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Review

Sympathetic nerve activity during sleep, exercise, and mental stress

Kenju Miki [a,*], Misa Yoshimoto [b]

[a] Department of Environmental Health, Life Science and Human Technology, Nara Women's University, Kita-Uoya Nishimachi, Nara 630-8506, Japan
[b] Department of Cardiac Physiology, National Cerebral & Cardiovascular Center Research Institute, Fujishiro-dai, Suita, Osaka 565-8565, Japan

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ABSTRACT

This brief review describes recent findings on the differential regulation of sympathetic nerve activity and its role in regulating systemic arterial pressure during rapid eye-movement sleep, non-rapid-eye movement sleep, exercise and freezing behavior (mental stress). We describe the mechanisms underlying the differential regulation of sympathetic outflows and how they act in concert to orchestrate adjustments of cardiovascular function for the whole body, which are optimized to match changes in organ activity in daily activity.

Contents

1. Introduction

Sympathetic nerves innervate most organs and play a dominant role in regulating organ blood flow and cardiac performance, and thus, arterial pressure. During daily activity, cardiovascular function exhibits patterned responses in a behavioral state-dependent manner (Rowell et al., 1996; Miki et al., 2003a). This is because each behavioral state is associated with patterned and differential changes in organ activity. For instance, exercise causes an increase in blood flow in the muscle to meet an increase in demands for oxygen and nutrients, while decreased splanchnic blood flow and increased cardiac output occur at the same time (Rowell, 1986). Redistribution of blood flow between muscles and splanchnic organs and changes in cardiac function are critical for maintaining organ perfusion pressure across the whole body during exercise. Other behavioral states, including

Abbreviations: AP, arterial pressure; RSNA, renal sympathetic nerve activity; LSNA, lumbar sympathetic nerve activity; REM, rapid-eye movement; NREM, non-rapid-eye movement; HR, heart rate; EEG, electroencephalogram; EMG, electromyogram.

* Corresponding author. Tel.: +81 742 20 3414; fax: +81 742 20 3499.
E-mail address: k.miki@cc.nara-wu.ac.jp (K. Miki).

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sleep, exercise and mental stress, are also associated with patterned changes in organ activity and organ blood flow, aimed at maintaining the optimal arterial pressure level.

It is of interest to know how the sympathetic nervous system orchestrates organ blood flows in an organ-dependent and differential manner, and how it influences cardiac performance. However, there is a lack of evidence showing how sympathetic nerve activity regulates organ blood flow in a differential manner in the daily sleep–wake cycle. This is partly because the majority of studies on sympathetic nerve activity have been carried out under acutely prepared and anesthetized conditions. Because central nervous systems cannot function normally under anesthesia, it is difficult to extrapolate from findings obtained under the anesthetized condition to the conscious awake state. Moreover, cardiovascular function is altered in different manners and directions by various anesthetics (Husby et al., 1998).

We have developed a method for continuous and simultaneous measurement of renal (RSNA) and lumbar sympathetic nerve activity (LSNA) in freely moving rats (Miki et al., 2002, 2004) and reported changes in RSNA and LSNA as well as a role for these changes in regulating organ blood flow and arterial pressure (AP) during the sleep–wake cycle (Miki et al., 2004; Yoshimoto et al., 2004). We hypothesized that areas of the central nervous system above the medulla could orchestrate organ blood flow differently through the control of sympathetic nerve activity. The aim of the present review is to categorize changes in sympathetic nerve activity during daily activity and to describe the role of such changes in regulating systemic AP. Situations in which sympathetic nerve activity orchestrates regional blood flow and cardiac performance, regulating AP throughout the whole body under various states including sleep, exercise and mental stress, are described.

2. Categorizing relationships between renal and lumbar sympathetic nerve activity during sleep and exercise

Fig. 1 shows the relationships between the changes in RSNA and LSNA (Fig. 1A) and between heart rate (HR) and AP (Fig. 1B) across behavioral states including rapid-eye movement (REM) sleep, non-REM (NREM) sleep, quiet awake, moving, grooming, and freezing behavior for which RSNA, LSNA, AP, and HR were measured simultaneously in the same rats (Yoshimoto et al., 2010, 2011). There was a significant linear relationship between RSNA and LSNA across the states of NREM sleep, quiet awake, moving and grooming. However, the relationship between RSNA and LSNA obtained during REM sleep was outside the range of the 95% confidence bands of the linear regression line. The relationship between HR and AP obtained during REM sleep was also dissociated from the linear regression line that was obtained across the states of NREM sleep, quiet awake, moving and grooming (Fig. 1B). These data suggest that 1) REM sleep seems to drive different mechanisms regulating sympathetic nerve activity, and hence AP, compared with the other behavioral states and 2) the sympathetic nervous system seems to be activated uniformly in proportion to the increase in physical activity level in the order of NREM, quiet awake, moving and grooming. This suggests that sympathetic nerve activity regulation during NREM, quiet awake, moving and grooming (voluntary exercise) is subject to the same control system.

Therefore, we discuss the regulation of sympathetic nerve activity during NREM sleep together with that during quiet awake, moving, grooming, and exercise, and not with that during REM sleep.

3. During REM sleep

3.1. Diverse changes in sympathetic nerve activity

REM sleep results in bidirectional changes in sympathetic nerve activity. Direct measurement of sympathetic nerve activity has been attempted during REM sleep in animals and humans. RSNA has been consistently shown to decrease during REM sleep in rats (Miki et al., 2003a; Nagura et al., 2004; Yoshimoto et al., 2004; Miki and Yoshimoto, 2005; Yoshimoto et al., 2011) and cats (Baust et al., 1968; Iwamura et al., 1969). The activity of sympathetic nerves projecting to muscles during REM sleep has been measured in humans using microneurography, and was found to consistently be increased (Hornyak et al., 1991; Okada et al., 1991; Somers et al., 1993). Somers et al. (1993) demonstrated that muscle sympathetic nerve activity

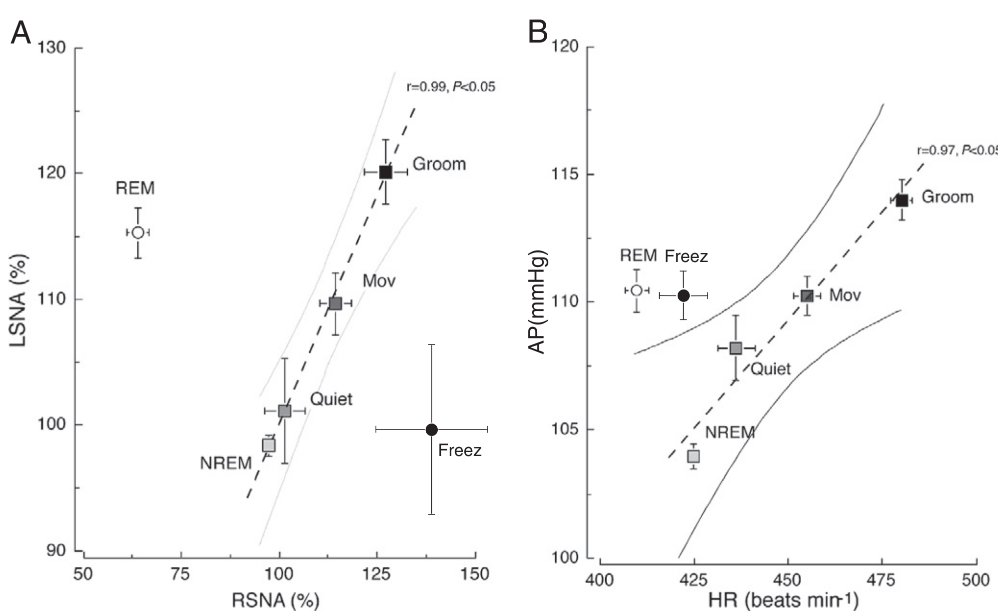

Fig. 1. Relationships between renal (RSNA) and lumbar (LSNA) sympathetic nerve activity (left panel, A) and between heart rate (HR) and systemic arterial pressure (AP, right panel, B) across behavioral states including NREM sleep, quiet awake (Quiet), moving (Mov), grooming (Groom), and freezing (Freez). Values are means ± SEM. The gray curved lines are the 95% confidence bands for the regression line (adapted from Yoshimoto et al., 2010, 2011).