NEURAL CONTROL OF THE KIDNEY IN A RAT MODEL OF HIGH OUTPUT HEART FAILURE: IMPACT OF NITRIC OXIDE.

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Heart failure initiates compensatory mechanisms particularly activation of the autonomic nervous system in response to decreased arterial pressure and cardiac output. The coronary artery ligation model of low output heart failure has been shown to increase renal sympathetic nerve activity (RSNA). This study utilized a model of high output heart failure to investigate the cardiopulmonary mediated reflex inhibition of RSNA in normal rats and those with cardiac damage induced by caffeine/isoprenaline. A further objective was to examine how this reflex might be modulated by nitric oxide (NO).

Groups of male Wistar rats (n=7) were maintained on a normal diet and drinking water or treated with caffeine (61.6 mg/L) in drinking water and isoprenaline (5 mg/kg every 72 h) for two weeks to induce cardiac damage (Burniston *et al*, 2002). Following anaesthesia (0.8-1.0 ml chloralose/urethane,16.5 and 250mg/ml) i.p., a femoral artery and femoral vein were cannulated for measurement of blood pressure (BP) and heart rate (HR) and saline infusion. The left kidney was exposed by a flank incision and the renal nerves placed on recording electrodes. All animals were subjected to two periods of volume expansion (VE) at a rate of 0.25% of body weight per minute for 30 min. After the first VE, there was a 30 min recovery period and then the nitric oxide synthase (NOS) inhibitor N-nitro-L-arginine methyl ester (L-NAME) was infused at 10μg/min/kg for 60 min (Lahera *et al.*, 1991). Thereafter, the animals were subjected to a second period of VE. Data, means ±SEM, were collected each five min. Comparisons between groups were performed using one-way ANOVA and profiles of the responses using two-ANOVA. Significance was taken at $P<0.05$.

Body weight of the normal group was higher than that of the treated group, 233±6 versus 224±5g respectively, as was the heart weight:body weight ratio, 0.003±0.00005 versus 0.004±0.001 (both $P<0.01$). HR, at 6 Hz was decreased ($P<0.01$) by 2 and 4% in the normal and treated groups during the 1st VE, and by 14 and 9% in the second VE. BP, at 90mmHg was increased ($P<0.05$) by 5 and 8% in the normal group while it was decreased ($P<0.05$) by 14 and 4% in the treated group during the 1st and 2nd VE respectively. VE in the normal group resulted in a 42% decrease ($P<0.001$) in RSNA at 30 min but, by contrast, RSNA did not change in the treated group. During the 2nd VE, RSNA was decreased by 78% and 33% (both $P<0.001$) for the normal and treated group, respectively which were responses larger (both $P<0.001$) than those obtained in the absence of L-NAME.

The RSNA suppression during VE illustrates the cardiopulmonary reflex and its absence in the treated group implies a deficit in the reflex residing either in the heart or within central pathways. Inhibition of NO with L-NAME enhanced the reflex RSNA suppression to VE in the normal rats, and re-established the VE induced renal sympatho-inhibition in the treated rats. These observations reflect a potential role of NO within the brain, possibly at the PVN.

Burniston *et al*., *J Appl Physiol* 2002;**93**: 1824-1832.
Lahera *et al.*, *Am J Physiol* 1991;**261**: F1033-F1037.