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Electroencephalographic Changes after a Marathon at 4300 M of Altitude

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ABSTRACT

Running at altitude is gaining greater popularity but it may expose participants to the risk of acute mountain sickness (AMS). The study investigated electroencephalographic (EEG) changes and eventual symptoms suggestive of AMS in 5 well-trained lowland native male runners (average age, 38.2 ± 4.6 years; VO_2 peak 61.4 ± 2.7 $mL \cdot kg^{-1} \cdot min^{-1}$ at sea level; best marathon performance at sea level under 3 hours), who completed a marathon at 4300 m altitude. EEG, percentage of peripheral arterial oxygen saturation (% $SpaO_2$) and heart rate (HR) were recorded during wakefulness at rest (supine position) and in comfort: 1) at sea level; 2) at 3600 m after 32 - 38 hours of acute acclimatization; 3) at 4300 m after 145 - 153 hours of chronic acclimatization; and 4) at 4300 m immediately after a marathon race. Symptoms of AMS were evaluated with the Lake Louise questionnaire before any ECG recording. There was a significant decrease in low-voltage high-frequency activities at rest after acute hypoxic-hypobaric exposure at 3600 m as compared to sea level. After six days of acclimatization at 4300 m there was a significant increase in the power of low-voltage high-frequency activities, particularly beta and gamma, indicating an aroused waking state and an integrated activity across widely distributed cortical regions. An increase in the power of low-voltage high-frequency activities over the entire cortex was observed, particularly after completion of the marathon at 4300 m. The increase in the high-frequency activities was probably due to direct and indirect reflex activation of the forebrain and reticular activating system involved in behavioral and metabolic integration of autonomic control and arousal and due to residual activation of the somatomotor and parietal cortex after the end of the marathon. Lake Louise score always resulted lower than 3, indicating no signs of AMS in all the runners. The results of this study indicate that in well-trained and acclimatized athletes, arousal has a protective role in preventing excessive oxygen deprivation also after an endurance exercise performed at high altitude. The absence of AMS fond in our study bear out that well trained and acclimatized runners, can safely participate in a marathon at high altitude that gives rise to temporary EEG changes without inducing paroxysmal phenomena.

Keywords: High Altitude; EEG Spectral Analysis; Reticular Activating System; Endurance Exercise

1. Introduction

With the increasing popularity of long-distance running, marathon races are now organized also at high altitude, where decreased barometric pressure and oxygen tension in the ambient air are the primary environmental changes affecting individual maximal aerobic power and consequently performances [1].

The natural hypobaric hypoxic environment gives rise to immediate and delayed physiological responses to compensate tissue hypoxia [2-4]. However, Acute Mountain Sickness (AMS) usually develops after rapid ascent to high altitude and/or soon after exercise performed before acclimatization to altitude [5].

Relative hypoxia can have also a direct influence on the Central Nervous System (CNS) and some typical consequences of exposure to high altitude (e.g. dehydration, lack of appetite, and AMS) are thought to be responsible for paroxysmal EEG phenomena [6,7], which resolve after adequate acclimatization and hydration [7,8].

It was demonstrated that exposure to high altitude leads to symptoms indicating impaired neuronal functions [2-4]. Electrocephalographic (EEG) abnormalities and sleep disruption are the major neurological symptoms following ascent to high altitude, and acute hypoxia is one of the main systemic factors that produces a widespread slowing down of the EEG and depression of its power [8]. Furthermore, Ozaki *et al*. [9] have suggested a link between AMS and EEG changes and that the EEG can be useful to predict the risk of developing AMS.

The aim of this study was to investigate cerebro-ele-

ctrical activity and the eventual onset of AMS symptoms in low-land native runners during acclimatization and after a marathon race performed at 4300 m altitude.

2. Material and Methods

2.1. Subjects

The study population was 5 male runners (mean age, 34.8 ± 4.9 years; body mass, 67.0 ± 4.8 kg; height, 176 ± 4 cm) who ran a marathon at high altitude. All were experienced high-altitude marathon runners whose best performance at sea level was under 2:42:04 ± 0:11:58 h:mm:ss.

Assessment included assessed administration of a medical and fitness history questionnaire and physical examination prior to EEG recording at sea level. Exclusion criteria were clinical evidence of hematochemical, cardiac, pulmonary, gastrointestinal, endocrine and psychological abnormalities.

The study protocol was approved by the Scientific Board of the International Federation for Sport at Altitude. The runners were recruited by advertisement as volunteers to participate in the study; they gave their written consent after having been fully informed of any risks or discomfort associated with the study.

2.2. Characteristics of the Marathon at Altitude

The marathon (42,195 m long) took place on the Tingri Plateau (Tibet, China) at 4300 m altitude. The marathon race route was flat along most of its course, with some areas of rough ground. The race began at 9:30 a.m. and ended before 3:30 p.m. (local time). There were restoration points every 6000 m along the marathon, and the runners were allowed to drink water and/or carbohydrate beverages *ad libitum*. The mean time taken to complete the race was 4:25:54 ± 0:54:30 h:mm:ss.

2.3. Journey to the Marathon Site

After about 13 hours flight time, the runners arrived in Lhasa (Tibet, China) at 3800 m altitude. The time difference between the sites of the start and the end of the fight was 7 hours.

The runners stayed for 3 days in Lhasa (2 nights) and then travelled by bus to Tingri (Tibet, China; 4300 m altitude) in 5 days (about 600 km/day), riding between 6 and 8 hours every day on the bus, and sleeping 4 nights in comfortable hotels. Before the marathon race, the runners stayed for 3 days (two nights) in Tingri. During the journey all the runners ran daily for 1 - 2 hours at intensity below the aerobic threshold.

2.4. Experimental Protocols

The aerobic characteristics of the subjects were determined at sea level, 4 to 9 weeks prior to the departure for the marathon. Measurements were performed by means of the standard open circuit spirometry breath-by-breath method (Sensorimedics 4000, TC, Yorba Linda, CA). For each athlete VO_{2peak} was measured at the end of an incremental running test on a treadmill, starting at 8 $km \cdot h^{-1}$, with increments of 2 $km \cdot h^{-1}$ every 3 minutes, until voluntary exhaustion.

2.5. Polygraphic Recording Procedures

EEG activity was recorded with six Ag/AgCl EEG scalp electrodes placed according to the international 10-20 system over both hemispheres on the frontal (F_3, F_4), parietal (P_3, P_4), and occipital (O_1, O_2) cortices. A referential electrode was clipped onto the right ear (A_2). The electrode assembly was fixed to the scalp with an elastic plastic cap and filled before and after fixing with a saline solution mixed with conductive Grass EEG betonies paste using a syringe with a smoothed needle. Resistance was checked before and after the end of EEG acquisition and was often found lower than 5 - 32 kΩ for a couple of electrodes. All the electrodes were colored with a saline solution before each recording session. The electrodes were positioned after having cleaned the skin with a solution composed of alcohol, ether and acetone at approximately 95% - 100% degree.

Using a high-impedance differential amplifier module, the EEG signals were balanced with different amplifications (×10, ×100 and ×1000) and then forwarded for acquisition. The module was composed of a DBK13 IOtech amplifier module and a multiplexer DaqBook/100 (IOtech, Cleveland, OH) accommodating 16 differential analogical amplifier input channels with an A/D converter and independent gain levels (1×, 10×, 100×, 1000×). The DaqBook was developed for the acquisition of analogical data (Data Acquisition System) for portable application. The DaqBook was matched with the parallel connector door to a laptop for data storage. The DaqBook/100 has 12/16 bit input channels with 1×, 2×, 4× and 8× gains with three amplifier stages with a wide gain range (from 10× up to 8,000,000×). The acquisition set was powered by a set of rechargeable lead batteries (Dryfit A500, Sonnenschein, Ft. Lauderdale, FL). The power supplies of all the instruments were battery assemblies that were recharged by internal, external or solar electrogenic groups. On-line signal visualization on the monitor enabled us to control the quality and the balance of the acquired signals.

Amplified EEG signals were acquired from F_3-F_4; F_3-P_3; P_3-A_2; F_4-P_4; P_4-A_2; P_3-O_1; P_4-O_2; O_1-O_2 derivations. To summarize, we report the results of the analysis of the amplified EEG signals that were acquired from F_3-P_3; P_3-A_2; O_1-O_2 derivations, at a frequency of 512 Hz,

sent to the computer equipped with software for on-line digitalization, signal recording and display (Extensa 355, Texas Instruments, Dallas, TX; DaqBook-100, IOtech) and for subsequent off-line spectral analysis (LabView, National Instruments, Austin, TX). The signals were analyzed using the rapid fast Fourier transform, by which the compressed prospected spectral arrays were developed. Each map represented 8 seconds of the EEG signal with a definition of 0.25 Hz. The maps were recorded on the hard disk as a numerical tabulation and visualized with Excel software. The relative and absolute power activity was determined in artefact-free 8-second spectra in the following bands: *Theta* (4.5 - 8.0 Hz); *Alpha* (8.5 - 11.5); *Beta* (15.5 - 30.0 Hz); and *Gamma* (30.5 - 47.0 Hz).

All signals were recorded in darkened room, or near the end of the finish line in a camp tent after the marathon. Efforts were made to reduce the noise in and outside of the rooms or around the camp tent.

During the EEG recording both ears were covered with 4 cm thick compressed gauze to reduce the discomfort of the plastic cap on the ears. All recordings were performed with the subject in a resting supine position and mentally relaxed, with both eyes closed and covered with a black mask. The medical staff informed the subjects to keep their eyes in a fixed position during the recording. Recordings were performed in the absence of muscle contractions of the face, the frontal-occipital skull and the neck. The neck was fixed with a plastic adaptable frame.

After completing the marathon and before starting the recordings, the runners towel-dried their bodies to avoid the effect of perspiration on the EEG. During data acquisition, they were instructed to keep their bodies as relaxed as possible**.**

2.6. Arterial Oxygen Saturation and Heart Rate

Peripheral arterial oxygen saturation (% $SpaO_2$) and heart rate (HR, beat·minute^{-1}) were measured during EEG recording. The % $SpaO_2$ was recorded with a pulse oxymetre (8500 Nonin Medical, Plymouth, MN) with a sensor placed on the middle finger of the left hand. Heart rate was recorded with cardiac monitors (Polar Vantage, Polar Electro, Kempele Finland).

2.7. Lake Louise Questionnaire

The Lake Louise scoring system was selected to diagnose and quantify AMS symptoms because it is short, easy to complete in difficult situations, and sensitive enough to detect AMS [5]. The diagnosis of AMS is based on a recent rise in altitude, the presence of headache and at least one of the following symptoms: gastrointestinal symptoms; fatigue; dizziness; and difficulty sleeping. The minimum total score is 3 (scoring range, from 0 to 15). The questionnaires were self-reported by each runner just before the EEG recordings.

The EEG recordings were done:

1) at sea level indoors for 30 minutes ([S_1] sea level; Brescia, Italy, P_b: 745 mm Hg);

2) at 3600 m altitude indoors for 20 minutes ([A_1] acute acclimatization) 32 - 38 hours after reaching Lhasa, (Tibet, China, P_b: 485 mm Hg);

3) at 4300 m altitude indoors for 20 minutes ([A_2] chronic acclimatization) 145 - 153 hours after reaching Tingri, Tibet, China, P_b: 444 mm Hg);

4) after the end of the marathon ([M_1] at Tingri Plateau (Tibet, China, P_b: 444 mm Hg) in a camp tent (22˚C - 24˚C) for 17 ± 4 minutes.

2.8. Statistical Analysis

Differences between values measured under the four conditions were assessed by means of the Student's paired *t*-test ($P < 0.05$).

3. Results

3.1. Maximal Aerobic Power

The maximal aerobic power (VO_{2peak}) at sea level was 4.1 ± 0.4 L·min^{-1} (*i.e.* 61.4 ± 2.7 mLO_2·kg^{-1}·min^{-1}).

3.2. Peripheral Arterial Oxygen Saturation and Heart Rate

The % $SpaO_2$ was higher at rest at S_1 than that recorded at A_1 ($P < 0.0005$) and A_2 ($P < 0.0005$); it was significantly lower ($P < 0.05$) after the marathon than that observed at A_2 (**Table 1**).

The heart rate recorded at S_1 was significantly lower

Table 1. Mean ± SEM values of peripheral arterial oxygen saturation ($SpaO_2$; %), heart rate (HR; bpm) and Lake Louise Questionnaire (LLQ) scores.

	S_1 Resting	A_1 Resting	A_2 Resting	M_1 after Marathon
Altitude (m)	**0**	**3600**	**4300**	**4300**
$SpaO_2$ (%)	96.5 ± 1.1	80.4 ± 3.9	83.1 ± 3.1	74.0 ± 8.0
HR (bpm)	53 ± 6	66 ± 12	61 ± 7	95 ± 9
LLQ scores	0.0 ± 0.0	1.0 ± 0.7	0.4 ± 0.5	1.6 ± 0.5

compared to that recorded at A_1 ($P < 0.05$) and A_2 ($P < 0.05$); it was significantly higher after the marathon than that observed at rest before the race ($P < 0.0025$) (**Table 1**).

3.3. EEG after Acute Acclimatization (A_1) versus Sea Level (S_1)

There was a significant decrease in *Theta* (F_3-P_3, A_2-P_3; $P < 0.0001$), *Alpha* (F_3-P_3, A_2-P_3, O_1-O_2; $P<0.001$), *Beta* (F_3-P_3, A_2-P_3, O_1-O_2; $P < 0.001$), and *Gamma* (F_3-P_3, A_2-P_3, O_1-O_2; $P < 0.005$) power activities over the entire scalp at A_1 at rest compared to S_1 (**Table 2**).

3.4. EEG after Chronic Acclimatization (A_2) versus Sea Level (S_1)

A decrease in *Theta* (F_3-P_3, A_2-P_3; $P < 0.0001$) and *Alpha* powers (F_3-P_3; $P < 0.05$) at A_2 compared to S_1. The *Beta* power decreased in the frontal (F_3-P_3; $P < 0.01$), parietal (A_2-P_3; $P < 0.001$) and occipital cortex (O_1-O_2; $P < 0.001$). The *Gamma* power was higher than at S_1 (F_3-P_3; $P < 0.05$) (**Table 2**).

3.5. EEG after Chronic Acclimatization (A_2) versus Acute Acclimatization (A_1)

There was a significant decrease in *Theta* power in the occipital cortex ($P < 0.01$) and an increase in *Alpha* (F_3-P_3; $P < 0.001$; A_2-P_3, $P < 0.001$; O_1-O_2; $P < 0.001$), *Beta* (F_3-P_3; $P < 0.001$; A_2-P_3; $P < 0.001$; O_1-O_2; $P < 0.001$) and *Gamma* (F_3-P_3; $P < 0.025$; A_2-P_3, $P < 0.001$; O_1-O_2; $P < 0.005$) powers at A_2 compared to A_1 (**Table 2**).

3.6. EEG after the Marathon (M_1) versus Chronic Acclimatization (A_2)

After the marathon (M_1), a decrease was noted in *Theta* power in the occipital cortex ($P < 0.01$) and an increase in the frontoparietal cortex ($P < 0.0005$). *Alpha* power increased ($P < 0.0005$) in the rostral cortex. *Beta* power increased over the parietal cortex ($P < 0.05$). The *Beta* (F_3-P_3; $P < 0.0005$) and *Gamma* (F_3-P_3; $P < 0.0005$) power activities increased significantly in the frontoparietal cortex, but the *Gamma* power decreased significantly ($P < 0.05$) over the parietal cortex (A_2-P_3) (**Table 3**).

Table 2. EEG activity (mV^2; mean and SEM) at rest at three different altitudes. Statistical differences are shown in the text.

F_3-P_3	***Theta* (4.5 - 8 Hz)**	***Alpha* (8 - 12 Hz)**	***Beta* (15.5 - 30 Hz)**	***Gamma* (30.5 - 47 Hz)**
Sea level (S_1)	0.87 ± 1.52	0.95 ± 1.51	0.24 ± 0.26	0.13 ± 0.10
3600 m (A_1)	0.45 ± 0.65	0.64 ± 1.35	0.14 ± 0.15	0.06 ± 0.05
4300 m (A_2)	0.48 ± 0.60	0.84 ± 1.53	0.20 ± 0.18	0.13 ± 0.10
A_2-P_3	***Theta* (4.5 - 8 Hz)**	***Alpha* (8 - 12 Hz)**	***Beta* (15.5 - 30 Hz)**	***Gamma* (30.5 - 47 Hz)**
Sea level (S_1)	1.02 ± 1.40	1.34 ± 2.00	0.33 ± 0.41	0.21 ± 0.27
3600 m (A_1)	0.69 ± 0.88	0.85 ± 1.37	0.15 ± 0.14	0.07 ± 0.07
4300 m (A_2)	0.71 ± 0.90	1.29 ± 2.52	0.26 ± 0.22	0.21 ± 0.20
O_1-O_2	***Theta* (4.5 - 8 Hz)**	***Alpha* (8 - 12 Hz)**	***Beta* (15.5 - 30 Hz)**	***Gamma* (30.5 - 47 Hz)**
Sea level (S_1)	0.39 ± 0.45	0.94 ± 1.63	0.18 ± 0.19	0.10 ± 0.07
3600 m (A_1)	0.38 ± 0.47	0.58 ± 1.02	0.09 ± 0.08	0.05 ± 0.04
4300 m (A_2)	0.33 ± 0.31	0.87 ± 1.78	0.15 ± 0.13	0.10 ± 0.08

Table 3. EEG activity (mV^2; mean and SEM) before at rest (A_2) and after the marathon (M_1) at 4300 m. Statistical differences are shown in the text.

F_3-P_3	***Theta* (4.5 - 8 Hz)**	***Alpha* (8 - 12 Hz)**	***Beta* (15.5 - 30 Hz)**	***Gamma* (30.5 - 47 Hz)**
Rest	0.48 ± 0.60	0.84 ± 1.53	0.20 ± 0.18	0.13 ± 0.10
After 5 - 7 min	0.44 ± 0.41	1.19 ± 2.19	0.22 ± 0.18	0.15 ± 0.15
After 5 - 22 min	0.52 ± 0.56	1.30 ± 2.27	0.23 ± 0.19	0.15 ± 0.13
A_2-P_3	***Theta* (4.5 - 8 Hz)**	***Alpha* (8 - 12 Hz)**	***Beta* (15.5 - 30 Hz)**	***Gamma* (30.5 - 47 Hz)**
Rest	0.71 ± 0.90	1.29 ± 2.52	0.26 ± 0.22	0.21 ± 0.20
After 5 - 7 min	1.19 ± 2.04	1.73 ± 2.65	0.40 ± 0.48	0.28 ± 0.40
After 5 - 22 min	0.98 ± 1.38	1.44 ± 2.19	0.29 ± 0.31	0.18 ± 0.26
O_1-O_2	***Theta* (4.5 - 8 Hz)**	***Alpha* (8 - 12 Hz)**	***Beta* (15.5 - 30 Hz)**	***Gamma* (30.5 - 47 Hz)**
Rest	0.33 ± 0.31	0.87 ± 1.78	0.15 ± 0.13	0.10 ± 0.08
After 5 - 7 min	0.26 ± 0.22	0.92 ± 1.56	0.18 ± 0.19	0.14 ± 0.16
After 5 - 22 min	0.29 ± 0.25	0.86 ± 1.31	0.00 ± 0.00	0.00 ± 0.00

4. Lake Louise Questionnaire

The Lake Louis Questionnaire scores prior to EEG recordings were <3 for all the runners.

5. Discussion

5.1. Acute Acclimatization at 3800 m Altitude (A_1)

A significant decrease in EEG power has been described during acute acclimatisation to altitude in low-land natives, in acclimatised subjects, and in high-altitude natives [10-12]. In agreement with these observations, we found a significant topographical decrease in *Theta*, *Alpha*, *Beta* and *Gamma* activities at A_1 and a slowing down of the high frequency component of *Alpha* activity and its anteriorization. These finding are suggestive of a deterioration in vigilance [9,12-16].

Moreover, acute hypoxia leads to hyperventilation and thus to arteriolar hypocapnia; this last may produce regional cerebral hypocapnic vasoconstriction, with changes in cerebral blood flow, alkalosis and increased pH, EEG synchronization and lethargy. The present data are in agreement with other observations showing that the slowing down of the EEG activity is one of the most constant features of cerebral hypoxia [3].

5.2. Chronic Acclimatisation at 4300 m Altitude (A_2)

There were significant increases in *Theta*, *Alpha*, *Beta* and *Gamma* activities over the entire scalp at A_2 as compared to A_1. These activities were consistently lower than those recorded at sea level (S_1). Also, there were some topographical variations in the power of the so-called "altitude sensitive" *Theta* and *Alpha* powers, but still indicating hypoxia-induced deterioration in vigilance.

We found also a positive correlation between the *Theta* activity in the frontal areas and hypoxemia ($y = 0.022x - 1.397$, $r^2 = 1{:}F_3P_3$). Moreover, a study with psychometric tests performed by the same subjects and published elsewhere showed that some brain functions of the left frontotemporal lobe were temporarily impaired under hypobaric-hypoxic conditions [17].

We suggest that the EEG increase in low-voltage high frequency observed after acclimatisation at 4300 m altitude was due to activation of the forebrain and reticular activating system involved in behavioural and metabolic integration of autonomic control and arousal. This is related to reflex activation of the ascending reticular activating system in the ventral medullary reticular and the central pontin-midbrain reticular formation, either directly via the carotid baroreceptors and/or indirectly on carotid and aortic chemoreceptors and/or hypocapnic-central chemoreceptors [2,4]. Indeed, it would not be surprising if exposure to hypobaric hypoxia were to elicit, in parallel with increased ventilation and cardiac output, stimulation of the catecholaminergic systems which activate the reticular activating system and the pituitary-adrenocortical system, cortical activation and arousal, together with slowing down of frontal EEG [18-24].

5.3. Marathon at Altitude (M_1)

After the marathon at altitude we found an increase in the *Theta*, *Alpha*, *Beta and Gamma* activities. Since our experiments involved well-trained and acclimatised runners, we suggest that the marathon race performed at altitude might have been responsible for the cortical arousal and, as at low altitude, is due to the stimulation of the reticular activating system involved in the behavioral and metabolic integration of autonomic control and arousal [25-29].

The increase in high-frequency rhythms recorded just after the end of the marathon document the persistence of motor tasks in the neocortical somatomotor cortices. The parallel increase in the so-called rhythmic slow activity on the parietal region just after the end of the race was probably due to residual activation of the chemical afferents from the subcortical nuclei of the limbic system reaching the frontal and parietal cortices through the cingulated cortex. As previously observed by Hobson [22], it is also possible that the increase in body temperature due to the long distance run might have influenced the EEG cortical activity as a result of an alteration in hypothalamic function. Above all, the results suggest that short-term arousal may have a protective role in preventing excessive oxygen deprivation at altitude [2, 11].

All EEG changes recorded after the marathon at altitude tended to return to A_2 values within 20 minutes (**Table 2**), indicating that the marathon-induced EEG changes were transitory and that the main changes recorded after acclimatization (*i.e*., at A_2) were due to the hypobaric hypoxic conditions typical of a high-altitude environment.

Furthermore, during acclimatization and after the race (A_2 and M_1) the runners showed no signs of AMS, as revealed by the Lake Louise Questionnaire, and we were unable to detect any pathological paroxysmal phenomena during the EEG recordings.

Exercise without EEG paroxysmal phenomena was reported to be possible at altitude only in subjects with an aerobic power of 60 - 65 $mL \cdot kg^{-1} \cdot min^{-1}$, a value very similar to that recorded at sea level in our subjects, and the most important characteristic for "extreme" physical performances at high altitude is claimed to be an excellent cardiorespiratory function [7,9,30].

Taken together these data indicate that running a mara-

thon at around 4300 m altitude is safe for well-trained mountain runners, as confirmed by other studies [8,31, 32].

6. Conclusions

After completion of a marathon at an altitude of 4300 m, the increase in the power of low-voltage high-frequency activities over the entire cortex was probably due to the direct and indirect reflex activation of the forebrain and the reticular activating system which has a protective role in preventing excessive cerebral oxygen deprivation.

Although exercise at high altitude, without oxygen supply, has been held to be unsafe [1,33], the results of this study indicate that arousal plays a protective role in preventing excessive oxygen deprivation. The absence of AMS fond in our study bear out that well trained and acclimatized runners can safely participate in a marathon at high altitude that gives rise to temporary EEG changes without inducing paroxysmal phenomena.

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