THE EFFECTS OF CHRONIC INTERMITTENT HYPOXIA ON INSULIN AND LEPTIN HOMEOSTASIS IN THE RAT

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I declare that this dissertation is my own, unaided work. It is being submitted for the Degree of Master of Science in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination in any other University.

Heidi Shira Romain

_____________ day of __________________________ 2005
ABSTRACT

There is a high prevalence of insulin and leptin resistance and increased cortisol concentrations in sleep apnoea patients, independent of obesity. Chronic intermittent hypoxia is used an experimental animal model to simulate the hypoxia occurring in sleep apnoea patients. The aim of this study was to measure plasma insulin and leptin concentrations and hypothalamic-pituitary-axis activity in rats exposed to either intermittent hypoxia (CIH) or sham hypoxia (SH) for fourteen days. To induce CIH plexiglass cylinders were flushed with 100% nitrogen for nine seconds every 90 seconds, seven hours/day. The rats were weighed each day during the exposure period. Venous blood samples for insulin and leptin were collected on days one, three, five, eight and fifteen. Faecal samples were collected to measure glucocorticoid metabolites. There was no significant difference in the daily change in body weight between the rats exposed to CIH compared to the rats exposed to SH (unpaired t-test). Plasma insulin concentrations were not affected by CIH. In both groups of rats plasma leptin concentrations were significantly higher on day fifteen compared to day five (p=0.03, unpaired t-test). Glucocorticoid metabolites were significantly increased in the intermittent hypoxia group on day two (p=0.003 one-way ANOVA). In conclusion, exposing normal weight rats to CIH for fourteen days resulted in a transient
increase in HPA axis activity on day two and an elevation in plasma leptin levels, in both groups of rats, at day fifteen.
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LIST OF ABBREVIATIONS

ACTH - adrenocorticotropic hormone
AHI - apnoea-hypopnoea index
BS - before surgery
CIH - chronic intermittent hypoxia
CPAP - continuous positive airway pressure
CRH - corticotropin releasing hormone
F\textsubscript{2}O\textsubscript{2} - fraction inspired oxygen
HPA - axis hypothalamic-pituitary-adrenal axis
IL-6 - interleukin 6
IU - international units
NaCl - sodium chloride
PaCO\textsubscript{2} - partial pressure of arterial carbon dioxide
PaO\textsubscript{2} - partial pressure of arterial oxygen
SH - sham hypoxia
T\textsubscript{a} - ambient temperature
TNF-\textalpha - tumor necrosis factor alpha