several parameters including Hb values to the residence altitude of about 70"000 Swiss men aged 18-22 years. We observed a significant increase of Hb values for every 300 meters of augmented altitude the young Swiss men live at. Thus, even a modest increase in the residence altitude significantly elevates Hb values. Apart from gender, age, ethnicity and socio-economical effects, altitude should be considered when defining the Hb threshold for a given population even when residing at altitudes below 1000 m above sea level.

S04-4 (O)

Alveolar oxygen respiratory oscillations measured in arterial blood.

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The partial pressure of oxygen in arterial blood can increase during inspiration and decrease during expiration in the presence of a variable shunt fraction, such as with cyclical atelectasis, but it is generally presumed to remain constant within a respiratory cycle in the healthy lung. In our experiments, arterial oxygen partial pressure was measured continuously with a fast intravascular sensor in the carotid artery of anaesthetized, mechanically ventilated pigs, without lung injury. Here we demonstrate that the partial pressure of arterial oxygen shows respiratory oscillations in the uninjured pig lung, in the absence of cyclical atelectasis (determined with dynamic computed tomography), with oscillation amplitudes that exceeded 50 mmHg, depending on the mechanical ventilation conditions. These respiratory oscillations in the partial pressure of arterial oxygen can be modelled from a single alveolar compartment and a constant oxygen uptake, without the requirement for an increased shunt fraction during expiration. Our results are likely to contribute to the interpretation of arterial oxygen respiratory oscillations observed during mechanical ventilation in animal models of the acute respiratory distress syndrome.

S04-5 (O)

Brain-derived neurotrophic factor mRNA expression in peripheral and cerebral vessels : Impact of physical training

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Questions:

For a long time, the neuron was considered as the preponderant cellular source of cerebral brain-derived neurotrophic factor (BDNF). However, we recently showed that the cardiovascular system contains as much BDNF as the brain with a prominent expression in endothelial cells and that physical training (PT) increases BDNF protein levels in both peripheral (aorta) and cerebral vessels. In this context, the aim of the present study was to determine i) if these vessels expressed BDNF mRNA and ii) the impact of PT on BDNF gene expression.

Methods:
Experiments were performed on 2 groups of WISTAR male rats: sedentary and exercised. Exercise was induced by a treadmill run (18 m/min, 30 min/day) for 7 consecutive days. BDNF, eNOS (as a marker of shear stress) and Tie2 (a specific marker of endothelial cells) mRNA expressions were measured by RT-qPCR in peripheral (abdominal aorta) and cerebral microvessels.

Results:
BDNF mRNA was expressed in both peripheral and cerebral vessels correlated with endothelial cells enrichment (Tie-2). However, while PT significantly increased eNOS and BDNF mRNA levels in cerebral microvessels, it was without effect in aorta.

Conclusions:
The present study is the first to show that both peripheral and cerebral vessels expressed BDNF gene. The differential expression between peripheral and cerebral vessels in response to PT could be explained either by differences in endothelial cells enrichment and/or in shear stress at the surface of the endothelium (inversely proportional to the diameter), which are both higher in cerebral microvessels than in aorta.

Symposium 05: Exhale negativity-chloride currents in the cardiovascular system

S05-1

What keeps Cl- out of equilibrium in the muscle cells of the cardiovascular system?

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In both vascular smooth muscle cells (SMC) and cardiomyocytes Cl- is in disequilibrium across the membrane. While the resting membrane potential is about – 50 mV in SMC and about – 80 mV in cardiomyocytes the Cl- equilibrium potential is about 25-30 mV in SMC and about 20-25 mV in cardiomyocytes. This means that increased Cl- conductance in SMC leads to depolarization because the membrane potential of SMC is probably always negative to the Cl- equilibrium potential. In the heart the effect of increasing the Cl- conductance may either contribute to repolarization from membrane potentials positive to the Cl- equilibrium potential or delay repolarization at membrane potentials negative to the Cl- equilibrium potential.

In both muscles two transporters are responsible for transporting Cl- in. One is the Cl,HCO3-exchanger (AE), which uses the energy of the HCO3- electrochemical gradient to transport Cl- into the cells in exchange for HCO3-. In the SMC the dominant AE is AE2 (the SLC4A2 gene product) while in the cardiomyocytes the dominant AE is AE3 (the SLC4A3 gene product). In addition to establishing the Cl- disequilibrium these transporters also play an important role in regulation of the muscle pH. The other transporter of importance for the Cl- disequilibrium is the Na,K,Cl-cotransporter (NKCC1) which is the SLC12A2 gene product. This transporter uses the energy in the electrochemical gradient for Na+ to transport Cl- into the cells. In addition to its contribution to establishing the Cl- disequlibrium this transporter is important for regulation the volume of the muscle cells.

S05-2

Calcium-activated chloride channels and vascular smooth muscle: AN(y)O1 know the answer?

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Arterial smooth muscle cells actively accumulate chloride ions (Cl-) so that activation of any Cl-channel will lead to Cl- efflux. The ensuing membrane depolarization increases the open probability of voltage-dependent calcium channels leading to smooth muscle contraction and reduced arterial diameter. Of the different types of Cl- channel identified the most extensively recorded in vascular smooth muscle cells is the calcium-activated chloride channel (CaCC), which for many years had no molecular identity. Since 2008 ANO1 (also termed TMEM16A) has been identified as a component of CaCCs. ANO1 is present in vascular smooth muscle and ANO1-sp[ecifc blockers alter vascular tone. However, there are a number of discrepancies and variations in the ANO1 story. This talk will review