OBESITY EFFECTS ON LUNG VOLUME, TRANSDIAPHRAGMATIC PRESSURE, UPPER AIRWAY DILATOR AND INSPIRATORY PUMP MUSCLE ACTIVITY IN OBSTRUCTIVE SLEEP APNOEA

by

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ABSTRACT

Obstructive sleep apnoea (OSA) is a common respiratory disorder characterised by repetitive periods of upper airway (UA) collapse during sleep. OSA is more common in males and the obese but the reasons why remain poorly understood. Abdominal obesity, particularly common in males, is likely to indirectly modulate the amount of tension (tracheal traction) exerted on the UA by the trachea and other intrathoracic structures, potentially leading to increased UA collapsibility. Other factors such as lung volume changes with obesity, altered drive to UA muscles and exaggerated arousal responses are also likely to contribute to UA instability. An investigation of these potential contributing factors forms the basis of this thesis.

In the first study, the effect of external abdominal compression on UA collapsibility during sleep was investigated in a group of obese male OSA patients. A large pneumatic cuff wrapped around the abdomen was inflated to increase intra-abdominal pressure, aiming to produce an upward force on the diaphragm, designed to reduce axial tension on the UA. Abdominal compression increased end-expiratory gastric (P_{GA}) and end-expiratory transdiaphragmatic (P_{DI}) pressure by ~50% and produced a significant rise in UA collapsibility compared to the cuff deflated condition. These data support that increased intra-abdominal pressure has a negative effect on UA function during sleep. This effect may help explain why obesity is the leading risk factor for OSA and why OSA affects men more than women, given that abdominal obesity is particularly common in obese males.

In the second study, differences in minimum expiratory (tonic) diaphragm activity during wakefulness were compared between 8 obese OSA patients and 8 healthy-weight controls. Changes in tonic diaphragm activity and lung volume following sleep onset were also compared between the two groups. There was no evidence of increased tonic diaphragmatic activity during wakefulness in obese OSA patients to support significant diaphragmatic compensation for abdominal compressive effects of obesity. There were small decrements in lung volume following sleep onset in both groups (<70 ml), with significantly greater lung volume and diaphragmatic EMG decrements when sleep onsets were immediately followed by respiratory events. While lung volume decrements at sleep onset were relatively small, this does not discount that UA function is not more sensitive to effects of reduced lung volume in obese OSA patients.

To more closely investigate the potential interactive effects of obesity on physiological variables likely influencing UA function, the third study investigated the temporal relationships between a comprehensive range of relevant physiological variables leading into and following the termination of obstructive apnoeas during sleep in 6 obese OSA patients. Prior to UA obstruction, diaphragm and genioglossus muscle activity decreased, while UA resistance increased. Lung volume and end-expiratory P_{GA} and end-expiratory P_{DI} also fell during this period, consistent with diaphragm ascent. There was a substantial increase in ventilation, muscle activity and lung volume immediately following the termination of obstructive events. Respiratory events and arousals occurred in close temporal proximity prior to and following obstructive apnoeas, supporting that cyclical respiratory events and arousals may both help to perpetuate further events. The

results from this study support that there is a ‘global’ loss in respiratory drive to UA dilator and pump muscles precipitating obstructive respiratory events. The associated decreases in UA dilator muscle activity and lung volume may therefore both contribute to the propensity for the UA to obstruct.

In summary, increased intra-abdominal pressure was shown to negatively impact UA airway collapsibility during sleep. A decrease in lung volume at sleep onset and prior to UA obstruction further support that lung volume decrement, coincident with a decline in overall respiratory drive, potentially contributes to the propensity for airway obstruction. Further studies are needed to elucidate the relative contribution of relatively small changes in lung volume versus changes in respiratory and UA muscle activity *per se* on UA patency in OSA patients.

PUBLICATIONS

The following are publications that have arisen from work conducted towards this thesis:

Journal article:

Stadler DL, McEvoy RD, Sprecher KE, Thomson KJ, Ryan MK, Thompson CC, Catcheside PG. Abdominal Compression Increases Upper Airway Collapsibility During Sleep in Obese Male Obstructive Sleep Apnea Patients. *Sleep* 2009; **32**(12):1579-1587.

Published abstracts:

D Stadler, RD McEvoy, D Paul, J Bradley, P Catcheside. Lung volume, Gastric and Transdiaphragmatic Pressure Changes Leading Into, During and Following Apnoea in Obese Male Obstructive Sleep Apnoea Patients. *Sleep Biol Rhythms* **7** (Suppl 1), A60, 2009

DL Stadler, PG Catcheside, D Paul, J Bradley, RD McEvoy. Changes in Lung Volume and Upper Airway Dilator Muscle Activity at Sleep Onset in Obese Male Obstructive Sleep Apnea Patients. *Am J Resp Crit Care Med* **179** A5405, 2009

D Stadler, P Catcheside, D Paul, J Bradley, R McEvoy. Changes in Lung Volume and Upper Airway Dilator Muscle Activity at Sleep Onset in Obese Male Obstructive Sleep Apnoea Patients. *Sleep Biol Rhythms* **6** (Suppl 1) A10, 2008

Stadler DL, Catcheside PG, George KE, Thomson K, Thompson CC, Ryan M, McEvoy RD. Abdominal compression increases upper airway collapsibility during sleep in obese male obstructive sleep apnea patients. *Proceedings of the American Thoracic Society* A51, 2007

Stadler DL, Catcheside PG, George K, Thompson C, Ryan M, McEvoy RD. The effect of abdominal compression on upper airway function during sleep in obese male obstructive sleep apnoea patients. *Sleep Biol Rhythms*, **4** (Supp 1) A23, 2006

Unpublished conference proceedings:

D Stadler, P Catcheside, J Bradley, D Paul and R Doug McEvoy. The Effect Of Sleep Onset On Lung Volume In Obese Male Obstructive Sleep Apnoea Patients. *Australian Society for Medical Research Annual Scientific Meeting, South Australian Branch, Adelaide, Australia*. 2008

DECLARATION

This work contains no material which has been accepted for the award of any other degree or diploma in any university or tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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GLOSSARY OF ABBREVIATIONS

ΔAP_{ABDO}	Change in abdominal anterior-posterior dimension
ΔAP_{CHEST}	Change in chest anterior-posterior dimension
AHI	Apnoea hypopnoea index (events·hr^{-1})
BMI	Body mass index (kg·m^{-2})
CPAP	Continuous positive airway pressure
ECG	Electrocardiography
EEG	Electroencephalography
EELV	End-expiratory lung volume
$eEMG_{DI}$	Average minimum tonic diaphragm activity
$eEMG_{GG}$	Average minimum tonic genioglossus activity
EMG	Electromyography
EMG_{DI}	Diaphragm muscle activity
EMG_{GG}	Genioglossus muscle activity
F_B	Breathing frequency (breaths·min^{-1})
FEV_1	Forced expiratory volume in 1 sec (% predicted)
FVC	Forced vital capacity (% predicted)
HC	Hip circumference (cm)
IAP	Intra-abdominal pressure
$iEMG_{DI}$	Average inspiratory diaphragm activity
$iEMG_{GG}$	Average inspiratory genioglossus activity
NREM sleep	Non rapid eye movement sleep
OSA	Obstructive sleep apnoea
OSAS	Obstructive sleep apnoea syndrome
P_{ACO_2}	Arterial CO_2
P_{CRIT}	Upper airway critical closing pressure

P_{CUFF}	Cuff pressure (cmH_2O)
P_{DI}	Transdiaphragmatic pressure (cmH_2O)
P_{EPI}	Epiglottic pressure (cmH_2O)
P_{ETCO_2}	End-tidal partial pressure of carbon dioxide (mmHg)
P_{GA}	Gastric pressure (cmH_2O)
PIF	Peak inspiratory flow ($L \cdot min^{-1}$)
P_{MASK}	Mask pressure (cmH_2O)
P_{OES}	Oesophageal pressure (cmH_2O)
REM sleep	Rapid eye movement sleep
R_{UA}	Upper airway resistance ($cmH_2O \cdot L^{-1} \cdot s$)
SDB	Sleep-disordered breathing
SEM	Standard error of the mean
SWS	Slow-wave sleep
T_E	Duration of expiration (secs)
T_I	Duration of inspiration (secs)
T_{TOT}	Total duration of inspiration and expiration (secs)
UA	Upper airway
UACP	Upper airway closing pressure (cmH_2O)
V_I	Inspiration minute ventilation ($L \cdot min^{-1}$)
V_T	Inspiration tidal volume (L)
WC	Waist circumference (cm)
WHR	Waist-to-hip ratio