Arousal, Sleep and Cardiovascular Responses to Intermittent Hypercapnic Hypoxia in Piglets.

By

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Statement of Originality

I declare that all work presented in this thesis is my own, except for the contribution of those acknowledged hereunder. The work was performed whilst the candidate was employed as Research Assistant with Dr Karen Waters in the Department of Medicine, University of Sydney, between July 2000 and November 2003. The methods utilised in these studies are modified from those used routinely in this laboratory and recently published in peer-reviewed journals (Waters and Tinworth 2001, Waters and Tinworth 2003).

General animal husbandry was performed by the Laboratory Animal Services staff at The University of Sydney. Surgical procedures and electrophysiological studies were performed by Dr Karen Waters, with the candidate’s assistance.

No part of this thesis has been previously submitted for any other degree or diploma at any University or Institution. No material in this thesis has been written or published by another individual, except where due credit has been given in the form of a reference.
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Introduction

Methods

The Piglets

Study Protocol
Abbreviations

ABP  arterial blood-gas
ALTE  apparent life-threatening event
ATP  adenosine triphosphate
ANOVA  analysis of variance antilogarithm
BE  base excess
BL  Baseline
BP  blood pressure
CNS  central nervous system
CO₂  carbon dioxide
CPAP  Continuous Positive Airway Pressure
CSF  cerebrospinal fluid
d  day
EEG  electroencephalogram
ECG  electrocardiogram
EMG  electromyogram
EOG  electrooculogram
H⁺  hydrogen ion
HCO₃⁻  bicarbonate ion
h  hour
HH  hypercapnic hypoxia, 8 % O₂ / 7% CO₂ / balance N₂
HR  heart rate
IHH  intermittent hypercapnic hypoxia
min  minute
N₂  nitrogen
NREM  non-rapid eye movement sleep
O₂  oxygen
OSA  obstructive sleep apnoea
PaCO₂  arterial partial pressure of CO₂
PaO₂  arterial partial pressure of O₂
PCO₂  partial pressure of CO₂
PO₂  partial pressure of O₂
Recovery  recovery, air: 21% O₂ / balance N₂
REM   rapid eye movement sleep
RR    respiratory rate
SIDS  Sudden Infant Death Syndrome
s     second
SD    standard deviation
TST   total sleep time
W     wake
Abstract

Clinical studies have demonstrated an arousal deficit in infants suffering Obstructive Sleep Apnoea (OSA), and that treatment to alleviate the symptoms of OSA appears to reverse the deficit in arousability. Some sudden infant deaths are thought to be contingent upon such an arousal deficit. This research utilised young piglets during early postnatal development, and exposed them to intermittent hypercapnic hypoxia (IHH) as a model of clinical respiratory diseases. Arousal responses of control animals were compared to the animals exposed to IHH. Comparisons were also made between successive exposures on the first and the fourth consecutive days of IHH. Time to arouse after the onset of the respiratory stimulus, and frequency of arousals during recovery, demonstrated that arousal deficits arose after successive exposures and that these were further exacerbated on the fourth study day. After an overnight recovery period, the arousal deficit was apparently dormant, and only triggered by HH exposure. These studies confirm that both acute and chronic deficits can be induced on a background of otherwise normal postnatal development, suggesting that deficits observed in the clinical setting may be a secondary phenomenon.