Autonomic Neuroscience: Basic and Clinical 180 (2014) 66–69

Contents lists available at ScienceDirect

Autonomic Neuroscience: Basic and Clinical

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

Short communication

Firing patterns of muscle sympathetic neurons during apnea in chronic heart failure patients and healthy controls

Petra Zubin Maslov [a], J. Kevin Shoemaker [b,c], Zeljko Dujic [a,*]

[a] Department of Physiology, University of Split School of Medicine, Soltanska 2, 21000 Split, Croatia
[b] Neurovascular Research Laboratory, School of Kinesiology, Western University, London, Ontario, Canada
[c] Department of Physiology and Pharmacology, Western University, London, Ontario, Canada

ARTICLE INFO

Article history:
Received 9 July 2013
Received in revised form 2 September 2013
Accepted 30 September 2013

Keywords:
Action potential detection
Sleep apnea
Cardiovascular disease

ABSTRACT

In the present study we investigated the influence of end-expiratory breathing cessation on firing activity of muscle sympathetic fibers in 6 stable chronic heart failure (CHF) patients and in 6 healthy age and gender matched controls. Integrated multi-unit bursts, as well as action potentials (APs), were identified from multi-unit muscle sympathetic nerve activity (MSNA) recordings during baseline and during functional residual capacity (FRC) apnea. Compared with controls, CHF patients had higher burst frequency and AP firing frequency ($P < 0.05$) at baseline. FRC apnea caused an increase in the number of APs per multi-unit sympathetic burst, in the AP frequency ($P < 0.05$) and in the number of active clusters per multi-unit sympathetic burst in both groups (controls $P < 0.06$, CHF group $P = 0.1$). The data suggest a comparable pattern of sympathetic activation associated with breath hold in healthy middle-aged individuals and in stable CHF patients. Thus, recruitment patterns for this stress are not affected by CHF despite their elevated sympathetic state.

Voluntary apnea is a powerful sympathetic stimulus through multiple mechanisms including hypoxia, hypercapnia and an increased central drive-to-breathe (Steinback et al., 2010a). Similar pathophysiological mechanisms are coupled with sleep-disordered breathing that occurs in 3–14% of middle aged population and in 30–50% chronic heart failure (CHF) patients (Augostini, 2012). Sleep apnea is recognized as an important risk factor for the development of hypertension as well as for progression of cardiac dysfunction in patients with CHF (Sin et al., 1999). During sleep apnea, tonic inhibition of sympathetic outflow by pulmonary stretch receptors ceases, while stimulation of peripheral and central chemoreceptors by hypoxia and hypercapnia further augments sympathetic nerve activity (Somers et al., 1995; Floras, 2009). Baseline sympathetic outflow increases in CHF patients and more if these patients experience sleep apnea. Cycles of apnea and arousal during the night expose the failing heart and peripheral circulation to repetitive norepinephrine release far greater than needed for circulatory homeostasis (Floras, 2009). The ability of sleep apnea to increase sympathetic outflow in CHF patients who already have marked elevations in neuronal activity, suggests that these patients retain the ability to increase sympathetic drive during the apneas. However, the underlying firing activity of the sympathetic neurons that occurs during sleep apnea in CHF patients is not completely understood. Previous studies with single-unit recordings of sympathetic fibers have shown increased multiple firing of the same sympathetic neuron during voluntary apnea (Elam et al., 2002). We have recently shown that stable CHF patients express a present, but diminished ability to recruit additional postganglionic sympathetic neurons in a response to hemodynamic stress such as premature ventricular contraction (PVC) (Maslov et al., 2012). In the present study voluntary cessation of breathing at functional residual capacity (FRC) level served as a model of physiological stimulus that can affect firing pattern of sympathetic neurons in stable CHF patients and in healthy,

Table 1
Hemodynamic parameters during baseline and during end-expiratory apnea.

	CHF patients (N = 6)		Controls (N = 6)	
	Baseline	End-exp apnea	Baseline	End-exp apnea
MAP (mm Hg)	82 ± 9**	91 ± 7*	96 ± 7	108 ± 9*
SBP (mm Hg)	126 ± 15	139 ± 15*	146 ± 17	164 ± 14*
DBP (mm Hg)	64 ± 8	71 ± 9*	70 ± 5	81 ± 10*
HR (bpm)	68 ± 5	68 ± 8	62 ± 5	65 ± 13
SV (mL)	88 ± 28	81 ± 24	115 ± 16	105 ± 20
CO (L/min)	5.9 ± 2	5.6 ± 2	7 ± 1	7 ± 1
TPR (a.u.)	15 ± 18	18 ± 7*	13 ± 1	16 ± 4*

Values are mean ± SD. MAP, mean arterial pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; SV, stroke volume; CO, cardiac output; TPR, total peripheral resistance.
* $P < 0.05$ compared to baseline.
** $P < 0.05$ compared to controls.

* Corresponding author. Tel.: +385 21 557 906; fax: +385 21 465 304.
E-mail address: zeljko.dujic@mefst.hr (Z. Dujic).

1566-0702/$ – see front matter.
http://dx.doi.org/10.1016/j.autneu.2013.09.016

age and gender matched controls. We hypothesized that despite chronic sympathoexcitation, stable CHF patients will manifest further activation of sympathetic reserve during end-expiratory apnea through increased firing of already active sympathetic fibers and through the recruitment of latent subpopulation of sympathetic fibers. For this purpose we used previously described technique that enables the identification and morphological classification of action potentials from raw, filtered signal of multi-unit muscle sympathetic nerve activity (MSNA) recordings (Salmanpour et al., 2010; Steinback et al., 2010b; Breskovic et al., 2011).

Data were obtained from six stable CHF patients and from six healthy control subjects matched for gender and age. Inclusion and exclusion criteria for CHF group were the same as for our previous studies (Maslov et al., 2012; Zubin et al., 2013). CHF patients were recruited from the Department of Cardiology, University Hospital of Split. Healthy volunteers free of cardiovascular disease were matched for age and gender and recruited as control group. All subjects gave written informed consent to participate in the study that was conducted in accordance with the Declaration of Helsinki and was approved by research ethics board at The University of Split, School of Medicine.

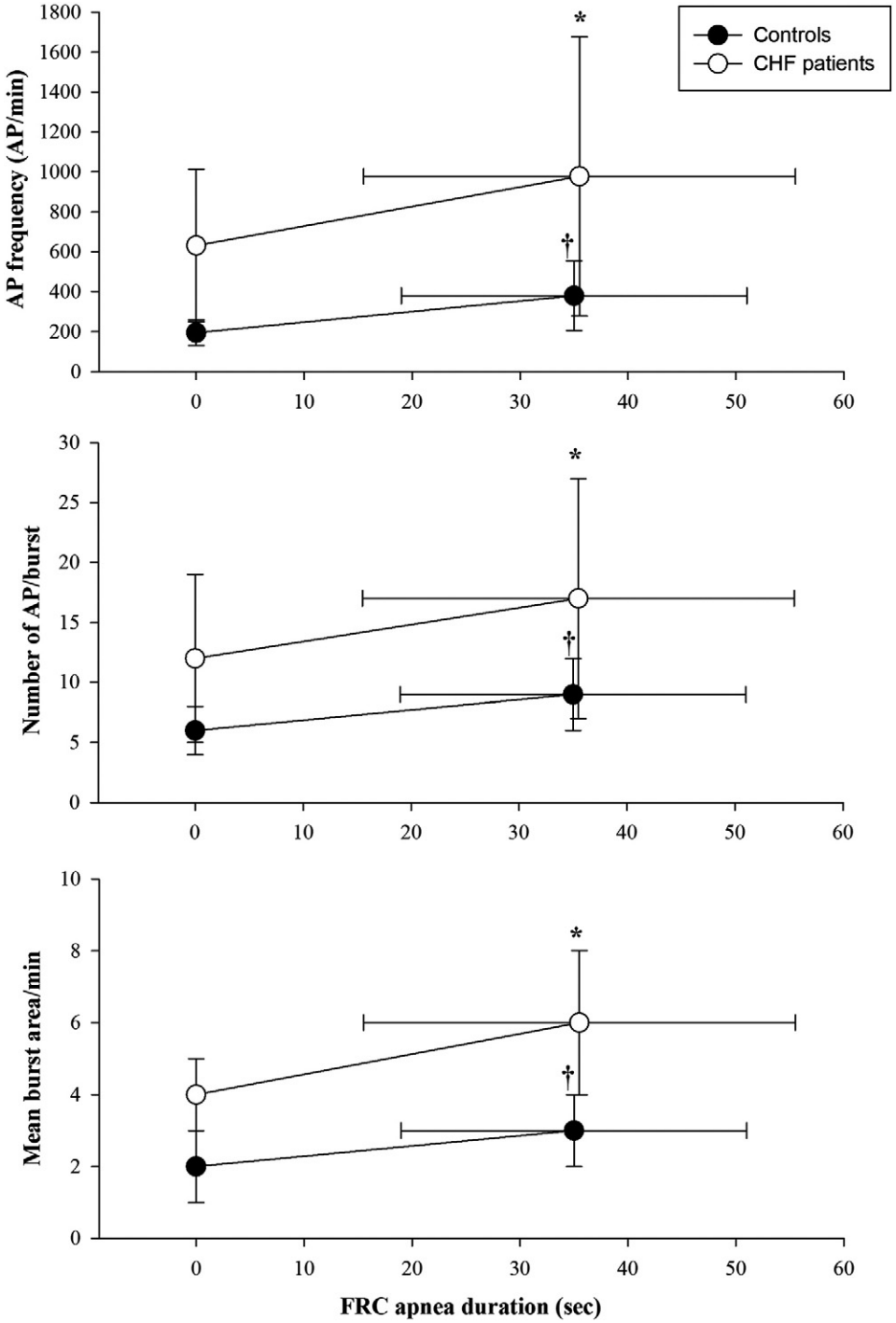

Fig. 1. Change in action potential (AP) parameters and mean burst area/min from baseline (0 s) to apnea at functional residual capacity (FRC) level. White circles represent chronic heart failure (CHF) patients and black circles represent controls. Values are means, bars represent SD. *, $P < 0.05$ compared to baseline for CHF group; †, $P < 0.05$ compared to baseline for control group.