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Baroreflex dysfunction in rats submitted to protein restriction

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Abstract

Earlier studies from the authors' laboratory showed that malnourishment induces alterations in the cardiovascular homeostasis increasing the basal mean arterial pressure and heart rate. In this study, the authors evaluated whether the sympathetic and parasympathetic efferent activities contribute to changes in the cardiovascular homeostasis through altered modulation of the arterial baroreflex of malnourished rats. After weaning, male Fischer rats were given 15% (Normal Protein—NP) or 6% (Low Protein—LP) protein diet for 35 d. The baroreflex gain and latency were evaluated before and after selective autonomic blockades in control and malnourished rats. It was observed that malnourishment affected the baroreflex gain in response to activation and deactivation of the arterial baroreflex. Moreover, malnourished rats showed increased baroreflex latency as compared to that of control rats. Regarding the autonomic efferent activity directed to the heart, the data showed increased sympathetic and decreased parasympathetic efferent activities in malnourished rats, and such alterations could be related to the observed changes in the arterial baroreflex gain as well as in the basal mean arterial pressure and heart rate.

Keywords: Autonomic dysfunction; Malnourishment; Baroreflex gain; Baroreflex latency; Methyl-atropine; Metoprolol

Introduction

Although the right to food and nutrition has been enshrined in the Universal Human Rights Declaration more than 50 years ago, malnourishment continues to be one of the most difficult problems of public health in developing countries (de Onis et al., 2000; Sawaya et al., 2003). Several studies suggest that low protein intake leads to biochemical, physiological, and cardiovascular alterations (Barker et al., 1989, 1990, 1993; Benabe et al., 1993a,b; Benabe and Martinez-Maldonado, 1993, 1998; Brawley et al., 2003; Mi et al., 2000). Blood pressure is under tonic autonomic control through sympathetic and parasympathetic branches of the autonomic nervous system whose efferent activities are adjusted every moment by integrating several neural cardiovascular reflexes to maintain the blood pressure within a narrow range of variation (Loewy, 1990). Among the cardiovascular neural mechanisms, the arterial baroreceptor reflex represents a homeostatic cardiovascular mechanism that maintains the mean arterial pressure within normal levels by coupling the cardiac output with the tissue demand (Machado et al., 1997; Machado, 2001). Baroreflex activation produces parasympathoexcitation and sympathoinhibition to "buffer" alterations produced by an increase in the arterial pressure (Machado et al., 1997; Machado, 2001). The sympathetic and parasympathetic contributions to the changes in the heart rate subsequent to baroreflex activation have distinct characteristics related to central pathways, latencies and abilities to increase or reduce the heart rate (Loewy, 1990). While the tachycardia observed in response to baroreflex deactivation seems to be determined by changes in both autonomic branches, including inhibition of parasympathetic activity and sympathetic activation (mainly), bradycardic responses during baroreflex activation seem to be dependent on rapid vagal discharges directed to

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the heart, because the sympathetic activity is slower to respond to sudden changes in mean arterial pressure (MAP) (Head and McCarty, 1987).

In earlier laboratory studies, the authors evidenced increased basal mean arterial pressure and heart rate (Oliveira et al., 2004), as well as increased baroreflex gain in rats subjected to a low protein diet (Tropia et al., 2001). The sympathetic vasomotor tonus in the experimental model also seems to have increased (Tropia et al., 2001). To further elucidate the cardiovascular autonomic changes associated with malnourishment, the present work was aimed at evaluating the involvement of the sympathetic and parasympathetic efferent activity directed to the heart in the modulation of the baroreflex function of malnourished animals.

Materials and methods

Animals

Male Fischer rats from the Experimental Nutrition Laboratory of the School of Nutrition at Federal University of Ouro Preto were used in this study. After birth, the offspring were randomly picked up and eight puppies were kept with each dam. The dams continued to receive commercial food (normal protein content) and water *ad libitum* and the pups were weaned after 28 d. After weaning, the male rats were divided into two groups: control group, receiving diet containing 15% protein (Normal Protein Diet—NP) and experimental malnourished group, receiving diet containing 6% protein (Low Protein Diet—LP) for the next 35 d. Thereafter, during the next 7 d, the rats underwent experimental protocols and continued receiving experimental rat chow (normal or low protein diet according to the experimental group). During all experimental protocols, the rats remained in controlled laboratory conditions (12/12 h light/darkness cycle, temperature: 23–25 °C).

Arterial blood pressure and heart rate recordings

Under tribromoethanol anesthesia (250 mg/kg, ip; Aldrich Chemical Company, Inc., Milwaukee, WI, USA), a polyethylene catheter (PE-10 connected to PE-50; Clay Adams, Parsippany, NJ, USA), filled with heparinized PBS (125 U/ml), was inserted into the abdominal aorta through the left femoral artery for measurement of pulsatile arterial pressure (PAP). Another catheter was inserted into the inferior vena cava through the left femoral vein for systemic administration of drugs. The free endings of both the catheters were tunneled subcutaneously and exteriorized through the back of the neck. The next day, at the time of cardiovascular recordings, the arterial catheters were connected to pressure transducer (Model MLT0699; ADInstruments Pty Ltd., Castle Hill, NSW Australia). The data acquisition was made through an analog-to-digital data acquisition system (Model PowerLab 400; ADInstruments Pty Ltd., Castle Hill, NSW Australia). The data were sampled at 12 bits using a 200-Hz sampling rate. Heart rate (HR) and mean arterial pressure (MAP) were derived off-line from PAP using the Chart for Windows software, version 4.1.2 (ADInstruments Pty Ltd., Castle Hill, NSW Australia). The baseline cardiovascular variables, MAP and HR, were recorded during the 15 min before each experimental trial. All trials were performed on conscious and unrestrained rats.

The baroreceptor reflex evaluation

Changes in MAP and HR were elicited by bolus injections of phenylephrine (0.25 to 4.0 μg/kg, i.v., Sigma, St. Louis, MO, USA) or sodium nitroprusside (0.7 to 10.0 μg/kg, i.v., Sigma, St. Louis, MO, USA). The difference between the baseline just before baroreflex activation or deactivation and the peak of the changes in the MAP and HR produced by baroreflex activation or deactivation were measured as ΔMAP and ΔHR, respectively.

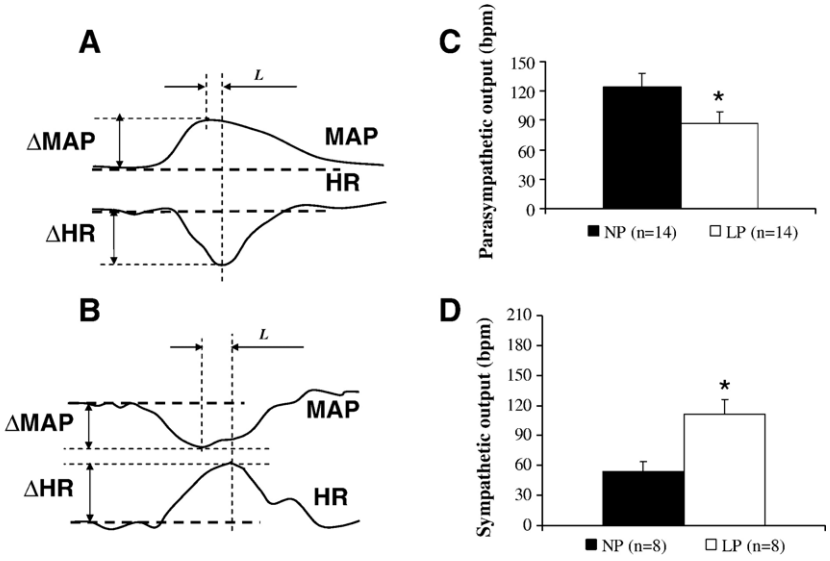

Fig. 1. The gain of the baroreflex was estimated by dividing the alteration in the heart rate (ΔHR, bpm) by the alteration in the mean arterial pressure (ΔMAP, mmHg) in the baroreflex activation (A) and deactivation (B). The latency (*L*) was calculated as the time lag between the peak of the change in the MAP and the peak of the change in the HR in response to baroreflex activation (A) and deactivation (B) in NP and LP rats. Parasympathetic (C) and sympathetic (D) tonus in the basal HR in malnourished (LP) and control (NP) groups (*=different from control group; $P<0.05$).