# AN EXAMINATION OF THE NATURE OF SLEEP FRAGMENTATION IN CHILDREN WITH UPPER AIRWAY OBSTRUCTION

---

**Scott Wade Coussens**

**Bachelor of Science, Bachelor of Science (Honours)**

**A thesis submitted for the degree of Doctor of Philosophy in Physiology by a mixed portfolio of publications, submitted manuscripts, manuscripts and traditional chapters**

**Discipline of Physiology**

**Faculty of Health Sciences**

**University of Adelaide**

**September 2015**

# TABLE OF CONTENTS

# TABLE OF CONTENTS (Tables)

# TABLE OF CONTENTS (Figures)

*Towards a Composite Index of Upper Airway Obstruction Severity in Children*

# i. Abstract

An examination of the nature of sleep fragmentation in children with upper airway obstruction.

**Introduction** – Sleep related upper airway obstruction (UAO) in children disrupts breathing in sleep, resulting in sleep fragmentation and subsequent neurocognitive and behavioural deficits. Unfortunately the nature of this fragmentation in children is poorly understood and a universally accepted, clinically valid, measure of sleep fragmentation has been elusive. This limits our ability to accurately determine and measure the consequences of sleep fragmentation on a child's development due to UAO, as well as the success of any treatment administered.

**General Aims -** The aim of the current study was to (i) examine the nature of sleep fragmentation in children with upper airway obstruction and (ii) to develop a new sleep fragmentation index for use in paediatric clinical populations with upper airway obstruction. When this study began no such index existed that was widely accepted and utilized. A range of sleep fragmentation measures already trialed in children with upper airway obstruction were reviewed to identify problems and limitations with current and previous methods of measuring sleep fragmentation in these children. An attempt was also made to identify other possible additional factors that mediate sleep fragmentation so as to develop a workable and generally applicable sleep fragmentation index for children with upper airway obstruction.

**Methods** – We performed a series of analyses on sleep and neurocognitive data from children with upper airway obstruction to identify and quantify neural activity associated with sleep fragmentation. We then used these measures and other mediating factors to create a composite measure of sleep fragmentation in children.

**Results** – We found that children with upper airway obstruction had characteristically altered neural activity as measured by electroencephalogram (e.g. changes in sleep spindle density,

decreased alpha and sigma power around spontaneous arousals from sleep). They also had an altered movement distribution in sleep (increased exponential distribution coefficient when sleep runs between movements are modeled on a survival curve), when compared to normal controls. The studies also demonstrated the potential ability of a composite measure of such sleep fragmentation markers and mediating vulnerability factors to more accurately and usefully quantify the negative impacts of upper airway obstruction.

**Conclusions** - Sleep fragmentation is a significant consequence of UAO in children, however the current measure of UAO severity is insufficient for determining the overall impact on a child's development. As this study demonstrates, the impact of sleep fragmentation is dependent on a complicated set of variables including: age, health factors (e.g. BMI), exposure time, disease severity (e.g. AHI), genetics, trait-like factors, social factors (e.g. SES) and family history. The arousals, or disruptions to sleep, are also altered in children with UAO compared to normal controls. We therefore propose a composite measure of these important factors as a more accurate tool for determining the impact of sleep fragmentation and overall severity of UAO in children.

# ii. *Signed Declaration*

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other 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. I give consent to this copy of my thesis when deposited in the University Library, being made available for loan and photocopying, subject to the provisions of the Copyright Act 1968. The author acknowledges that copyright of published works contained within this thesis (as listed below) resides with the copyright holders of those works.

Chatburn, A., S. Coussens, K. Lushington, D. Kennedy, M. Baumert, and M. Kohler. (2013) "**Sleep spindle activity and cognitive performance in healthy children**." *Sleep,* 36(2): pp. 237-243.

Coussens, S., M. Kohler, M. Baumert, J. Martin, D. Kennedy, K. Lushington, D. Saint, and Y. Pamula. "**EEG spectral changes associated with spontaneous arousals in children with upper airway obstruction."** In The Journal of Sleep Research, vol. 20, (2008): pp. 52-52.

Coussens, S., Baumert, M., Kohler, M., Martin, J., Kennedy, D., Lushington, K., & Pamula, Y. (2014). “**Movement distribution: a new measure of sleep fragmentation in children with upper airway obstruction**.” *Sleep*, *37*(12), pp. 2025-2034.

Scott Coussens Date 29th January 2014

# iii. *Acknowledgements*

First and foremost I would like to thank my supervisors Dr. David Saint and Dr. Yvonne Pamula for the opportunity. I am extremely grateful for your patience and guidance over the last several years. I especially would like to thank Yvonne for the constant motivation and support. You taught me the skills that have been vital for my growth from an undergraduate student to an independent scientist. I would also like to thank David Parsons for giving me a chance and beginning my research career. Your initial and continued support has helped me to become the enthusiastic researcher I am today.

I extend my gratitude to Department of Respiratory and Sleep Medicine Team, particularly Dr. Declan Kennedy and Dr. James Martin; The Women's and Children's Hospital including Kurt Lushington; and to the Department of Electrical and Electronic Engineering at Adelaide University including Matthew Berryman, Derek Abbott, Cosma Shalizi, and Andrew Allison. It has been a valuable experience working and learning from you all, without which this project would not be possible.

I would also like to acknowledge Dr. Mark Kohler for his invaluable knowledge, encouragement and selfless dedication to helping myself and others. Thank you for taking the time to read through, assist and provide feedback on my thesis, your sage council and the various studies and projects you have generously included me in. There is no way that this thesis would have been finished without you and I look forward to many years of working in research together.

Finally I would like to thank my colleagues, both past and present, for accompanying me on this journey. Your help, advice and encouragement has been greatly appreciated during the course of this research. In particular I would like to thank Alex Chatburn for sharing my passion for research.

I look forward to many collaborations in the future, and many more insightful discussions. And to Melissa Cava, my ‘editor in chief’. Thank you for your personal and professional support over the last 5+ years.

This research was generously funded by The Women’s and Children’s Hospital, The University of Adelaide, Australian Research Council, NHMRC and Australasian Sleep Association.

## *iv. Publications*

Baraglia, D. P., M. J. Berryman, S. W. Coussens, Y. Pamula, D. Kennedy, A. J. Martin, and D. Abbott. "**Automated sleep scoring and sleep apnea detection in children** [6039-35]." In *PROCEEDINGS-SPIE THE INTERNATIONAL SOCIETY FOR OPTICAL ENGINEERING*, vol. 6039, p. 60390T. International Society for Optical Engineering; 1999, 2006.

Baraglia, David P., Matthew J. Berryman, Scott W. Coussens, Yvonne Pamula, Declan Kennedy, A. James Martin, and Derek Abbott. "**Automated sleep scoring and sleep apnea detection in children**." In Microelectronics, MEMS, and Nanotechnology, pp. 60390T-60390T. International Society for Optics and Photonics, 2005.

Blunden, Sarah, Emily Watson, Gabby Rigney, Siobhan Banks, Scott Coussens, Gilly Hendrie, and Mark Kohler. "**TO-136 the effects of a high sugar diet on sleep quality and attentional capacity in prepubescent girls: a preliminary study**." Sleep Medicine 12 (2011): S94.

Chatburn, A., S. Coussens, K. Lushington, D. Kennedy, M. Baumert, and M. Kohler. "**Sleep spindle activity and cognitive performance in healthy children**." *Sleep* 36, no. 2 (2013): 237-243.

Coussens, S., M. Kohler, M. Baumert, J. Martin, D. Kennedy, K. Lushington, D. Saint, and Y. Pamula. "**EEG spectral changes associated with spontaneous arousals in children with upper airway obstruction."** In JOURNAL OF SLEEP RESEARCH, vol. 20, pp. 52-52. COMMERCE PLACE, 350 MAIN ST, MALDEN 02148, MA USA: WILEY-BLACKWELL, 2011

Matthew Berryman, Scott Coussens, Martin, James A., David A. Saint, Derek Abbott, Yvonne Pamula, Declan Kennedy, Kurt Lushington, Cosma Shalizi, and Andrew Allison. "**Nonlinear aspects of the EEG during sleep in children**." In *PROCEEDINGS-SPIE THE 3rd INTERNATIONAL SYMPOSIUM ON FLUCTUATIONS AND NOISE*, pp40-48, vol. 6039, p. 60390T. International Society for Optics and Photonics. 2005.

Pamula, Y., A. Campbell, S. Coussens, M. Davey, M. Griffiths, J. Martin, J. Maul *et al*. "**ASTA/ASA addendum to the AASM guidelines for the recording and scoring of paediatric sleep**." In Journal of Sleep Research, vol. 20, no. Supp. 1, pp. 4-4. Wiley-Blackwell Publishing, 2011.

Coussens, S., Baumert, M., Kohler, M., Martin, J., Kennedy, D., Lushington, K., & Pamula, Y. "**Movement distribution: a new measure of sleep fragmentation in children with upper airway obstruction**". Sleep, 37(12), 2025-2034.2014.

## v. *Style and Referencing Format of Jointly Authored Papers, Documents and Unpublished Manuscripts*

The manuscript style and referencing format for chapters 1,2,3,5,7 and 8 are that prescribed by the journal Sleep Medicine.

The manuscript style and referencing format for Chapters 4 and 6 are that prescribed by the journal Sleep.

## vi. Abbreviations

| | |
|---|---|
| *α* | *Alpha Wave Form In EEG (~ 9 – 12 Hz)* |
| ACPT | Auditory Continuous Performance Test |
| Adolescents | 12-18 Years Old |
| AHI | Apnoea-Hypopnea Index |
| ANOVA | One Way Analysis Of Variance |
| Artotl | Total Arousal Index |
| BMI | Body Mass Index |
| C | Control |
| CA | Central Apnoea |
| CBCL | Child Behaviour Check-List |
| Children | 4-11 Years Old |
| CPRS | Conner's Parents Rating Scale |
| CRS-R | Conner's Rating Scale – Revised (Conners 1997) |
| DAS | Differential Abilities Scale |
| DBP | Diastolic Blood Pressure; |
| DS | Daytime Sleepiness |
| DTVMI | The Developmental Test Of Visual-Motor Integration |
| EMG (SM) | Electromyogram (Submental) – Chin Electrode Measuring Local Muscle Activity |
| ESS | Epworth Sleepiness Scales. A Subjective Measure Of Daytime Sleepiness |
| GDSVD - s | The Gordon Diagnostic System Vigilance And Distractibility Subtests (Gordon 1983) |
| Infants | 1-3 Year Old |
| MAP | Mean Arterial Pressure |
| MDI | Mental Development Index |

| | |
|---|---|
| ME | Movement Events |
| MSLT | Multiple Sleep Latency Test. An Objective Measure Of Daytime Sleepiness |
| nCPAP | Nasal Continuous Positive Airway Pressure |
| NEPSY | Neuropsychological Developmental Assessment (Korkman 2001) |
| NIPPV | Nocturnal Non-Invasive Positive Pressure Ventilation |
| NN | SFI Calculated Using A Neural Network Approach To Complicated To Be Summarized In This Paper |
| ns | Not Significant |
| nt | Night Of Study Including Clinical PSG |
| OA | Obstructive Apnoea |
| OAI | Obstructive Apnoea Index |
| OSAS | Obstructive Sleep Apnea Syndrome |
| OSLER | Oxford Sleep Resistance Test. An Objective Measure Of Daytime Sleepiness |
| PeS | Esophageal Pressure Monitoring |
| PLMI | Periodic Limb Movement Index |
| PS | Primary Snoring |
| R/K | Remember/Know (R/K) Procedure (Tulving 1985) |
| RAI | Respiratory Arousal Index |
| REM | Sleep Stage REM (Rapid Eye Movement) |
| S1, S2, S3, S4 | Sleep Stage 1, 2, 3 And 4 Respectively |
| SAI | Spontaneous Arousal Index |
| $SaO_2$ | Arterial Oxyhaemoglobin Saturation |
| SBP | Systolic Blood Pressure |
| SPT | Sleep Period Total |
| TAC | Thoracoabdominal Asynchrony |
| TCAoSAS | Subjects From The Tucson Children’s Assessment Of Sleep Apnoea Study (Mulvaney 2005) |

| | |
|---|---|
| TST | Total Sleep Time (In Hours) |
| TWT | Total Wake Time In Hours |
| Ua | Unattended In Home PSG |
| WASI | The Wechsler Abbreviated Scales Of Intelligence |
| WCST- 64 | The Wisconsin Card Sorting Test-64 Card Version |
| WISC-III | Wechsler Intelligence Scale For Children-Third Edition |
| wk | Weeks |
| WPPSI-R | Wechsler Pre-School And Primary Scale Of Intelligence–Revised |
| WRAML | Wide Range Assessment Of Memory And Learning |