Neuroscience Letters 591 (2015) 144–148

Contents lists available at ScienceDirect

Neuroscience Letters

journal homepage: www.elsevier.com/locate/neulet

Research article

L-Carnosine's dose-dependent effects on muscle sympathetic nerves and blood flow

Yuko Horii[a,*], Yoshiyuki Fujisaki[a], Risa Fuyuki[a], Katsuya Nagai[a,b]

[a] ANBAS Corporation, 4-12-10 Toyosaki Kita-ku, Osaka 531-0072, Japan
[b] Osaka University, 1-1 Yamadaoka, Suita, Osaka 565-0871, Japan

HIGHLIGHTS

- L-Carnosine has dose-dependent effects on muscle sympathetic nerve activity.
- L-Carnosine has dose-dependent effects on muscle blood flow.
- The increase in muscle blood flow was realized via β-adrenergic receptor.

ARTICLE INFO

Article history:
Received 24 November 2014
Received in revised form 10 February 2015
Accepted 16 February 2015
Available online 19 February 2015

Keywords:
Sympathetic nerve activity
Skeletal muscle
Muscle blood flow
β-Adrenergic receptor
Propranolol
Rats

ABSTRACT

L-Carnosine is synthesized in mammalian muscles and brain and affects autonomic neurotransmission and physiological phenomena. To clarify the role of L-carnosine, the effects of intraduodenal administration of L-carnosine on muscle sympathetic nerve activity (muscle-SNA) and blood flow (BF) were examined. The changes in muscle-SNA and BF were examined using electrophysiological and Doppler flowmeter in urethane-anesthetized rats. The effect of propranolol, a β-adrenergic antagonist, on the increase in muscle BF due to L-carnosine was also examined. Low dose (1 μg/300 g body weight [bw]) of L-carnosine increased both muscle-SNA and muscle BF, while high dese (100 mg/300 g bw) of L-carnosine decreased both muscle-SNA and muscle BF. Furthermore, propranolol eliminated the increase in muscle BF caused by a low dose of L-carnosine. These results suggest that L-carnosine has dose-dependent effects on muscle BF via changes in muscle-SNA, and the β-adrenergic receptor is implicated in the increase in muscle BF due to L-carnosine.

1. Introduction

L-Carnosine (CAR) is a dipeptide composed of β-alanine and L-histidine. CAR is synthesized by carnosine synthetase in the skeletal muscles and brain [1]. L-Carnosine is reported to be involved in the cardiovascular function, metabolism, and energy expenditure likely owing to its actions as an anti-oxidant, pH-buffering, metal-ion chelating, and carbonylation agent [1–3].

In our previous work, evidence was found suggesting that CAR is released during physical exercise [4] and affects autonomic neurotransmission and physiological phenomena in a dose-dependent manner [5–11]. That is, CAR affects blood glucose, blood pressure, body temperature, lipolysis, and tumor immunity via changes in autonomic neurotransmission. In this regard, it is also known that the concentration of CAR in muscle has a positive effect on exercise performance and capacity [3,12,13]. Therefore, we investigated whether CAR affects the activity of the sympathetic nerves innervating the skeletal muscle. In this trial, it was observed that intraduodenal (ID) administration of CAR affected skeletal muscle sympathetic nerve activity (muscle-SNA) in a dose-dependent manner. Furthermore, it was found that L-carnosine has dose-dependent effects on muscle blood flow (BF). This paper outlines these results.

2. Materials and methods

2.1. Animals

Male Wistar rats (Kiwa Laboratory Animals, Co. Ltd., Wakayama, Japan), weighing 300–350 g, were used. The rats were housed in a room maintained at 24 ± 1 °C and illuminated for 12 h (0800–2000 h) daily, and freely given food and water for at least 1 week before the experiment. All animal care and handling pro-

* Corresponding author. Tel.: +81 6 6486 1080; fax: +81 6 6486 1081.
E-mail address: yhorii@anbas.co.jp (Y. Horii).

http://dx.doi.org/10.1016/j.neulet.2015.02.044
0304-3940/

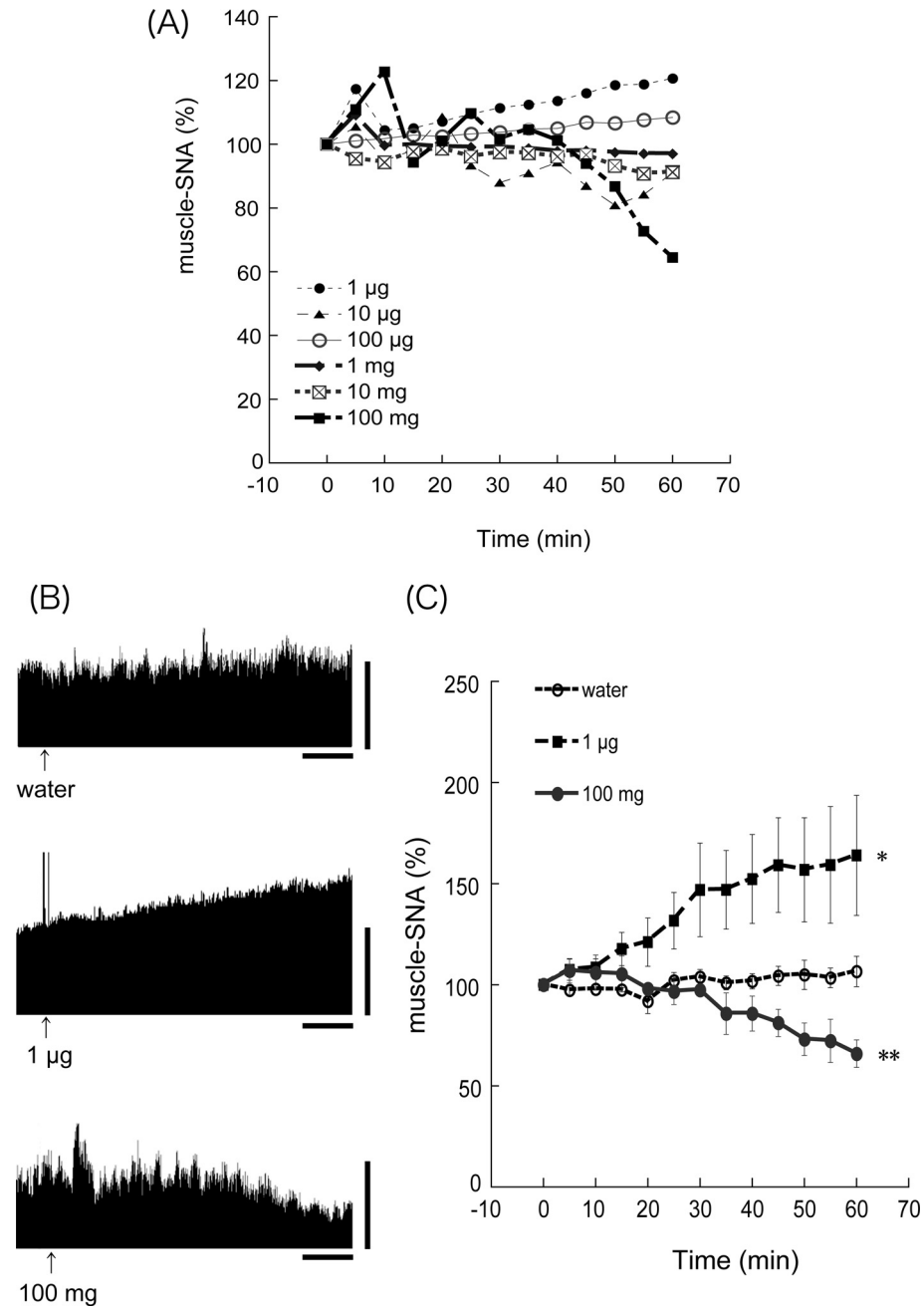

Fig. 1. Effect of intraduodenal administration of L-carnosine on the muscle sympathetic nerve activity (muscle-SNA) in urethane-anesthetized rats. (A) The changes in neural activity after intraduodenal administration of several dose of L-carnosine. (B) Representative images of changes in the neural activity. Vertical scale bars on the right side of the recording represent the neural discharge rate (200 spikes per 5 s; horizontal bar, 10 min). (C) The changes in neural activity after intraduodenal administration of water, 1 μg of L-carnosine, or 100 mg of L-carnosine are expressed as a percentage of the baseline value. Data (mean ± S.E.M.) are expressed as the percentage of change in the values from baseline ($n = 3$). *The significant differences ($p < 0.05$) between the values recorded from 5 to 60 min after intraduodenal injection of water or 1 μg of L-carnosine were analyzed by analysis of variance with repeated measures. **The significant differences ($p < 0.05$) between the values recorded from 5 to 60 min after intraduodenal injection of water or 100 mg of L-carnosine were analyzed by analysis of variance with repeated measures.

cedures were approved by the Institutional Animal Care and Use Committee of the ANBAS Corporation.

2.2. Electrophysiological study

On the day of experimentation, food was removed 3–4 h before the start of surgery. General preparations were performed as described previously [7]. The animals were anesthetized with 1 g/kg body weight (bw) urethane injected into the intraperitoneal (IP) cavity. A polyethylene catheter was inserted into the duodenal cavity for ID injection. The animals were then fixed in a stereotaxic apparatus, body temperature was maintained at 37–37.5 °C using a heating pad, and a tracheal cannula was inserted for assuring respiration.

A longitudinal incision was made in the middle of the left femoral region and the sympathetic nerve, which innervates the vastus medialis of the quadriceps femoris muscle, was exposed under a dissecting microscope. The distal end of the nerve was ligated and hooked up to a pair of silver wire electrodes for recording efferent nerve activity. Liquid paraffin oil was then liberally poured over the recording electrodes until the electrodes were completely immersed to prevent dehydration and for electrical insulation. The