Changes in cerebral blood flow and vasoreactivity to CO2 measured by Arterial Spin Labeling after 6 days at 4,350 m

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Target audience: Neuroradiologists, Methodologists

PURPOSE The changes in cerebral perfusion and CO_2 cerebrovascular reactivity occurring during and immediately after a sojourn at high altitude remain largely unknown but may be critical for acclimatization. The aim of the present study was to assess the effects of a sojourn of 6 days at 4,350 m on cerebral perfusion and cerebrovascular reactivity (CVR) to CO_2 using arterial spin labeling (ASL) magnetic resonance imaging at sea level and to compare it with transcranial Doppler (TCD) results at altitude.

METHODS Eleven healthy male subjects, non-acclimatized to altitude, stayed for 6 days at 4,350 m (Observatoire Vallot, massif du Mont-Blanc). Acute mountain sickness (AMS) symptoms were assessed using the Lake Louise Score (LLS, 5 items) [1] and the cerebral subscore of the Environmental Symptom Questionnaire (ESQ-III AMS-C, 11 items) [2]. Prior to the stay and within 6 h after returning to sea level, subjects were investigated using pseudo-continuous ASL at 3 T during a block-design CO_2-inhalation paradigm to measure basal cerebral blood flow (CBF) and CO_2 CVR. Data were acquired on a 3T Philips Achieva TX scanner using 32-channel receive arrays: T_1-weighted structural scan; one 12min series of pseudo-continuous ASL data [3] (1650 ms label, 1525 ms post-label delay, 3x3x6 mm^3 voxels, TR/TE 4000/12 ms); ASL reference scan; rapid T_1 map for CBF quantification. Capnia was modulated in a 1/2/1 min paradigm (3 cycles) by alternating administration of medical air and an air/CO2 mixture (7% CO_2, 21% O_2, balance N_2). End-tidal CO_2 ($EtCO_2$) and respiration were monitored via nasal cannula (Maglife, Schiller Medical). Data were analyzed using Matlab, the SPM software and custom routines. Images were realigned and individual frames exhibiting strong motion were excluded from the analysis. Vasoreactivity regressors were built using the baseline-corrected $EtCO_2$ for each subject. Structural images were segmented and all images were normalized to the MNI template. CBF and CVR were averaged over all voxels with significant baseline perfusion ($p<0.05$ FDR) within gray matter (GM fraction > 90%), separately in three vascular territories (Fig. 1). Subjects were also examined using TCD prior to the altitude exposure and on day 5 of the stay at altitude to measure blood velocity in the middle cerebral artery (MCAv) and CO_2 CVR. CO_2 CVR was expressed as percent change in ASL CBF or TCD MCAv per mmHg change in $EtCO_2$.

RESULTS According to the LLS (AMS-C) scores 9 (6) subjects suffered from AMS. All physiologic parameters in Table 1 were modified at altitude compared to the prior sea-level exam, but most of them returned to normal immediately after descent. Only $EtCO_2$ remained significantly decreased 6 h after return to sea level. Increases were observed in TCD MCAv (+20.5±15.5%) on day 5 at altitude (Fig. 2b) and in ASL CBF post-altitude in the MCA (+22.0±24.1%, Fig 2a) and the anterior (+20.5 ± 20.3 %) territories. TCD CVR tended to decrease after 5 days at 4,350 m (-12.3±54.5%, Fig 3b), while the ASL CVR in the MCA territory was significantly decreased post-altitude (-29.5±19.8%, Fig 3a). Significant correlation between changes in TCD CVR and changes in ASL CVR was detected (Spearman $\rho=0.86$; $p<0.01$). No correlation was observed between cerebral hemodynamic changes and symptoms of acute mountain sickness at high altitude.

	SpO_2 [%]	$EtCO_2$ [mmHg]	Breathing Freq. [min^{-1}]	Heart Rate [min^{-1}]	MABP [mmHg]
Before altitude (212 m)	97.2±0.5	40.9±4.9	13.8±2.7	61.2±7.7	104.4±6.1
Day 5 altitude (4,350 m)	87.6±1.3 (*)	30.5±3.1 (*)	19.2±2.7 (*)	77.9±16.1 (*)	115.6±6.7 (*)
6h after altitude (212 m)	97.8±0.7	33.2±4.0 (*)	14.9±2.9	63.1±8.2	105.8±8.1

Table 1: Physiological data before, at day 5 and after 6 days at high altitude.

DISCUSSION & CONCLUSION This study is the first to measure cerebral perfusion and vasoreactivity with ASL after a prolonged stay at high altitude. Prolonged exposure to high altitude significantly decreases CO_2 CVR. Since TCD MCAv on day 5 and normoxic ASL CBF after descend were similarly increased, the increase in CBF is not only the consequence of the vasodilating effect of hypoxia but likely involves other mechanisms such as changes in cerebral autoregulation or angiogenesis. The reduction in CO_2 CVR at high altitude may be critical for ventilatory acclimatization.

REFERENCES

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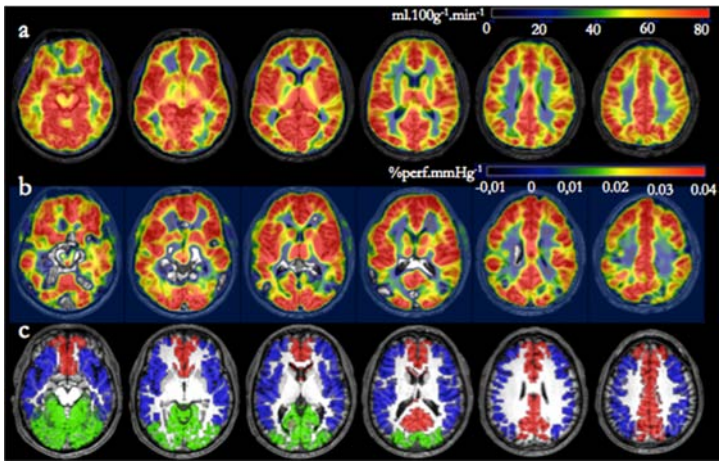

Figure 3: CBF map (a) obtained using ASL in ml/100g/min, CVR map (b) obtained using ASL in % of perfusion increase/mmHg increase of $EtCO_2$, regions of interest in the vascular territories (MCA in blue, anterior in green, posterior in red), for one subject before altitude.

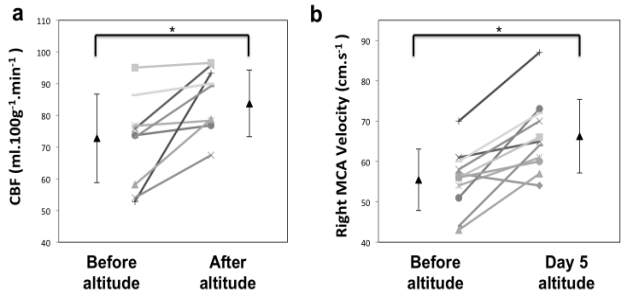

Figure 1: Perfusion in the MCA territory measured using ASL (a) before and after altitude, and using TCD (b) before and at day 5 at altitude, for each subjects and their mean values.

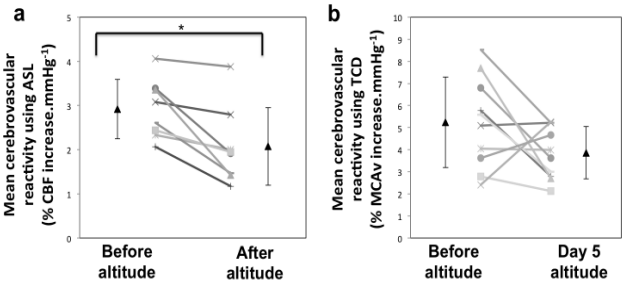

Figure 2: Cerebral reactivity in the MCA territory using ASL (a) and using TCD (b).