



# The role of brain natriuretic peptide during strenuous endurance exercise and appetite regulation

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The pre-pro-hormone brain natriuretic peptide (BNP) is synthesized in the myocytes and is the precursor of two forms of polypeptides: the inactive N-terminal pro-B-type natriuretic peptide (NT-proBNP) and the bioactive peptide BNP.

The changes in NT-proBNP observed with strenuous endurance exercise (e.g., ultramarathon events) are directly linked to an increased cardiac workload. Further mechanisms, such as vasodilatation, diuresis, sodium excretion, inhibition of renin secretion, and suppression of aldosterone synthesis, are also associated with NT-proBNP release. It has been recently demonstrated that there is a substantial increase in NT-proBNP levels up to 24 hours after a 100 km ultramarathon event.<sup>1</sup> Other remarkable responses to such events can be attributed to significant loss in body weight ( $-2.6\% \pm 1.6\%$  immediately following the race and  $-1.1\% \pm 2.0\%$  24 hours after the race) and subsequent renin-angiotensin-aldosterone system (RAAS) activation, with a significant increase in serum renin and aldosterone concentrations. These changes lead to the identification of a linkage between the cardiac and renal systems, which actively cooperate during exercise in order to maintain hemodynamic stability and perfect perfusion in essential organs. The importance of this linkage has been particularly highlighted in consideration of the high cardiovascular risk in patients with minor renal dysfunction.<sup>2</sup> Indeed, patients with diabetes have been initially identified for having impairment in heart-kidney interaction.<sup>3</sup> However, strenuous endurance exercise could also represent a risk for health, due to high physiological demands, and induce electrolyte imbalance, rhabdomyolysis, acute kidney injury, and cardiac arrest.

In this regard, an essential strategy to counteract the acute responses to strenuous endurance exercise is rehydration, as it can decrease the level of NT-proBNP during the recovery phase. Sufficient volume of fluid, with addition of electrolytes (in

particular sodium), carbohydrate, and milk protein, should be ingested after exercise to efficiently promote recovery and avoid negative effects on subsequent exercises.<sup>4</sup>

Therefore, the comprehension of changes in NT-proBNP is of great value for the understanding of the interaction between the cardiac and renal systems and the related alterations in hydration status, neurohormonal and inflammatory pathways, activation of the sympathetic nervous system and RAAS following strenuous endurance exercise. However, further systemic interactions exist in the human body via BNP action. In fact, the heart-gut-brain axis can regulate appetite through the anorexigenic properties of BNP. It has been found that BNP can reduce circulating ghrelin concentration, especially acyl ghrelin, hence decreasing hunger and increasing the feeling of satiety in healthy people.<sup>5</sup> Several members play an important role on those mechanisms. BNP, with its hormonal properties, can induce natriuresis, diuresis, and vasodilatation.<sup>6</sup> Thus, a relation between heart dysfunction and appetite regulation may exist on the so called "heart-gut axis." Moreover, the brain contains numerous BNP receptors, hence the potential direct effects of BNP on appetite regulating centers can be expected. Ghrelin is a gut-derived hormone involved in the modulation of appetite<sup>6-8</sup> in the short-term, on energy balance<sup>9-11</sup> in the long-term, and in the stimulation of left ventricular function, vasodilatation, and anti-inflammatory effects. These mechanisms are considered relevant in patients with heart failure.<sup>12</sup> Conversely, no evidence is available to fully explain the mechanisms of the heart-gut-brain axis and the central role played by the BNP during strenuous endurance exercise. Therefore, the understanding of all the properties of the BNP still requires further investigations.

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