Machine Learning-based Sleep Staging in Sleep Apnea Patients Using a Single Mandibular Movement Signal

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Word Count: 1089 with 2 figures

Author Contributions

N-N.L-D. conceived and designed the project, analyzed the data, drafted the initial manuscript, and reviewed and revised the manuscript; J-B.M. conceived and designed the study, performed the research, analyzed the data, drafted the initial manuscript, reviewed and revised the manuscript; N.C.

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performed the research and participated in data acquisition; V.C. performed the research and participated in data acquisition; R.T. reviewed and revised the manuscript; S.B. analyzed the data, and reviewed and revised the manuscript; J-L.P. conceived and designed the study and analyzed the data, reviewed and revised the manuscript. All authors helped revise the manuscript and approved it for submission.

Financial support

J-L.P., R.T. and S.B. are supported by the French National Research Agency in the framework of the "Investissements d'avenir" program (ANR-15-IDEX-02) and the "e-health and integrated care and trajectories medicine and MIAI artificial intelligence" Chairs of excellence from the Grenoble Alpes University Foundation. This work has been partially supported by MIAI @ Grenoble Alpes, (ANR-19-P3IA-0003). N-N.L-D is an employee of Sunrise. The devices used in the study were provided by Sunrise, Namur, Belgium.

Running head

Mandibular jaw movements for automated sleep staging

Subject category list: 15.10

AJRCCM Articles in Press. Published July 23, 2021 as 10.1164/rccm.202103-0680LE

To the Editor,

We all sleep, and sleep patterns and architecture influence our health and wellbeing. At present, the gold standard method for recording detailed sleep patterns to detect and monitor sleep disorders is in-laboratory overnight polysomnography (PSG), requiring specialized equipment and trained staff. This is no longer feasible in view of the size of the population with suspected sleep disorders, and especially in the Covid-19 era.[1]

Mandibular movements reveal the changes in trigeminal motor nucleus activity driven by brainstem centers involved in sleep/wake transitions.[2,3] The activity of upper airway muscles anchored on the mandibular jaw is the net result of the activation of brainstem respiratory and sleep centers and their respective interactions. This produces specific mandibular movement patterns reflecting the interactions between sleep stages and respiratory control. We previously demonstrated that sleep mandibular movements represent a powerful tool for characterizing respiratory disturbances in obstructive sleep apnea (OSA).[4-6]

Figure 1 gives examples of how the different sleep stages each have typical mandibular movement signal patterns.

Recordings of mandibular movements throughout the night provide hundreds of temporal-spatial signals for modeling and identifying the different sleep stages. Our objective was to develop, train and then validate an artificial intelligence algorithm to stage sleep using a single sensor detecting mandibular movements.

This prospective study included 1026 adults with suspected OSA referred for overnight in-laboratory PSG and simultaneous recordings of mandibular movements using the Sunrise system (Sunrise, Namur, Belgium) (IRB 00004890 - number B707201523388).

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The PSG data (Somnoscreen Plus, Somnomedics, Germany) were manually scored by two experienced sleep technicians (interobserver agreement: 92.1% (95%CI: 0.89-0.94; p<0.001) in accordance with criteria of the American Academy of Sleep Medicine.[7]

The Sunrise system is composed of a coin-sized sensor attached by the sleep technician to the chin of the patient (Figure 1). The embedded inertial measurement device senses mandibular movements and is externally controlled by a smartphone application via Bluetooth, automatically transferring nightly data to a cloud-based infrastructure.[2]

Using the Extreme Gradient Boosting classifier as the core algorithm we developed and progressively trained a machine learning sleep staging algorithm[8] using the overnight PSG and mandibular movement recordings from 800 of the patients. The algorithm automatically classified each 30s epoch of mandibular movement patterns as wake, light non-REM (N1+N2), deep non-REM (N3), or REM sleep stage (Figure 1). N1 and N2 stages were combined in the automated scoring to reach the best compromise between clinical relevance and best model performances. The extracted features consisted of a combination of raw signals along the 3 axes of the accelerometer/gyroscope, processing modes (filters with different frequency bands, moving average), and statistical functions. The statistics applied to the above features were: tendency toward centrality (mean, median), extreme values (min, max), quartiles, standard deviation, as well as the normal standardized version of all above features. The programming language was Python.

Patients in the machine learning training set (n=800 (451 males)) were aged 48.4 yrs (16.7), with body mass index 29.1 kg/m^2 (10.2), and neck circumference 40.0 cm (5.0) all median (IQR) respectively. PSG recordings showed apnea-hypopnea, respiratory disturbance and micro-arousal indexes of 17.1 (27.5), 23.9 (28.5), 24.2 (20.2), all median events/h (IQR); and

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PSG sleep parameters: total sleep time 372 min (122.7), sleep efficiency 85.1% (13.7), and wake time 12.2% (16.5), all median (IQR).

Patients in a separate validation set (n=226 (116 males)) had similar characteristics: 46.5 yrs (17.5), 32.3 kg/m^2 (11.5), and 40.0 cm (5.0) all median (IQR); similar PSG indexes (20.3 (23.5), 27.0 (23.6), 25.0 (20.3) for apnea-hypopnea, respiratory disturbance and micro-arousal, all median (IQR) respectively) and sleep parameters: 397 min (95.7), 87.1% (11.8), 11.5% (12.2) all median (IQR) for total sleep time, sleep efficiency and wake time respectively.

In the validation set, quantitative agreement analysis between machine learning and human scorings was estimated using a linear mixed-model by a two-way intraclass correlation coefficient: ICC (A,1) (95%CI) for total sleep time, wake time, light NREM, deep NREM and REM sleep stages: 0.94 (0.93-0.96), 0.90 (0.88-0.92), 0.70 (0.63-0.76), 0.66 (0.58-0.73) and 0.65 (0.56-0.72), respectively. The mean (95%CI) measurement bias for total sleep time and the four sleep stages (as above) were -13.0 min (-52.9 to +19.0), +3.8% (-6.8 to +16.8), -14.9% (-31.1 to +1.8), +6.0% (-6.0 to +21.2) and +8.4 (-21.3 to +2.4).

The algorithm classified sleep epochs with substantial qualitative agreement with manual PSG scorers, which improved as the size of the learning set was progressively increased (Kappa = 0.71 and accuracy = 78.3% using the full machine learning dataset of 800 patients). As shown in Figure 2, a sleep stage-wise ROC curve analysis confirmed the well-balanced performance for each target sleep stage.

Wakefulness was clearly discriminated from sleep states with a sensitivity of 88% [95%CI: 71% to 99%] and a specificity of 94% [85% to 98%]. Moreover, the algorithm performed well in detecting REM sleep (sensitivity 83% [64% to 97%], specificity 89% [76% to 97%]) and deep

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sleep (sensitivity 84% [59% to 100%], specificity 90% [79% to 98%]). Light NREM sleep was slightly less well detected (sensitivity 60% [36% to 82%], specificity 88% [79% to 96%]).

These findings indicate that machine learning analysis of mandibular movements identifies sleep stages with good agreement to that of individual manual scorers of PSG data.

A strength of this work is that it was conducted using a real-life cohort consisting both of subjects for whom PSG detected no OSA and patients with a broad spectrum of OSA, and randomly sampled into training and validation sets.

Clear advantages of our approach are that it relies on a highly-performant sleep staging algorithm processing signals from a single mandibular movement, facilitating the complex process of signal treatment and improving sleep staging reproducibility.

Our study was designed to avoid the limitations occurring in other studies. First, PSG sleep staging was carried out by two experienced technicians. Second, data from an independent set of patients was used to validate the algorithm. The input data were balanced using a random resampling (SMOTE) technique to minimize the effect of data imbalance. A conventional algorithmic framework implying manual feature extraction and a structured data-driven algorithm was adopted for better control and understanding of input data. Furthermore, the XGBoost algorithm offers several advantages over classical methods, including high efficiency in computation and resources, allowing fast training and execution speed.

In conclusion, the mandibular movement signal acquired from a compact inertial measurement device is suitable for automated sleep staging in adults presenting a broad spectrum of OSA severity. The proposed algorithm performs well for clinical applications and

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could present a major step forward towards unobtrusive, reliable and cost-effective home-based sleep assessment, and value-based care.[9]

Acknowledgements

We thank Ravzat Ashurlaeva (CHU-UCL Namur, Belgium) who kindly spent innumerable hours providing secretarial assistance and Alison Foote PhD (Grenoble-Alpes University Hospital, France) for critical reading and substantial editing of the letter.

Conflicts of interest

NNL-D is an employee of Sunrise; and the devices used in the study to record mandibular movements were provided by Sunrise, Namur, Belgium. J-BM, NC, VC, RT, SB and J-LP have no conflicts of interest directly related to this work.

Data Sharing statement

The de-identified data used in this study are not publicly available at present. Parties interested in data access should contact Dr. Nhat-Nam Le Dong (nam@hellosunrise.com) for queries related to the Extreme Gradient Boosting (XGB) classifier and Dr. JB Martinot (martinot.j@respisom.be) for queries related to the sleep laboratory dataset. The data sets generated and/or analyzed during the current study are available from the corresponding author on reasonable request. Applications will need to undergo ethical and legal approvals by the respective institutions. Those interested in research collaborations should contact JBM (martinot.j@respisom.be).

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Figure 1. The mandibular movements signal processed by machine learning to provide sleep staging

Typical example of 2 of the 6 channels (upper and lower trace) of the mandibular movements signal recorded by a single sensor during the 4 sleep stages in a single individual. Each trace represents a 210 seconds (3.5 minutes) time span of MM recordings by the Sunrise system (inertial measurement with 6 channels) during wakefulness (top), REM sleep, light sleep and deep sleep (bottom)). Thirty second epochs were used for sleep stage classification. Sleep is detected when mandibular movements occur at the breathing frequency. During light sleep (N2) the amplitude of mandibular movements reach several tenths of a mm and vary slightly. The movements during quiet respiration and light sleep are repeated at a frequency ranging between 0.15 and 0.60 Hz depending on central drive output. Deepening of sleep (N3) increases the upper airway's resistance, and this is reflected by an increase in the amplitude of movement, which is also more stable than during light (N2) sleep. REM sleep is easily identified by irregular frequencies and changing amplitudes in mandibular movements that are on average smaller compared to non-REM sleep amplitudes. Cartoon Images adapted from Freepik.com.

Figure 2. Stage-wise ROC curve analysis

This consisted of extracting prediction scores for each target stage (wake, light sleep, deep sleep and REM sleep) and for each patient, then estimating the false and true positive rates of a binary one-versus-rest classification rule to establish the ROC curve. The 95%CIs of the area under the curve (AUC) and smoothing effect were obtained from empirical data (without using any resampling). The diagonal dotted line serves as a reference and shows the performance if sleep staging had been made randomly. The algorithm performed well in

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detecting REM sleep with a ROC-AUC of 0.96 [0.90 to 0.99] and NREM deep sleep with a ROC-AUC of 0.97 [0.91 to 0.99]. Only light NREM sleep was slightly less well detected with a ROC-AUC of 0.86 [0.77 to 0.94].

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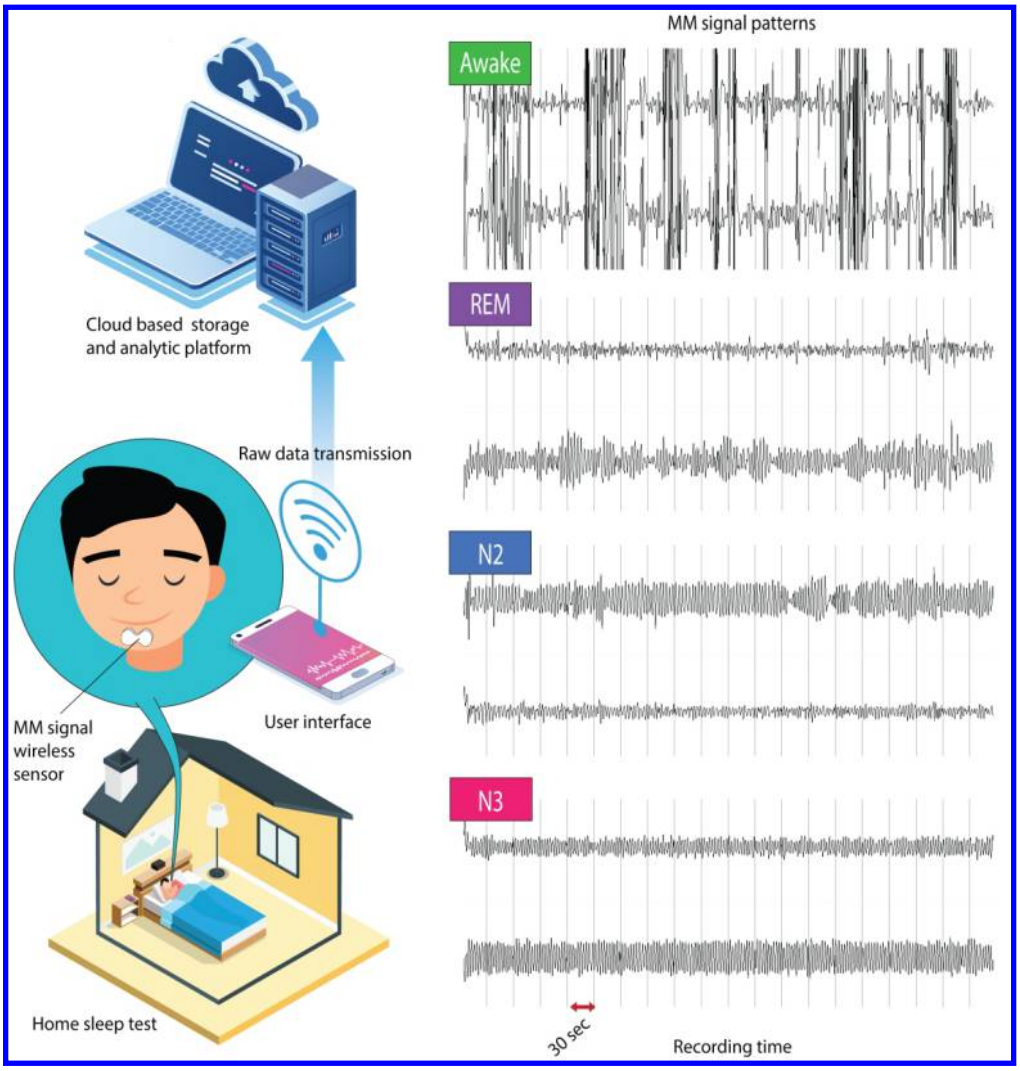

Figure 1. The mandibular movements signal processed by machine learning to provide sleep staging

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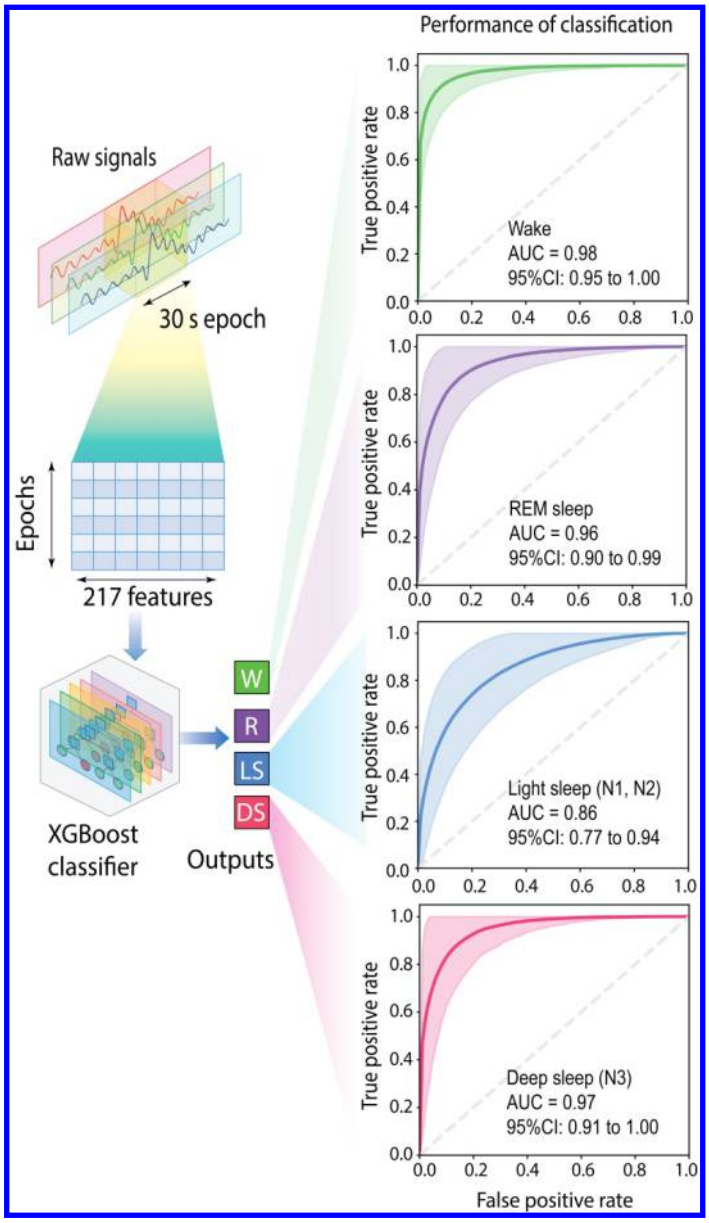

Figure 2. Stage-wise ROC curve analysis

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