INTRODUCTION

Long term exposure to intermittent hypoxia (e.g. obstructive sleep apnoea) elevates urinary and plasma catecholamines, muscle sympathetic nerve activity and systemic arterial blood pressure (Fletcher 2000).

Functionally, enhanced sympathetic activity may be due to reduced bioavailability of nitric oxide (NO) since activation of the NO-cGMP pathway decreases central sympathetic activity (Zanzinger et al. 1997), the peripheral pre-synaptic release of noradrenaline (NA) (Schwarz et al. 1995) and the heart rate (HR) response to sympathetic nerve stimulation (SNS) (Choate and Paterson 1999).

AIMS

To investigate whether:

a) Intermittent hypoxia (IH) enhances the heart rate (HR) response to peripheral sympathetic nerve stimulation (SNS) in the guinea-pig atria in-vitro.

b) NO plays a role in the HR response to SNS following IH.

METHODS

TRAINING PROTOCOL

• Animals undergoing IH were placed inside a purpose-built hypoxic chamber.

• Manual adjustments to the flow of nitrogen and air maintained F_{CO2} at 0.3-0.35%.

• Animals underwent IH for 21 consecutive days. Control animals remained in an ambient atmosphere (F_{CO2} :21%, F_{CO2}:0.04%) for the same duration.

RESULTS: ROLE OF NITRIC OXIDE

• Western blot analysis of nNOS protein expression, using a specific monoclonal antibody in the atria from control (n=4) and IH (n=4) animals. A 120 kDa protein band compatible with the nNOS was absent in IH samples, but was identifiable in control samples (Panel A).

• A 120 kDa protein band compatible with the nNOS variant was lower (f=52%) in the IH group compared to the control group (Panel B). Isolated guinea pig small intestine (we control) and guinea pig fore-brain (+ve control) were used to verify nNOS antibody specificity (Panel C).

RESULTS: HR RESPONSE TO PERIPHERAL SNS AND BATH APPLIED NORADRENALINE

• The positive chronotropic response to SNS at 3Hz was significantly enhanced in IH atria (*p<0.05, n=13-14).

• The effect NOS inhibition with L-NA (100µM) and its reversal with L-arginine (1mM) on the increase in heart rate with SNS at 3 Hz (n=7 control, n=7 IH).

• IH atria demonstrated typical responses to hypoxic exposure, characterised by significantly (p<0.05) lower body weights, reduced growth rates and increased heart weight/body weight ratios.

RESULTS: PHYSICAL CHARACTERISTICS

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REFERENCES


