CHRONIC AND INCREMENTAL EFFECT OF HYPOXIA DUE TO EXTREME HIGH-ALTITUDE EXPOSURE RELATE WITH ATROPHY IN MOTOR-FUNCTION RELATED BRAIN AREAS.

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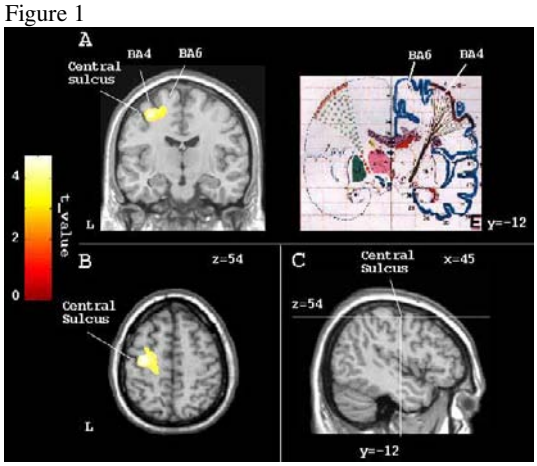
Background. At high-altitude the barometric pressure is reduced, thus resulting in less quantity of oxygen that can be inhaled. A reduced presence of oxygen in the brain tissue determines structural abnormalities and cognitive deficits (West 2004). Previous MRI studies to assess brain changes in subjects who suffered from 'high-altitude illness' have reported controversial results. The present study was designed to explore the effect of high altitude exposure in a group of world-class mountain climbers, using Voxel-Based Morphometry (Good et al.,2001), which is a spatially-specific and unbiased method of analysis of MR images reflecting the regional gray and white matter volume and/or density at a voxel scale.

Methods. We studied nine mountain climbers before (baseline) and after (follow-up) partaking an extremely high-altitude escalation to Everest and to K2. Using Optimazed Voxel-Based Morphometry we investigated the effects due to reiterated high-altitude exposures (chronic effect) by comparing mountain climbers scans obtained at baseline with those from 19 age- and sex-matched controls. Furthermore we measured the effects following a single high-altitude expedition (incremental effect) by comparing mountain climbers scans obtained at baseline and follow-up.

Results. The average whole brain volume was not significantly different between mountain climbers and controls [mean value (SD)=1540 (290) and 1529 (220) ml respectively; p=0.33, n.s.]. When regional anatomical differences were investigated, we found a region of reduced white matter density in the left pyramidal tract nearby the primary (BA 4) and supplementary (BA 6) motor cortex in mountain climbers at baseline compared to controls (p= 0.003, corrected at cluster level) (see Figure 1), while no gray matter changes were detectable. When we compared mountain climbers scans obtained before and after the expedition, we found a region of reduced decreased gray matter density in the left angular gyrus (BA 39) at follow-up (p= 0.002, corrected at cluster level), with no significant white matter changes,

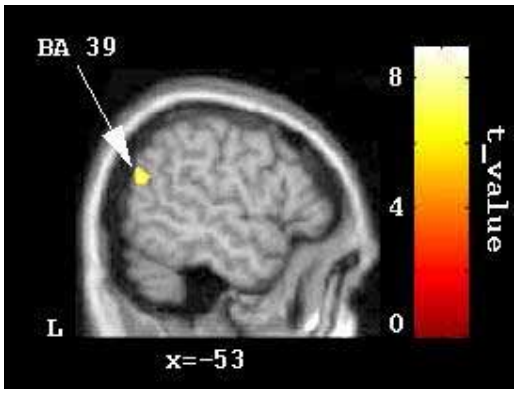
Conclusions. These findings reveal that repeated extreme high-altitude exposures may result in subtle white and gray matter changes, which mainly affect those brain regions that are implicated in motor activity during the escalation. Previous fMRI (Dai et al., 2001) and PET (Dettmers et al 1996; Korotkov et al., 2005) studies, examining the changes of cerebral activation due to intense muscular activity, found that the primary motor and somatosensory areas, the supplementary motor area, and the somatosensory association areas are strongly activated in generating motor commands and processing additional sensory-motor information during important muscle activation. Moreover Gonzalez-Alonso et al (2004) has shown that fatigue during maximal exercise (such as climbing can be considered) is associated in healthy subjects with an enhanced rather than impaired brain uptake of oxygen. Thus, we hypothesize that during climbing the motor areas are mainly engaged, and under a fatigue condition they require more oxygen. Since the motor activity (extreme high climbing) is performed in a particular environment, characterized by a low level of oxygen, the unbalance between oxygen needed and oxygen available can determine a sufferance of those brain areas. Furthermore the motor impairment has been frequently reported as a long-term effect of high-altitude exposure. Therefore we conclude that the pattern of atrophy involving the pyramidal tract and the angular gyrus might explain, at different level of complexity, a long-term motor deficit. Finally this experimental study may represent a possible experimental model to better understand the potential role of chronic hypoxia in normal aging.

Figure 1



Regional reduction in white matter density of MC at baseline compared with controls. The area involves the left pyramidal tract nearby the primary (BA 4) and supplementary (BA 6) motor cortex. **Panel A** shows the thresholded map of *t*-statistic values (coronal section, y=-12) of this region superimposed on the single subject T1-weighted normalized brain of SPM (left side). The correspondent slice from the Talairach and Tournoux atlas (right side) shows the pyramidal tract. **Panel B** shows the thresholded map of *t*-statistic values of the same region (axial section, z=54). **Panel C** shows the position of the slices considered in panel A (coronal) and B (axial) superimposed on the single subject T1-weighted normalized brain of SPM (sagittal section, x=45). L= left.

Figure 2



Results of the longitudinal VBM analysis that compared the scans obtained from MC before (baseline) and after (follow-up) an extremely high-altitude expedition. A reduction in GM density is detectable in the left angular gyrus (BA 39). There is here reported the thresholded map of *t*-statistic values (sagittal section, x=-53) of this region superimposed on the single subject T1-weighted normalized brain of SPM. L= left.