Acute Hypoxic Pulmonary Artery Responses in the WKY and BN Rodent Strains

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Background
- We previously showed that the acute hypoxic stimulus response could be determined in an intact sedated rodent model.
- Alhashe et al. suggested that the acute hypoxic response could predict the development of pulmonary artery hypertension (1)
- Hypoxic stimulus response curve was compared for two rodent strains: Wistar Kyoto (WKY) and Brown Norway (BN) rats which differ significantly in their right ventricular hypertrophic response to chronic hypoxia (91% vs 84% increase in the right ventricular to left ventricular ratio respectively).
- We hypothesized that the BN would have a higher acute response predicting the higher chronic hypoxic response.

Objectives
- Compare the hypoxic dose response curves in two rodent strains known to differ significantly in their right ventricular hypertrophic response to chronic hypoxia
- Determine whether the acute response could predict the chronic hypoxic effects in these two strains
- Identify potential genetic differences and design of future studies

Setup
- Pressure transducer
- Infusion pump
- Pulmonary and femoral artery catheters
- Cardiac output
- ECG
- Core temperature
- CO2 and O2 analyser
- Nitrogen

Methods
- Rodents were anesthetized and paralyzed to inhibit the hypoxic ventilatory response (urethane and vecuronium)
- Stimulus response curve was obtained in 8 BN rats and compared to our prior data in WKY rats
- Heart rate
- Sauration
- Temperature
- ECG
- PA pressure
- Femoral artery pressure
- CO pressure
- Cardiac output
- Artery CO2
- Artery pressure
- Ntirch/Nitric oxide

Determining the hypoxic stimulus response
- 30sec hypoxic challenges (40-0%)
- 5min rest between episodes
- Continuous hemodynamic monitoring
- PA response measured as % increase from baseline at each hypoxic challenge

Representative response to 8% FiO2 for 30sec (WKY rat)
- Baseline
- Response
- % Change

Results
- WKY rats
- BN rats

Conclusion
- Contrary to the hypothesis generated from the existing literature, the BN rats are distinguished from the WKY rats by a trend toward a higher maximal response, with a relatively higher inflection point.

Future Directions
- Effect of chronic hypoxia on the pulmonary artery acute dose response curve
- Effects of drugs on the dose response curve and the potential use of this response for pre-clinical testing

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References