



BRIEF OBSERVATION

Evidence of Brain Damage after High-altitude Climbing by Means of Magnetic Resonance Imaging

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ABSTRACT

PURPOSE: There are only anecdotal and small reports on brain systematic magnetic resonance imaging (MRI) studies in mountain climbers. The purpose of our work is to study the risk of brain lesions in mountain climbers by means of conventional MRI and magnetic resonance spectroscopy (MRS).

METHODS: We recruited 35 climbers consecutively (12 were professional and 23 were amateur) in 4 expeditions without supplementary oxygen: 12 professionals and one amateur went up to Mt. Everest (8848 m), 8 amateurs to Mt. Aconcagua (6959 m), 7 amateurs to Mont Blanc (4810 m), and 7 amateurs to Mt. Kilimanjaro (5895 m). The mean age was 33.8 years (range: 22-46). All of them underwent general medical examination, standard blood tests, and MRI of the brain after the expeditions. MRI also was carried out in a control group of 20 healthy subjects. Single-voxel MR spectroscopy was carried out in 14 amateur subjects after the expeditions and in 10 healthy controls. As outcome measures, we evaluated changes in the hematocrit value, presence of cerebral lesions on MRI, as well as atrophy and dilatation of Virchow-Robin spaces, and differences in the metabolite ratios obtained from brain MRS in comparison with controls.

RESULTS: Only 1 in 13 of the Everest climbers had a normal MRI; the amateur showed frontal subcortical lesions, and the remainder had cortical atrophy and enlargement of Virchow-Robin spaces but no lesions. Among the remaining amateurs, 13 showed symptoms of high-altitude illness, 5 had subcortical irreversible lesions, and 10 had innumerable widened Virchow-Robin spaces. Conversely, we did not see any lesion in the control group. We found no significant differences in the metabolite ratios between climbers and controls.

CONCLUSIONS: We conclude that there is enough evidence of brain damage after high altitude climbing; the amateur climbers seem to be at higher risk of suffering brain damage than professional climbers. © 2006 Elsevier Inc. All rights reserved.

KEY WORDS: Mountain climbers; Brain magnetic resonance imaging and spectroscopy

Climbing mountains is a risky activity. As more people practice this sport every year, with little experience on many occasions, a public health problem may emerge with important consequences. High-altitude illness is the most common disturbance in climbers and mountain trekkers and refers to cerebral and pulmonary syndromes that occur in unacclimatized trekkers shortly after ascent, in general at altitudes above

2500 m.¹ The minor form is called “acute mountain sickness,” which is characterized by headache, insomnia, dizziness, lassitude or fatigue, anorexia, and nausea or vomiting. The major form is called “high-altitude cerebral edema”, and it is defined by the additional presence of ataxia and impaired consciousness. The syndrome is caused by hypoxia, which produces hyperperfusion, elevation of capillary pressure, and leakage from cerebral and pulmonary microcirculation.¹ Additionally or separately, other neurological conditions have been observed such as mental disturbances,² focal neurological deficits,³ and transient global amnesia.⁴

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Although the brain is the organ most harmed by hypoxia, there are few neuroimaging studies in mountain climbers. Three cases of high-altitude cerebral edema showed bilateral lesions in the globus pallidus on neuroimaging techniques; one of them with important personality changes after recovery⁵ and 2 with irreversible subcortical dementia and severe neuropsychiatric symptoms.⁶ An MRI study in 9 subjects with high-altitude cerebral edema in the acute phase showed increased T2 signal in the splenium of the corpus callosum in 7 of them. The abnormalities resolved on subsequent MRI study, and all patients had complete clinical recovery.⁷ Systematic MRI studies in mountain climbers are anecdotal. In a study conducted in 26 Spanish climbers who ascended over 7000 m without oxygen, abnormalities were seen in 46%; cortical atrophy in 5 and periventricular hyperintensity lesions in other 5. The lesions were not related to age, clinical symptoms, maximal altitude reached, or length of exposure to extreme altitude, and images were obtained later than 20 days after return to sea level.⁸ In another study of 9 climbers with MRI before and after ascent, cortical atrophy and white matter hyperintensities were seen before climbing in 5 subjects and new lesions in 2 climbers who had symptoms of high-altitude illness.⁹ No MRI changes were observed in a series of 8 climbers that participated in 3 expeditions ascending 7100 m.¹⁰

The aim of this study is to measure the brain damage by means of magnetic resonance imaging and spectroscopy in a series of climbers enrolled from 4 different expeditions. Secondly, we want to elucidate whether or not the encountered lesions are reversible.

METHODS

We included a total of 35 climbers involved in 4 different expeditions to high mountains without supplementary oxygen. The mean age was 33.8 years (range: 22-46). The first expedition went up Mt. Everest (8848 m) in Asia and was composed of 12 experienced climbers with histories of scaling other extremely high mountains and one amateur. The ascent lasted 10 days to 5400 m and 3 months thereafter. The expedition took place from February to June 1992. The second expedition went up Mt. Aconcagua (6959 m) in South America with 8 amateur climbers from December 17, 1997, to January 1, 1998, after only 6 days of acclimatization. The third expedition went up Mont Blanc

(4810 m) in Europe with 7 amateur trekkers in March 1998 and it lasted 2 days. The fourth one was composed of 7 amateurs who went up Mt. Kilimanjaro (5895 m) in Africa from April 13 to April 19, 2004. Only 2 climbers were women (amateur). All of the climbers participating in the study lived and are living at an altitude no higher than 200 m over the sea level. None of the amateur climbers had previously ascended an altitude higher than 3000 m.

Before and after every expedition the climbers underwent general medical examination, standard blood tests, and electrocardiogram. Within 7-15 days after expedition we carried out an MRI of the brain on a 1.5-T clinical scanner (Signa Horizon, General Electric Medical Systems, Milwaukee, Wis). Axial T1 spin-echo images were obtained with the scanner set at the following parameters: Repetition Time (TR): 500 msec; Echo Time: 14 msec; matrix: 256 × 192; number of excitations: 2; slice thickness: 5 mm; interslice space: 2.5 mm. For T2 axial images it was as follows: TR: 4020 msec; TE: 126 msec, matrix: 256 × 256; slice thickness: 5 mm;

interslice space: 2.5 mm; number of excitations: 3. FLAIR (fluid attenuated inversion recovery) sequences were possible only in the amateur group.

We searched for signal alterations suggestive of lesions, enlargement of Virchow-Robin spaces, white matter hyperintensities, and signs of atrophy. The scans of the climbers were compared with those of 20 healthy controls (mean age: 32.1, range 20-44 years; sex: 17 men and 3 women). The climbers who showed cerebral lesions underwent another MRI study 3 years after the expedition, in order to determine the irreversibility of the lesions. Unlike ischemic lesions (hyperintense in fluid attenuated inversion recovery sequences), the widened Virchow-Robin spaces were defined as punctuate signals, surrounding perforating arteries, isointense on T1 and fluid attenuated inversion recovery sequences and hyperintense on T2 scans in the subcortical white matter.^{11,12} MR images were evaluated by 2 radiologists and a neurologist. The abnormalities reported in the results section were only those found by clear consensus.

We also performed proton MR spectroscopy of the brain on 14 amateur climbers after the respective expeditions: 7 from the Aconcagua, 6 from the Kilimanjaro, and 1 from the Mont Blanc. Every imaging spectroscopy was performed on 1.5-T clinical scanner (Signa Horizon). Sagittal T1-weighted topogram and T2-weighted axial localizing series were used

CLINICAL SIGNIFICANCE

- High-altitude climbing carries non-negligible risks for health.
- Acute mountain sickness and brain edema are the most common events in climbers but an appropriate acclimatization decreases the incidence of these conditions.
- Previous reports with MRI pointed to the risk of brain damage after high-altitude expeditions.
- The present study showed cortical atrophy and enlargement of the perivascular Virchow-Robin spaces on MRI of most climbers. Subcortical lesions were also present in climbers who were inexperienced and not properly acclimatized.

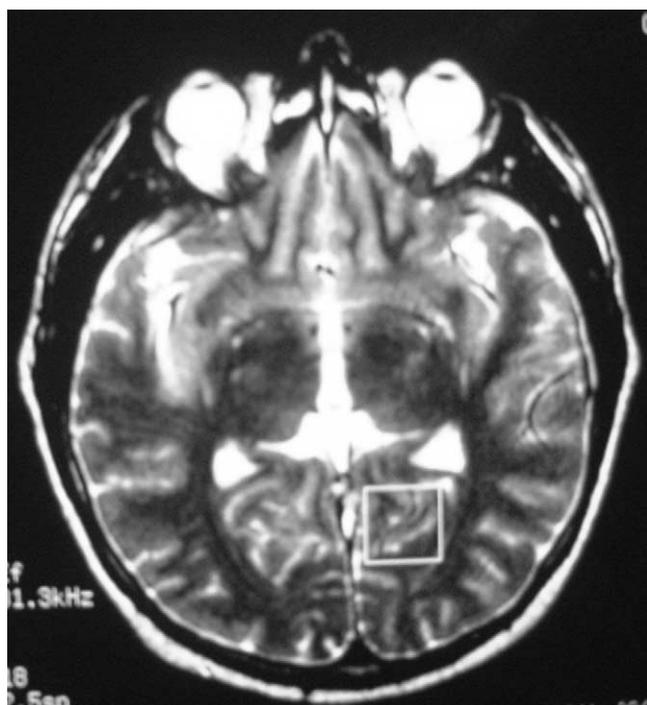


Figure 1 T2-weighted MRI with the single voxel placed in the left parasagittal parieto-occipital area.

to place volume (8 cm³) in the left parasagittal parieto-occipital area (Figure 1). We chose this area because it is rich in grey matter and located far from ventricles in order to avoid partial volume effect. Single voxel ¹H-MRS was performed by means of an echo time (TE) of 144 msec and a repetition time (TR) of 2000 msec with spin-echo technique that uses selective excitation with gradient spoiling for water suppression. The mode of spectral acquisition was Probe-s (STEAM technique). The matrix was 256 × 152 and the number of excitations was 8. The spectrum was automatically fitted to 4 peaks corresponding to levels of N-acetyl aspartate (NAA), 2.02 ppm; total creatine (Cr), 3.03 ppm; choline-containing compounds (Ch), 3.23 ppm; and myo-inositol (mI), 3.56 ppm. We also obtained the peak-amplitude of the metabolites relative to creatine in the area of exploration. The data were analyzed with the software provided by General Electric (SAGE).

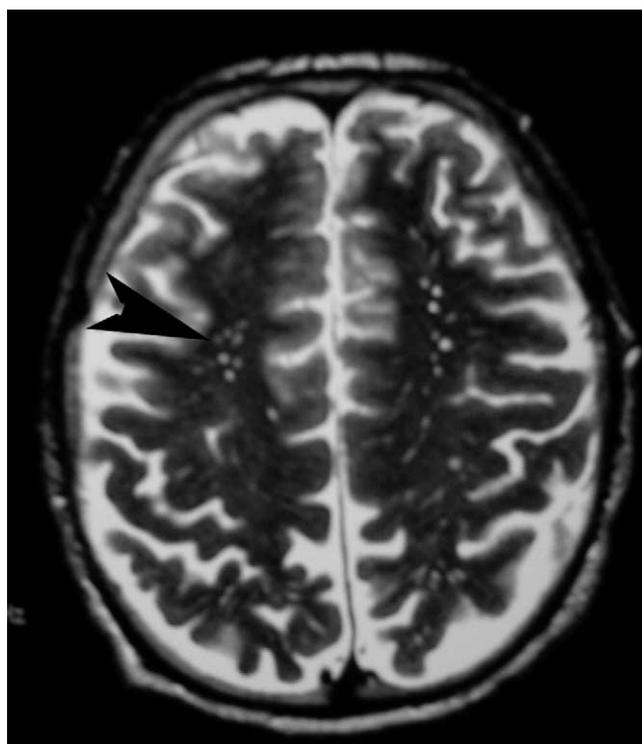


Figure 2 T2-weighted MRI showing multiple enlarged Virchow Robin spaces (arrow) in the centrum semiovale bilaterally. Image obtained from a climber of the Aconcagua expedition.

For comparison purposes we also recruited a group of 10 young healthy subjects on whom we performed MRS of the brain with the same protocol as that used in climbers.

Statistical differences for quantitative variables (hematocrit values and metabolite ratios obtained from MRS) were analyzed with 2-tailed *t*-test for paired samples and also with the Wilcoxon nonparametric test.

All the subjects participating in the study gave explicit and informed consent to carry out magnetic resonance techniques.

RESULTS

The findings of the MRI scans are summarized in the Table. In the expedition of Everest no major events occurred and none of the 12 professionals suffered from high altitude

Table The most common abnormalities found on brain MRI by expeditions

Type of abnormality	Number of climbers by every expedition and number of climbers showing abnormalities			
	Everest (n = 13)	Aconcagua (n = 8)	Mont Blanc (n = 7)	Kilimanjaro (n = 7)
Cortical atrophy	8	8	1	0
Enlargement of VRS	11	7	2	1
Subcortical lesions	1 (amateur)	4	1	0
Normality in the MRI scan	1	0	4	5

VRS = Virchow-Robin spaces.

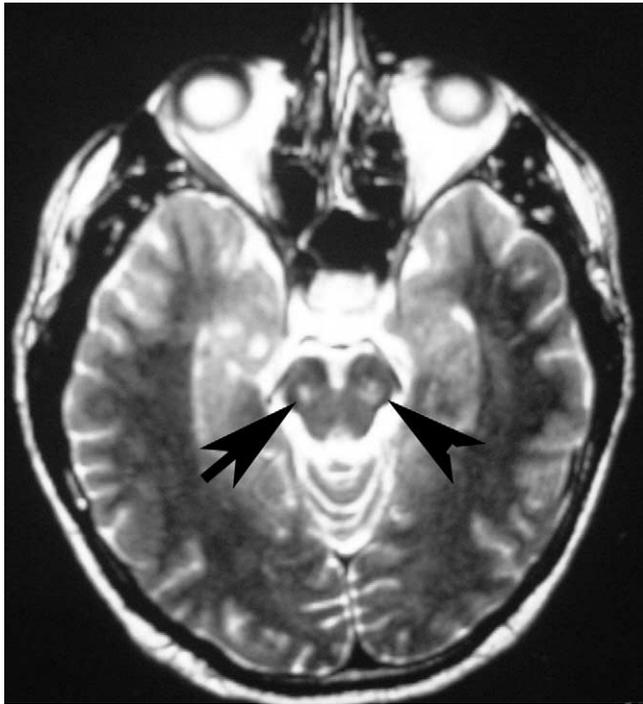


Figure 3 T2 weighted MRI showing enlargement of Virchow-Robin spaces in the midbrain, corresponding to the collicular arteries (arrows). Image obtained from another climber of the Aconcagua expedition.

illness. Only 3 reached the summit, 3 ascended to 8100 m, and the remainder ascended to 6500-7500 m. We did not observe lesions on MRI after the expedition; only 1 had a normal MRI, 8 showed diffuse cortical atrophy, and 11 showed enlargement of the Virchow-Robin spaces. However, the amateur climber suffered from high-altitude illness with respiratory involvement and a hematocrit elevation from 43.5% to 59.9%, needing a blood extraction of 450 cc. MRI after return showed bilateral subcortical frontal lesions. The 12 experienced climbers had previously ascended to mountains higher than 7000 m and they had undergone a previous MRI of the brain. We did not see differences between the 2 scans.

In the expedition to Aconcagua, 2 climbers reached the summit, 5 ascended to 6000-6400 m, and 1 reached only 5500 m. Symptoms of acute mountain sickness appeared in 3 climbers and symptoms of brain edema in 2. One of these 2 climbers had nominal aphasia from which he recovered 6 months later. After returning from the expedition, 2 climbers complained of transient memory loss and 3 others from bradypsychia. All climbers showed cortical atrophy on MRI, 7 showed widespread enlargement of Virchow-Robin spaces in the basal ganglia and the centrum semiovale (Figure 2) and in the midbrain in 2 cases (Figure 3). We encountered multiple subcortical lesions on T2-weighted MRI (Figure 4) in 4 subjects. Three years later, with no other expedition in between, the lesions persisted on T2 and fluid attenuated inversion recovery sequences (Figure 5) as well as atrophy and Virchow-Robin spaces widening.

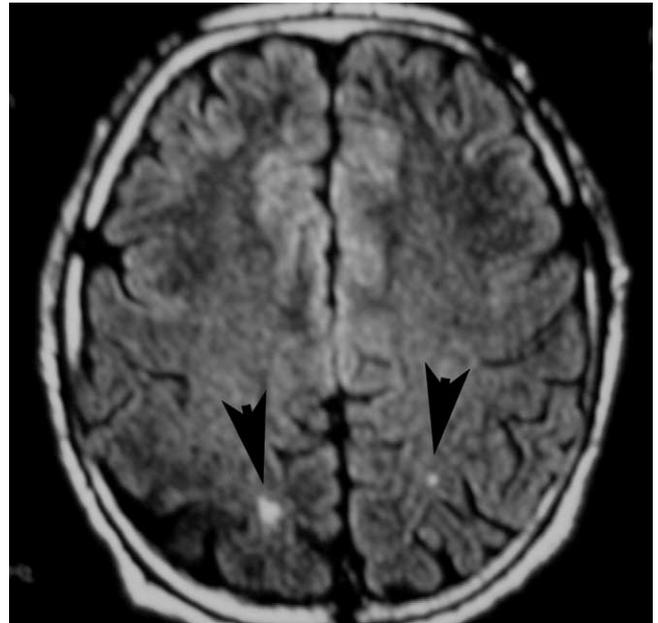


Figure 4 Fluid attenuated inversion recovery sequences after the expedition to Aconcagua obtained from a 32-year-old climber. Hyperintense subcortical lesions (arrows) in the parietal lobes and cortical atrophy are visible.

In the Mont Blanc expedition there was neither any noticeable event nor acute mountain sickness. All of the 7 climbers reached the summit. Only 1 climber showed a subcortical lesion on MRI, and 2 showed dilatation of multiple VRS in the basal ganglia.

In the last expedition (Kilimanjaro), 3 climbers reached the summit, 2 ascended to 4600 m, 1 to 5000 m, and another

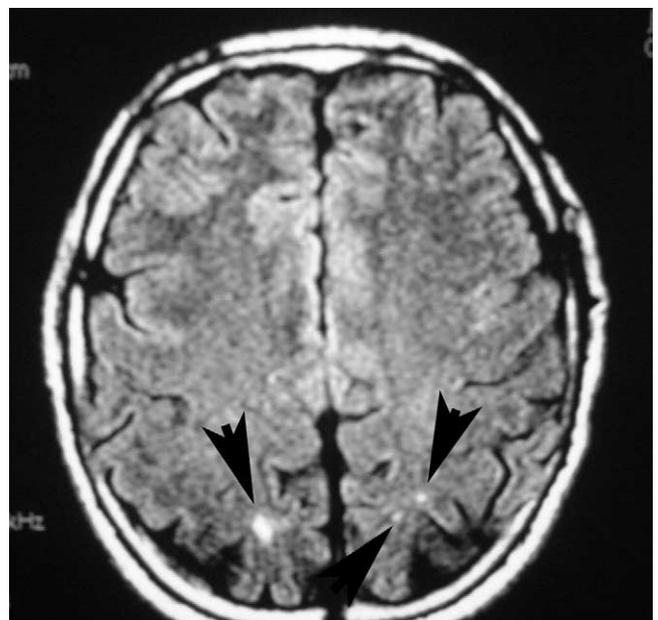


Figure 5 Fluid attenuated inversion recovery sequences in the same subject 3 years later. The bilateral lesions are still visible (arrows) with marked cortical atrophy.

1 quit the expedition at lower altitude. All of them had symptoms of acute mountain sickness but not of brain edema. On MRI, only 1 climber showed enlargement of VRS and none of them had lesions. All of them had MRI scan before the expedition without showing Virchow-Robin spaces enlargement in any of them.

In the control group we did not see either lesions or atrophy, and only 2 subjects showed 2 and 3 Virchow-Robin spaces enlarged, respectively.

In the blood tests the most striking change was observed in the hematocrit value. Before the expeditions the mean value was 44.1%, whereas after the expeditions it was 49.3% ($P = .003$ on t -test for paired data). The mean elevation of the hematocrit value was 3.2 points for amateurs and 8.7 for experienced climbers. However, the amateurs showed lesions and the professionals did not.

On MRS we did not observe significant differences in the metabolite ratios between climbers and controls. The mean NAA/Cr ratio for climbers was 1.78 and for controls it was 1.76 ($P = .7$).

DISCUSSION

The number of professional and recreational high-altitude climbers is growing every year; approximately 5000 climbers ascend every year to Himalayan peaks.¹³ Currently there is an open debate on whether the exposure to hypoxia at high altitude produces irreversible brain damage. Some neuropsychological studies did not find mental dysfunction after climbing;^{10,14} however other studies did so. Verbal and visual long-term memory was impaired after ascent in a study with 35 mountaineers.¹⁵ Another study including 17 mountaineers observed short-term memory impairment in relation to the presence of acute mountain sickness within a 24-48 hour stay at high altitude.¹⁶

In this study we have found radiological evidence of irreversible lesions in the brain of amateur climbers and cortical atrophy in professionals, which suggests some degree of chronic damage. Cortical atrophy was also a frequent finding in 2 previous studies.^{8,9} The lack of spectroscopic changes in the parieto-occipital area where no lesions were found does not confirm widespread damage. We do not know the exact mechanism of the lesions because of the lack of images in the acute phase of the high-altitude illness. Although the most likely agent is hypoxia, a vascular component cannot be completely discarded because the hematocrit values increased significantly. Hackett et al attributed the lesions observed in the acute phase of high-altitude brain edema to vasogenic mechanism because of reversibility.⁷ However, the irreversibility of the lesions in climbers with symptomatic disease in our study points to an additional role of cytotoxic edema and axonal damage. An experimental 31P-MRS study with 4 subjects before and after 7 days in a hypobaric chamber demonstrated intracellular acidosis on return to normoxia.¹⁷

It is also noteworthy to comment on the enlargement of the Virchow-Robin spaces, which were found in extensive

subcortical areas of the brain and especially in the centrum semiovale. These widened spaces are present in the elderly and rarely in young people.¹² These enlarged spaces maintain isointensity with cerebrospinal fluid on all pulse sequences and are usually seen in 2 locations: along the anterior commissure into the lower basal ganglia and the brain vertex.¹⁸ The pathophysiologic mechanism is not well known. They may be an expression of atrophy because they are associated with white matter lesions and cortical atrophy.¹⁹ Taking into account the pathophysiology of high-altitude brain edema,¹ we hypothesize that these enlargements might be caused by the vasodilatation and perivascular edema that would have occurred in the ascent at high altitude.

The fact that brain damage is more likely to occur in nonproperly acclimatized climbers also was corroborated in another study with Sherpas (native mountaineers of Nepal). These people were more resistant to high altitude than lowland climbers, as only 1 in 7 had symptoms at extreme altitude and periventricular lesions, compared with 13 of 21 lowland climbers.²⁰

The results disclosed in relation to MRS deserve some comments. NAA is one of the most abundant amino acids in the central nervous system, located predominantly in neurons, axons, and dendrites. Its function is not well known so far and remains speculative. It has been thought to play a role in lipid and protein synthesis, but also it may be a product of N-acetyl-aspartyl-glutamate degradation, or an osmolyte. As long as this metabolite decreases in degenerative diseases of the brain it has been regarded as a marker of neuronal integrity.²¹ Myo-inositol is a sugar-alcohol compound that may act as osmoregulator, intracellular messenger, and detoxication agent; it is also regarded as a marker of glial cells.²² We found no differences in metabolite ratios, but only a single area of the brain was explored.

We are aware of some drawbacks of our study. First, this is not a homogeneous cohort because we included experienced and amateur climbers with different altitudes reached. Second, cortical atrophy was evaluated in a visual way and, therefore, it could have been in some way overestimated. Although no differences were found in the metabolite ratios, it cannot be discarded that some differences in NAA/r may be found in other areas. Subcortical lesions and the marked and diffuse enlargements of the Virchow-Robin spaces are clear evidence of brain damage, because these alterations did not appear in controls.

We conclude that high-altitude climbing carries a non-negligible risk of developing cerebral lesions and atrophy on MR and that the risk looks higher in nonproperly acclimatized subjects.

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