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YEAR 1 PROGRESS REPORT

Project / Program Title		Obesity Hypoventilation Syndrome and Neurocognitive Dysfunction
Name		Dr Sheila Sivam
Award Received		2015 RACP NHMRC Dixon Award for Excellence
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Chief Investigator / Supervisor		Dr Sheila Sivam / Prof Ron Grunstein
Administering Institution		University of Sydney
Funding Period	Start Date:	1 February 2015
	Finish Date:	31 January 2018

PROJECT SUMMARY

Prior studies in this area have focused on hypoxia and sleep fragmentation, but an important source of morbidity may relate to the presence of hypercapnia. This project will provide novel insights on

the severity of neurocognitive dysfunction in patients with obesity hypoventilation, and determine how hypercapnia contributes to this impairment. The risk of cardiometabolic events appears to be only partially reversed with therapy. If it is established that individuals with obesity hypoventilation syndrome (OHS) also have more neurocognitive impairment than those with eucapnic obstructive sleep apnea (OSA), it would provide further impetus to identify these individuals early, before irreversible changes occur.

PROJECT AIMS / OBJECTIVES

Aims:

1. To ascertain the neurocognitive deficits associated with obesity hypoventilation syndrome (OHS), and how these relate to alterations in sleep physiology and nocturnal gas exchange.

2. To determine the extent to which these deficits are reversed with effective positive airway pressure therapy (PAP).

3. To identify obese patients who are at risk of developing OHS by investigating the relationship between daytime measures (including supine hypercapnia, distribution of body fat, and lung volumes) with the presence of hypoventilation during sleep, particularly REM hypoventilation, thought to represent a prodromal state for OHS.

Hypotheses:

1. Patients with OHS exhibit greater cognitive impairment than obese patients with obstructive sleep apnea (OSA), but without daytime hypercapnia.

2. Patients with sleep hypoventilation have less sleep fragmentation but greater neurocognitive impairment arising from a longer exposure to hypercarbia

3. Although correction of hypercapnia with PAP treatment will at least partially improve cognitive function, patients with OHS may remain impaired relative to treated OSA patients without hypercapnia.

4. Supine hypercapnia is a useful marker for identifying sleep hypoventilation, an early sign of the development of OHS.

Aims 1 and 2:

This will be an observational study of morbidly obese patients, examining the effect of hypercapnia and its reduction with treatment, on a battery of neurocognitive tests. This will be administered before and after a 3 month trial of PAP therapy. Patients with daytime hypercapnia (PCO 2 >45mmHg, OHS group) will be compared at baseline with obese OSA patients without daytime hypercapnia (OSA group).

Aim 3:

For this cross-sectional study, patients with a BMI >40kg/m2, sufficiently mobile for blood sampling and able to provide informed consent, will be invited to participate. Subjects will undergo upright and supine arterialised venous blood gas sampling (with the order of testing randomised) prior to their diagnostic sleep test. Neck, weight and hip circumference will be measured in triplicate to determine upper body (WHR > 0.95) vs lower body fat. A simple bedside spirometry to record supine and upright slow VC in addition to FEV1 and FVC will be performed as per American Thoracic Society guidelines. The sagittal height of the abdomen will also be measured in the supine lying position.

SIGNIFICANCE AND OUTCOMES

Prior studies in this area have focused on hypoxia and sleep fragmentation, but an important source of morbidity may relate to the presence of hypercapnia. This project will provide novel insights on

the severity of neurocognitive dysfunction in patients with obesity hypoventilation, and determine how hypercapnia contributes to this impairment . Early detection and correction of hypercapnia

may be an important step in the prevention of neurocognitive dysfunction. Currently, the identification of nocturnal hypoventilation requires monitoring of CO2 during sleep. This is not

routinely carried out in many sleep laboratories and not performed in the home setting. Consequently, nocturnal hypercapnia may be present in some patients with severe OSA despite

daytime normocapnia, with the problem going undetected. The presence of supine hypercapnia could be a useful marker for identifying sleep hypoventilation, an early sign of the development

of OHS. The risk of cardiometabolic events appears to be only partially reversed with therapy. If it is established that individuals with OHS also have more neurocognitive impairment thanthose with eucapnic OSA, it would provide further impetus to identify these individuals early, before irreversible changes occur.

PUBLICATIONS / PRESENTATIONS