ACUTE MOUNTAIN SICKNESS SUSCEPTIBILITY AND BASIC COGNITIVE FUNCTION AFTER A BRIEF SIMULATED ALTITUDE OF 4800 M.

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ABSTRACT: Twelve climbers with not been exposed in the last 12 months at high altitude were evaluated using verbal, spatial, reasoning and numerical tasks from Thurstone's (1969) Primary Mental Abilities (PMA) test. These tasks were undertaken before and immediately after completing the Richalet et al. (1988) Normobaric Hypoxic (NH) test, which evaluates the acute mountain sickness (AMS) risk using a FiO_2 of 11.5% during rest and exercise. A control group of eight climbers did not perform the NH test, so as to rule out the possible learning effect of the PMA test. Four participants (33%) from the experimental group were classified as having high-susceptibility to AMS. However, the PMA test performed after the NH test did not significantly differ from the one carried out before the NH test or from the cognitive abilities measured in the control group ($p > .05$).

KEYWORDS: Acute mountain sickness, normobaric hypoxia, basic cognitive function.

SUSCEPTIBILIDAD DEL MAL AGUDO DE MONTAÑA Y FUNCIONES COGNITIVAS BÁSICAS TRAS UNA BREVE EXPOSICIÓN A UNA ALTITUD SIMULADA DE 4.800 M

RESUMEN: Se evaluaron doce escaladores, que no habían estado expuestos en los últimos 12 meses a gran altitud, utilizando el test de Aptitudes Mentales Primarias (PMA) de Thurstone (1969). Se realizó el test antes e inmediatamente después de completar el test de Hipoxia Normobárica (HN) de Richalet et al. (1988) que evalúa el riesgo del mal agudo de montaña (MAM) usando una FiO2 de 11.5% durante el ejercicio y en reposo. Un grupo control de ocho escaladores, no realizó la prueba de HN, con el fin de descartar el posible efecto de aprendizaje del test PMA. Cuatro participantes (33%) del grupo experimental fueron clasificados como de alta susceptibilidad al MAM. Sin embargo, los resultados del PMA realizado después del test de HN no fue significativamente diferente del llevado a cabo antes de la prueba HN en ninguna de las habilidades cognitivas medidas en el grupo control ($p > .05$).

PALABRAS CLAVE: Mal agudo de montaña, hipoxia normobárica, funciones cognitivas básicas.

SUSCETIBILIDADE DO MAL AGUDO DE MONTANHA E FUNÇÕES COGNITIVAS BÁSICAS APÓS UMA BREVE EXPOSIÇÃO A UMA ALTITUDE SIMULADA DE 4.800 M

RESUMO: Foram avaliados doze escaladores, que não tinham estado expostos nos últimos 12 meses a grande altitude, utilizando o teste de Aptidões Mentais Primárias (PMA) de Thurstone (1969). O teste foi realizado antes e imediatamente depois de completar o teste de Hipoxia Normobárica (HN) de Richalet et al. (1988) que avalia o risco do mal agudo de montanha (MAM) usando uma FiO2 de 11.5% durante o exercício e em repouso. Um grupo de controlo de oito escaladores não realizou a prova de HN a fim de excluir o possível efeito de aprendizagem do teste de PMA. Quatro participantes (33%) do grupo experimental foram classificados como de alta suscetibilidade ao MAM. Contudo, os resultados do PMA realizado depois do teste de HN não foram significativamente diferentes dos obtidos antes da prova de HN em nenhuma das habilidades cognitivas medidas no grupo de controlo ($p > .05$).

PALAVRAS CHAVE: mal agudo de montanha, hipoxia normobárica, funções cognitivas básicas.

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The impact of environmental hypoxia on the central nervous system has been a topic of scientific interest for many decades. A varied picture of neuropsychological disturbances (memory, learning, attention, processing speed, decision-making, sensorial perception, motor control or cognitive flexibility) has emerged from analyses during or after exposure to a wide range of real or simulated high and extreme altitudes (Virués-Ortega, Buela-Casal, Garrido, & Alcázar, 2004). Cerebral function may be affected in relation to altitude level and ascent rate (Wilson, Newmans, & Imray, 2009). Cognitive processes show particular sensitivity to brain oxygen availability, although at altitudes below 3000 m there seems to be little effect on human performance (Banderet & Burse, 1991).

In agreement to Marsillas, Rial, Isorna & Alonso (2014), although we take in account that different studies have made efforts to identify the psychological variables that can be on the basis of sports performance, there is no agreement yet about which may truly be the most relevant. Nevertheless, "On the mountain there is no only the need to be prepared technically and physically but also psychologically. The combination of these three variables provides a good mountaineer preparation" (Allueva, Nerín, Ayora, Morandeira, & San Vicente, 2010, p. 133).

Nowadays, a large number of people ascend to high altitudes for recreational or professional purposes, and the risk of suffering from the various forms of altitude illness, and especially acute mountain sickness (AMS), is well known (Hackett & Roach, 2001). In recent years, an increasing number of mountaineering enthusiasts have also begun to practice sports requiring rapid ascents, very brief stays and fast withdrawal from high altitude (above 4000 m, in a substantial amount of cases); although the time period is usually insufficient to develop AMS, the neuropsychological risk derived from acute hypoxia does exist. Such is the case when practicing heli-skiing, skydiving, and other activities involving flying for short periods using different types of non-engine propelled aerial devices such as hang-gliders and paragliders. Such activities require accurate cognitive performance in the aforementioned environmental conditions, both at peak altitude and during descent. Even when light exercise is performed just before hypoxia reverts, hypoxemia normalization seems to be considerably delayed (Smith, 2007).

Although it is believed that people who suffer from AMS are especially susceptible to cognitive change (Mackintosh, Thomas, Olive, Chesner, & Knight, 1988; Regard et al., 1991; White, 1984), there is evidence of dissociation between the time course of both disorders. The functioning of some neurocognitive domains begins to decline relatively quickly under moderate-to-severe acute hypoxia (Fowler & Nathoo, 1997; Koller, Bischoff, Bührer, Felder, & Schopen, 1991; Truszczyński, Mieczyslaw, Biernacki, & Kowalczuk, 2009; Tsarouchas, Benedek, Bezerianos, Benedek, & Keri, 2008; Van der Post et al., 2002), although performance impairment may be delayed and tends to improve after several hours of sustained exposure when AMS symptoms usually start to appear (Banderet & Shukitt-Hale, 2002; Shukitt-Hale, Banderet, & Lieberman, 1991). Nevertheless, the minimum threshold, duration and speed of onset of transient hypoxic stress, resulting from different situations, required to impair human brain function, and especially the recovery from such stress, are controversial issues (Bahrke & Shukitt-Hale, 1993; Fowler, Paul, Porlier, Elcombe, & Taylor, 1985; Hopkins & Jackson, 2006; Hornbein, Townes, Schoene, Sutton, & Houston, 1989; Lim, Alexander, LaFleche, Schnyer, & Verfaellie, 2004; Truszczyński et al., 2009). What is more, the possible link between residual cognitive impairment induced by brief normobaric hypoxic exposure and AMS risk has not been established.

With the main purpose of establishing whether single and brief exposure to simulated high-altitude could be useful to relate AMS and cognitive risks, we aimed to evaluate the basic cognitive abilities before and just after performing a hypoxic test specific for AMS susceptibility, by measuring the physiological response to a sudden oxygen reduction.

METHOD

Participants

The experimental group (EG) was made up of 12 male non-acclimatized climbers aged 36.8 (*SD* = 6.2) years on average, with a mean height of 175.1 (*SD* = 6.7) cm, and average body weight of 75.7 (*SD* = 8.5) kg. All of them were members of the Spanish Armed Forces' High Mountain Military Group (GMAM). One subject (no. 10) had climbed to an altitude of almost 5000 m. Five participants (nos. 1, 4, 7, 8 and 9) had achieved altitudes of over 6000 m, three participants (nos. 2, 5 and 6) had ascended to over 7000 m, and the remaining three (nos. 3, 11 and 12) had climbed to over 8000 m. The altitudes attained ranged from 4850 m to 8201 m. Altogether, the climbers had participated in a total of 19 expeditions to mountains over 7000 m, with 593 hours and 64 hours of accumulated exposure above 7000 m and 8000 m, respectively, and had never used supplementary oxygen when climbing. All of them lived at altitudes below 1000 m, and during the previous 4 months they had not ascended to over 2500 m. Some of the climbers (nos. 3, 4, 5, 7, 9 and 11) had occasionally experienced slight headaches at high-altitude, but none had suffered from the severe forms of altitude sickness attributed to hypoxia, although they had never previously been administered a specific questionnaire for AMS. None of them had ever taken analgesics or acetazolamide for AMS prophylaxis. All the participants were non-smokers who did not habitually consume pharmacological substances or have a medical history of neuropsychological disturbances. One climber (subject no. 13), who suffered a syncope induced by the hypoxic test, was duly excluded from the study.

Materials and Procedure

The study protocol was approved in advance by the local University Institutional Ethical Review Committee, and each subject provided written informed consent before participating.

Hypoxic test

The exercise laboratory was located 200 m above sea level, with a barometric pressure ranging between 1002-1009 hPa, a temperature between 19ºC and 22ºC, and relative humidity between 40% and 60%. One week before the Normobaric Hypoxic (NH) test, participants were evaluated by means of a cardiovascular physical examination, resting electrocardiogram and maximal exercise test, with the main objective of ruling out myocardial ischemia and arrhythmias. The entire NH test took place in the morning, 3 hours after a light breakfast that did not include beverages with potential depressant or stimulant effects. The NH test was designed by Richalet et al. (1988) to identify populations with particular susceptibility to AMS, and involves 4 successive phases each lasting 4 to 5 minutes. Acute forms of normoxia (N) and hypoxia (H) conditions are alternated during rest and exercise. The participants' cardiac function was continuously monitored throughout the NH test by means of a 12-lead telemetric electrocardiogram (X-Scribe II, Mortara Inst., Milwaukee, WI, USA). Pulmonary gas exchange was measured using a breath-by-breath automated gas analysis system (Vmax Spectra 29 C, SensorMedics Co., Yorba Linda, CA, USA), which was calibrated before each test in relation to volume, flow and O_2 and CO_2 reference mixtures balanced in nitrogen. Pulmonary samples were obtained by means of a facial mask (Hans

Rudolph, Kansas, CO, USA) joined to a bi-directional pneumotachograph connected to a two-way valve. Hypoxic gas was obtained by a mixture production system (Altitrainer 200, SMTEC, Geneva, Switzerland) using nitrogen from a tank. It was calibrated before each test to obtain a simulated altitude of 4800 m. The gas mixture was readjusted during the first seconds of the hypoxic phase until a stable fractional concentration of 11.5% of oxygen was obtained in inspired gas (FiO_2) for 10 minutes (5 minutes resting, and 5 minutes during exercise). The FiO_2 was reduced in the acute form, as the FiO_2 is 20.9% in normoxia. Arterial oxygen saturation was continuously measured by indirect oximetry (Oximax Nelcor N-595, Tyco, Pleasanton, CA, USA) with an infrared sensor situated in the earlobe. Blood pressure was manually measured every 2 minutes in the left arm using an analogical sphygmomanometer. The exercise in the N (5 minutes) and H (5 minutes) phases was performed using an electromagnetic cycle ergometer (Ergoline 900 OEM, Ergometrics, Bitz, Germany). Participants aimed to cycle at 60 r.p.m. and a different work rate (WR) was selected for each subject to obtain a metabolic steady state. The aim was to stabilize cardiac frequency between 130 and 150 beats·min^{-1}. To discard the potential psychological influence of the test, participants were unable to see the displays and monitors, which were situated both behind and in front of them. In addition, participants were not told when they were breathing ambient air or the hypoxic mixture. The following 4 main physiological parameters were recorded for the NH test evaluation: pulmonary ventilation (VE, L·min^{-1} BTPS), respiratory rate (RR, min^{-1}), heart rate (HR, min^{-1}), and peripheral oxygen saturation (SpO_2, %). For the final evaluation, we calculated the average of the instantaneous data obtained during the final 2 minutes of each phase when the steady state was achieved. For the stratification of the AMS risk, we also applied the following data proposed by Richalet et al. (1988) & Richalet & Herry (2006): CRE: HR response in relation to SpO_2 during exercise under N and H phases ($\Delta HR \cdot \Delta SpO_2^{-1}$; normal value > .56 beat·min^{-1}·%$^{-1}$); VRE: VE response in relation to SpO_2 during exercise under N and H phases in relation to the body weight ($\Delta VE \cdot \Delta SpO_2^{-1}$/kg; normal value > .36 L·min^{-1}·%$^{-1}$·kg^{-1}); ΔSpO_2E: difference in SpO_2 between N and H phases during exercise (normal value < 26%); ΔSpO_2R: difference of SpO_2 between N and H phases during rest (normal value < 15%); RREH: RR during exercise under H (normal value < 26 beat·min^{-1}). Criteria for high-risk of AMS were defined as abnormal data in at least one of the first three parameters, and increased risk was characterized by abnormal data in one of the last two parameters (Richalet & Herry, 2006).

Cognitive assessment

The EG was submitted to cognitive evaluation by means of Thurstone's Primary Mental Abilities (PMA) test (Thurstone, 1969), which is a practical instrument in applied psychology to assess mental processing speed by means of a simple model of independent group factors of intelligence. Each subject was invited to perform the PMA test before and immediately after completing the NH test. Participants answered 4 of the 5 PMA sub-tests: 1) Factor V (verbal comprehension), which involves the ability to understand and express ideas through the written or spoken word by means of a vocabulary test. This sub-test consists of multiple choice questions in which the participants are requested to find synonyms for the proposed words. 2) The Factor S (spatial visualization) involves the ability to imagine and conceive objects in two or three dimensions. It is measured by a test requiring the mental rotation of images depicting different objects. This sub-test includes different elements, each featuring a geometric model and 6 similar figures. Participants must determine which of a series of figures, presented in different positions, coincides with the geometric model, even though this may have been rotated in the same plane. 3) Factor R (inductive reasoning) involves the capacity to resolve logical problems and to predict and plan, and assesses inductive and deductive reasoning. Such aptitudes are required for problem solving and planning. Participants are requested to determine the following letter in a given series, once they have deduced the logical series linking the letters. 4) Factor N (numerical calculation) involves the capacity to handle numbers and resolve quantitative problems rapidly. This ability is necessary in resolving tasks requiring a simple mathematical problem-solving test. The subtest consists of elements or problems-solving in which the participants are required to determine whether or not the sum of four two-digit numbers is correct. 5) Factor F (verbal fluency) was not undertaken, as it was not considered particularly relevant to the present study. In addition, to keep the PMA test short, each subject was invited to answer items with even numbers before the NH test (pre-PMA) and items with odd numbers after completing the NH test (post-PMA), respectively. Factor V involves attempting 25 elements in a maximum of 120 seconds, Factor S involves 10 elements in 150 seconds, Factor R includes 15 elements in 180 seconds and Factor N involves 35 elements in 180 seconds. Each neurocognitive assessment took 630 seconds in total, and the total number of correct answers was calculated. EG participants began the post-PMA test immediately after they had completed the NH test, which was around 3 minutes after oxygen saturation had recovered normal values (SpO_2 > 95%). The study was a blind two-period trial and, therefore, both the climbers and the psychologists carrying out the evaluation were unaware of the NH test results.

To detect a learning effect and discard the possible influence of exercise in the laboratory, the PMA test was also performed twice by a control group (CG), whose participants did not take the NH test. The CG was made up of 8 age and sex-matched climbers, who were also GMAM members with similar experience in high and extreme altitudes. CG participants had not undertaken a recent ascent over 2500 m in the previous 4 months. The CG was invited to perform even and odd items of the PMA test, administered before (pre-PMA) and after 30 minutes of resting (post-PMA), respectively. Each subject in both the EG and CG groups performed the PMA test alone in a silent and comfortable room.

Statistical analysis

The Kolmogorov-Smirnov test was applied to establish the normal distribution of the all samples. Repeated measures ANOVA was then used to assess the differences between the two groups (EG and CG) at different time points (pre-PMA and post-PMA). The data are expressed as mean ± SD and a significance level of $p < .05$ was used. The statistical analysis was performed using SPSS v.17 (SPSS Inc., Chicago, USA).

RESULTS

EG climbers tolerated the NH test well, although they experienced a certain sensation of light-headedness. The climbers showed an abrupt drop of SpO_2 from the beginning of the hypoxic phase. However, this was particularly marked during physical exercise, when participants achieved the worst peak mean values in SpO_2: 71%, during the mean peak in HR: 139 beats·min^{-1}. However, as previously mentioned in the methods section, the average of all the different parameter values was obtained by computing the last two minutes of each phase, once a steady state was achieved. Physical exercise in H and N was performed (*M* and *SD*) at WR: 134.6 (*SD* = 23.7) watts, with VE in H: 60.4 (*SD* = 13.2) L·min^{-1}, VE in N: 48.3 (*SD* = 10) L·min^{-1}, HR in H: 134.3 (*SD* = 9.8) beats·min^{-1}, HR in N: 113.8 (*SD* = 11.3) beats·min^{-1}, SpO_2 in H: 73.9 (*SD* = 6.1) %, SpO_2 in N: 98.6 (*SD* = 1.1) %, RR in H: 22.2 (*SD* = 5.9) beats·min^{-1}. Resting SpO_2 in H was 90.2 (*SD* = 2.9) % and resting SpO_2 in N was 99.5 (*SD* = 0.7) %. Table 1 shows the data for individual AMS susceptibility, individual global pre-PMA and post-PMA tests, and the total number of correct answers given by each EG subject.

Data for each subject in the experimental group obtained by means of the normobaric hypoxic test simulating an altitude of 4800 m., the susceptibility of acute mountain sickness (AMS), and the total number of correct answers in the cognitive test performed before (pre-PMA) and after (post-PMA) the hypoxic test. See the methods section for the following definitions: CRE, VRE, ΔSpO_2E, ΔSpO_2R, and RREH. *Abnormal data and AMS susceptibility according to Richalet & Herry (2006). Six participants (nos. 1, 3, 4, 6, 9 and 10) had at least one parameter outside the normal range. One subject (no. 1) had 3 parameters outside the normal range, three (nos. 3, 6 and 10) had at least one main parameter outside the normal range. The other two participants (nos. 4 and 9) had only one secondary parameter outside the normal range. Although the latter two probably had a greater susceptibility to AMS, given that their breathing was shallower during the hypoxic exercise, only four participants were classified as having a higher risk of AMS (nos. 1, 3, 6 and 10). The 4 climbers who had the most pronounced peak hypoxemias (SpO_2 < 70%) during the NH test (nos. 1, 3, 6 and 10), gave a higher number of correct answers in the post-PMA test.

Table 1

Individual AMS susceptibility, individual global pre-PMA and post-PMA tests, and the total of correct answers given by each EG subject.

Subject	CRE beat·min^{-1}·%$^{-1}$	VRE L·min^{-1}·%$^{-1}$· kg^{-1}	ΔSpO_2E %	ΔSpO_2R %	RREH beat·min^{-1}	AMS risk	pre-PMA	post-PMA
1	0.88	0.1 *	33 *	13	28 *	High	57	64
2	0.86	1.03	21	8	23	Low	72	69
3	0.82	0.53	28 *	10	20	High	75	78
4	0.77	1.43	18	3	29 *	Increased	61	62
5	1.08	0.98	24	10	24	Low	70	78
6	0.64	0.39	37 *	11	20	High	49	60
7	1.04	1.07	26	11	26	Low	48	57
8	0.59	0.59	22	9	21	Low	78	71
9	0.64	0.85	17	8	31 *	Increased	74	72
10	0.8	0.47	31 *	13	11	High	49	56
11	0.65	0.42	20	10	18	Low	47	46
12	1.16	0.55	19	5	15	Low	53	47

Table 2 shows the total number of correct answers and the 4 factors of the PMA test performed by EG before and immediately after they had finished the NH test, compared with the CG that was not exposed to hypoxia. The results did not show any statistically significant differences between the groups (p > .05).

Table 2

Correct answers and the 4 factors of the PMA test performed by EG before and immediately after they had finished the NH test, compared with the CG that was not exposed to hypoxia.

PMA Factor	intervention	EG *n* = 12	CG *n* = 8	significance
V	pre	19.4 ± 2.7	19.3 ± 3.1	p > .05
	post	23.3 ± 2.6	22.6 ± 1.8	
S	pre	17.3 ± 6.6	13.5 ± 6.4	p > .05
	post	17.3 ± 7.2	16.1 ± 7.3	
R	pre	10.3 ± 2.9	7.6 ± 2.4	p > .05
	post	8.9 ± 2.9	6.8 ± 2.8	
N	pre	14.0 ± 6.3	12.9 ± 5.8	p > .05
	post	13.9 ± 6.3	14.1 ± 6.5	
Total	pre	61.1 ± 12.0	53.3 ± 8.9	p > .05
	post	63.3 ± 10.7	59.6 ± 11.6	

Data expressed as number of correct answers (mean and standard deviation) with respect to the verbal (V), spatial (S), reasoning (R) and numerical (N) factors and total cognitive PMA test performed by the experimental group (EG) before (pre) and just-after (post) the hypoxic test simulating an altitude of 4800 m, compared with the pre-post PMA by the control group (CG) not exposed to hypoxia. ANOVA for repeated measures in pre- and post-intervention between the two groups did not show statistical significance (p > .05).

DISCUSSION AND CONCLUSION

Overall cognitive function did not show a significant decline immediately after acute and brief exposure to hypoxia simulating an altitude of 4800 m, nor was it linked to high susceptibility to AMS using a specific NH test. The objective of our study was not to correlate the altitude symptoms with the results obtained in the NH test, as no specific AMS scores (e.g. Environmental Symptoms Questionnaire) were recorded during the climbers' previous expeditions. We observed that only half of the participants who recalled having suffered from hypoxia-related altitude symptoms (slight headache) also showed increased susceptibility to AMS in the NH test. Obviously, our sample was too small to obtain an overall prediction from this NH test, which has been shown to have high accuracy (80%) in distinguishing AMS susceptibility in extensive samples of climbers (Richalet et al., 1988), as well as in less trained populations (Rathat, Richalet, Herry, & Larmignat, 1992). We consider that the low incidence of altitude symptoms shown by

all our climbers may be explained by the fact that they are members of a professional mountaineering team and are accustomed to spending the recommended acclimatization time for high-mountain environments. However, more recently reported hypoxic tests have shown new data as to the estimative severity of AMS and the general degree of maladaptation to high altitude, although such tests do not involve physical exercise and the simulated altitude is slightly lower (Savourey et al., 2007).

To our knowledge, only six studies have been specifically designed to relate AMS incidence with cognitive status by using real or simulated altitudes. White (1984) reported impairment in auditory addition and memory in participants affected by AMS symptoms at 3600 m, but not in those taking acetazolamide at the same altitude. Forster (1985) found a lower incidence of AMS symptoms and better numerate memory and psychomotor ability in participants after several days at the summit of Mt. Mauna Kea (4200 m) than in participants tested six hours after reaching the same altitude. Mackintosh et al. (1988) reported that reaction time was increased in those participants with marked symptoms of AMS at 4790 m and 5008 m during mountaineering expeditions. Shukitt-Hale et al. (1991) reported a correlation between AMS incidence and cognitive performance deficit in males within several hours of acute exposure to a simulated altitude of 4700 m. Regard et al. (1991) used conceptual tasks to detect a mild impairment of short-term memory, albeit with an improvement in cognitive flexibility, in mountaineers who developed AMS within several hours after a rapid ascent to 4559 m, compared to participants who did not suffer from AMS. Crowley et al. (1992) found that participants who were affected by AMS showed a more gradual improvement in cognitive performance during the hours following an acute ascent to a simulated altitude of 4300 m. All these studies involve lengths of exposure to hypoxia ranging from hours to days, which is the time needed to develop AMS symptoms, and therefore differed considerably from the short-term hypoxic exposure applied in the present study. Our main objective was to use the same procedure (specific hypoxic test) to determine whether AMS susceptibility in non-acclimatized participants could also be related to cognitive transient changes, at least residual ones, without having to provoke any type of high altitude illness.

Persistent neurocognitive impairment after withdrawal from a single exposure to prolonged severe hypoxia or after repeated ascents to extremely high-altitudes is well-documented (Garrido et al., 1996; Hornbein et al., 1989; Paola et al., 2008; Regard, Oelz, Brugger, & Landis, 1989). Cognitive performance suffers an abrupt deterioration if such altitudes are reached rapidly. However, there is some disagreement concerning the cognitive slowing down induced by acute and short-term exposure to lower altitudes. In the experimental field, Kida & Imai (1993) did not detect any major changes in reaction time tasks in some participants exposed either to simulated altitude of 6000 m, or when short adaptation was carried out by means of intermittent simulated altitudes of up to 7000 m (Leifflen et al., 1997). Lindeis, Nathoo, & Fowler (1996) did not find any slow stimulus identification in a mental rotation task during arterial blood oxygen saturation at 64% while breathing gas mixtures. Noble, Jones, & Davis (1993) found that only minor, insignificant psychomotor effects with moderate hypoxemia (SaO_2 ~78%) were induced by a similar duration and reduction in FiO_2 as we applied in our study. Van der Post et al. (2002) detected significant cognitive impairment in simple reaction times, binary choice task and in serial word recognition in healthy participants a few minutes after they began to maintain a SpO_2 of 80% when breathing gas mixtures. Wu, Li, Han, Wang, & Wei (1998) have reported reductions in arithmetic performance and reaction time one hour after a simulated altitude of almost 5000 m inside a hypobaric chamber, and Bartholomew et al. (1999) reported short-term memory deficit after spending 90 minutes at a simulated altitude of 3800 m. Comparing acclimatized and non-acclimatized participants exposed to 6000 m inside a hypobaric chamber, Koller et al. (1991) reported significant mental arithmetic errors only in the latter group. Nevertheless, few studies have introduced physical exercise during the hypoxic exposure, and therefore a significant increase in the degree of hypoxia would be expected. Paul & Fraser (1994) did not detect any impairment in the ability to learn new tasks when participants performed light physical exercise at simulated altitudes below 3700 m. Knight, Schlichting, Fulco, & Cymerman (1990) demonstrated that several hours of exposure at the same simulated altitude (FiO_2 13%) seemed sufficient to develop psychomotor impairment, but this, however, was not related to submaximal exercise. Moreover, it has been suggested that helicopter aircrews should be aware that even very light physical activity (4 minutes cycling at a work rate of 60 watts) under acute exposure as low as 2134 m may produce hypoxemia and mental symptoms similar to those normally expected in a person resting at an altitude approximately between 3600 m and 4600 m (Smith, 2007). Likewise, an interesting topic of study is the effects on cognitive processes immediately after a hypoxic situation, as occurs in some critical illnesses. The presence of residual neuropsychological effects may depend on the length and degree of decreased oxygen delivery to the brain, and neurocognitive sequelae seem common and may be permanent (Hopkins & Jackson, 2006). However, impairment may slowly improve within several months of an early post-acute confusional state caused by sudden and brief hypoxic episode (Lim et al., 2004).

We observed that our participants in both EG and CG groups provided slightly more correct answers during the second PMA test, due to an improvement in Factor V. This may be the result of a learning effect, as this particular factor requires the simplest cognitive task, in that it tests basic verbal comprehension abilities related to daily language use. Although, with the exception of factor S, cognition tended to decline in the other two cognitive factors (R and N) in tests performed by EG participants, we did not find any significant differences between their pre-PMA and post-PMA scores. However, the four participants who had the lowest peak values of SpO_2 during the NH test, and consequently those with the highest AMS susceptibility, unexpectedly performed slightly better in the post-PMA test. The other participants (with the exception of nos. 5 and 7) who had a brisk ventilatory response to hypoxia, showed a greater decline in scores on the post-PMA test. We cannot rule out the possibility that this observation may be related to the complex mechanisms involved in cerebral blood flow regulation during altitude exposure, which depends mainly on the degree of hypoxia and on individual sensitivity to oxygen and carbon dioxide balance

(Brugniaux, Hodges, Hanly, & Poulin, 2007). The NH test designed by Richalet et al. (1988) assesses the ventilatory response in the poikilocapnic hypoxia condition. In other words, the alveolar carbon dioxide pressure is free to vary as a consequence of ventilation changes with hypoxia. This condition has been shown to cause a biphasic response of cerebrovascular resistance, with an initial drop in blood flow mediated by hypocapnia within the first minutes of acute inhalation of half of the normal alveolar oxygen pressure (Steinback & Poulin, 2008). A higher level of hypocapnia induced by physical exercise following intermittent hypoxia exposure has been shown to cause a significant decrease in cerebral oxygenation at a simulated altitude of around 3200 m (Ainslie, Hamlin, Hellemans, Rasmussen, & Ogoh, 2008). Nevertheless, a more recent study challenged the notion that hypocapnia was the main deoxygenation mechanism in cognitive prefrontal brain areas during peak exercise under acute and short-term exposure to a simulated altitude of 4700 m (Subudhi, Miramon, Granger, & Roach, 2009).

Nor did we detect any significant differences between the groups in the four PMA subtests; however, the worst performance was in Factor R, which tended to decline more sharply in climbers who underwent the NH test. This sub-test explores inductive reasoning related to the function of the frontal lobe brain areas, which are particularly vulnerable to hypoxic insults. Comprehension processing difficulty was strongly associated with damage to prefrontal cortex pathways in extreme altitude climbers (Lieberman, Protopapas, Reed, Young, & Kanki, 1994). Recent findings have shown hypoxia-induced performance deficits using electromagnetic tomography after short exposure (40 minutes) to a simulated altitude of approximately 4000 m, and such deficits have been related to changes in the cortical activity of prefrontal areas (Schneider & Strüder, 2009). However, although changes in cerebral excitability caused by a lack of oxygen seem to be an important factor in producing AMS symptoms, hypoxia cannot probably explain the whole neuropsychological and clinical picture of this altitude sickness, as was recently reported (Miscio et al., 2009). It is probable that a variety of mechanisms are involved, due to the evidence of the dissociation of the time course between AMS, cognitive changes and also moods during sustained hypoxic exposure (Banderet & Burse, 1991; Shukitt-Hale et al., 1991).

Psychological reactions brought on by the hazardous environment of high altitudes, whether terrestrial or aerial, were rejected on the basis of an NH test performed in a laboratory. However, our study did not assess cognitive function during the hypoxic exposure, even though the climbers performed the post-PMA immediately after completing the NH test. If this type of hypoxic test causes a significant cognitive slowing down, recovery must occur rapidly a few minutes after the hypoxia stops. We must take into account that this type of NH test consists of a sudden hypoxic stress that adds physical exercise and is consequently more aggressive to brain oxygenation than acute hypoxia, in which the peak degree is achieved progressively in several steps within minutes or hours while resting. In our experience, this type of NH test induces a hypoxic syncope in a few cases, but tends to provoke a certain dazed sensation in many people. Therefore, we do not rule out the possibility that there may be some transient mental dysfunction during the hypoxic phases of the test. Technical problems make it impossible to perform the PMA test during this type of NH test, as gas exchange is continuously monitored by means of a pneumotachograph connected to mouth valve multipiece tubes, while the subject performs relatively intense physical exercise while both checking a display in order to maintain a steady cycling pace and holding the handle bar of the cycle ergometer. This test situation may produce methodological errors, even during a simple cognitive assessment, that are not associated exclusively with the hypoxic stress. Finally, the Thurstone test was included in a study in mountaineers that enabled detection of the presence of cognitive impairment after repeated extremely high-altitude climbs (Regard et al., 1989), and we consider that the PMA test could be useful for cognitive evaluation during stances in high mountains, due to its simplicity, rapid execution and easy interpretation, even by non-scientific personal. Nevertheless, the results do not support our initial hypothesis, and consequently, for prior detection of participants who are at particular AMS and cognitive risks, we suggest that complex task performance needs to be evaluated by applying other specific tests of normobaric or hypobaric hypoxia characterized by longer exposure to oxygen deprivation, like some recently reported models (Savourey et al., 2007).

Basic cognitive function does not seem to be impaired immediately after short and sudden hypoxic exposure corresponding to an altitude of almost 5000 m, and no link was established between AMS risk and cognitive dysfunction by means of the procedures applied. Our results suggest that rapid ascents with very brief stays below extreme altitudes, even when performing moderate physical exercise, as is the case in some aerial or mountain activities, seem to be cognitively safe despite the susceptibility to AMS, at least in non-acclimatized males with previous experience of high terrestrial altitudes. Nevertheless, future studies including complex task evaluation in larger numbers of participants are necessary if we are to provide a predictive value between AMS and cognitive susceptibilities on the basis of a single, and probably longer, hypoxic test. Can also be incorporated studies of Event-Related Potential (ERP), widely used to assess how the human brain normally processes information (Hernández, 2007).

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