# Published Papers
# Cardio Pulmonary Coupling

| Author(s) | Title |
|---|---|
| Thomas RJ, Mietus JE, Peng CK, Goldberger AL | An electrocardiogram-based technique to assess cardiopulmonary coupling (CPC) during sleep |

| Journal | Summary | Practical Significance |
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| SLEEP 2005; 28:1151-61 | O: Evaluate a new automated measure of cardiopulmonary coupling during sleep using a single-lead electrocardiographic (EKG) signal<br><br>C: A sleep spectrogram derived from information in a single lead electrocardiogram can be used to dynamically track cardiopulmonary interactions. The 2 distinct (bimodal) regimes demonstrate a closer relationship with visual cyclic alternating pattern and non-cyclic alternating pattern states than with standard sleep stages. This technique may provide a complementary approach to the conventional characterization of graded non-rapid eye movement sleep stages | This seminal work establishes the link between high frequency cardio pulmonary coupling and good sleep quality and low frequency cardio pulmonary coupling and poor quality sleep |

| Thomas RJ, Mietus JE, Peng CK, Gilmartin G, Daly RW, Goldberger AL, Gottlie DJ. | Differentiating obstructive from central and complex sleep apnea using an automated electrocardiogram-based method |
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| SLEEP 2007; 30:1756-1769 | O: Complex sleep apnea is defined as sleep disordered breathing secondary to simultaneous upper airway obstruction and respiratory control dysfunction. The objective of this study was to assess the utility of an electrocardiogram (ECG) based CPC technique to distinguish obstructive from central or complex sleep apnea.<br><br>C: ECG based spectral analysis allows automated, operator-independent characterization of probable interactions between respiratory dyscontrol and upper airway anatomical obstruction. The clinical utility of spectrographic phenotyping, especially in predicting failure of positive airway pressure therapy, remains to be more thoroughly tested. | Using the Heart Health Study population of 3989 subjects this study shows that CPC not only differentiated obstructive vs central vs complex sleep apnea, it positively correlated with periodic breathing episodes in PSG and was the strongest predictor of success or failure with PAP titration. |

| Author(s) | Title |
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| Thomas RJ, Weiss MD, Mietus JE, Peng CK, Goldberger AL. | Prevalent hypertension and stroke in the sleep heart health study: association with an ECG-derived spectrographic marker of cardiopulmonary coupling |

| Journal | Summary | Practical Significance |
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| SLEEP 2009 32:897-904 | O: The ECG-based sleep spectrogram generates a map of CPC based on heart rate variability and respiration derived from QRS amplitude variations. A distinct spectrographic phenotype, designated as e-LFCnb, has been associated with central apneas and periodic breathing and predicts sleep laboratory failure of continuous positive airway pressure therapy. This study assesses, at a population level, the associations of this spectrographic biomarker with prevalent cardiovascular disease using the Sleep Heart Health Study (SHHS)-I dataset. C: An ECG derived spectrographic marker related to low frequency cardiopulmonary coupling is associated with greater sleep apnea severity. Whether this biomarker is solely a sign of more severe disease or whether it reflects primary alterations in sleep apnea pathophysiology, which may either cause or result from sleep apnea, is unknown. This ECG-based spectral marker is associated with a higher prevalence of hypertension and stroke. | The presence of e-LFCnb represents the first time a biomarker for sleep disordered breathing independent of age, sex and body mass has been described. |

| Schramm PJ, Madison S. | An electrocardiogram-based technique to identify complex sleep apnea in patients with diabetes and sleep disordered breathing |
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| Under Review SLEEP http://www.journalsleep.org/PDF/AbstractBook2010.pdf | O: The objective of this study was to examine the utility of an (ECG)‑based CPC technique to identify complex sleep apnea in a diabetic population suspected of having sleep disordered breathing (SDB) who were seen in clinical sleep labs. C: The findings from the present study indicate that 30% of the diabetic population being evaluated for obstructive sleep apnea is identifiable by the presence of eLFCNB band as having complex sleep apnea. | This study demonstrates that in addition to being able to identify apnea in a diabetic population, CPC demonstrates the high correlation between complex sleep apnea and diabetes using the e-LFCnb . |

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| Author(s) | Title |
|---|---|
| Baker D, Schramm PJ, Neville AN, Thomas R., Madison S | An Assessment of Sleep Quality using Cardiopulmonary Coupling: Validation in Patients Suspected with Sleep Disordered Breathing |

| Journal | Summary | Practical Significance |
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| Sleep<br><br>2009;32:A82.<br><br><br>http://www.journalsleep.org/PDF/AbstractBook2009.pdf | O: To assess automated sleep quality analysis software using cardiopulmonary coupling (CPC) from one EKG channel, polysomnographs from 69 patients suspected of sleep disordered breathing (SDB).<br><br><br>C: The RemLogic CPC analyzer accurately reproduces sleep quality results from Beth Israel and is comparable to the work of Thomas et al. 2007. | The RemLogic CPC tool is validated against the CPC algorithm created by Dr. Robert Thomas of Beth Israel University, an affiliate of Harvard University as seen in the 2007 study *Differentiating obstructive from central and complex sleep apnea using an automated electrocardiogram-based method.* |

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| Schramm PJ, Neville AG, Madison S, Thomas RJ, Baker DN. | Cardio-pulmonary coupling (CPC) measures correlate to standard sleep variables in a random clinical sample of patients suspected with sleep disordered breathing (SDB) | |

| Journal | Summary | Practical Significance |
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| SLEEP<br><br>2009 Vol. 32:A373 | O: Scoring rules of sleep variables measured in sleep medicine were recently revised. Some of these variables were reported in subjects selected from the Sleep Heart Health study in addition to cardio-pulmonary coupling (CPC) measures. This study's objective is to determine the correlation of CPC variables to standard sleep variables in a random clinical sample.<br><br>C: The RemLogic CPC analysis variables correlate with standard sleep metrics in a clinical population suspected with OSA, but seem to detect complementary aspects of sleep physiology | CPC variables compliment various aspects of sleep physiology obtained using standard sleep metrics. |

| Author(s) | Title |
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| Thomas RJ, Mietus JE, Peng CK, Goldberger AL. Crofford LJ and Chervin RD | Impaired Sleep Quality in Fibromyalgia: Detection and Quantification with ECG-based Cardiopulmonary Coupling Spectrograms |

| Journal | Summary | Practical Significance |
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| Sleep Med. 2010 May;11(5):497-8. Epub 2009 Dec 16 | O: To retrospectively analyze the PSG ECG with CPC from patients with fibromyalgia and compare to matched controls.<br><br>C: Both ECG and EEG approaches yield consistent findings in this syndrome further solidifying the hypothesis of altered sleep stability in fibromyalgia. | This study shows the favorable comparison of CPC findings over time with traditional PSG findings and the pain diaries of patients suffering from Fibromyalgia. |

| Schramm PJ. | An Early Indicator of Complex Sleep Apnea |
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| Journal | Summary | Practical Significance |
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| Advance for Managers in Respiratory Care and Sleep<br><br>June 2010 | O: Demonstration of the impact on a Complex Sleep Apnea patient's sleep quality with CPAP versus ASV using CPC to detect stable and unstable sleep<br><br>C: CPC variables indicated that the patient's sleep quality had improved objectively. Subjectively, the patient reported his sleep more restful when using the combination of ASV at 9 cm H2O and added dead space compared to CPAP. | This study highlights the fact that the presence of eLFCnb is capable of identifying complex sleep apnea both before and after initiation of PAP therapy. A follow up CPC study following the application of ASV with dead space showed improved quality of sleep in the form of increased HFC and this agreed with the patients subjective findings as well |

| Author(s) | Title |
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| Schramm PJ, Neville AN, Baker D, | The Sleep Quality Recovery of a Snorer's Bed Partner |

| Journal | Summary | Practical Significance |
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| Respiratory Therapy Magazine<br><br>June/July 2010<br><br>Volume 5, No | O: To demonstrate through the use of CPC technology the negative impact of snoring and OSA and the response to PAP initiation. on the bed partner's sleep quality<br><br>C: Both the snorer and his bed partner's sleep quality improved significantly with the application of PAP therapy. | Proof to a reticent CPAP user of the benefit to their bed partner as well as themselves of CPAP compliance. |

| Feldman BS, Schramm PJ, Thomas RJ. | Complex Sleep Apnea Syndrome: Response to Continuous Positive Airway Pressure, Auto Servo Ventilation and Auto Servo-Ventilation plus Dead Space |
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| Under Review<br><br>Journal of Clinical Sleep Medicine (submitted 2010) | O: The goal of the present report is to describe a case of Complex SAS that failed CPAP and ASV but responded to ASV with adjunctive dead space, along with the associated CPC patterns of obstructive and chemoreflex modulated sleep apnea.<br><br>C: The response to $CO_2$ adjunct therapy and positive airway ventilation was a normalization of sleep respiration. | This study is further validation of the ability of CPC to phenotype complex sleep apnea and act as a guide to the use of ASV and its adjunct use of dead space to promote $CO_2$ re-breathing. |

| Author(s) | Title |
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| Ibrahim LH, Jacono FJ, Patel SR, Thomas RJ, Larkin EK, Mietus JE, Peng CK, Goldberg AL, Redline S | Heritability of Abnormalities in Cardiopulmonary Coupling in Sleep Apnea: Use of an Electrocardiogram-based Technique |

| Journal | Summary | Practical Significance |
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| SLEEP 2010;33(5):643-646 | O: To evaluate the familial aggregation of distinctive spectrographic biomarkers of unstable sleep, related to elevated-low frequency cardiopulmonary coupling (e-LFC), and to assess their utility in genetic studies.<br><br>C: Approximately 30% of the variability of e-LFC, measured from a continuous ECG during sleep, is explained by familial factors other than BMI. ECG-based spectrographic measures of cardiopulmonary coupling may provide novel phenotypes for characterizing subgroups of individuals with different propensities and genetic etiologies for sleep apnea or for other conditions associated with sleep fragmentation. | This study suggests the opportunity that CPC provides to enhance our understanding of the genetics of OSA by identifying intermediate traits with high heritability. |

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| Essick G, Weisner J, Schramm P | Use of Cardiopulmonary Coupling to Titrate a Mas: An Initial Case Report |

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| Under Review<br><br>AADSM 2011 (submitted 2010) | O: Using a type III home sleep monitoring device (Embletta Gold), determine whether novel measures of CPC might be sensitive to changes in SDB associated with jaw advancement.<br><br>C: Five nights of data were obtained from a 48 yr old non-CPAP adherent male, previously diagnosed by PSG with severe OSA (RDI=39; LSAT=82%) showed the AHI (mean=11.9 events/hr; range=6.6-19.5) did not vary significantly with %JA (rho=-0.32, p>0.6); however, elevated broad-band low-frequency CPC (eBB-LFC) decreased (rho=-0.95, p<0.02). Low-frequency CPC (LFC) increased (rho=0.95, p<0.02), suggesting that while sleep fragmentation improved, overall sleep instability remained excessive. | CPC measures provide evidence of a patient's sleep quality that might be useful in determining the end-point of jaw advancement with a MAS. |