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Eur. Pharm. J. LXIII, 2016 (1): 23-24.
ISSN 1338-6786 (online) and ISSN 2453-6725 (print version),
DOI: 10.1515/afpuc-2016-0010

EUROPEAN PHARMACEUTICAL JOURNAL

Effect of Chronic Social Stress on Endothelial Function of the Mesenteric Artery of Normotensive and Spontaneously Hypertensive Rats

Vplyv chronického sociálneho stresu na funkciu endotelu mezenterickej artérie normotenzných a spontánne hypertenzných potkanov

Original research article

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Received 4 August, 2016, accepted 12 August, 2016

Abstract The aim of the work was to study the effect of chronic social stress induced by increased population density, "crowding stress" on blood pressure and endothelial function of arteries of male normotensive Wistar and spontaneously hypertensive (SHR) rats. Based on the results, we assume that social stress-induced reduction in endothelium-dependent relaxation and increased blood pressure of SHR rats is most likely associated with decreased bioavailability of nitric oxide.

Slovak abstract Cieľom práce bolo zistiť vplyv chronického sociálneho stresu vyvolaného zvýšením hustoty populácie, tzv. crowding stresom, na arteriálny tlak a funkciu endotelu arterií samcov normotenzných Wistar a spontánne hypertenzných (SHR) potkanov. Na základe výsledkov predpokladáme, že redukovaná relaxácia závislá od endotelu a zvýšenie krvného tlaku spôsobené stresom u SHR potkanov pravdepodobne súvisia so zníženou biologickou dostupnosťou oxidu dusnatého.

Keywords *Endothelium – SHR – Nitric Oxide – Social stress*

Kľúčové slová: *endotel – SHR potkany – oxid dusnatý – sociálny stres*

INTRODUCTION

The vascular endothelium is significantly involved in the regulation of vascular resistance and blood pressure (BP), mainly by the production of nitric oxide (NO), which is one of the most potent vasodilator substances. In different pathological situations, reduction in the bioavailability of NO is caused by lowered expression and activity of endothelial NO-synthase (e.g. Jankyova et al., 2013). In the vascular system, this may result in hypertension. Bernatova et al. (1999) found reduced vasodilatation, thickening of the vessel wall and subsequent hypertension in normotensive rats after inhibiton of NO synthesis. Social stress was found to impair the endothelium by both NO-dependent and -independent mechanisms. Thus, for example, Non et al. (2014) reported significantly higher levels of the endothelial biomarker sVCAM-1 in stressed humans. These findings may suggest that endothelial dysfunction is an important biological mechanism linking social stress with cardiovascular health outcomes.

MATERIAL AND METHODS

Wistar (W) and spontaneously hypertensive rats (SHR) were exposed to 8-week lasting crowding stress (stressed in cages - cca 200 cm2/rat vs controls cca 480 cm2/rat). BP was

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*Table 1. Blood pressure in mmHg, measured by tail-cuff plethysmography after 8-weeks of social stress. * p <0.05 vs respective control, x p <0.05 vs W.*

Fenotype	Control	Stressed
W, n=8	111±3	112±2
SHR, n=8	185±2^{x}	193±2^{x}*

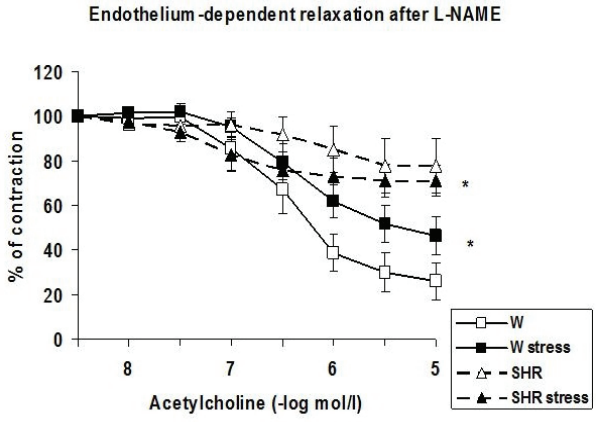

*Figure 1. Responses of the mesenteric arteries of SHR and W rats precontracted by phenylephrine (1 µmol/l) to Ach after inhibition of NO synthase (L-NAME 100 µmol/l) and prostaglandin synthesis (indomethacin, 10 µmol/l). Arteries were obtained from animals reared under normal conditons (□, Δ) and conditions of social stress (■, ▲). Data are means ± SEM obtained from 8 experiments. * p <0.05 vs control*

measured by tail-cuff plethysmography. After the animals had been sacrificed in tiopenthal anesthesia, the function of the endothelium of the superior mesenteric artery (SMA) was monitored in in vitro conditions by evaluation of the responses of the precontracted arteries to acetylcholine (Ach) before and after NO-synthase and prostaglandin inhibition.

Results

In control conditions, SHR had significantly higher BP than W rats. Stress caused an increase in BP in SHR, but not in W (Table 1). In control W, Ach evoked relaxation with a large proportion of the L-NAME-resistant component. SHR responded to Ach with smaller relaxation compared to W. Moreover, the L-NAME-resistant part of the response was also lower. In W, crowding reduced only the L-NAME resistant part of relaxation. However, the stressed SHR animals had decreased response to Ach compared to W and the L-NAME-resistant part of the endothelium-dependent relaxation (EDR) was augmented (Fig. 1).

DISCUSSION

In our work, the increased BP in SHR rats that underwent crowding stress, in contrast to the unchanged BP in normotensive rats, indicated differences in the vascular response to stress. Indeed, we found that the EDR of SMA of SHR rats was smaller than that of Wistar rats. Even smaller was the L-NAME-resistant part, which is assumed to be mediated by the hyperpolarizing factor released from the endothelium, EDHF. Our results correspond with the results of Bennett et al. (1996) who found impaired EDR in SHR rats. Damaged EDHF release has been suggested to be one of the participating mechanisms (Fujii et al., 1993). In our experiments, crowding stress did not affect the responses of Wistars´SMA to Ach but it reduced the EDHF component, thus relatively increasing the proportion of relaxation evoked by NO. In contrast, crowding reduced the EDR in SHR, while the proportion of EDHF increased at the expense of the NO-component. Thus it appears that normotensive rats are able to maintain BP and unchanged EDR by increased bioavailability of NO. This mechanism may not work in SHR rats, which results in increased BP and reduced EDR.

ACKNOWLEDGEMENT

This work was supported by grants VEGA 2/0084/14, and 2/0054/15.

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