
Cerebral blood flow in high-altitude native children

Julien Brugniaux^{*1}, Vincent Bonin², Aurélien Pichon³, Emeric Stauffer⁴, Anthony Costa¹, Paul Robach^{5,6}, Stéphane Doutreleau⁷, Benoit Champigneulle⁸, Jose Luis Macarlupu⁹, Manuel Gasco¹⁰, Jorge Sotomayor Perals¹¹, Ramon Figueroa¹², Luis Jimenez¹³, Jorge Galdos Tejadas¹³, Gustavo Gonzales¹⁴, Philippe Connes¹⁵, and Samuel Verges¹⁶

¹Univ. Grenoble Alpes, Inserm, CHU Grenoble Alpes, HP2, 38000 Grenoble, France – Université Grenoble Alpes – France

²Univ. Grenoble Alpes, Inserm, CHU Grenoble Alpes, HP2, 38000 Grenoble, France – Univ Grenoble Alpes – France

³Laboratoire Mobilité, Vieillesse, Exercice – Université de Poitiers = University of Poitiers – France

⁴Laboratoire Interuniversitaire de Biologie de la Motricité (LIBM) EA7424, Equipe “Biologie Vasculaire et du Globule Rouge”, Université Claude Bernard Lyon 1, Lyon, France – Université Claude Bernard-Lyon I - UCBL (FRANCE), Hôpital de la Croix-Rousse [CHU - HCL] – France

⁵Hypoxie et PhysioPathologie – Institut National de la Santé et de la Recherche Médicale, Université Grenoble Alpes – France

⁶Ecole Nationale des Sports de Montagne – Ecole Nationale des Sports de Montagne – France

⁷Univ. Grenoble Alpes, Inserm, CHU Grenoble Alpes, HP2, 38000 Grenoble, France – Institut National de la Santé et de la Recherche Médicale - INSERM : U1300, Université Grenoble Alpes, CHU Grenoble, Institut National de la Santé et de la Recherche Médicale - INSERM – France

⁸Univ. Grenoble Alpes, Inserm, CHU Grenoble Alpes, HP2, 38000 Grenoble, France – CHU Grenoble – France

⁹Laboratorio de Fisiología Comparada, Instituto de Investigaciones de la Altura, Universidad Peruana Cayetano Heredia, Lima, Perú – Pérou

¹⁰Laboratorio de Endocrinología y Reproducción, Instituto de Investigaciones de la Altura, Universidad Peruana Cayetano Heredia, Lima, Perú – Pérou

¹¹Centro de Salud, Juliaca, Perú – Pérou

¹²Universidad Nacional de San Antonio Abad del Cusco, Cusco, Perú – Pérou

¹³Universidad Nacional de San Antonio Abad del Cusco, Cusco, Perú – Pérou

¹⁴Facultad de Ciencias de la Salud, Universidad San Ignacio de Loyola, Lima, Perú – Pérou

¹⁵VBRBC – Université Claude Bernard - Lyon 1 – France

¹⁶Univ. Grenoble Alpes, Inserm, CHU Grenoble Alpes, HP2, 38000 Grenoble, France – Institut National de la Santé et de la Recherche Médicale - INSERM, Univ Grenoble Alpes – France

Résumé

Introduction

Since it has virtually no local reserve, the brain is known to be utterly sensitive to the lack

*Intervenant

of oxygen as experienced during hypoxia. Therefore, sufficient perfusion must be ensured to maintain cerebral oxygen delivery (CDO₂) in spite of the reduced O₂ partial pressure (Brugniaux et al., 2007). While cerebral blood flow (CBF) regulation has already been studied with adult high-altitude natives of various ethnicities, including Andeans, presenting with lower CBF (Bailey et al., 2019), little is known about resting patterns of CBF in children born and bred at altitude. Therefore, the aim of this study was to quantify CBF in children of Andean descent living at 5,100 m and compare them to children living at lower altitudes and to lowlander children at sea-level.

Methods

A total of 160 children (80 boys) aged 8–12 years, living at sea level (Lima, n = 40, 28 boys), 3,400m (Cusco, n=38, 13 boys), 3,800 m (Juliaca, n =40, 17 boys) or 5,100 m (La Rinconada, n = 42, 22 boys) were recruited in this study. All were of Aymaran or Quechua descent. High-altitude native children were all born above 3,000m and raised at their respective altitudes of residence and testing.

After at least 10min of supine rest, volumetric measures of CBF within the common carotid artery (CCA), internal carotid artery (ICA), and vertebral artery (VA) was assessed using a 10-MHz multi-frequency linear array duplex ultrasound (e-Cube i7, Alpinion, Republic of Korea) according to published technical recommendations (Thomas et al., 2015). Vessel diameter was measured using B-mode imaging, whereas pulse-wave mode was used to simultaneously measure peak envelope blood velocity. Global CBF (gCBF) was estimated as twice the sum of the unilateral ICA and VA measurements, which were calculated using peak velocity and the cross-sectional area of the respective vessels. Associated measurements included hemoglobin ((Hb)) concentration, hematocrit (Hct), plasma volume (PV) and blood viscosity. One-way ANOVAs were used to detect differences between groups with Tukey post hoc comparisons when applicable (Jamovi, v.2.5.7.0).

Results

There were no differences regarding the age and anthropometric characteristics, between the 4 groups, but as expected, (Hb) increased with altitude. There was an overall effect of altitude on gCBF ($P=0.032$), but post hoc analyses did not reveal any further differences. However, there were regional differences, since blood flow in the VA was significantly lower in Juliaca than in the other 3 altitudes, while now alteration was observed in the ICA.

Discussion

Maintained gCBF at the extreme altitude of La Rinconada, may seem counterintuitive, however, this is accompanied by an elevation in Hb and hence in oxygen content, contributing to defend CDO₂ and consequently, reducing the need to increase CBF. Nevertheless, higher CBF was associated with increased HR and PV, both probably stimulating the endothelium to relax via shear-mediated mechanisms. Conversely, an increase in Hct and/or viscosity, that were both observed herein, have been suggested to be associated with lower gCBF, which we are confirming here. Taken together, these opposing mechanisms probably explain the relatively stable gCBF.

Posterior brain circulation being involved in the development of cognition (and overall homeostasis), the lower VA blood flow observed in Juliaca, and the global lack of response to altitude is intriguing and warrants further research.

Conclusions

Despite altitude-induced hypoxemia, brain perfusion appears well-preserved. Nevertheless, regional differences seem to exist. The potential consequences of these differences on the (cognitive) development of these children remain to be elucidated.

References

Bailey, D. M., Brugniaux, J. V., Filipponi, T., Marley, C. J., Stacey, B., Soria, R., Rimoldi, S. F., Cerny, D., Rexhaj, E., Pratali, L., Salmon, C. S., Murillo Jauregui, C., Villena, M., Smirl, J. D., Ogoh, S., Pietri, S., Scherrer, U., & Sartori, C. (2019, Jan). Exaggerated systemic oxidative-inflammatory-nitrosative stress in chronic mountain sickness is associated with cognitive decline and depression. *J Physiol*, *597*(2), 611-629. <https://doi.org/10.1113/JP276898>

Brugniaux, J. V., Hodges, A. N., Hanly, P. J., & Poulin, M. J. (2007, Sep 30). Cerebrovascular responses to altitude. *Respir Physiol Neurobiol*, *158*(2-3), 212-223. <https://doi.org/10.1016/j.resp.2007.04.008>

Thomas, K. N., Lewis, N. C. S., Hill, B. G., & Ainslie, P. N. (2015). Technical recommendations for the use of carotid duplex ultrasound for the assessment of extracranial blood flow. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, *309*(7), R707-R720. <https://doi.org/10.1152/ajpregu.00211.2015>