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The key role of the mandible in modulating airflow amplitude during sleep

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A R T I C L E I N F O

Keywords:
Mouth opening
Mandibular movements
Dental appliance
Sleep apnea syndrome

A B S T R A C T

Rationale: Mandibular position and motion during sleep rely on the balance between mandibular elevators and depressors. We hypothesized that vertical mandibular position (VMP) modulates airflow amplitude during sleep.
Methods: VMP, tidal nasal flow pressure (NFP) and concurrent surface electromyographic activity of the masseters (sEMG-m) were recorded and processed by a customized algorithm from 100 polysomnographic fragments including a micro-arousal (25 obstructive sleep apnea patients). The relationship between mandibular position and changes in airflow was analysed.
Result: Concurrent VMP and sEMG-m activity changes routinely occurred before a new steady state of airflow documented by NFP. Vertical mandible depression was associated with a median (95% CI) reduction in NFP of 40.9% (14.6%–71.3%, $p = 0.007$) while vertical mandible elevation and mouth closure were associated with a median (95% CI) relative increase in NFP after arousal of 52.6% (17.9%–56.2%, $p = 0.001$).
Conclusion: Elevation and lowering of the mandible were associated with changes in masseteric EMG activity modulating airflow amplitude during sleep.

1. Introduction

It is known during sleep that mouth opening (a lower position of the mandible) increases upper airway collapsibility and resistance which in turn negatively impacts airflow amplitude by decreasing pharyngeal diameters (Inazawa et al., 2005; Isono et al., 1995; Meurice et al., 1996). It is also known that the decrease in apnea/hypopnea index (AHI) when a dental appliance (DA) is used to treat obstructive sleep apnea hypopnea syndrome (OSAHS) is accompanied by a decrease in the vertical mandibular movements amplitude and a more stable position of the mandible (Martinot et al., 2018).

Two types of mandibular movements (MM) have been described during sleep. The first are vertical oscillations of the mandible accompanying the respiratory cycle whose amplitude is known to be a reliable marker of respiratory effort (Martinot et al., 2017a). The second type is a large vertical abrupt displacement of the mandible concurrently with the cortical arousal and mouth closing ending a period of breathing disorder with a significant increase in nasal airflow (Martinot et al., 2017b). These findings draw attention to a possible causal relationship between the vertical mandibular movements, vertical mandibular positions (VMP) and the changes in airflow notably on arousal.

The impact of VMP is also a key research question when evaluating dental DA efficacy. Most studies examining the efficacy of DA during the titration of mandibular advancement keep the inter-incisal distance (the vertical dimension) constant and how to optimize the inter-incisal distance for maximal reduction in AHI remains an open question (Aarab et al., 2010; Dieltjens et al., 2012; Gauthier et al., 2009; Milano et al., 2018; Pitsis et al., 2002). Allowing the inter-incisal distance to vary might increase comfort and tolerability but this should not participate in a deterioration in size effect range (Hamoda et al., 2018).

The two study objectives can be summarized as follow (Hill, 2015): 1/ Is a change in VMP associated with a change in NFP amplitude (specificity and physiological gradient)? 2/ Is a change in VMP systematically preceding the change in NFP signal (temporality)?

Abbreviations: DA, dental appliance, type mandibular advancement splint; OSAHS, obstructive sleepapnea/hypopnea syndrome; AHI, apnea/hypopnea index; MM, mandibular movements at the breathing frequency; NFP, nasal airflow pressure; sEMG-m, surface EMG activity of the masseter; PSG, Polysomnography; RE, respiratory effort; SpO2, O2 saturation; SumRIP, sum of the respiratory inductance plethysmography thoracic and abdominal belts signals; VMM, vertical mandibular movements; VMP, vertical position of the mandible

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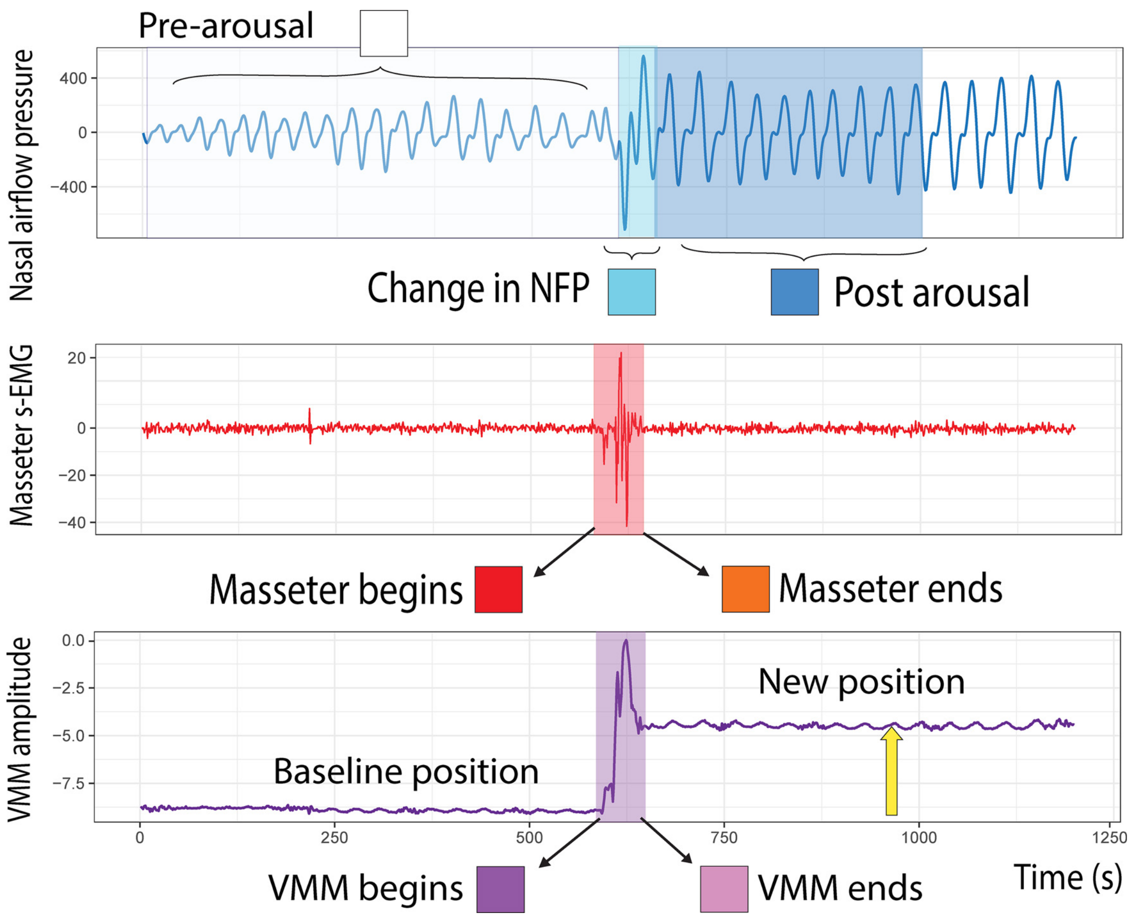

Fig. 1. Sequential analysis in a fragment of nasal airflow pressure (NFP) changes, vertical mandibular movements (VMM) and sEMG-masseter activity Caption: The data recorded in each fragment can be presented as a sequence of 7 components: 1) baseline pre arousal nasal airflow pressure (white), 2) instantaneous change in nasal airflow (lighter blue), 3) post arousal nasal stabilized airflow pressure (blue), 4) VMM beginning (violet), 5) VMM ending (magenta), 6) masseter sEMG activity starting to increase (red) and 7) terminating (orange). The vertical arrow (yellow) measured the difference in mean vertical mandibular position (VMP) between baseline and post arousal levels.

2. Materials and methods

2.1. Study subjects

Adult patients referred for suspected obstructive sleep apnea hypopnea syndrome in a single sleep center (CHU UCL Namur, Saint Elisabeth site, Namur, Belgium) were enrolled. All participants had symptoms suggestive of underlying OSAHS. The study was approved by the local human ethics committee (IRB 00,004,890 – number B707201523388), and all participants provided a written informed consent.

2.2. Study design

This was a prospective cross-sectional study based on multichannel segments, randomly selected from the raw data acquired during a single night polysomnography (PSG).

2.3. Measurements and data acquisition

Laboratory-based video assisted PSG was recorded with a commercial digital acquisition system (Somnoscreen Plus, Somnomedics, Randersacken, Germany). The monitored parameters included EEG (Fz-A+, Cz-A+, Pz-A+), right and left electro-occulogram, submental EMG, tibial EMG, chest and abdominal wall motion by respiratory inductance plethysmography (SleepSense S.L.P.Inc, St. Charles, IL, USA), nasal and oral flows respectively with a pressure transducer and an oral thermistor, and O2 saturation (SpO2) by digital oximeter displaying pulse wave form (Nonin, Nonin Medical, Plymouth, MN, USA). The PSG was supplemented by the surface EMG recording of the right and the left masseter (sEMG-m) as previously described (Walters et al., 2007).

2.4. Mandibular movements

These were assessed with a midsagittal mandibular movement (MM) magnetic sensor (Brizzy® Nomics, Liege, Belgium) which measures the distance between two parallel, coupled, resonant circuits placed on the forehead and on the chin. It was used to record MM (Gray and Barnes, 2017). The transmitter generates a pulsed magnetic wave of low energy. The change in the magnetic field recorded at the receiver is inversely related to the cube of the distance between the chin and forehead probes. The distance between two probes is measured in mm with a resolution of 0.1 mm. Basically, this signal provides the instantaneous position of the mandible (e-Figure 1) and its change concurrently to an arousal.

2.5. Polysomnography scoring

PSG scoring was performed by one certified technician who was blinded to the study aims and according to the American Academy of Sleep Medicine 2012 rules (Berry et al., 2012).

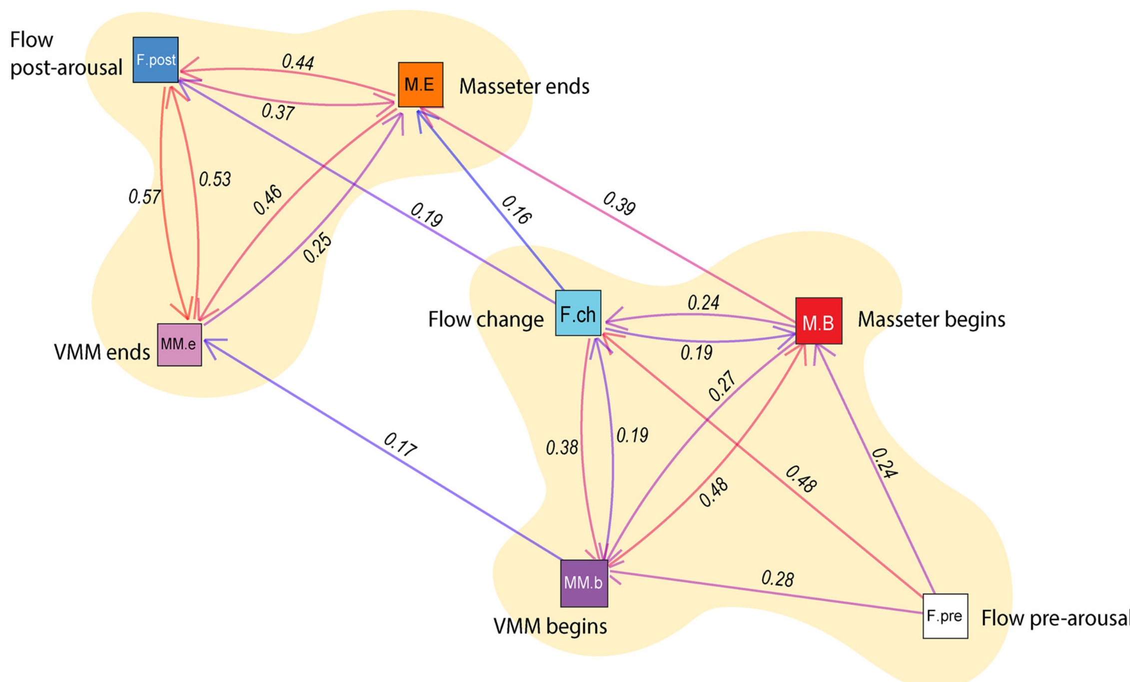

Fig. 2. Directed network showing the probabilities of all possible transitions from each state or event to another Caption: Basically, the data recorded in each fragment could be presented as a sequence of 7 components: baseline pre-arousal nasal airflow pressure (white), instantaneous fluctuation in nasal airflow (lighter blue), post arousal nasal stabilized airflow pressure (blue) VMM beginning (violet), VMM ending (magenta), masseter EMG activity starting to increase (red) and terminating (orange). The directed network summarizes the probabilities of all possible transitions from each event to another. The links connecting the nodes represent the direction of transition. The numbers indicate probabilities for a direct transition.

2.6. PSG fragment selection

The selection was performed in a blinded fashion to the scorer after exportation of the raw data into an excel table by a proprietary algorithm coded in R-language. The algorithm searched for isolated and brief cortical arousals (< 15 s) without any change in body position or in sleep stage during a fragment of time of about 2 min. One hundred fragments were then randomly selected for further processing when constant oral thermal flow was observed during the fragment.

2.7. Further data processing and statistical analysis

We aimed at establishing a causal relationship between the VMP and the changes in airflow amplitude documented by NFP signal through a 3 steps analysis applied to the selected fragment.

The first step focused on the temporality question, to verify whether VMP would occur *before* the effective change in NFP signal and how sEMG-m activity participated in this pattern. Empirical answer to this question was obtained from a descriptive sequence analysis. A binary segmentation algorithm was applied separately to MM, NFP and sEMG-m signals in the fragment to determine the beginning and the end of VMP, masseters contractions and NFP changes around the micro-arousal. The results were transformed into categorical sequence data (two NFP states and 5 brief events). The algorithm identified the signal patterns of successive states or events and calculated their probabilities of occurrence (Fig. 1). The differences between NFP means and amplitudes before and post-arousal signals were measured (Gabadinho et al., 2011). The signals were analysed at 10 hz.

During the second step, a causal association between the occurrence of a vertical mandibular movements (VMM) event and posterior changes in NFP signal was explored using the Causal Impact analysis process. Basically, the algorithm built a Bayesian structural time series model based on the baseline NFP signals (the time series recorded before VMP change) and used the model to forecast a new synthetic sequential baseline, which was a sequence of NFP values we would have expected without the impacting VMP. Then we could quantify the impact of a change in VMP on NFP in 100 data blocks by measuring the differences between the synthetic baseline and the real observed data. A statistically significant difference allowed to assume a significant causal impact of VMP on NFP (Killick and Eckley, 2014; Scott and Varian, 2013; Brodersen et al., 2015).

Finally, we compared the sums of abdomen and thoracic RIP signal amplitudes between the two groups identified by the direction taken by the mandibular movement on arousal to close or open the mouth using bootstrapped Student's *t*-test. This step is a cross validation by an additional technique of volume variations in relation with nasal pressure changes

All analyses were performed in R statistical programming language (TR Core Team, 2012). Null-hypothesis testing was done at significance level of 0.05.

3. Results

3.1. Exploratory data analysis

The patient characteristics ($n = 25$) are reported in e-Table 1. In this study population, 100 data blocks were randomly extracted by the algorithm during NREM sleep periods. The characteristics of these blocks are presented in e-Table 2.

Each data block included the 4 signals: NFP, MM/VMM, sEMG-m and sum of the respiratory inductance plethysmography thoracic and abdominal belts signals (SumRIP). The NFP signal showed a 3-phase pattern, including baseline state, a brief signal fluctuation and then a period of time where the signal amplitude and mean airflow increased or decreased relative to baseline (Fig. 1). VMM events were detectable in all fragments, with a mean ± SD duration of VMM of 22.4 ± 19.1 s. A distinct change in sEMG-m was successfully detected by the algorithm in 90/100 fragments. The duration of sEMG-m was shorter (11.8 ± 11.1 s) than VMM.

3.2. Events sequences analysis

The binary segmentation algorithm identified 5 events chronologically matched in the fragment: 1) instantaneous change in NFP on arousal, 2) start of VMP, 3) termination of VMP, 4) sEMG-m activity starting to increase and 5) sEMG-m terminating (Fig. 1). The algorithm analysed the amplitude and the mean of the NFP before and after the arousal. Fig. 2 is a directed network that summarizes the probabilities of all possible transitions from each state or event to another. These graphs exhibit together that VMM is directly associated to an increase in sEMG-m activity. The associated following events, micro-arousal (with a brief change in airflow), beginning of VMP change and sEMG-m activity always preceded the NFP re-stabilization after arousal.

3.3. The causal impact of VMP on NFP amplitude

We applied the Kay Brodersen's causal impact model to estimate the effect of a change in VMP on NFP. The impact of VMP on NFP was significant in 80/90 fragments. These included 29 fragments with a drop in NFP amplitude (mean relative causal impact of -40.9 % (95%CI: -14.6% to – 71.3%, $p = 0.007$) and 51 fragments with an increase in NFP amplitude (mean relative impact of +52.6% (95%CI: +17.9 to +56.2%, $p = 0.001$) when the mouth is opening or closing, respectively (Fig. 3).

The positive impact ($n = 51$) was characterized by an increase of NFP amplitude from 101.9–148.4 µV and the mean NFP value from 57.7–81.5, whilst a fall from 174.9–142.0 µV in amplitude and the mean NFP value from 97.9–59.8 µV were observed in the negative impact group ($n = 29$). e-Figure 2 shows a significant change in both the mean ($p = 0.0001$) and the peak-to-peak amplitude ($p < 0.0001$) of NFP before and after a change in VMP.

The analysis of the sequences confirmed that a change in mandibular position did always occur before the new steady state of NFP observed after arousal.

3.3.1. Differences in the means of VMP and in the sum of RIP belts amplitudes between the positive and negative causal impact groups

We found that the mouth was more close (VMP significantly higher (mean difference of 2.03 mm 95%CI: 0.92–3.37, $p = 0.0024$)) and the sum RIP belts amplitudes higher (mean difference of 179 µV (95%CI: 79.1–349, $p = 0.0082$) in the group of fragments showing an increased NFP (positive causal impact) compared to the group where NFP decreased (negative causal impact).

4. Discussion

Our study has established for the first time that the changes in VMP are the cause of the change observed in NFP and the consequence of a change in sEMG-m activity (Fig. 3).

The categorical sequence analysis identified two clusters regrouping the landmarks with the highest probabilities to observe a temporal direct transition between two events or two states: the causative cluster of events regrouped the state of baseline flow, the beginning of an increase in sEMG-m activity, VMM and the change in NFP; the consecutive cluster included the end of the increase sEMG-m activity, the end of the mandibular position changes and the state of the restabilized NFP. Fig. 2 shows the network of probabilities linking the knots of interest where the causal factor must precede temporally the occurrence of the outcome.

The strength of the study was provided by the automated binary analytic algorithm which was applied blindly to the human visual scoring. Each fragment included one brief cortical arousal inserted between two periods of stabilized NFP. These are infrequent and discrete events in absence of sleep stages or body position changes (Fig. 1). We showed that the increase in NFP was associated to a positive change in mandibular position following arousal (mouth is closing). The opposite could also be demonstrated (Fig. 3). In absence of a change in oral thermic flow, we assumed that the change in NFP was related to a change in a global air ventilation and not to airflow re-orientation between the mouth and the nose when mouth is closing or opening.

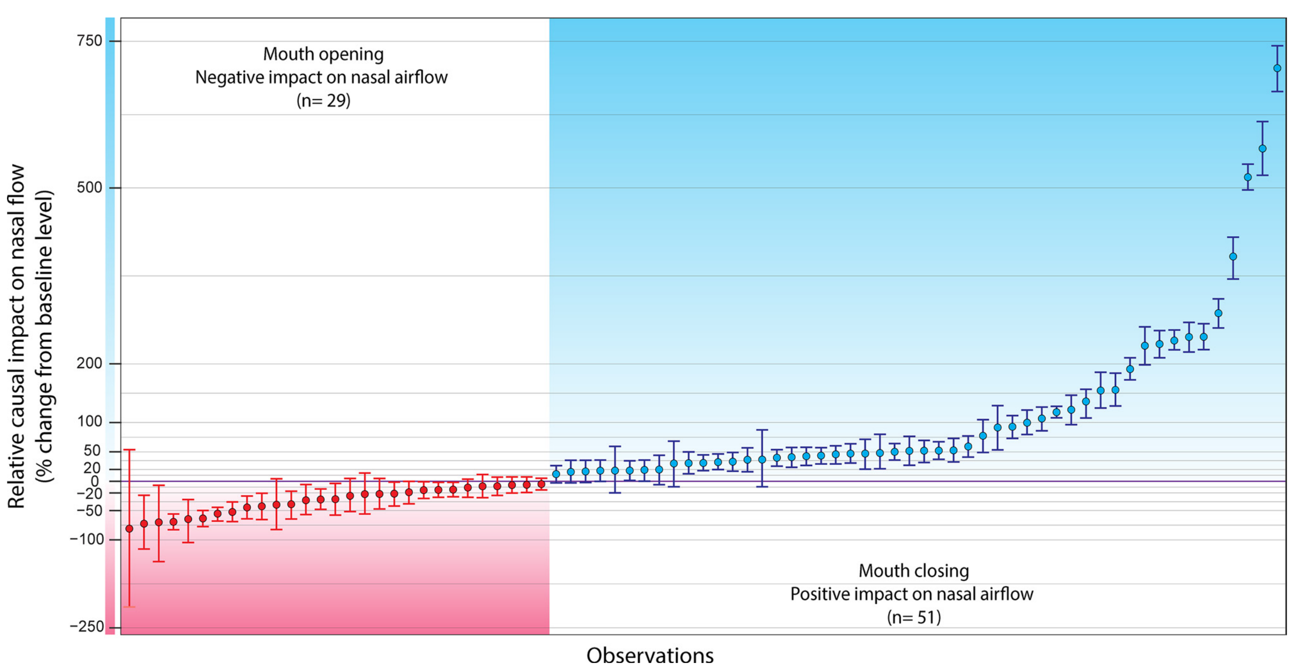

Fig. 3. Causal association between vertical mandibular movements and variations in airflow amplitude Caption: The figure represents the relative causal impacts of a vertical mandibular displacement on the nasal airflow pressure, estimated as the percentage of change in nasal flow amplitude after the beginning of the vertical mandibular movement, compared to its baseline level (if the vertical mandibular movement did not occur). The circle indicates the mean and the error bars represent the 95 % confident interval of this impact. Negative impact (red color) corresponds to a drop in nasal flow amplitude caused by mouth opening ($n = 29$) whilst positive impact (blue color) indicates an improvement in nasal flow from low baseline level as a consequence of a mouth closing ($n = 51$). Those impacts were all statistically significant ($p < 0.05$).

Indeed, the ventilation was not measured here by pneumotachography due to the possible interference of a naso-buccal mask on VMP (Lebret et al., 2017). Here we could demonstrate that the sum of the abdominal and thoracic RIP belts signals changed similarly to NFP depending on the direction taken by MM (more or less mouth opening). This strongly suggests that the mandible position is a mean to stretch the upper airway allowing an increase in nasal airflow.

It is known that the change in airflow on arousal at the end of a period of respiratory disorder is associated with a change in mandibular position. Jaw closure at the end of an obstructive apnea or hypopnea is frequently reported by the sleep partner especially in presence of gasping and choking episodes. Physiological issue of these large displacements of the mandible have been investigated in the past (Hollowell and Suratt, 1991; Miyamoto et al., 1999). Arousal intensity drives motor responsiveness in a hierarchical way, and it is known that motor activation of the peripheral limbs is also frequently observed in response to arousal terminating obstructive breathing events. In this way, Kato et al. concluded that on arousal, jaw muscles recruitment (i.e. masseters contractions) was a non-specific and general motor manifestation without any airflow determinism (predictable issue) (Isono et al., 1995; Kato et al., 2013). Upper airway re-opening is commonly associated with the arousal (Eckert and Younes, 2014) and elevation of the mandible could impact the patency of the upper airway by stretching the local musculature. Considering these data, controlling vertical dimensions of mouth opening during oral appliance titration might be critical to ensure successful response. A 2-components DA with a minimal freedom for mouth opening was reported more effective than a monobloc DA to reduce AHI (Hamoda et al., 2018). The addition of rubber bands to the DA is known to increase DA success in positional obstructive sleep apnea/hypopnea (OSAH) (Milano et al., 2018). This has technical implications because DA has material thickness causing an increase in the vertical dimension and therefore pushing the mandible to a more caudal position. On the other hand, allowing some mandibular movements is known to increase DA adherence because providing more comfort. However, if allowed this must be compensated by additional mandibular advancement. Therefore, it is critical that DA can control respiratory MM amplitudes in their normal range by positioning the mandible in a forward and elevated position while allowing mild displacement on arousal.

5. Limitations

It is known that algorithms dedicated to the detection of abrupt changes in biological signals are highly sensitive even for short periods of time. Indeed, biological signals are not monotonous but to be plausible the results must find meaning in the comprehensive physiology.

6. Conclusions

The activities of the jaw antagonistic muscles are causally associated to the change in mandibular positions on arousal. The changes in the mandibular position during sleep are responsible for variations in the nasal inspiratory flow pressure and global changes in ventilation. This demonstrates the interest of monitoring MM during sleep and the needs for controlling mouth opening to optimize the effects of oral appliance therapy.

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Declaration of Competing Interest

The authors have no conflicts of interest to disclose linked to this work or direct involvement in the development of the device used here to measure mandibular movements.

CRediT authorship contribution statement

Jean-Benoit Martinot: Conceptualization, Methodology, Writing - original draft, Data curation, Formal analysis, Investigation, Project administration, Resources, Supervision, Validation, Visualization. **Nhat Nam Le-Dong:** Writing - original draft, Formal analysis, Software, Validation, Visualization. **Valérie Cuthbert:** Visualization, Data curation, Investigation. **Stéphane Denison:** Visualization, Data curation, Investigation. **Philip Silkoff:** Writing - review & editing, Formal analysis, Project administration, Supervision. **Jean Christian Borel:** Conceptualization, Methodology, Writing - review & editing, Formal analysis, Investigation, Project administration. **Jean Louis Pépin:** Funding acquisition, Conceptualization, Methodology, Writing - review & editing, Formal analysis, Investigation, Project administration, Resources, Supervision, Validation, Visualization.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.resp.2020.103447.

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