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Heart Rate and Cardiovascular Variability at High Altitude

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Abstract— **Primary effect of hypobaric hypoxia on the circulation is a direct vasodilatory effect on the peripheral circulation, which is normally prevented by a sympathetic-induced vasoconstriction. Most of the clinical methods for testing the baroreflex sensitivity only evaluate the cardiac-vagal branch of the baroreflex, but at altitude it is also of importance to test the vascular effects of the baroreflex. This is possible by directly measuring sympathetic efferent activity (by microneurography) or by directly stimulating the carotid baroreceptors (by the neck suction). By cyclical stimulation of the carotid baroreceptors, neck suction-synchronous reflex oscillations could be observed in a large number of signals, including RR interval, blood pressure, microcirculation, muscle sympathetic nerve activity. An increase in fluctuations at the same frequency of the stimulus was considered an evidence of the ability of the carotid baroreceptors to modulate a given physiological signal. The sinusoidal neck suction was set at 0.10 Hz (low-frequency stimulation), or to a frequency close to- but distinct from- the respiratory signal (0.20 Hz, high frequency stimulation, whereas respiration was fixed to 0.25 Hz). The method is noninvasive, without side effects connected to use of drugs, and evaluates both the response to the heart and to the blood pressure of the baroreflex. The altitude-induced sympathetic activation was evidenced in sea level natives by a decrease in RR interval, an increase in blood pressure and in the 0.1Hz components of cardiac and vascular signals. The arterial baroreflex was active on RR interval and also in blood pressure, even during acute exposure to high altitude, thus indicating that it was counteracting and modulating the increase in sympathetic tone. Signs of exaggerated sympathetic activation were evident in subjects with severe acute mountain sickness, while successful therapy was associated with a restoration of autonomic modulation. Conversely, sympathetic activation was reduced (and baroreflex enhanced) in himalayan high altitude natives. In conclusion, a comprehensive understanding of the mechanisms taking place during the adaptation to high altitude requires a multisignal approach, also integrated with equipment designed to provide specific provocative tests, such as those necessary to measure the cardiorespiratory interactions.**

I. Introduction

HYPOXIA (due to endogenous or atmospheric causes) primarily affects ventilatory control, but, due to strong reciprocal influences, also greatly influence autonomic cardiovascular regulation in normal as well as in pathologic conditions, such as chronic cardiac and respiratory failure. While in pathologic conditions the effects of chronic hypoxia superimpose and complicate other aspects of the underlying disease, exposure to high altitude of healthy subjects provides a unique model to study specific adaptations to acute and prolonged hypoxia independently from pre-existing pathology.

Ascent to high altitude is characterized by adjustments in the sympatho-vagal balance, which induce changes in the cardiovascular system, including increases in heart rate, in blood pressure and systemic vascular resistances, and in the metabolism. Evidence of a sympathetic activation has been derived by studies of plasma and urinary levels of norepinephrine and epinephrine, whose increases were correlated with the increases in blood pressure, heart rate and systemic vascular resistance. Resting and exercise associated heart rates are increased but a defined decrease in maximal heart rate above 3000m has been observed, probably as a result of a down regulation of the beta adrenoceptors.

Power spectrum analysis of heart rate has led to an improvement in understanding the autonomic changes during adaptation to high altitude and has demonstrated that the heart rate increase observed after acute exposure to high altitude is the result of both sympatho-adrenal activation and parasympathetic withdrawal. Nevertheless, the absence of respiratory signals from these previous investigations and the presence of frequent altitude-induced respiratory abnormalities limit the value of these observations. In fact, the need (too often overlooked) to simultaneously perform analysis of the respiratory signal even at sea-level, it is still even more crucial at altitude, when the expected large increases in ventilation are a major determinant of the respiratory component of heart rate variability. In a series of studies carried out in the altitude chamber and in the field (in Himalayan and the Andean regions) we had chance to examine the heart rate variability and its relation with cardiovascular and respiratory control in different groups of subjects: subjects born and living at sea level, under various degrees of adaptations to high altitude, spanning from almost no symptoms to severe degrees of acute mountain sickness, and also native highlanders, studied at sea-level and a high altitude, in their own environment. Finally, we also have observed how specific patterns of cardiovascular and respiratory adaptations could help reaching high or even extreme altitudes. In order to perform these studies, several specific equipment have been designed and tested, with the aim of performing multi-signal acquisition and analysis, ultimately resulting in useful by-products, both in terms of new design and search for portable, low power and more reliable equipment. One of the most relevant had been the

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design of a new method for testing the baroreflex.

II. Testing Baroreflex Sensitivity at High Altitude

The primary effect of hypoxia is a direct vasodilatory effect on the peripheral and cerebral circulation. When exposure to severe hypoxia occurs very rapidly it may occasionally induce a marked hypotension and syncope. However, the latter is in normally prevented by a sympathetic-induced vasoconstriction (and appropriate hydration). The picture is further complicated by the tight relationship between the rapid changes in concentration of blood gases, the changes in sympathetic activation and their effects on cerebral circulation. Thus, to be able to capture the complexity of these many different phenomena, all strictly inter-connected, simple clinical methods useful at sea-level, here may prove insufficient.

Most of the clinical methods for testing the baroreflex sensitivity only evaluate the cardiac-vagal branch of the baroreflex, but at altitude it is also of importance to test the vascular effects of the baroreflex. This is possible by directly measuring sympathetic efferent activity (by microneurography) or by directly stimulating the carotid baroreceptors (by the neck suction). Our model stimulates the carotid baroreceptors using a sinusoidal function.

The neck-suction was applied by a semi-flexible plastic or lead collar connected to a vacuum cleaner whose power was modulated by a computer driven phase-control power unit via a digital-to-analog interface, or, in a subsequent model, using a rotating exhausting valve with a variable hole of variable diameter, and so keeping the vacuum power constant. By selecting the appropriate signal amplitude and frequency we could then obtain a sinusoidal suction with desired characteristics (suction from 0 to -30 mmHg), whose amount was continuously monitored by a piezoresistive transducer. By cyclical stimulation of the carotid baroreceptors, neck suction-synchronous reflex oscillations could be observed in a large number of signals, including RR interval, blood pressure, microcirculation, muscle sympathetic nerve activity, with only minor changes in mean values. An increase in fluctuations (at the same frequency of the stimulus) from no neck suction to neck suction was considered an evidence of the ability of the carotid baroreceptors to modulate a given physiological signal. The sinusoidal neck suction was set at 0.10 Hz (low-frequency stimulation), or to a frequency close to- but distinct from- the respiratory signal (0.20 Hz, high frequency stimulation, whereas respiration was fixed to 0.25 Hz). Previous studies [1] have shown that the low frequency stimulation can modulate the sympathetic activity in the vasculature (blood pressure, skin microcirculation, cerebral circulation), whereas faster stimulation is almost exclusively effective on the heart via the parasympathetic system. The purpose of controlling the breathing rate was to avoid spurious slow breaths which would have created spurious respiratory slow fluctuations in the other signals. After a 4 minute recording during controlled respiration only, low- or high- frequency neck suction stimulation were performed for periods of 2 minutes.

This technique presents several advantages with respect to other methods used to evaluate the baroreflex, including the noninvasiveness, the absence of side effects connected to use of drugs, and the possibility to evaluate both the response to the heart and to the blood pressure of the baroreflex. Possible disadvantages are the fixed rate of breathing in order to avoid superimposition of respiratory- and neck suction-induced oscillations.

III. Clinical and Physiological Results

In a first study [2] we showed the effects of high altitude on autonomic modulation not only of the RR interval, but also on the blood pressure and on the microcirculation. The altitude sympathetic activation was evidenced in sea level natives by a decrease in RR interval, an increase in blood pressure, in the 0.1Hz components of cardiac and vascular signals, and from a marked skin vasoconstriction, likely due to the progressive increase in circulating norepinephrine levels during the first days of exposure. The changes observed in spectral components consist of an increase in the 0.1Hz components in both RR interval and blood pressure, at least in sea-level natives. Despite evidence of sympathetic activation, the arterial baroreflex, as assessed by the neck suction technique, was active on RR interval and blood pressure, even during acute exposure to high altitude, thus indicating that the arterial baroreflex was modulating the increase in sympathetic tone. However, the increase in blood pressure suggests that the baroreflex activity was not sufficient to completely counteract the catecholamine-induced increase in vasoconstriction. Signs of exaggerated sympathetic activation were found in subjects with severe acute mountain sickness, characterised by a loss of autonomic modulation (similar to that occurring under submaximal exercise at sea level). Successful medical therapy was associated with a restoration of autonomic modulation (as observed during recovery from exercise). At the opposite, sympathetic overactivation was blunted in himalayan high altitude natives [2]. Conversely, cardiovascular autonomic modulation of himalayan high altitude natives, living at 4700m, appeared similar to that of sea level natives at sea level [3] suggesting that subjects with better coping with hypoxia had lower sympathetic activation, greater heart rate variability, higher baroreflex and lower chemoreflex sensitivity, together with lower increases in ventilation as a consequence of higher tolerance to hypoxia and higher respiratory efficiency. This was particularly evident subjects practicing yoga, when exposed to both acute, subacute and simulated altitudes [4], and also successful in elite climbers during the 2004 Italian Expedition to Everest and K2. Here, those climbers who were able to reach those summits without oxygen support where those with lower relative increases in ventilation and

in chemoreflex sensitivity, but with higher ventilatory efficiency, and thus less sympathetic activation and higher baroreflex and heart rate variability [5]. In most of these conditions, we observed that breathing at 0.1Hz (either spontaneous or done as a test) induced a resonance in the cardiovascular system, improving cardiovascular reflexes, and also increasing arterial oxygen saturation by improving respiratory efficiency.

IV. Conclusion

In conclusion, a comprehensive understanding of the mechanisms taking place during the acute phase of adaptation to high altitude requires a multisignal approach, also integrated with equipment designed to provide specific provocative tests, such as those necessary to measure the cardiorespiratory interactions.

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