Autonomic Neuroscience: Basic and Clinical 177 (2013) 266–270

Contents lists available at ScienceDirect

Autonomic Neuroscience: Basic and Clinical

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

Arterial pressure oscillation and muscle sympathetic nerve activity after 20 days of head-down bed rest

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ARTICLE INFO

Article history:
Received 26 October 2012
Received in revised form 24 January 2013
Accepted 28 February 2013

Keywords:
Power spectral analysis
Low-frequency component
Microgravity

ABSTRACT

Both spectral power within the low-frequency component, i.e., 0.04 to 0.15 Hz, of systolic pressure and muscle sympathetic nerve activity are increased during head-up tilt. The nerve activity during tilt is altered after space flight and exposure to simulated microgravity. In the present study, correlations of the low-frequency component and the nerve activity were analyzed before and after 20 days of −6° of head-down bed rest. Measurements were performed at −6° head-down bed rest, 0° (flat), and 30° and 60° head-up tilt (HUT). Mean arterial pressure during HUT was not different between pre- and post-bed rest, but muscle sympathetic nerve activity in post-bed rest significantly increased at tilt angles of −6°, 0°, 30°, and 60° compared with those during pre-bed rest. The low-frequency component of systolic pressure also significantly increased during post-bed rest compared with pre-bed rest at tilts of 0°, 30°, and 60°. The nerve activity and the frequency component were linearly correlated for individual (r^2 = 0.51–0.88) and averaged (r^2 = 0.60) values when the values included both pre- and post-bed rest. Thus, the low-frequency component of systolic pressure could be an index of the muscle sympathetic nerve activity during tilt during pre- and post-bed rest.

1. Introduction

Long-term exposure to a microgravity environment and simulation of such conditions, as in head-down bed rest, causes various adaptations and deconditioning such as body fluid loss, cardiac atrophy, changes in antigravity muscle mass, and change in vestibular function (Alfrey et al., 1996; Convertino et al., 1997a; Levine et al., 1997, 2002; Jarchow and Young, 2010). Cardiovascular deconditioning is considered to induce orthostatic intolerance after returning from space missions, and crew members experience presyncope in the standing position (Buckey et al., 1996; Fritsch-Yelle et al., 1996). Sympathetic nerve activity in the postflight supine position is higher than that in the preflight supine position, but the response of the nerve to posture changes or to changes in the stroke volume before presyncope is maintained via the baroreflexes (Levine et al., 2002). Thus, increases in heart rate (HR) and total peripheral resistance compensate for cardiac atrophy and decreased stroke volume, and arterial pressure (AP) is maintained before presyncope.

Sympathetic nerve activity controls vascular contraction and induces fluctuation of AP. Both systolic AP (SAP) and muscle sympathetic nerve activity (MSNA) have oscillation of around 0.1 Hz, which is similar to the low frequency (LF) of HR or RR interval variability in human subjects (Pagani et al., 1986; Julien, 2006). The LF component of MSNA variability ($MSNA_{LF}$) is positively and tightly correlated with the LF components of RR interval and SAP (SAP_{LF}) (Pagani et al., 1997), and both are increased during head-up tilt (HUT) (Pagani et al., 1986; Furlan et al., 2000). $MSNA_{LF}$ is linearly correlated with MSNA as evaluated by number of the spikes (Furlan et al., 2000). Thus, it is not difficult to anticipate that MSNA is correlated with SAP_{LF} during HUT, but the correlation is not directly evaluated. During lower body negative pressure (LBNP), which induces footward fluid shift similar to that during HUT, SAP_{LF} is correlated with MSNA on a group level, but not in individual healthy subjects (Ryan et al., 2011). During HUT, subjects must support their body weight with the muscle and bones of the lower limbs, but the weight is mostly supported by the back during LBNP in the supine position. The lower limb muscle contraction enhances venous return and suppresses blood pooling on the lower body (Ludbrook, 1966). Thus, local myogenic responses for vascular resistance and SAP_{LF}, which is affected by the blood pooling, might be different from those during LBNP (Shoemaker et al., 2000; O'Leary et al., 2004).

In the present study, we hypothesized that SAP_{LF} and MSNA are correlated during HUT, and the relationship would change after adaptation to a microgravity environment. To examine the hypothesis, we evaluated SAP_{LF} and MSNA before and after long-term exposure to a simulated microgravity environment.

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http://dx.doi.org/10.1016/j.autneu.2013.02.025

2. Methods

Ten healthy male subjects (23 ± 2 years old, 168.6 ± 1.2 cm height, and 63.9 ± 5.0 kg body weight [mean ± SE]) volunteered for the study. This study was approved by the Institutional Review Board at Aichi Medical School and performed in accordance with the ethical standards laid down in the 2008 version of the Declaration of Helsinki. Informed written consent was obtained from all participating subjects. Subjects consumed meals of 2300 kcal/day (Na, 2540 mg; K, 2418 mg; Ca, 530 mg). They were instructed to drink only water or caffeine-free tea. The 24-hour urine volume was measured daily, and subjects were encouraged to drink the same volume of fluid as the urine volume of the previous day (Sato et al., 2009). For 20 days, subjects remained in 6° head-down tilt except during showers, at which time they were horizontal (30–40 min/day). All measurements were performed at room temperature of approximately 26 °C. Before and after 20 days of head-down bed rest, a tilt test was performed. The subjects were in the supine position throughout the measurements, but the angle of the body was set at −6° (head down), 0° (flat), 30° and 60° of HUT. Each angle was maintained for 15 min. AP and MSNA were measured simultaneously and continuously. AP at the heart level was measured using a continuous blood pressure monitor (Model 2300; Finapres, Ohmeda, CO). MSNA was measured using microneurography (Wallin and Fagius, 1988). A tungsten microelectrode (Model 26-05-1; Frederick Haer and Company, Bowdoin, ME) was percutaneously inserted into the muscle nerve fascicles of the tibial nerve at the left or right popliteal fossa. Nerve signals were fed into a preamplifier (Kohno Instruments, Aichi, Japan) with band-pass filters set between 500 and 5000 Hz and were monitored with a speaker. MSNA was identified according to the following discharge characteristics: *1*) pulse-synchronous and spontaneous efferent discharges; and *2*) afferent activity evoked by tapping the calf muscles but not in response to a gentle skin touch (Wallin and Fagius, 1988).

For analysis of AP, a stable period of 256 s at each posture angle was used. Beat-to-beat SAP values were derived from the maximum values of the AP waveform. Mean AP (MAP) and HR were calculated from the waveform. The SAP time series was interpolated by the cubic spline function and resampled at 1 Hz to obtain equidistant time intervals. The resampled series were analyzed using autoregressive power spectral analysis (Lipsitz et al., 1998; Mainardi et al., 2009). Power spectral density within the frequency of 0.04 to 0.15 Hz was integrated. For analysis of MSNA, the number of bursts with signal-to-noise ratios of approximately 3:1 during the same period was counted.

For statistical analysis, the Wilcoxon signed-rank test was employed to compare SAP, MAP, diastolic AP (DAP), HR, SAP_{LF}, and MSNA during pre- and post-bed rest at each tilt angle. Regression between MSNA and SAP_{LF} was analyzed for individual and group data. For comparison of correlation coefficients, the Z-transform was used. Data were expressed as mean ± SE. P values were shown in the text and figures.

3. Results

MSNA could not be detected in one subject at −6° during pre-bed rest. One subject did not complete the measurements at 60° during post-bed rest, and the AP signal of another subject could not be clearly analyzed because of electric noise during pre-bed rest. Fig. 1 shows typical responses of AP and MSNA during pre-bed rest (upper panels) and post-bed rest (lower panels) in the supine position (left panels) and at HUT of 60° (right panels). MAP during pre- and post-bed rest was similar, but the oscillation during post-bed rest was larger than that during pre-bed rest. MSNA during post-bed rest was also larger than that during pre-bed rest.

Fig. 2 shows the typical power spectral density of SAP during pre-bed rest (upper panels) and post-bed rest (lower panels) in the supine position (left panels) and at HUT of 60° (right panels). The vertical scale of the right lower panel or HUT during post-bed rest

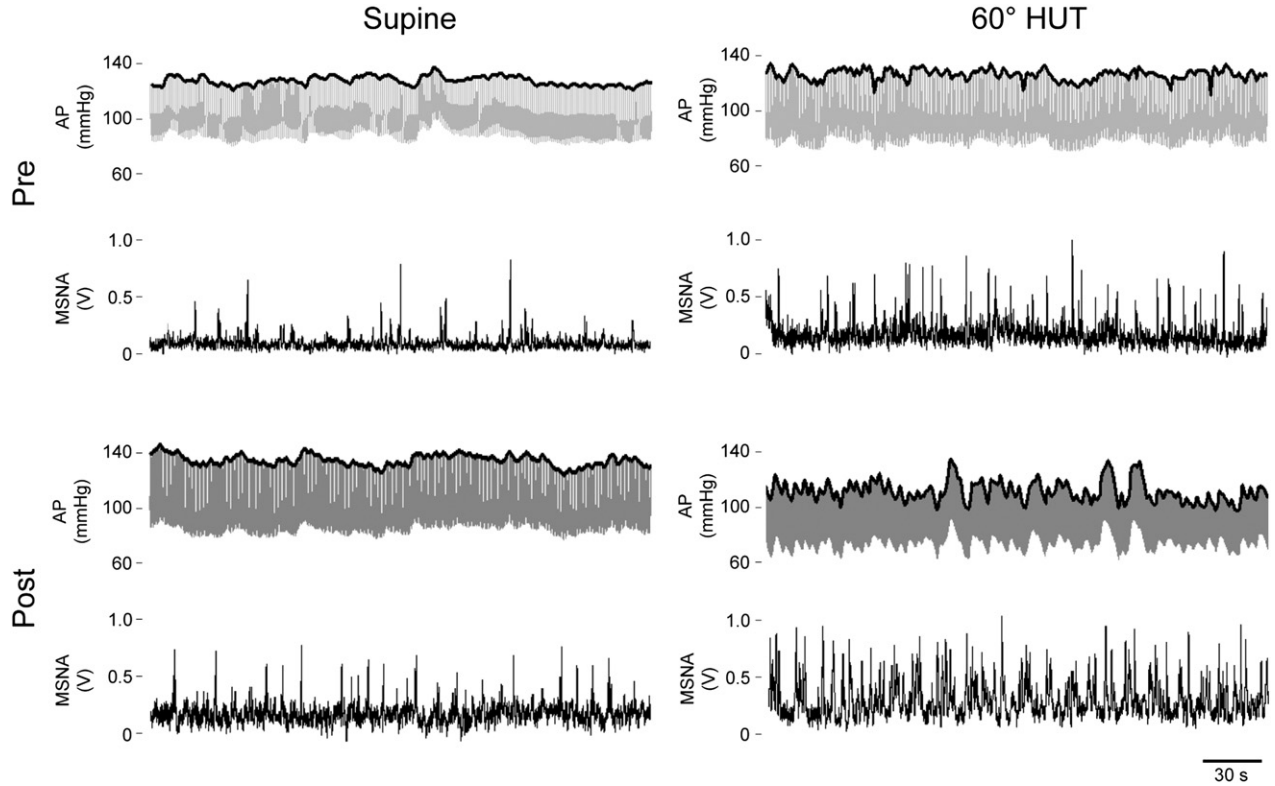

Fig. 1. Typical responses in arterial pressure (AP) and muscle sympathetic nerve activity (MSNA) in the supine position (left panels) and 60° of head-up tilt (HUT, right panels) during pre-bed rest (upper panels) and post-bed rest (lower panels) in one subject.