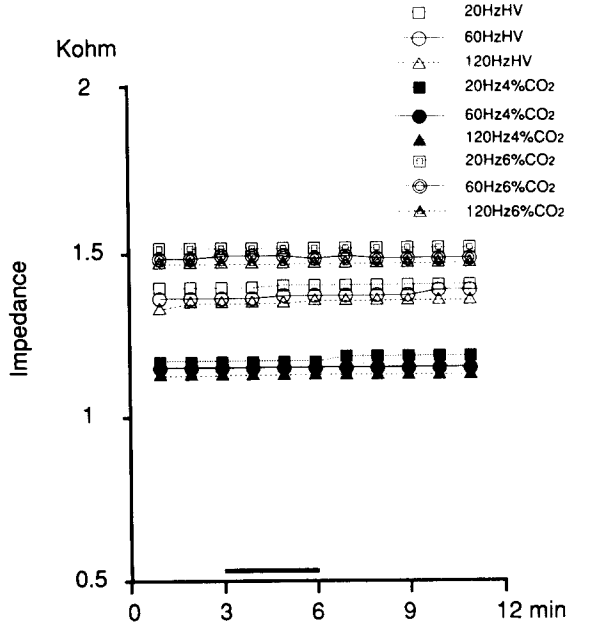

Fig. 5. The influence of HV, inhalations of high CO_2 content air (4%, 6% CO_2) on impedance (average values, $n = 7$) between the electrodes on scalp (Cz) and linked earlobes. A horizontal bar indicates each respective session between 3 and 6 min.

similar order of several mV with HV as that of ours. However, the magnitude of the shifts observed by Bülow et al. and Rockstroh was about one fifteenth, and the magnitude of shift reported by Marshall et al. was about one third, respectively, of that observed in our present results. A possible source of the differences in the magnitude might be the differences in the extent of changes in the P_{ACO_2} level, which these authors did not measure.

Caspers et al. (1987) have indicated in the animal experiments that a lowering of the P_{ACO_2} in the cortical tissues or administration of 100% O_2 during HV evoked a negative DC shift. In the present study, the end-tidal P_{AO_2} level increased to 136.9 mmHg during HV, and an inhalation of 100% O_2 during HV induced the negative DC shift of the same magnitude as HV, but an inhalation of high CO_2 content air during HV decreased the negative DC shift by 53% as compared to that during HV. These results suggest that a negative DC shift during HV may be attributed to hypocapnia rather than hyperoxia.

This is the first paper to report on the positive shift of the DC potential in humans during HYPO while inhaling high CO_2 content air. The mean magnitudes were +127.5 μV during HYPO + 4% CO_2 and +280.6 μV during HYPO + 6% CO_2, respectively. There was a significant correlation ($r = 0.78$, $P < 0.0001$) between P_{ACO_2} and the magnitude of DC shifts in both negative and positive polarities.

During HYPO, as shown in Fig. 2, the DC potential shifted to a negative direction and the end-tidal P_{ACO_2} level showed a slight increase by 6.5 mmHg during the initial 30 s after the start of HYPO. Then, the DC potential kept shifting to the negative side and the P_{ACO_2} level showed a gradual decrease throughout HYPO. The relation between the DC shift and the end-tidal P_{ACO_2} level in the initial phase was not a parallel one. There is a possibility that the subject in the initial phase made an effort to pace the breathing frequency with the rate indicated by the sound from a speaker. This mental effort may induce a more dominant negative shift in the DC potential than the slight increase in P_{ACO_2} level. It is interesting that such an interaction between a mental effort and the P_{ACO_2} level on the DC potential shift was observed during breath-holding, where negative-positive DC displacements were exhibited in this experiment.

To summarize, shifts of scalp-recorded DC potential are correlated with the changes in P_{ACO_2} rather than P_{AO_2}, with a negative shift being coincident with a reduced P_{ACO_2} and a positive shift with an increased P_{ACO_2}. Since these are in line with the cortically recorded DC potential shift, the scalp-recorded DC potential shift may reflect cortical DC potential shift and, consequently, reflect changes in cortical excitability.

Acknowledgements

The authors would like to express their appreciation to Prof. M. Kato of Kyushu University for his valuable comments on the manuscript.

References

Bechtereva, N.P. DC changes associated with the sleep-wakefulness cycle. In: A. Rémond (Ed.), Handbook of Electroencephalography and Clinical Neurophysiology, Vol. 10A, Section IV. Elsevier, Amsterdam, 1974, pp. 25–32.

Bullard, R.W. Effects of carbon dioxide inhalation on sweating. J. Appl. Physiol., 1964, 19: 137–141.

Bülow, I.V., Elbert, T., Rockstroh, B., Luzenberger, W., Canavan, A. and Birbaumer, N. Effects of hyperventilation on EEG frequency and slow cortical potentials in relation to an anticonvulsant and epilepsy. J. Psychophysiol., 1989, 3: 147–154.

Caspers, H. DC potentials of the brain. In: W. Haschke, A.I. Roitbak and E.-J. Speckmann (Eds.), Slow Potential Changes in the Brain. Birkhäuser, Boston, 1993, pp. 9–20.

Caspers, H. and Speckmann, E.-J. Cortical DC shifts associated with changes of gas tensions in blood and tissue. In: A. Rémond (Ed.), Handbook of Electroencephalography and Clinical Neurophysiology, Vol. 10A, Section VI. Elsevier, Amsterdam, 1974, pp. 41–65.

Caspers, H., Speckmann, E.-J. and Lehmenkühler, A. DC potentials of the cerebral cortex seizure activity and changes in gas pressures. Rev. Physiol. Biochem. Pharmacol., 1987, 106: 127–178.

Chatrian, G.E., Somasundaram, M. and Tassinari, C.A. DC changes recorded transcranially during 'typical' three per second spike and wave discharge in man. Epilepsia, 1968, 9: 185–209.

Cohn, R. DC recordings of paroxysmal disorders in man. Electroenceph. clin. Neurophysiol., 1964, 17: 17–24.

Cowen, M.A. The brain as generator of transcephalically measured direct current potentials. Psychophysiology, 1974, 11: 321–335.

Girton, D.G. and Kamiya, J. A very stable electrode system for recording human scalp potentials with direct-coupled amplifiers. Electroenceph. clin. Neurophysiol., 1974, 37: 85–88.

Goldring, S. DC shifts released by direct and afferent stimulation. In: A. Rémond (Ed.), Handbook of Electroencephalography and Clinical Neurophysiology, Vol. 10A, Section III. Elsevier, Amsterdam, 1974, pp. 12–24.

Goodman, R.M., Wachs, K., Keller, S. and Black, P. Spontaneous spinal cord 'injury potential' in the rat. Neurosurgery, 1985, 17: 757–759.

Gumnit, R.J. DC potential changes from auditory cortex of cat. J. Neurophysiol., 1960, 23: 667–675.

Klass, D. and Bickford, R.G. Glossokinetic potentials appearing in the electroencephalogram. Electroenceph. clin. Neurophysiol., 1960, 12: 239.

Lang, W., Starr, A., Lang, V., Lindinger, G. and Deecke, L. Cortical DC potential shifts accompanying auditory and visual short-term memory. Electroenceph. clin. Neurophysiol., 1992, 82: 285–295.

Marshall, L., Mölle, M., Schreiber, H., Fehm, H.L. and Born, J. Scalp recorded direct current potential shifts associated with the transition to sleep in man. Electroenceph. clin. Neurophysiol., 1994, 91: 346–352.

McCallum, W.C., Cooper, R. and Pocock, P.V. Brain slow potential and ERP changes associated with operator load in a visual tracking task. Electroenceph. clin. Neurophysiol., 1988, 69: 453–468.

Picton, T.W. and Hillyard, S.A. Cephalic skin potentials in electroencephalography. Electroenceph. clin. Neurophysiol., 1972, 33: 419–424.

Picton, T.W., Pivik, R.T. and Godbout, R. Scalp-recorded DC potential shifts associated with hyperventilation in human subjects. Can. J. Neurol. Sci., 1979, 6: 380.

Robinson, S.M. and King, A.B. Hypocapnia-induced increases in rectal temperature in man during heat exposure. J. Appl. Physiol., 1971, 31: 656–658.

Rockstroh, B. Hyperventilation-induced EEG changes in humans and their modulation by an anticonvulsant drug. Epilepsy Res., 1990, 7: 146–154.

Simons, R. Event-related slow brain potentials: a perspective from ANS psychophysiology. In: P.K. Ackles, J.R. Jennings and M.G.H. Coles (Eds.), Advances in Psychophysiology, Vol. 3. JAI Press, 1988, pp. 223–267.

Speckmann, E.-J. and Elger, C.E. Introduction to the neurophysiological basis of the EEG and DC potentials. In: E. Niedermeyer and F. Lopes da Silva (Eds.), Electroencephalography. Urban and Schwarzenberg, Baltimore, MD, 1987, pp. 1–13.

Tomita, S., Ikemi, A., Nakamura, T. and Hayashida, Y. The reduction of CNV amplitude during relaxation related to DC potential shift. Neurosciences, 1990, 16: 285–289.

Uhl, F., Kretschmer, T., Lindinger, G., Goldenberg, G., Lang, W., Oder, W. and Deeke, L. Tactile mental imagery in sighted persons and in patients suffering from peripheral blindness early in life. Electroenceph. clin. Neurophysiol., 1994, 91: 249–255.