The Role of Cyclooxygenases-derived Metabolites on the Contraction Induced by Angiotensin II in Carotid Artery from Rat Exposed to Stress

H Côco¹, AHP Lopes¹, TM Cunha¹, SY Fukada², AM Oliveira²

¹Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto, São Paulo, Brazil, ²Faculty of Pharmaceutical Sciences of Ribeirão Preto, University of São Paulo, Ribeirão Preto, São Paulo, Brazil

Cyclooxygenase (COX) isoforms are involved in sympathetic activation due to restraint stress (1). COXs-derived metabolites modulate angiotensin (Ang) II-induced contraction in diabetic rat carotid artery (2). The aim of this study was to investigate the participation of metabolites derived from COX-1 and COX-2 on the contraction evoked by Ang II in carotid artery from control or exposed to restraint stress rats.

Adult male Wistar rats (n≥8) were exposed or not to 3h restraint stress for 5 days and experiments were performed on the 5th day. Concentration-response curves for Ang II were obtained in endothelium-intact or endothelium-denuded carotid rings from control (C) or exposed to restrain stress (RS) rats, in the absence or presence of the selective COX-1 inhibitor, SC-560 (9nmol/L) or the selective COX-2 inhibitor, SC-236 (10nmol/L). Protein expression was assessed by western blot in carotid artery from both groups.

In RS rat endothelium-intact carotids, SC-560 and SC-236 reduced the maximum effect (Emax) for Ang II when compared to absence of the inhibitor and to respective control group (Fig. 1). In the absence of endothelium, the selective inhibitors of COX isoforms did not alter the Ang II Emax in RS rat carotid arteries in relation to respective control group (SC-560: 1.06±0.07 vs. 1.20±0.07g/mg; SC-236: 1.17±0.08 vs.1.40±0.05g/mg). Repeated restrain stress enhanced the protein expression of COX-1 in rat carotid arteries and it did not alter the protein expression of COX-2 (Fig. 2).

On the exposure to restrain stress, it is observed that endothelium-dependent metabolites derived from COX-1 and COX-2 with contractile properties participate in the modulation of the contraction induced by Ang II. This participation is restricted to animals exposed to stress and it seems to be mediated by increased protein expression of COX-1 in this group. As the expression of COX-2 in RS rat carotids is not altered when compared to control, changes in
its activity might be responsible for participation of metabolites derived from this isoform on Ang II-induced contraction in RS rat carotid.

(1) Yamaguchi N et al, Neuroscience 170:773-781, 2010