Mini-Symposia Title:

ADVANCES IN SLEEP BIOENGINEERING III: New developments in the quantitative assessment of sleep, daytime sleepiness and obstructive sleep apnea

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S Mini-Symposia Speaker Name & Affiliation 5:

Mini-Symposia Speaker Name & Affiliation 6:

Theme:

- ○ 01. Biomedical Signal Processing
- ○ 02. Biomedical Imaging and Image Processing
- ○ 03. Micro/ Nano-bioengineering; Cellular/ Tissue Engineering &
- ○ 04. Computational Systems & Synthetic Biology; Multiscale modeling
- ◉ 05. Cardiovascular and Respiratory Systems Engineering
- ○ 06. Neural and Rehabilitation Engineering
- ○ 07. Biomedical Sensors and Wearable Systems
- ○ 08. Biorobotics and Biomechanics
- ○ 09. Therapeutic & Diagnostic Systems and Technologies
- ○ 10. Biomedical & Health Informatics
- ○ 11. Biomedical Engineering Education and Society
- ○ 12. Translational Engineering for Healthcare Innovation and Commercialization

Mini-Symposia Synopsis— Max 2000 Characters

Insufficient or fragmented sleep has been identified as a public health epidemic. The most prevalent causes include chronic insomnia and obstructive sleep apnea (OSA), which affect almost a billion people. OSA is associated with increased risk of developing a rapidly expanding list of medical comorbidities such as hypertension, cardiac arrhythmias, ischemic heart disease, stroke, diabetes, learning and attention deficits, and depression and mental illness. While the underlying pathophysiology of various endotypes of OSA and their impact on other organ systems remain to be completely understood, the availability of low-cost "smart" technology, along with increasing computational power, are fueling novel advances in improved methods of nonintrusive diagnostics and therapeutic management of the syndrome. In this series of 3 minisymposia, established experts in the fields of cardiorespiratory and sleep research will present their latest findings in a broad spectrum of areas in sleep medicine. This proposal continues the tradition of similarly themed minisymposia series on sleep that we have organized for EMBC over the past 8 years, which have attracted considerable interest among EMBC attendees. This third minisymposium session will focus on the use of novel methods for quantifying sleep, sleepiness and the severity of OSA, as well as the effects of OSA in patients with chronic obstructive pulmonary disease. Brief speaker biographies: (1) Timo Leppänen, PhD, Adjunct Professor, Department of Applied Physis, University of Eastern Finland, Kuopio, Finland (2) Ignasi Ferrer-Lluis, Researcher, Institute of Bioengineering of Catalunia (IBEC), Barcelona, Spain (3) AbdelKebir Sabil, PhD, researcher, SOS oxygene, Paris, France (4) Thomas Penzel, PhD, Professor of Physiology, Charite University Hospital, Berlin, Germany.

SleepRevolution project - Automatic analysis of sleep and respiratory events with deep learning

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***Abstract*— EU Horizon 2020 project *SleepRevolution* aims to develop deep learning approaches to better estimate the severity of obstructive sleep apnea (OSA) and personalize treatment options to improve health outcomes and quality of life. The deep learning approaches will be implemented to new wearables developed within the project to alleviate the costs and increase the availability of sleep recordings. The aim is also to design a digital platform that functions as a bridge between researchers, patients, and clinicians. Here, two different deep learning approaches are presented; one for automatic respiratory event scoring and one for a detailed assessment of sleep architecture.**

I. INTRODUCTION

OSA is currently diagnosed based on the number of respiratory events during sleep (i.e., the apnea-hypopnea index (AHI)) and the presence of daytime symptoms [1]. The respiratory events and sleep stages are scored manually from polysomnographic (PSG) recordings, which is highly laborious, expensive, and susceptible to human errors. In the current clinical practice, sleep stages are annotated with non-overlapping 30-sec epochs [2]. This arbitrary division is a historical remnant from the era when electroencephalographies were printed on paper and this division lacks a solid physiological basis [3,4]. Also, even though some automatic respiratory event scoring algorithms exist, the accuracy of those is relatively poor and manual review is still required [5]. Thus, novel advanced automatic scoring methods could significantly improve the efficiency and accuracy of the diagnosis of OSA and release the clinical resources from manual scoring to other important areas of sleep medicine. Here, the aims were to develop using the deep neural network approaches an automatic respiratory event scoring tool [5] and analyze the sleep architecture in a more detailed manner compared to traditional 30-sec epochs [6].

II. METHODS

For automatic respiratory event scoring, a long short-term memory (LSTM) network utilizing oxygen saturation, nasal pressure, thermistor, and thorax respiratory movement signals as an input, was developed. Out of the 887 PSGs, 787 were used for training and 100 for testing the neural network [5].

For sleep staging, a pretrained [7] combined convolutional and recurrent neural network was developed to perform sleep staging in a sequence-to-sequence manner. Sleep stages were identified with the traditional 30-sec approach and by using overlapping epochs with 15, 5, 1, or 0.5-sec epoch-to-epoch duration. PSGs of 446 suspected OSA patients, not used during training of the network, were utilized and the differences in the sleep architecture between OSA severity groups were evaluated [6].

III. RESULTS

The epoch-wise agreement between automatic LSTM network scoring and manual scoring was 88.9% with a kappa value of 0.728. Furthermore, the AHI calculated based on automated scorings differed only minimally from the manually determined AHI: a mean absolute error was 3.0 events/hour and an intraclass correlation coefficient 0.985 [5].

As a result of shorter epoch-to-epoch duration (i.e., higher resolution hypnogram), the amount of detected wake increased while REM and sleep stage 3 decreased in severe OSA. However, the amount of sleep stage 1 and wake decreased and sleep stage 3 increased within the other OSA severity groups. When epoch-to-epoch duration was 1-sec, the hazard ratios (HRs) for the risk of fragmented sleep were 1.14 (p=0.39), 1.59 (p<0.01), and 4.13 (p<0.01) for mild, moderate, and severe OSA, respectively, compared to the non-OSA group. These HRs were 1.20 (p=0.21), 1.68 (p<0.01), and 3.73 (p<0.01) respectively, based on manually analyzed 30-sec epochs. Also, the use of shorter epoch-to-epoch durations led to increased total sleep time and sleep efficiency in the non-OSA group while these values decreased in severe OSA [6].

IV. DISCUSSION & CONCLUSION

High accuracy and good agreement with manual scoring were achieved with the automatic respiratory event scoring tool. The LSTM network could be used e.g., for re-analysis of large research datasets with the latest scoring rules, which are not feasible to re-score manually. Also, a more detailed automatic analysis of sleep architecture reveals highly fragmented sleep in severe OSA patients as well as the current sleep staging practice. The results highlight the need for a more detailed automatic sleep analysis when assessing sleep disorders.

These preliminary results of the *SleepRevolution* project are highly promising and support that the ambitious goals of the project can be achieved. A total of 37 research institutions, sleep centers and industry partners will work together to assess and validate the new diagnostic algorithms, wearables, and platforms. Finally, with the commitment of the European Sleep Research Society and the Assembly of National Sleep Societies, the *SleepRevolution* has the unique possibility to create new standardized guidelines for sleep medicine in Europe.

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*This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement 965417, Academy of Finland (323536), VTR, Business Finland (5133/31/2018), and several private non-profit foundations.

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Sleep Apnea & COPD: data analysis to explore comorbidities

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***Abstract*— Obstructive sleep apnea (OSA) and chronic obstructive pulmonary disease (COPD) are highly prevalent diseases. The study of COPD as a OSA comorbidity suggests an increased risk of suffering OSA due to hypoventilation. In this study, we evaluated how COPD affects OSA in a multivariate demographic database including polysomnographic signals.**

***Clinical Relevance*— COPD increases the OSA risk due to hypoventilation and microarousals.**

I. INTRODUCTION

Obstructive sleep apnea (OSA) and chronic obstructive pulmonary disease (COPD) are two important and prevalent diseases. Their interaction is of interest because COPD patients usually have hypoventilation [1], which affects OSA. OSA-COPD patients tend to avoid supine position [2] and have an increased apnea-hypopnea index (AHI) due to a higher microarousals number [3]. Some studies recommend the use of CPAP plus oxygen supply to revert the OSA and hypoventilation, respectively [4].

II. METHODS & RESULTS

We analyzed data from the Study of Health In Pomerania (SHIP) database to determine the effects of COPD in OSA. This database contains data from 1181 subjects from the region of Pomerania, in Germany, who underwent sleep studies. We discarded 95 subjects due to missing values.

As seen in Table I, we found 83 subjects (7.6%) matching the criteria for COPD diagnosis (FEV1/FVC < 0.7), vs. 1005 subjects in the control group, which agrees with the COPD prevalence in the general population. The database is balanced in terms of gender, age and BMI.

In Figure 1 we can observe how the AHI is related to the oxygen desaturation index (ODI). The lower slope of the regression line in the COPD group suggests that these patients had more events linked to microarousals than the control group, since they had less oxygen desaturation episodes.

TABLE I. DATABASE DESCRIPTION

	Groups				
	Control	***COPD***	***Gold1***	***Gold 2***	***Gold 3***
Subjects	1005	83	41	36	6
Female	473	25	14	10	1
Male	532	58	27	26	5
Female age ($\bar{x} \pm$ std)	53 ± 13	56 ± 13	52 ± 11	59 ± 13	74 ± 0
Male age ($\bar{x} \pm$ std)	54 ± 14	55 ± 15	50 ± 17	59 ± 11	58 ± 12
Female BMI ($\bar{x} \pm$ std)	28 ± 5	27 ± 7	28 ± 9	26 ± 5	25 ± 0
Male BMI ($\bar{x} \pm$ std)	29 ± 4	27 ± 5	27 ± 5	28 ± 5	29 ± 3
Female AHI ($\bar{x} \pm$ std)	7 ± 11	7 ± 9	5 ± 7	11 ± 12	1 ± 0
Male AHI ($\bar{x} \pm$ std)	14 ± 16	14 ± 16	13 ± 17	15 ± 16	10 ± 6
% subjects mild OSA	26	19	15	19	50
% subjects moderate OSA	15	19	15	25	17
% subjects severe OSA	8	8	7	11	0

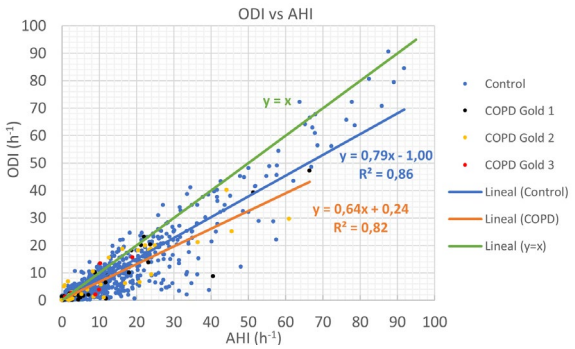

Figure 1. ODI as a function of AHI in COPD and Control subjects.

III. DISCUSSION & CONCLUSION

These findings suggest that COPD rises the risk to suffer a moderate-severe OSA due hypoventilation and an increased occurrence of microarousals. In addition, the presence of OSA-COPD modifies the sleep behavior, can be affected by sleep position, and reduces the sleep quality.

ACKNOWLEDGMENT

Thanks to the Universitätsmedizin Greifswald research team and technicians for accessibility to the SHIP database.

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*This work was supported in part by the "La Caixa" Foundation (ID 100010434) under fellowship codes LCF/BQ/DI17/11620029 and LCF/BQ/DE18/11670019, in part by the European Union's Horizon 2020 Research and Innovation Program under the Marie Sklodowska-Curie Grant number 713673; in part by the CERCA Program/Generalitat de Catalunya, in part by the Secretaria d'Universitats i Recerca de la Generalitat de Catalunya under grant GRC 2017 SGR 01770; in part by the Spanish Ministry of Science, Innovation and Universities under grant RTI2018-098472-B-I00 MCIU/AEI/FEDER, UE.

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Polysomnography Analysis Beyond the Apnea Hypopnea Index

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Abstract— **Obstructive sleep apnea (OSA) is a heterogeneous disorder in terms of clinical phenotype, treatment response and disease outcome. Polysomnography (PSG) software solutions should offer more clinically valuable parameters that would be automatically derived from the recorded signals. Such advanced analysis of PSG recordings could provide biomarkers with potential implications for diagnosis, treatment, and consequences of OSA.**

I. INTRODUCTION

Several studies have reported a high prevalence of cardiovascular comorbidities and risk factors in OSA patients.[1] The distribution of comorbidities and risk factors differed between OSA patients and the burden progressively increases with OSA severity. However, the diagnosis, treatment and monitoring of OSA is oversimplified in many patients, focusing primarily on the apnea–hypopnea index (AHI), resulting in inadequate clinical characterization with unclear and unexpected outcomes. Phenotypes of OSA based on recent concepts such as hypoxic burden and heart rate variability (HRV) or pulse rate variability (PRV) indices provide opportunities for a better understanding and individualized therapy of the disorder as well as certain diseases' risk stratification. These physiological markers are easily derived from PSG signals. However, they are not yet readily available in routine sleep recordings.

II. METHODS

The gold standard OSA diagnostic test, PSG, uses multiple sensors with simultaneous recording of cardiorespiratory and electrophysiological signals. Additional sensors may evaluate actimetry, body position, allow video and audio monitoring and sometimes tracheal sound recording, peripheral arterial tone and jaw movements. Apnea–hypopnea index (AHI) remains the standard metric from PSG analysis used to define OSA and its severity. However, it poorly correlates to clinical consequences and oversimplifies the complexity of the disorder. Thus, given the breadth of information that could be extracted from various PSG signals, several recent studies have proposed a more advanced analysis of certain PSG signals. We analyzed 4 studies that used algorithms to derive indices from the oximetry SpO_2 and the PPG signals available in routine overnight PSG recordings. Within population-based cohorts, Azarbarzin et al. have shown that the hypoxic burden of sleep apnea, evaluated from the oximetry SpO_2 signal, predicts cardiovascular disease-related mortality[2] and that pulse rate response (ΔHR) specific to OSA, evaluated from the oximetry photoplethysmography (PPG) signal predicts cardiovascular morbidity and mortality[3]. In the multicenter Pays de la Loire Clinic-based cohort, we have also demonstrated lately that the PSG derived indices of hypoxic burden and HRV, may provide an opportunity to allow for stroke risk stratification in patients with OSA[4]. We have also shown in another study that nocturnal hypoxemia and PRV indices derived from single-channel pulse oximetry were independent predictors of atrial fibrillation incidence[5].

III. RESULTS

Reference	Used signals	Used indices	End-organ impact
Azarbarzin et al. 2019	SpO_2	Hypoxic burden (+)	CVD mortality
Azarbarzin et al. 2021	PPG	ΔHR (+)&(-)	Cardiovascular morbidity and mortality
Blanchard et al. 2020	HRV SpO_2	ln LF(-), ln HF(+), ln LF/HF(-) T90(+), Hypoxic burden(+)	Stroke
Blanchard et al. 2021	PRV SpO2	SDNN(+), RMSSD(+), LF/HF(-) T90(+)	Atrial fibrillation

Table 1: Summary of used PSG signals, indices, and associated end-organ impact from 4 studies. For further information on the used algorithms, please refer to the original published papers (2,3,4 and 5). Abbreviations: SpO_2 = Oxygen saturation measured with a pulse oximeter, PPG = Pulse Photoplethysmography evaluated by an oximeter, HRV = Heart Rate Variation evaluated from the ECG signal, PRV = Pulse Rate Variation evaluated from the PPG signal, ΔHR = Pulse Rate Response to Respiratory Events evaluated from the PPG signal, ln = natural log, LF = Low Frequency (0.04–0.15Hz) power, HF= High Frequency (0.15–0.4Hz) power, LF/HF= frequency power ratio evaluating balance between sympathetic and parasympathetic systems, SDNN = Standard Deviation Of Normal-To-Normal (NN) beat intervals, RMSSD = Root Mean Square of Successive NN Differences, (+) = a higher value of the index is associated with the end-organ impact, (-) = a lower value of the index is associated with the end-organ impact, CVD = Cardiovascular Disease.

IV. DISCUSSION & CONCLUSION

We have presented in this paper 4 examples illustrating the extent of information that could be extracted from just a couple of PSG signals. Similar studies have suggested more sophisticated analysis of other PSG signals providing biomarkers with potential implications for diagnosis, treatment, and consequences of OSA. Using appropriate signal processing techniques, indices from PSG signals provide important physiological information about comorbidities associated with OSA. Added to the usual AHI, these indices would make pathophysiological information more reliable, improve sleep studies and help phenotype OSA patients more precisely. Future PSG analysis software should offer algorithms that would automatically derive clinically valuable indices from the recorded signals.

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Comparison of methodologies for quantitative assessment of Sleepiness during daytime

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***Abstract* — Sleep should restore performance and physiological functions for satisfying daytime performance. Sleep disorders impairs daytime performance and increases sleepiness. Quantitative assessment of sleepiness is important to evaluate fitness to drive once the underlying sleep disorder is treated.**

Methods: Scales can help to assess subjective sleepiness, such as the Epworth Sleepiness Scale (ESS), the Karolinska Sleepiness Scale (KSS), and the Stanford Sleepiness Scale (SSS). EEG recording can help to quantify objectively and the corresponding tests are the Maintenance of wakefulness test (MWT), and the Multiple Sleep latency test (MSLT). Because the recording and evaluation of EEG requires significant effort in terms of testing site, equipment, and analysis, simplified objective tests were introduced. These are the psychomotor vigilance test (PVT), the Oxford sleep latency test (OSLER), and the divided attention steering test (DASS). In this study these different tests and scales were systematically compared for subjects without and with considerable sleepiness. Reliability and feasibility of these tests were compared and are presented.

Results: Tests were good, but cover different aspects of attention and sleepiness. Motivation does play a role not only when completing subjective scores, but also when performing tests. Even tests with EEG recording may be biased by motivation.

INTRODUCTION

Disturbed sleep, possibly caused by sleep disorders, does lead to impairment of daytime functions such as attention during driving [1]. To investigate daytime attention / sleepiness is of particular importance to drivers and people in supervision tasks. When these people suffer from sleep disorders, a treatment follow up with an objective control of daytime function is important.

METHODS

To investigate sleepiness in drivers objectively, the established methods include testing of the likelihood to fall asleep under controlled conditions. For a test, first a sleep study needs to be performed, to know the starting conditions. The subsequent day, a Multiple Sleep Latency Test (MSLT) or a Maintenance of Wakefulness Test (MWT) has to be performed. Mathematical models of simulating dynamics of the sleep wakefulness continuum may be of some help to predict sleepiness [2]. However, more important is the development and testing of new methods which are simplier than MSLT or MWT during the next day. Such tests are the Oxford Sleep Resistance (OSLER) Test [3] and the Divided Attention Steering (DASS) Test [4]. These tests were systematically evaluated against MSLT in patients with sleepiness.

RESULTS

The baseline sleep study is important to have standardized starting conditions. The MSLT and MWT together with sleepiness scales are standard tools with some weaknesses. The new tests OSLER and DASS cover different aspects of sleepiness, resistance against monotony, and reaction time testing. A combination of tests is optimal.

ACKNOWLEDGMENT

We thank the Megagrant for providing support for these projects. We thank the Heinen and Löwenstein Foundation for their grant support of validating the SONATA equipment for sleep testing.

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*Research is supported by European Union Horizon 2020 grant no 965417 (SLEEPREVOLUTION) and Government Russian Federation megagrant no 075-15-2019-1885.

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