

ALTITUD y RIESGO NEUROLÓGICO

Alpinistas Europeos *versus* Sherpas del Himalaya

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Barcelona

1997

Are Himalayan Sherpas better protected against brain damage associated with extreme altitude climbs?

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(Received 19 June/19 September 1995; accepted 16 October 1995)

1. The potential risk of brain damage when lowlanders attempt to climb the highest summits is a well-known fact. However, very little is known about what occurs to Himalayan natives, perfectly adapted to high altitude, when performing the same type of activity.

2. Taking into account their long-life climbing experience at extreme altitudes, we examined seven of the most recognized Sherpas with the aim of performing a comprehensive neurological evaluation based on medical history, physical examination and magnetic resonance brain imaging. We compared them with one group of 21 lowland elite climbers who had ascended to altitudes of over 8000 m, and another control group of 21 healthy individuals who had never been exposed to high altitude.

3. While all of the lowland climbers presented psychoneurological symptoms during or after the expeditions, and 13 of them (61%) showed magnetic resonance abnormalities (signs of mild cortical atrophy and/or periventricular high-intensity signal areas in the white matter), only one Sherpa (14%) showed similar changes in the scans, presenting neurological symptoms at extreme altitude. The neurological examination was normal in all three groups, and no neuroimaging abnormalities were detected in the control group.

4. The significant differences, in both clinical and neuroimaging terms, suggest that Sherpa highlanders have better brain protection when exposed to extreme altitude. Although the key to protection against cerebral hypoxia cannot be established, it is possible that an increase in the usually short period of acclimatization could minimize brain damage in those lowlanders who attempt the highest summits without supplementary oxygen.

may produce brain injury [1–3]. Cerebral blood flow is highly sensitive to changes in carbon dioxide tension [4] and the increased ventilation shown by humans at extreme altitude may enhance the situation of hypoxia in the nervous system resulting from a reduction of blood flow to the brain, secondary to the marked hypocapnia observed in these circumstances [5]. This situation, which can be expressed clinically as 'mountain sickness', can be quickly relieved by inhaling air enriched in carbon dioxide [6]. It is also known that those subjects who show a higher ventilatory response when in a hypoxic atmosphere exhibit more residual neurobehavioural impairment after returning to lower altitudes [7]; Himalayan highlanders, when in a hypoxic environment, respond with a lower degree of hyperventilation than acclimatized lowlanders [8]. Recent observations made using magnetic resonance imaging (MRI) in lowland residents, suggest that repeated climbing at high altitude without supplementary oxygen is associated with a high incidence of cortical atrophy [9], with further MRI changes in the white matter after only one climb to extreme altitude [10].

The Himalayan Sherpas are a unique ethnic group of high-altitude natives who specialize in ascents to the highest peaks of the world. Although their extraordinary adaptation at high altitude is well known, it has not been established whether the brains of these chronic hypoxia-adapted highlanders are affected by repeated exposure to extreme high-altitude when climbing without the use of supplementary oxygen.

METHODS

In order to evaluate the existence of potential brain damage among these mountaineers, we selected the eight most recognized Himalayan Sherpa climbers, paying particular attention to their climbing experience and especially their total ex-

INTRODUCTION

The low oxygen pressure present at high altitude

Key words: altitude, brain, climbing, hypoxia, magnetic resonance, neurological symptoms, Sherpas.

Abbreviations: MRI, magnetic resonance imaging.

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Table 1. Median and range of the characteristics of the two groups of climbers studied. *, statistical significance.

	Age (years)	Climbs over 7000 m	Climbs over 8000 m	Time over 7000 m (h)	Time over 8000 m (h)	Time of each climb over 7000 m (h)	Time of each climb over 8000 m (h)	Subjects with MRI brain changes
Sherpas (n = 7)	33 (5)	7 (12)	4 (8)	239 (631)	34 (79)	26.6 (107.1)	3.6 (15)	1
Lowland climbers (n = 21)	31 (7)	3 (7)	1.5 (5)	445 (1390)	56.5 (293)	116.7 (430)	26.3 (72.5)	13
Comparison (Sherpas versus low climbers)	P > 0.05	*P < 0.01	*P < 0.05	P > 0.05	P > 0.05	*P < 0.005	*P = 0.01	*P < 0.05

posure to extreme altitude, with the purpose of examining them on the basis of medical history, physical examination, and brain MRI. The native males, aged 36 (7SD) years, were born and had spent most of their life between altitudes ranging from 2500 m to 4800 m in the *Solu-Khumbu* Everest area of north-eastern Nepal. Climbs of over 6000 m were quite common for each of them and, as a whole, they had participated in 80 expeditions over 7000 m, of which 52 were over 8000 m. On 29 occasions they had reached the top of the highest peaks, including 15 ascents to the summit of Mt Everest. They had never used supplementary oxygen during the climbs.

Through medical histories, obtained with the help of an expert translator (a Nepali who works as a translator in the Nepal Consulate in Spain), we obtained detailed information with special attention to head injuries, toxic habits, metabolic disorders and other medical problems. These medical histories were especially aimed at detecting biological, cognitive, emotional, motivational, perceptual and neuro-motor dysfunctions or abnormalities experienced during the high-altitude acclimatization period, exposure time to extreme altitude and descent time home. Four Sherpas had recently withdrawn from altitudes of above 8000 m (48 days), and the other four subjects had done so eight or more months before the study (between 8 and 34 months). None of the highlanders showed signs of hypertension. Four of them were light tobacco smokers (less than 10 cigarettes per day). The oldest Sherpa in the group (53 years old) proved to have a long history of chronic alcoholism. Since his youth, he had been drinking high quantities of *rakshi* and *chhang* (distilled and fermented Tibetan beverages), and for the last 9 years he had been addicted to beer and whisky with an average daily intake of alcohol corresponding to about 70 g of pure ethanol. He was therefore excluded from the final evaluation which consisted of seven Sherpas with a mean age of 34 (1SD) years, as indicated in Table 1.

The clinical examination included complete standard neurological testing. The cranial MRI was performed at sea level on a 1.5 T superconducting magnet (General Electric, U.S.A.) equipped with a

quadrature polarized head coil. From a sagittal T₁ image (TE:20, TR:575), used as a localizer, axial and coronal series were planned, and T₂-weighted spin-echo images (TE:40–100, TR:2000) were obtained. Twenty 4-mm-thick cranial sections (1 mm gap) on a 256² matrix were obtained. In each MRI study the number, pattern and site of the lesions were analysed qualitatively by two independent neuro-radiologists who had no previous knowledge of the subjects, and who were kept blindfolded as to the clinical data, the previous medical history of the subjects and the diagnosis made by their fellow colleague. An arbitrary scoring system was used in order to localize lesions or abnormalities for the following anatomical zones: centrum semi-ovale, periventricular areas, brain stem, basal ganglia, internal capsula, thalamus, cerebellum, hemispheric brain sulci and ventricles.

The group of seven Sherpas was compared with a group of 21 age and sex-matched elite mountaineers, lowland residents who had performed at least one climb of over 8000 m without supplementary oxygen. The time elapsed between the last ascent at extreme altitude (above 8000 m) and the examination date ranged between 21 and 56 days (mean of 35 days) for 12 of the lowland climbers, and more than 8 months (with a range of between 8 and 27 months) for the other nine lowland resident climbers. None of them had a history of arterial hypertension or cerebrovascular disease nor were they habitual alcohol drinkers. Only three members of this group were occasional or light tobacco smokers (less than 10 cigarettes per day). We also included a control group of 21 age and sex-matched healthy lowlanders who had never been exposed to altitudes above 2500 m. The control group was made up of members of the University staff, none of whom showed signs of central nervous system pathology nor the presence of any neurological risk factors. The three groups were all studied within a year of each other in Barcelona (Spain) using the same clinical assessment, neuroimaging techniques and procedures, and with the same equipment and team of physicians and neuro-radiologists. After approval from the institution's ethics committee, consent was obtained from all

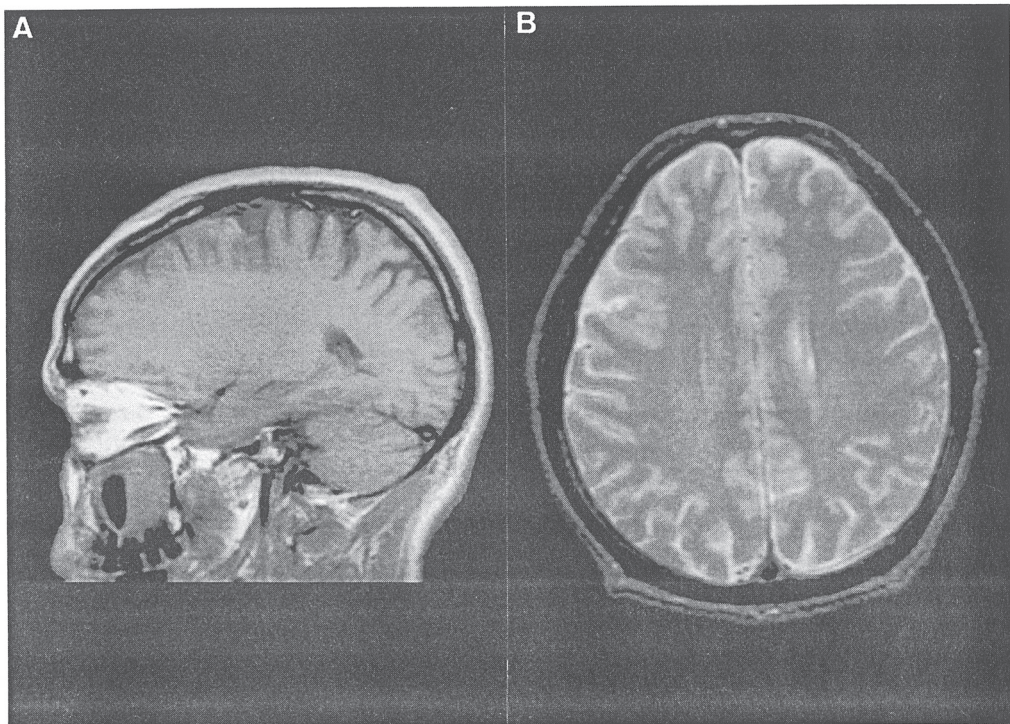


Fig. 1. The only Sherpa (33-year-old) who showed brain MRI abnormalities. (A) Sagittal T_1 -weighted image showing signs of mild parietal-posterior cortical atrophy; (B) axial T_2 -weighted image showing a left white-matter periventricular high-intensity signal.

subjects after explaining the purpose of the study to them.

We compared the two groups exposed to high altitude, both the Sherpas and lowland climbers, with the aim of determining the possible differences in the response to environment. The mean age of the two groups was compared using Student's *t*-test, differences in the incidence of MRI abnormalities (expressed as the statistical proportion of the corresponding event) by means of Fisher's exact test, and the other variables (number of climbs and total time at extreme altitude, and the time of each climb at extreme altitude) by means of the Mann-Whitney test, a non-parametric test.

RESULTS

All members of the group of lowland climbers have experienced some kind of high-altitude related psychoneurological disorder. They reported several symptoms such as headache, insomnia, ataxia, lack of vision, aphasia, irritability, hallucination, behaviour abnormalities or others, and almost half of them also presented symptomatology after completing expeditions, such as memory disturbances, depression syndrome or poorer intellectual efficiency. Although none of the individuals showed the presence of neurological dysfunction upon physical examination, 13 climbers (61%) presented brain MRI changes: signs of cortical atrophy and/or high-intensity signal areas. Sagittal T_1 -weighted images showed sulci enlargement and prominent parietal subarachnoid spaces. The high-intensity

signal lesions were always identified on proton density and T_2 -weighted images, and never on T_1 , predominantly in the atrial and posterior horns of the periventricular white matter.

Only one (14%) of the seven Sherpas showed MRI abnormalities (Fig. 1), which proved to be similar to those detected in the lowland climbers, and on the basis of the lower incidence of lesions in the Sherpas compared with the lowland climbers, we detected a significant difference ($P < 0.05$). This Sherpa was also the only member of his group who had experienced neurological symptoms: severe headache followed by transitory hemianopsia at 8200m 5 years previously, and 2 years before this he had also had to spend one night at 8650m during a slow descent from the summit of Mt Everest. The clinical neurological examinations of the Sherpas were completely normal, and we did not detect any clinical dysfunctions or brain MRI abnormalities in the control group.

We have not found any relation between the changes or abnormalities detected by MRI and the type, extension and severity of the psychoneurological symptomatology, the number of climbs, the time of exposure to extreme altitude, the time elapsed from the last ascent or tobacco consumption.

DISCUSSION

The Sherpa natives surpassed severalfold the group of European climbers in the number of times exposed to extreme high-altitude without supple-

mentary oxygen. If the accumulation of severe hypoxic episodes was responsible for the structural damage, an increased frequency of brain MRI changes could be expected in the Sherpas. This, however, was not the case. Parenchymal hyperintensity areas, signs of moderate cortical atrophy, or both, were observed in a large percentage of the lowland climbers, while no brain MRI abnormalities were found in the control group. It is also worth noting that all members of the group of lowland climbers had experienced several high-altitude related psychoneurological disorders, as compared with the single Sherpa group member. Due to language problems there was the potential danger of imprecision when recording the Sherpa group's medical history, despite the fact that some of the members could communicate in English. Nevertheless, we decided to overcome this possible risk, first with the help of the best possible Nepali translator, and second, by performing an extensive and detailed medical interview using simple questions as advised by experts in this field [11].

The periventricular white matter high-intensity signal MRI areas observed by us were described by Hachinski et al. [12], and were probably related to brain atrophy due to cortical-subcortical lesions. These findings are relatively common in elderly people, especially in relation to cerebrovascular risk factors, and are associated with slowness in the performance of complex mental processes [13]. This slowness can be similar to that observed in the so-called 'acute organic brain syndrome' described by Ryn [14], which appears frequently under extreme altitude environmental stress. Furthermore, chronic alcoholism is a well-established cause of neuronal shrinkage [15], a fact that prompted us to exclude the 53-year-old Sherpa.

The differences observed, both in terms of clinical events and of neuroimaging abnormalities, suggest that these Himalayan natives are better protected against the deleterious effects of extreme altitude. Particular genetic resistance to hypoxia [16], in addition to a physiological adaptation in the adult [17–19], may explain this brain defence. It is worth mentioning that the highland Sherpas show, only occasionally, a minor Cheyne–Stokes breathing pattern typically exhibited by lowlanders for sustained periods of time during sleep at high altitude [20]. This fact, in part attributed to the special characteristics of the respiratory control system of the Sherpa highlanders, precludes the important fall in blood oxygen that occurs during the very frequent and prolonged periods of apnoea in lowlanders sleeping at low barometric pressures [20, 21]. Another fact that should be taken into account is the extraordinary endurance capacity and strength shown by the Sherpas selected in this study, which had allowed them to perform a large number of ascents and descents during each expedition, and consequently minimized continuous exposure to the

severe hypoxic conditions of extreme altitude environment. While this fact could explain that the European climbers exceeded the Sherpas in the number of hours or total time spent above 7000 m, it has not yet been established if humans show a greater tolerance to a higher number of brain aggressions of brief duration or to a lower number of aggressions albeit of longer duration. Finally, the unique development of the nervous system, and in particular the brain, during early life at high altitude could determine a special metabolic rate with lower energy and oxygen requirements. This seems to be in accordance with the results of a recent study which reports a low metabolism in the brain of Amerindian Quechuas considered as a result of an adaptation of the central nervous system against chronic hypobaric hypoxia [22].

Although the mechanism for brain protection against severe hypoxia in climbers cannot be established, we consider that some physiological factors, conditioned genetically or induced by training, may prevent brain damage from occurring even in cases of extreme high-altitude exposure. It is possible that by increasing the habitually short periods of acclimatization or by following special training programmes, the occurrence of brain injury in those lowland dwellers who ascend the highest mountains could be minimized. It is worth noting that lowlanders take more than a year at high altitude to recover autonomic nervous balance completely [23].

At present, it is difficult to determine with reasonable precision the clinical and physiopathological significance of such MRI findings in climbers, and their mid- and long-term evolution remains to be seen. However, they seem to be consistent with the hypothesis that exposure to extreme high-altitude constitutes a potential risk of brain damage for lowlanders, but not for highland natives, as shown for the first time by the present study performed on a group of Himalayan Sherpas.

Finally, we would like to warn those lowland dwellers who, every year, attempt to reach the world's highest summits about the potential risk of brain damage when climbing to extreme altitudes, especially without an adequate adaptation period to this new environment. We would also urge physicians to inform their team colleagues about the potential danger of such enterprises, if undertaken without the use of supplementary oxygen.

ACKNOWLEDGMENTS

We thank the following people and institutions for their support: Sandoz Sport Research; the Nepal Consulate in Spain; the Spanish Embassy in India; Mr Raju Shakya for his translation and interpreting in Nepalese and Tibetan; Mrs B. Campos, Assistant Professor of the Department of Biostatistics of the University of Barcelona; Mr G. Fannon for his English correction of the paper; and Prof. S. Goldstein, Henry Ford Hospital, Detroit.

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