Elbrus Dragon 2008

Report of an Expedition to Investigate Cerebral Risk Factors for Acute Mountain Sickness

Mt Elbrus, Caucasus Mountains, Russia.
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Abstract

Elbrus Dragon 2008 was a collaborative venture between medical undergraduate students of Swansea University Wilderness Medicine Society and researchers based at the University of Heidelberg (Germany), Cardiff University Brain Research Imaging Centre and the Hypoxia Research Unit at the University of Glamorgan (UK). The aim was to investigate risk factors for Acute Mountain Sickness (AMS), and attempt to predict individual susceptibility to AMS. The project took place in July 2008, with 18 participants. Prior to departure, each team member was investigated using magnetic resonance imaging (MRI) and trans-cranial Doppler (TCD) to assess various morphological and physiological parameters including vascular reactivity and cerebral autoregulation. Twice daily during the expedition, participants completed validated questionnaires to assess AMS severity and recorded arterial oxygenation values. Within four days of return to the UK, participants underwent further MRI assessment to investigate any morphological changes evident post-exposure to high altitude. Data analysis is ongoing; we hope to have preliminary results available in early 2009.

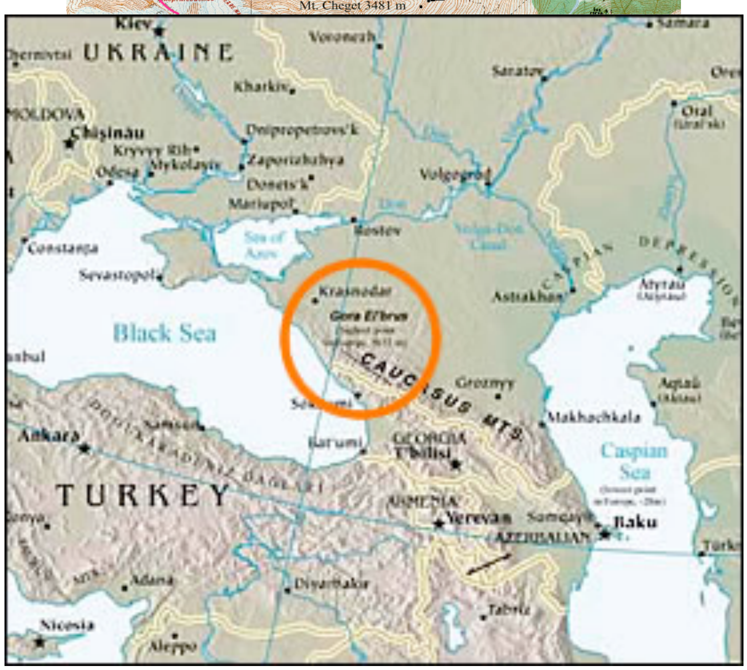
Unfortunately the expedition did not meet its mountaineering objective; the summit attempt was terminated at approximately 4900m due to inclement weather conditions. However, the expedition should be considered a success. The team achieved a high camp at 4100m and gave a number of team members the opportunity to attempt the ascent of Europe's highest mountain. The development of personal skills and qualities in all team members, particularly the expedition leaders, will feed into further research and mountaineering projects, whilst the quality of research data obtained is expected to be excellent. We would like to thank the Mount Everest Foundation for their generous support of this expedition.

Introduction

Research into the effects of altitude on human physiology has recently received substantial media interest, due to increasing numbers of tourists having easy access to high altitude with rapid ascent times. Elbrus Dragon was a research expedition undertaken this summer by 18 individuals from Swansea and Cardiff Universities, and planned by medical students from Swansea University's Graduate Entry Medical Programme.

The research aimed to identify predicting factors for those at risk of Acute Mountain Sickness, or AMS; at present there are no reliable indicators for those at risk. All of the participants were required to undergo MRI scans both before and after acute exposure to altitude. A number of scans were done on each subject including measurements of brain to skull size ratio and functional MRI (fMRI) to measure blood flow changes to the brain in response to mild hypoxia. Blood flow in the middle cerebral artery was also measured by trans-cranial Doppler ultrasound (TCD) in response to a number of hypoxic challenges to assess subjects' vascular reactivity and cerebral autoregulation. Over two weeks, whilst at altitude, participants were asked to complete several scientifically validated questionnaires used to score severity of AMS and to take measurements of their oxygen saturations and pulse rate using portable pulse oximeters. Professor Damian Bailey, a world authority on altitude physiology, led the research program.

Maps



Expedition Members

Nick Cochand, Mike Wild, Jon Bailey, Damian Bailey, Peter Davies, Ross Whitehead, Jamie Naughton, Ian Lane, Alex Patau, Sam Harrison, Jo Organ, Rhodri Evans, Cicely Warren, Sile Murphy, Sarah Buszard, Kevin Evans, Sabina Aziz, Caroline Taylor.

Admin and Logistics

Destination: Mt Elbrus is located at the North West end of the Baksan Valley approximately 4 hours drive south of the nearest airport in the town of Mineralnye Vody (MV). MV is regularly served by Russian domestic airlines (eg. S7, formerly Siberian Airlines), only a 4 hour flight from Moscow.

Transport from MV to the Baksan valley is best organised ahead of time by private bus as public transport is irregular and difficult to organise. The company organising transport from the airport can also arrange to 'smooth' the way through the numerous police checkpoints.

There are two main towns at the base of the mountain. The larger village of Terskol is 2 miles from the cable car base station and has a number of shops, bars, and restaurants, although they are quite basic. Azau is the town at the cable car station and is made up of a collection of hotels, and market stalls.

Research Materials: There are very few guidebooks to the Elbrus region, and the any maps are of poor standard in comparison to British OS maps. The only guidebook we were able to get hold of was *Mount Elbruz Region guide and maps*, by Robin Collomb published by West Col Productions in 1992 and is very out of date.

Permission and Permits: A number of permits are required for climbing Mt. Elbrus. First a Russian Visa is needed which requires an invitation from someone within Russia. On arrival in the Elbrus region you then must register with the local police, and obtain a national park permit and border zone permit due to the proximity to the Georgian border. A number of local tour companies can organise all of the above for a small fee.

Insurance: Insurance is a difficult issue for Mt. Elbrus as current FCO advice is against all but essential travel to the region due to the relative proximity to Chechnya and Georgia. As a result most insurance companies will not cover travel in that region. We were able to insure the expedition with AULT Insurance Co. (West Bromwich) who continue to insure the large number of commercial expeditions to the mountain.

Food: Due to weight restrictions we were only able to bring approximately half of our food supplies from the UK in the form of high calorie freeze-dried meals. All of the rest could be purchased in local shops in Terskol. The two huts on the mountain can also provide food if arranged in advanced.

Accommodation: In order to register with the local police you need to spend at least one night in a local hotel. There are a number around and more being built who can provide accommodation with dinner and breakfast for about 30 Euros per person per night. There is a large well used campsite in the wood behind the village of Terskol, which is another excellent and free option.

Communication: Communication with our host company was via email and telephone from the UK. There is excellent mobile phone coverage on the mountain although expensive. VHF radios can be hired but the quality and battery life is questionable, therefore more reliable radios should be brought from the UK.

Medical arrangements: We were fortunate to have two very experienced doctors on the trip, one of whom was the dedicated expedition medic. As we were expecting to encounter some level of AMS within the expedition, the doctor was on prophylactic medication to prevent AMS. We carried a comprehensive medical kit with a particular focus on AMS medication. Medical infrastucture in the area is poor. There is a clinic 40 minutes drive from Terskol with limited facilities. The nearest major hospital is a 2 hour drive from the base of the mountain and is not open 24 hours. There is a rescue helicopter in the region but this is not always working and cannot be relied on.

Environmental impact: Although Mt Elbrus is climbed by hundreds if not thousands of people every year, the infrastructure to support this number of people is very poorly developed. The area around the top of the chairlift is strewn with rubbish and human waste. A new outhouse has been constructed to replace the older facilities, known as 'the worst outhouse in the world', however no effort appears to have been made to remove any of the rubbish. Considering the volume of traffic one would expect more to be done to look after the mountain. The impression we received is that the majority of climbers on the mountain are taken up and down very rapidly by any number of commercial guiding companies, therefore these companies receive most of the money coming into the area and very little is actually fed into the local economy.

Fuel: Our expedition relied on multi-fuel liquid stoves. There is one good quality mountaineering store (Alpindustria, Terskol) but although it sells and rents liquid fuel stoves, nowhere in town actually sells liquid fuel. The nearest petrol station is 6km down the Baksan valley. It is possible to buy butane canisters for stoves in Terskol, but supplies are unreliable.

Log

Access to the village of Azau at the foot of Mt Elbrus, described as the 'Chamonix of the East', is not quite as simple as for its French counterpart. Flying to Mineralnye Vody via Moscow, and following a 4 hour bus ride, the party arrived tired but excited. Following a day to get to know Azau and buy food for the coming days, the main research phase began with acute exposure to altitude. The team ascended from Azau (2200m) by cable car to 'the barrels' hut at 3800m. After two nights at 2200m and a full 6 hours spent exercising vigorously at 3800m, one third of the team began to show symptoms of mild to moderate AMS. They were carefully monitored by the expedition doctor who was on prophylaxis against AMS, and at the end of the day the team descended by cable car to Azau where they recovered rapidly.

With the main research completed, only the task of summiting Mt Elbrus, at a height of 5642m, remained. Over the next 5 days, the group acclimatised through a series of ascents of lesser local peaks, culminating in the ascent of Mt Cheget at 3772m, and an overnight camp at 3000m.

On July 26th the team ascended again to ‘the barrels’ where we pitched camp on a spine of rock splitting two massive glaciers. The weather, which had been clear and calm for the previous week began to turn and the team spent a night battered by high winds and heavy rain. The following day thick cloud obscured the mountain and the three parties made their way up the slope to the Priut hut at 4100m, which was to be the site of the summit base camp. One of the team members began to experience symptoms of AMS once more and as we were turning one group around to return to camp, a number of Russian military personnel arrived to tell us we had to move, as they would be detonating explosions on a nearby pile of rock for a purpose we were unable to elicit. As one team returned to camp, two teams continued to scout out a suitable site for base camp to the sound of large booms echoing up the mountainside.

The next day was spent moving the camp to the site scouted out by the Priut hut, and moving away from the barrels, which was surrounded, by human garbage and excrement, noticeably raised the team’s spirits. The previous afternoon the expedition doctor started treatment with dexamethasone for the climber suffering with AMS, and by morning he was feeling better. He was watched closely as we continued the ascent, but showed no further signs of illness. Once at the barrels it was all hands on deck to dig the expedition tents into the snow to protect them from the winds where were starting to howl over the shoulder of the mountain. As we finished setting up camp the clouds cleared to give a spectacular sunset and our first up close view of our goal.

Unfortunately the weather was not to last and the acclimatisation trek the following morning was through thick cloud and high winds. The team managed to reach the goal for that day, the Pashtukova rocks at 4800m. The wind started to gust at close to 70mph and as we turned back one of the guides got onto his snowboard and disappeared into the cloud leaving one guide in front and myself bringing up the rear. On the way up one party had to turn back as a team member began to experience worrying signs. She was already very slow and began to stumble, and when asked if she was all right was unable to answer due to marked dysphasia. The team quickly turned back and the party member was rapidly evacuated off the mountain first by snow cat and then by cable car, where she was taken to the local hospital. As the expedition leaders returned to summit base camp to decide on the best course of action two more team members developed symptoms of moderate to severe AMS and these were both evacuated down on the snow cat to spend the night at the barrels where they recovered quickly.

With all the illnesses safely evacuated and treated the team could now prepare for their assault on the summit. The plan was to leave at 0200 with an estimated summit time of 0900. If the teams had not reached the summit in 7 hours they would turn back. We said good night to the guides and retired to our tents to rest and eat.

0200 dawned crisp and cold, but with an ominous lack of stars in the sky. However the team set off back up towards the Pashtukova rocks with high spirits. As we neared the previous day's altitude the wind and hail began to pick up once more. From the Pashtukova rocks the trail, which has been climbing the shoulder of the East summit turns to traverse the 45^{o} slope to the saddle. By 0400 the team had only made it to about 4900m but the decision was made that the wind was too strong to attempt the traverse, as one wrong step on the narrow path would lead to a long steep slide ending in a large crevasse field. The team turned back and the guides suggested to shelter in the Pashtukova rocks until sunrise to see if the wind would drop. However many of the team were very cold and to do so would have put many members of the expedition at risk of developing severe frostbite so the team continued back to base camp.

By the morning of the 31st July we had used both our allotted summit days and although there was potential for a third, in light of the illnesses already experienced and the tiredness of the team we decided to descend the mountain. We made it back to Azau by afternoon on the 31st where we were reunited with the rest of the team members, who had already been enjoying soft beds and hot showers and were in a much better state than the rest of us! The remaining few days were well earned R&R for the team involving a number of treks to the nearby Georgian border and getting to know the local Russian mountain rescue team.

The expedition achieved a number of its goals so although we didn't manage to reach the highest point in Europe, we made the right choice in turning back and we would still consider it a success. We were able to collect a wealth of new data on AMS which when analysed should help our understanding of this serious condition. We, the expedition leaders, gained a huge amount of experience not only in leadership but also in the organisation and logistics required to get 18 people up a mountain in a foreign country. And most importantly we had fun and gave a number of people the chance to experience high altitude mountaineering.

The Elbrus Dragon 2008 team

Expedition Research

Background

Elbrus Dragon 2008 was a scientific expedition aiming to study risk factors for developing Acute Mountain Sickness (AMS) during the ascent of Mt. Elbrus, Russia. It was a collaborative venture between medical undergraduate students of Swansea University Wilderness Medicine Society and researchers based at the University of Heidelberg (Germany), Cardiff University Brain Research Imaging Centre and the Hypoxia Research Unit at the University of Glamorgan (UK).The aim of the expedition was to investigate factors which might predispose individuals to the development of AMS, and thereby develop strategies which might allow prediction of AMS susceptibility in individuals at sea-level.

Each year, thousands of UK residents travel to moderate and high altitudes for work and leisure activities. With approximately 15-25% of those visiting moderate altitude succumbing to AMS, this creates a significant burden of illness, with treatment costing insurance companies and health services tens of thousands of pounds. Lost working days and travel cancellations further widens the economic impact of the condition. With significant morbidity, and mortality associated with the more serious sequelae of high altitude pulmonary and cerebral oedema, the search for non-invasive techniques which can identify those individuals susceptible prior to travel is a worthwhile and justifiable project.

The project was in three phases:

1. A pre-expedition phase. This involved the sea-level research into risk factors for acute mountain sickness (AMS). All participants visited both the University of Glamorgan and Cardiff University Brain Research Imaging Centre (CUBRIC) for magnetic resonance imaging (MRI) brain scanning and assessment of clinical and physiological parameters considered likely to pre-dispose individuals to AMS.
2. The expedition phase. The team travelled to Mt. Elbrus and performed a series of non-invasive assessments to assess indices of AMS in each individual. These tests were largely questionnaire-based.
3. Post-expedition phase. Most members of the team returned to CUBRIC for a post-expedition MRI brain scan, to investigate any morphological changes evident post-exposure to high altitude.

Mt Elbrus was chosen as the study area for two main reasons:

1. The area has a well developed ski tourism and mountaineering infrastructure. The cable cars allowed rapid ascent to an altitude sufficient for development of AMS symptoms, and subsequent safe, rapid descent.

2. As Europe's highest mountain, Mt Elbrus provided a realistic, yet challenging mountaineering objective for the team.

Research Programme Details

'Cerebral risk factors for acute mountain sickness; focus on intracranial buffering capacity and capillary "stress failure"'

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Introduction

The research was a prospective investigation of twenty healthy mountaineers. Using conventional 3T MRI techniques, our team examined if selected morphological features of the healthy human brain at sea-level could predict susceptibility to acute mountain sickness (AMS) during ascent to terrestrial high-altitude.

Background to AMS

Symptoms of AMS: AMS describes a collection of non-specific vegetative symptoms that include headache, anorexia, nausea, vomiting, fatigue, dizziness and insomnia experienced by non-acclimatized mountaineers within 6-12h of arrival to altitudes above 2500m [1,2]. It is considered a primary disorder of the central nervous system since headache, indistinguishable from that encountered during migraine without aura, is the most common feature.

Pathophysiology: Fig 1 provides a theoretical overview of the major factors implicated in the pathophysiology of AMS. The schema describes how chemical and hemodynamic forces act in concert to promote edema and brain swelling with AMS as the minor and HACE as the major variant. Though the subject of current controversy, intracranial hypertension subsequent to an increase in intracranial volume (ICV) is considered the "unifying" risk factor since the mechanical compression of pain-sensitive structures that reside within the trigeminovascular system provides an elegant explanation for headache and thus by consequence, AMS. The events that conspire to increase ICV and cause brain swelling are considered by many as the key to understanding its pathophysiology.

The hemodynamic pathway describes the formation of extracellular vasogenic edema since hypoxia can result in cerebral over-perfusion subsequent to sustained vasodilatation and autoregulatory breakthrough to cause a transient opening of the blood-brain barrier[1]. Two recent studies provided convincing evidence for vasogenic edematous brain swelling in hypoxia as indicated by a mild increase in brain volume [3], T_2 relaxation time (T_2rt) and apparent diffusion co-efficient (ADC) score confined mainly to the splenium and genu of the corpus callosum (CC) [3,4].

Since the human brain is so exquisitely sensitive to damaging redox reactions, the chemical pathway may also contribute to barrier dysfunction. It describes how a selfperpetuating cascade of iron-catalyzed reactive oxygen and nitrogen species (ROS/RNS) can result in membrane destabilization leading to increased permeability, vascular damage and inflammation. Pump failure subsequent to hypoxia and/or a free radical-mediated reduction in the expression and/or activity of Na/K-ATPase may prove the mechanism responsible for the astrocytic swelling recently observed in AMS [3].

However, no study to date has provided convincing evidence for any relationship between volumetrics, relaxometry and symptoms suggesting that vasogenic edematous brain swelling *per se* is a "normal" reaction to hypoxia. Since brain swelling *per se* isn't totally predictive of AMS, alternative, predominantly anthropometric factors may be involved. In 1985, Ross [5] speculated that random anatomical differences in an individual's craniospinal volume-buffering capacity may contribute to the inherent susceptibility to AMS. He suggested that a smaller intracranial and intraspinal cerebrospinal fluid (CSF) volume would predispose to AMS since the individual would be less able to accommodate brain swelling causing the brain to compress against fixed pain-sensitive structures in a non-compliant cranium.

Preliminary findings: We recently provided preliminary evidence in support of this hypothesis by establishing an intrinsically higher brain volume to intracranial volume ratio (BV:ICV) as a surrogate measure of craniospinal buffering capacity in subjects who developed AMS compared to those who remained resistant [3]. Thus, it would appear that the "tight-fit" brain may prove an anatomical risk factor for AMS in the setting of volume overload initiated by mechanical and/or chemical factors. However, there are no studies to the best of our knowledge that have tested this hypothesis in a field setting at high-altitude.

More recently, we revealed MR evidence for hemosiderin deposits confined to the parenchyma of the corpus callosum in non-lethal HACE (Kallenberg *et al*, unpublished observations). These micro-hemorrhages remained detectable for up to 31 months post-event and suggest that HACE is associated with disruption of the blood brain barrier resulting in cerebral capillary "stress failure", extravasation of red blood cells and subsequent accumulation of insoluble iron (III) oxide-hydroxide. Autoregulatory breakthrough is a likely cause that has also been documented in AMS and may indeed account for the predilection of micro-bleeds to the corpus callosum which is especially vulnerable to hypoxic vasodilatation and autoregulatory failure. However, whether micro-bleeds persist in severe AMS following a physically demanding ascent to high-altitude to confirm if AMS and HACE do indeed share a common pathophysiology related to barrier disruption and cerebral capillary "stress failure" remains to be explored.

Hypotheses

This research aimed to extend these preliminary findings and identify morphological features of the healthy human brain at sea-level that are predictive of AMS at high-altitude. Our specific aims and hypotheses are outlined below:

Specific aim (1): Determine the potential relationship between intracranial buffering capacity measured at sea-level and AMS.

Hypothesis (1): Mountaineers characterized by an intrinsically higher BV:ICV ("tight-fit" brain) and lower craniospinal axis "buffering" capacity that may be exceeded during the "normal" course of brain swelling at high-altitude will be more prone to AMS.

Specific aim (2): Determine the potential relationship between AMS, cranio-spinal morphology and density of micro-bleeds confined to the corpus callosum following return to sea-level.
Hypothesis (2): Hemosiderin deposits will be detectable only in those mountaineers diagnozed with severe AMS who exhibit a "higher" BV:ICV. The existence of micro-bleeds will provide indirect evidence for autoregulatory failure, barrier disruption and cerebral capillary "stress failure".

Design and Methods
Design:
Prospective, correlational and comparative that involved measurements at sea-level and at high-altitude.

Subjects:
Eighteen healthy mountaineers, aged between 21-60 years, were recruited as part of an organized expedition to Mt. Elbrus. There were 13 males and 5 females

Methods:
Phase 1-Sea-level measurements
Following ethical approval and after having obtained written informed consent, 18 volunteers were individually scheduled for a thorough medical examination. All AMS and MRI measurements were performed at sea-level before and within 4 days following return from Mt. Elbrus.

AMS and headache*:* AMS was assessed using the Lake Louise (LL) [6] and Environmental Symptoms Questionnaires (ESQ) [7]. Headache was determined using a clinically-validated visual analogue scale ([8]. Clinical AMS (AMS+ versus AMS-) was defined as a total LL score (self assessment + clinical scores) of ≥5 points in the presence of a headache *and* an ESQ cerebral symptoms (ESQ-C) score ≥0.7 points as previously described [3,9].

MRI: MR-images were acquired on a clinical 3-Tesla whole-body scanner (GE HDx) using a 8-channel-phased-array receive-only head-coil. MR-sequences were obtained with the following parameters:

BV:ICV: T1 weighted gradient-echo sequence (axial orientation; TE 4.4ms; TR 30ms; Flip angle 30°; FOV 256; 85 slices, thickness 2.0) covering the whole brain to the level of the Foramen Magnum.

Hemosiderin deposits: T2 contrast: Axial; TR/TE 4710/18; flip angle 148; number of slices/thickness 20/4mm; field of view 220; acquisitions/time of acquisition 2/3:15min.

T2* contrast: Axial, TR/TE 503/20; flip angle 20; number of slices/thickness 20/6mm; field of view 220; acquisitions/time of acquisition 2/1:42min.

Susceptibility-weighted imaging (SWI): Primary axial 3D-dataset; TR/TE 28/20; flip angle 15; number of slices/thickness 72/1.2mm; field of view 230; acquisitions/time of acquisition 1/6:38.

Post-processing: Data will be visualized and processed using FSL (FMRIB Software Library; http://www.fmrib.ox.ac.uk/fsl/) and SIENA (Structural Image Evaluation, using Normalization, of Atrophy) [10].

Phase 2-High-altitude measurements
AMS, headache and arterial hemoglobin saturation (pulse oximetry) was assessed every morning (on waking) and evening (prior to bed-rest) during each day of ascent to HA.

Data analysis
Statistical analyses will be performed using SPSS software. The mathematical distribution of all selected dependent variables will be assessed using Shapiro W Wilks tests. Changes in selected dependent variables at the various altitudes will be assessed using a one factor repeated measures analysis of variance (ANOVA) and Bonferroni-corrected paired samples *t*-tests. Differences between AMS subgroups will be examined using a two factor (between-clinical state: AMS+ *vs.* AMS- *x* within-location: SL *vs.* location) repeated measures analysis of variance and appropriate *a posteriori* tests. The relationship between AMS and selected variables will be examined using a Pearson Product-Moment Correlation. Significance for all two-tailed tests will be established at $P < 0.05$ and data expressed as mean ± SD.

Time frame
Sea-level measurements were conducted within 14 days prior to the expedition with follow-up measurements performed within 4 days return to the UK. The expedition took place in July 2008 and lasted for 15 days depending. Sea-level measurements each took approximately 2h to complete and altitude measurements 30 min/day.

Facilities
Professor Bailey provided the scientific leadership to Messrs Cochand and Wild and provided all scientific training/equipment required. All MR scans were performed at Cardiff University Brain Research Imaging Centre under the auspices of Dr Richard Wise (http://www.cardiff.ac.uk/psych/cubric/facilities/mri/index.html).

Research Results
Due to the relatively recent nature of the expedition, and complexities of the research outlined above, we are still in the process of collating the results. Although no deadline has been set for the completion of data analysis, it is hoped this will be completed by early 2009 and preliminary results will therefore be available from this time.

Conclusions
Although the expedition did not meet its mountaineering objective, we are confident that the research data collected during the project is of excellent quality. The infrastructure of the Mt Elbrus region, although not advanced by Western standards, does lend itself well to projects of this nature where rapid ascent to high altitude is required.

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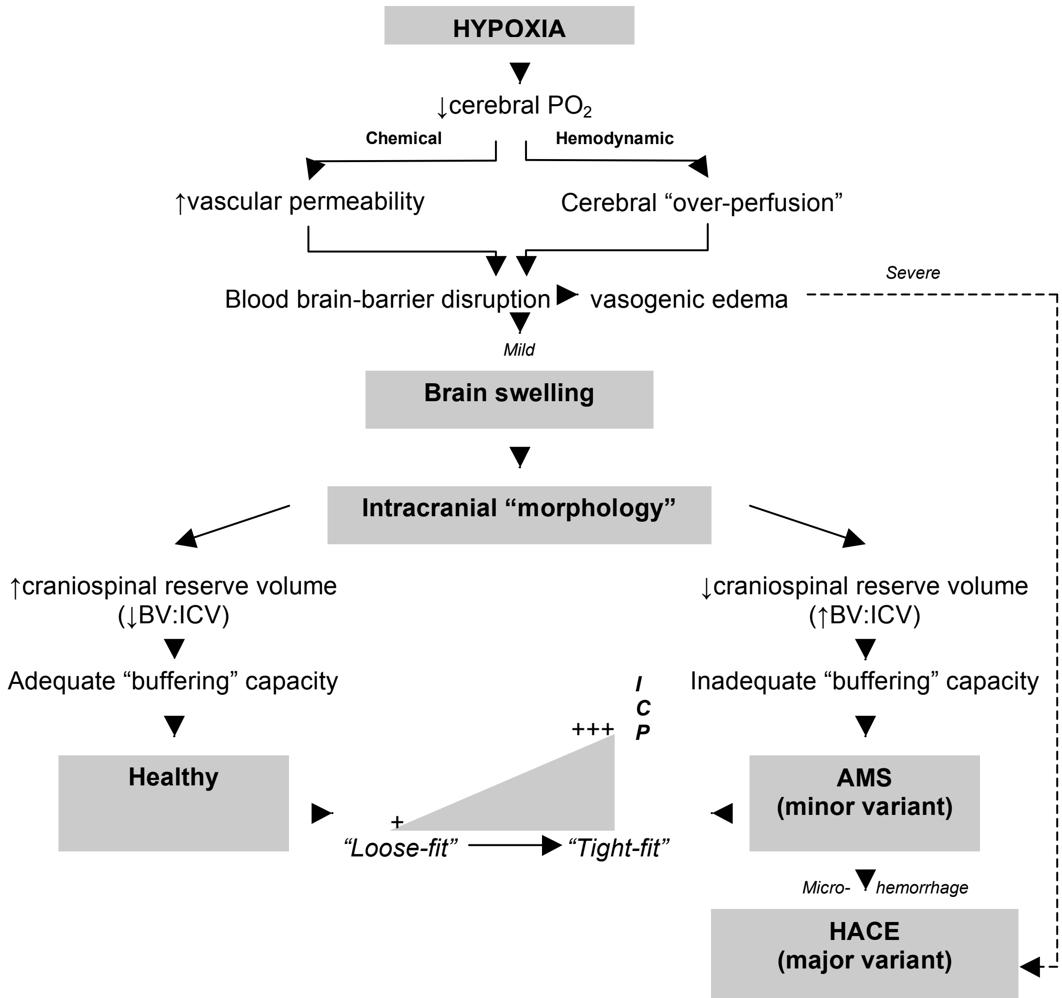

Fig 1. Pathophysiology of AMS and HACE.