

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.

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_____ 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 as 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 - adrenocorticotrophic hormone

AHI - apnoea-hypopnoea index

BS - before surgery

CIH - chronic intermittent hypoxia

CPAP - continuous positive airway pressure

CRH - corticotropin releasing hormone

F_IO₂ - fraction inspired oxygen

HPA - axis hypothalamic-pituitary-adrenal axis

IL-6 - interleukin 6

IU - international units

NaCl - sodium chloride

PaCO₂ - partial pressure of arterial carbon dioxide

PaO₂ - partial pressure of arterial oxygen

SH - sham hypoxia

T_a - ambient temperature

TNF- α - tumor necrosis factor alpha