Chapter 2 – Part 1
Added value of a Mandible Movement Automated Analysis in the screening of Obstructive Sleep Apnoea

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SUMMARY

In-laboratory polysomnography is the "gold standard" for diagnosing obstructive sleep apnoea syndrome but is time-consuming and costly with long waiting list in many sleep laboratories. Therefore, the search for alternative methods to detect respiratory events is growing.

In this prospective study, we compared attended polysomnography to 2 methods, with or without mandible movement automated analysis provided by a distance meter and added to airflow and oxygen saturation analysis for the detection of respiratory events. The mandible movement automated analysis allows for the detection of salient mandible movement which is a surrogate for arousal. All parameters were recorded simultaneously in 570 consecutive patients (M/F: 381/189; age: 50 ± 14; BMI : 29 ± 7 kg/m²) visiting a sleep laboratory.

Most frequent main diagnoses were obstructive sleep apnoea (344; 60 %), insomnia/ anxiety/ depression (75; 13 %) and upper airway resistance syndrome (25; 4 %). Correlation between polysomnography and the method with mandible movement automated analysis was excellent (r : 0.95; $p < 0.001$). Accuracy characteristics of the methods showed a statistical improvement in sensitivity and negative predictive value with the addition of mandible movement automated analysis. This was true for different diagnostic thresholds of obstructive sleep severity,

with an excellent efficiency for moderate to severe index (AHI ≥ 15/h). A Bland & Altman plot corroborated the analysis.

The addition of mandible movement automated analysis significantly improves the respiratory index calculation accuracy as compared to an airflow and oxygen saturation analysis. This is an attractive method for the screening of obstructive sleep apnoea syndrome, increasing the ability to detect hypopnoea thanks to the salient mandible movement as a marker of arousals.

INTRODUCTION

As related in chapter 1, obstructive sleep apnoea syndrome (OSAS) is a frequent disease associated with multiple co-morbidities. Untreated, OSAS has important health and socioeconomic consequences but efficient therapies are available and consequently its diagnosis is important. However, a large number of patients with OSAS remain undiagnosed.

Several less elaborated sleep monitoring equipments have been developed for the diagnosis of OSAS.

Respiratory sleep disorders are thought to be associated with typical mouth opening and closing movements. Miyamoto et al. have described a common pattern consisting in a gradual opening and a quick closure of the mouth, mostly following an arousal response in normal and OSAS patients.[1,2]

The quick closure of the mouth is hereunder called salient mandible movement (SMM) which could also start as a lowering of the mandible. T.T. Sjöholm et al. studied a small group of 21 patients with OSAS and analysed masseter (masticatory muscle and elevator of the mandible) contraction episodes[3]. They found that masseter contraction episodes were associated with the termination of apnoea or hypopnoea. We postulated that mandible movement automated analysis (MMAA) could improve accuracy in respiratory event recognition, mainly through a better detection of hyponoea thanks to the associated SMM as described by F. Senny et al.[4] According to the definition used for hypopnoea in this study, SMM is considered as an arousal marker.

MATERIAL AND METHODS

1. Setting

The sleep laboratory of the CHU Liège. This laboratory is linked to a neurological unit.

2. Participants

We prospectively included 629 consecutive subjects referred for diagnostic PSG who had a recording in one of the room of the sleep laboratory of the CHU Liège between January 2006 and March 2010. There was no intentional selection for assignment of the patients in this particular room. The only exclusion criterion was ongoing CPAP treatment. The test has been recorded with additional oxygen (nasal canula) in one patient. The experiments were conducted in accordance with the principles of Declaration of Helsinki for Human Experimentation and after approval of Ethics Review Board; the patients were informed of the aim of the study and gave consent.

3. Recordings

We compared attended full PSG with 2 methods combining nasal airflow (NAF) and pulse oximetry (SpO_2) recordings, with or without MMAA.
All subjects underwent attended PSG (S7000 or N7000 polysomnographs, EMBLA Medcare, Denver, US) and Jawsens® (Nomics, Liège, Belgium) recording. The PSG included the following neurophysiology signals : a three-channel electroencephalography (EEG, C3-A2, C4-A1, FZ-CZ), left and right electrooculography (EOG), submental electromyography (chin EMG) for sleep staging and arousal

scoring, two (left and right) tibial EMG for periodic leg movement evaluation; cardiorespiratory signals including ECG, nasal cannula/pressure transducer (NAF) (Protech, Mukilteo, USA), chest and abdominal inductance plethysmography belts, a plethypulse, a pulse oximetry (SpO_2, Nonin, Plymouth, USA), a snoring detection (piezzoelectric sensor from EMBLA), and a body position (body position sensor Protech) recordings. Oximetry sampling was done at 2 Hertz.

MMAA was performed by means of a distance-meter called Jawsens® (Jaw sensor, the recorded signal is called "Jawac" for jaw activity) based on the principle of magnetometry.

4. Analysis

The number of respiratory events (apnoeas and hypopnoeas) per hour was calculated using as denominator the time between lights out and lights on called the total dark time (TDT) for the 2 methods and TST (total NREM stages 1 to 4 and REM sleep) providing an apnoea hypopnoea index (AHI) for PSG. The primary measures were the RDI for the 2 automated methods that were compared with the visual analysis for PSG. The first RDI was defined as respiratory events provided by the NAF and SpO_2 analysis divided by the TDT. The second RDI was called SMM-RDI and was defined as the number of respiratory events recognized by the NAF, SpO_2 and MMAA analysis divided by the TDT. Recordings of PSG and the 2 alternative methods were performed simultaneously but on separate acquisition channels in each patient.

All sleep studies (PSG) were manually analysed either by a competent certified polysomnography technician or two sleep physicians that were blind to the mandibular movement signal. The sleep analysis was performed by visual analysis of successive 30 seconds epochs. The sleep stages were defined according to the scoring rules of A. Rechtschaffen

and A. Kales.[5] Arousals were reported as recommended by the ASDA and defined as an acceleration of the EEG frequencies in NREM sleep, associated with an increase of chin EMG amplitude in REM sleep, occurring at least during 3 seconds with at least 10 seconds of stable sleep preceding the change.[6]

Apnoea, hypopnoea and UARS are defined in Annex 1. Furthermore, a reduction of flow as defined in Annex 1, associated with a cortical arousal, was also defined as a hypopnoea for PSG recordings and a reduction of airflow as defined above was defined as a hypopnoea when associated with a SMM on automated analysis.

To perform the statistical analysis, we selected three cut-offs for the AHI. An abnormal AHI was considered when ≥ 5/h. Moderate to severe and severe OSA corresponded respectively to AHI ≥ 15/h and ≥ 30/h.

Apnoea, hypopnoea or central and obstructive respiratory events were not differentiated for the present study.

The number of OSAS (clinical diagnosis) mentioned in the table 1 “main final diagnoses” and allowing population characterization, was not exactly the same as sleep apnoea (OSA, pure respiratory event analysis, including AHI ≥ 5/h disregarding the symptoms).

The main relevant diagnosis was determined based on the complaints and history of the patient and established by the specialists in charge of the final results (Table 1).

Table 1 : Final clinical diagnoses	
Final diagnosis	**Main**
OSAS	344 (60)
Insomnia/ anxiety/ depression	75 (13)
UARS/RERA	25 (4.4)
Circadian rhythm sleep disorder	20 (3.5)
Restless legs syndrome	17 (3)
Periodic limb movement syndrome	14 (2.5)
Inadequate sleep hygiene, caffeine	13 (2.3)
Hypersomnia	7 (1.3)
Narcolepsy	2 (0.35)
Parasomnia: Primary snoring REM sleep disorder	11 (1.9) 9 (1.6) 2 (0.35)
Unknown	24 (4.2)
Normal	10 (1.8)
Other medical disease	8 (1.4)

Results are provided in n (%). Other medical disease known before sleep investigation and maintained as final diagnoses : fibromyalgia, pain, gastroesophageal reflux.

Signal processing of the mandible movement signal for the recognition of sleep-disordered breathing comprises the following stages. First, NAF and SpO_2 were automatically analysed based on the above mentioned definition. SMM were pointed as respiratory arousals if they were associated with a reduction of airflow (10 seconds or more) below 70 % of the reference value in order to respect the hypopnoea definition used. SMM were identified by the continuous wavelet transform as described by F. Senny et al.[4] Each mandibular movement was characterized by a value that depends on its amplitude and its sharpness (the more discontinuous or sharp was the movement, the greater the value was). A SMM was considered as a relevant arousal for hypopnoea definition if its maximal value was greater or equal to 1 (which corresponds to a movement of around 1mm) and twice greater than the average of the movement values during the related event. Based on this sequential analysis, considered SMM were always associated with a hypopnoea not associated with an oxygen desaturation. The SMM-RDI was defined as the total apnoeas and hypopnoeas number recorded by the automated analysis of NAF, SpO_2 and the MMAA divided by the time (expressed in hours) between lights out and lights on.

These automated analyses (RDI and SMM-RDI) were performed randomly and collected by an engineer that was blind to the results of the PSG.

In order to avoid a bias linked to technical divergences of sensors, NAF and SpO_2 signals were common for PSG and the 2 automated methods. Each patient had one NAF and one digital pulse oximetry. NAF and SpO_2 signals were electronically derived to feed both the automated analysis and the PSG.

In order to assess how SMM was linked to cortical arousals associated with hypopnoea not defined by the presence of desaturation, we performed a post hoc analysis. For each patient, the number of

hypopnoeas associated with arousal (visual analysis) but without any arterial oxygen desaturation was measured and compared to the number of hypopnoeas (without desaturation) associated with SMM, detected by the automatic system. The only requirement was that the SMM had to be in a time interval of -5 and +15 seconds of the end of the respiratory event detected by the nasal airflow.

The PSG scorer was blind to jaw activity, the analysis was entirely automated. The number of hypopnoea linked to arousal or SMM detected was divided by the TST to calculate a Hypopnoea Index (HI).

5. Statistical analysis

Sensitivity (Se) and specificity (Sp), positive and negative predictive value (PPV and NPV), likelihood ratio (LR) compared to the reference (PSG) were determined for mild (AHI $\geq$ 5/h), moderate to severe (AHI $\geq$ 15/h) and severe (AHI $\geq$ 30/h) SA patients. Exact confidence intervals were computed by F distribution. Sensitivity and specificity were compared by binomial test.

Paired Student t test was applied for comparison of the difference between the two methods compared to standard diagnosis.

Linear regression and Pearson correlation between the 2 indexes were also calculated on the entire studied population for assessing association between parameters. Correlations were compared by the Hotelling test described by A. Cohen.[7]

Bland & Altman graphs were performed with MedCalc (Mariakerke, Belgium) on the entire studied population. For the Bland Altman plot, each data point represents the difference between the two measurements (AHI-RDI) plotted against the mean for each patient ([AHI+RDI]/2). Mean difference and limits of agreement (Bland & Altman) are reported, where the limits of agreement have been defined as $\pm$ 1.96 SD of the difference. The same was done with SMM-RDI.

All statistical tests are two-tailed. Statistical significance was set at $p < 0.05$. Analyses were done with NCSS version 2007 (Kaysville, Utah) and SPSS 15.0 (SPSS Inc., Chicago Ill.)

RESULTS

Data were collected in 629 patients visiting the sleep laboratory, and 570 were considered for the analysis. 59 patients were excluded for the analysis. Lost data occurred in 22 patients due to technical problem : loss of NAF signal (n = 4), loss of jaw activity signal during the night (n = 4), no jaw activity signal (n = 12) and loss of SpO_2 (n = 2). It means that 3.5 % of the recordings were excluded due to technical problem. Thirty-seven patients had a history of OSA diagnosed by PSG. To avoid impact on predictive parameters, they were excluded from this analysis. The final study population (570 patients; M/F : 381/189) had a mean age : 50 ± 14; min : 13; max : 85; BMI : 29 ± 7 kg/m²; min : 14, max : 57. Main complaints are listed in Table 2. In one third of the cases, these complaints were snoring and/or sleepiness, sometimes in association. The mean Epworth Sleepiness Score was 11 ± 7/24.

The most frequent final diagnoses were OSAS (344; 60 %), insomnia/anxiety/depression (75; 13 %) and UARS (25; 4 %) (Table 1). These were mostly dyssomnia as described in the International Classification of Sleep Disorders (2005). [16]

Table 2 : Patients characteristics	
N	**570**
M/F (n (%)	381(67)/189(33)
Age	50 ± 14
BMI (kg/m²)	29 ± 7
Complaints - Snoring - Sleepiness - Apnoea (witness) - Tiredness - Lack of sleep - Not refreshing sleep - Frequent awakenings - Gasping	 204 (36) 175 (31) 111 (19.5) 100 (17.5) 53 (9) 24 (4) 12 (2) 9 (1.6)
Epworth sleepiness scale	11 ± 7
Shift work	14 (2.5)
Known smoking habits (Current/Former /Non smoker/unknown)	134(23.5)/302(53)/103(18)/31(5.4)
Current BzD use	90 (16)
HTA	192 (66.7)
Chronic respiratory disease Asthma/ COPD/ Others*	58 (10) 25/24/4
Cardiovascular disease (cardiopathy and peripheric vascular disease)	64 (11.3)
Psychiatric disorder	94 (16.5)
Neurological disease Ischemic event/ MS/ Epilepsy/others**	 113 (19.8) 21/7/9/76
Transplantation (solid organ)/ RA	4 (0.7)/3 (0.5)
Nose & Throat disease Uvulo-palatal surgery	111 (19.5) 15 (2.6)
Surgical mandible treatment	9 (1.6)

n (%); M : male; F : female; BMI : Boby Mass Index. Complaints are those related by the patients, sometimes in association, which is not mentioned. BzD : benzodiazepine; HTA : hypertension; COPD : chronic obstructive pulmonary disease. * : bronchiectasis, pulmonary fibrosis, thoraco-pulmonary sequellae. MS : multiple sclerosis. ** muscular dystrophy, traumatic injury, headache. RA : Rhumatoid Arthritis.

The mean total analysed period was 553.6 ± 89.7 min for the 2 RDI calculation and 419 ± 8.4 for the AHI (total sleep time).

Using the AHI cut-off of 5/h combined with symptoms, OSAS was the main diagnosis in 60 % (n = 344) in this population. For the whole studied population, the mean PSG AHI was 24.3 ± 23.3 events per hour while the mean SMM-RDI was 19.2 ± 18.6 events per hour and 14.3 ± 18.3 for RDI. Simple regression analysis was used to study correlation between AHI and the 2 RDI. The relation was linear and direct. Correlations were strong between PSG AHI and SMM-RDI (r : 0.95) accounting for 90 % variance ($p < 0.001$) and between PSG AHI and RDI (r : 0.93; $p < 0.001$) (figure 1 and 2). Correlations were significantly different ($p < 0.001$).

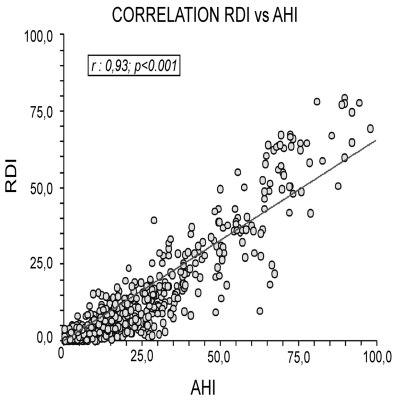


Figure 1 : Correlation graph between RDI and AHI.

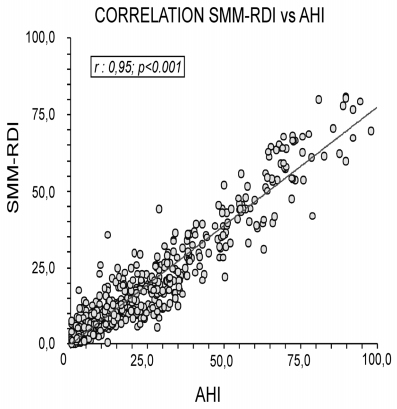


Figure 2 : Correlation graph between SMM-RDI and AHI.

AHI : apnoea hypopnoea index (PSG). RDI : respiratory disturbance index (nasal airflow and SpO_2. SMM-RDI : respiratory disturbance index based on nasal airflow, SpO_2 and MMAA. The estimated model for regression is (0.8) + (0.76 x AHI PSG) for correlation between AHI and SMM-RDI.

Bland & Altman plot corroborated the analysis. The mean difference between AHI and SMM-RDI was 5.1 ± 8 ($p < 0.001$) versus 10 ± 9.23 ($p < 0.001$) for RDI. With MMAA, agreement was good with few points outside the limits of agreement (figure 3 and 4). Limits of agreement were [-8.1; 28.1] for AHI-RDI and [-10.7; 20.9] for AHI - SMM-RDI.

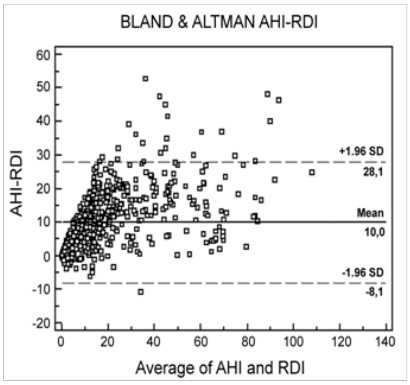


Figure 3 : Bland & Altman Graph for AHI - RDI

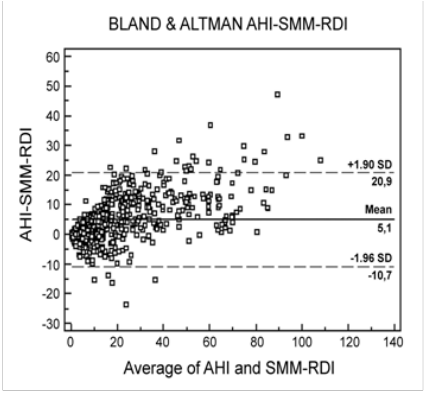


Figure 4 : Bland & Altman Graph for AHI - SMM-RDI

Respectively 462 (81 %), 307 (54 %) and 169 (30 %) patients had an AHI ≥ 5/h, ≥ 15/h and ≥ 30/h. Accuracy characteristics of the method with or without MMAA for the different AHI cut-offs are described in table 3. We found a statistically significant improvement in sensitivity and negative predictive value with the addition of MMAA (SMM-RDI) for each AHI cut-off : ≥ 5/h (93 and 72 %), ≥ 15/h (75 and 77 %) compared to RDI with the same thresholds ≥ 5/h (69 and 43 %), ≥ 15/h (54 and 65 %). There was no significant loss of PPV and the values of Sp for moderate to severe and severe AHI were excellent. For severe patients (≥ 30/h), sensitivity and negative predictive value improved by adding MMAA (respectively 52 and 83 % for RDI; 68 and 88 % for SMM-RDI). Although not formally significant, there was an improvement in NPV in this severe group.

Positive and negative likelihood ratios were comparable for the 2 methods for moderate to severe index (AHI ≥ 15/h).

In order to assess how hypopnoeas related to arousal are the hypopnoeas linked to SMM, we performed a post hoc analysis on the entire population. The results showed that 62.7 % of hypopnoeas associated with cortical arousals but without desaturation on PSG were associated with a SMM. The HI calculated for PSG and for MMAA added to airflow analysis were respectively 6.0 ± 6.0/h and 3.8 ± 4.2/h. The correlation coefficient between these two indices was excellent (r : 0.92). The mean difference from B&A plots was 2.2 ± 2.7/h.

Table 3 : Sensitivity, Specificity, PPV, NPV and likelihood ratio derived from the 2 methods and compared to simultaneous polysomnography

AHI	**≥ 5/h N = 462 (81 %)**			**≥ 15/h N = 307 (54 %)**			**≥ 30/h N = 169 (30 %)**		
	RDI	SMM-RDI	p	RDI	SMM-RDI	p	RDI	SMM-RDI	p
Se	69 [65.13; 73.74]	93 [90.57; 95.38]	< 0.001	54 [48.64; 60.06]	75 [70.02; 79.97]	< 0.001	52 [44.27; 59.81]	68 [60.45; 75.00]	< 0.001
Sp	96 [90.95; 99.00]	72 [62.44; 79.99]	< 0.001	99 [96.7; 99.76]	95 [92.16; 97.62]	< 0.05	99.7 [98.62; 99.99]	99 [97.83; 99.85]	NS
PPV	99 [96.87; 99.66]	93 [90.57; 95.38]		98 [94.93; 99.63]	95 [91.53; 97.42]		99 [93.90; 99.97]	97 [92.75; 99.47]	
NPV	43 [36.92; 49.53]	72 [62.44; 79.99]		65 [60.10; 69.67]	77 [71.79; 81.23]		83 [79.51; 86.40]	88 [84.70; 90.89]	
LR +	19.13 [7.30; 50.16]	3.32 [2.47;4.54]		47.69 [15.41;147]	16.49 [9.45;28.77]		208 [29.33;1486]	90.96 [29.32;282.16]	
LR -	0.32 [0.27;0.36]	0.1 [0.07;0.137]		0.46 [0.41;0.52]	0.26 [0.21;0.32]		0.48 [0.41;0.56]	0.32 [0.26;0.40]	

AHI : apnoea hypopnoea index (PSG). RDI : respiratory disturbance index (nasal airflow and SpO_2). SMM-RDI : respiratory disturbance index based on nasal airflow, SpO_2 and MMAA. Se : sensitivity; Sp : specificity; PPV : positive predictive value; NPV : negative predictive value; LR + : positive likelihood ratio; LR- : negative likelihood ratio. Exact confidence intervals are based on F distribution. NS : Not Significant.

DISCUSSION

In the present study, we found that adding MMAA to nasal airflow and pulse oximetry automated analysis allowed a significant increase in sensitivity and negative predictive value for the diagnosis of moderate to severe OSA (AHI ≥ 15/h) without a significant drop in positive predictive value.

Globally, correlation was excellent between AHI and SMM-RDI. There was a bias underestimating respiratory events index (Bland & Altman mean difference is 5.1 ± 8). This bias was significantly smaller than with RDI ($p < 0.001$). As seen on the Bland & Altman graphs (Figure 3 and 4), there was a linear trend between the bias (AHI-RDI; for positive and negative differences) and AHI below 30/h for both methods. Another large cohort related by J.F. Masa et al.showed the same trends.[8] Moreover, limits of agreement are narrower for SMM-RDI compared to RDI, showing more accuracy in the concordance.

Thanks to the SMM, used as an arousal marker, the accuracy in respiratory events detection improved by increasing the ability to detect hypopnoea.

For defining hypopnoeas in the present study, we used the criteria of A.L. Meoli et al.which are currently the approved hypopnoea definition for the Centers for Medicaire and Medicaid Services in the United States but also considering arousals.[9,10] A hypopnoea was pointed if an airflow reduction occurred with either a desaturation or an arousal. A post hoc analysis between all the hypopnoeas with cortical arousals (without desaturation) and all the hypopnoeas with SMM (without desaturation) showed that 62.7 % of this type of hypopnoea could be automatically detected using MMAA. The fact that only 62.7 % were recognized is probably due to the automatic thresholds that were imposed. This mainly concerns the minimal SMM amplitude for the automatic recognition. A SMM was considered as a relevant arousal for hypopnoea definition if its maximal value was greater or equal to 1 (which corresponds to a movement of around 1mm) and twice greater than the average of the movement values during the related event.

The 2 components of the SMM definition are important for the recognition of SMM as a marker of respiratory arousal. This explains why the HI derived from MMAA is strongly correlated with HI derived from PSG (r : 0.92).

As shown by W.R. Ruehland et al., all differences in hypopnoea criteria would induce variable final AHI, leading to misclassified OSA.[11] By using SMM to detect arousals included in our hypopnoea definition, MMAA significantly improved predictive parameters, suggesting that the combination of SMM with SpO_2 and NAF analysis in a simple device could be an attractive solution for the screening of OSA.

Lost data occurred in 22 (3.5 %) patients which is acceptable. This was due to variable technical problems detailed in the results section.

The difference in respiratory events index could be explained by several factors. First, there is variability in scoring respiratory events between automatic and manual (human perception) analysis. This is the case for very short events but considered by the reviewer as sufficient to reach 10 seconds or for very long events (mainly hyponoea) considered as one or multiple events. Moreover, a drop greater than 30 % in airflow to detect hypopnoea is not so easy to assess for human eyes but automatic analysis will always measure it and stick to the definition. This could explain a part of the variability. Second, a comparison was made between AHI and RDI : the analysed period is different (mean difference RDI-AHI in the present study : 134 minutes). The denominator used for RDI and SMM-RDI is the total dark time which includes sleep latency; wake periods during the night and short onset awakening before lights on. Different denominators explain variability in respiratory events index. This is an important point, explaining higher AHI than RDI and SMM-RDI.

Third, the maximal value of MMAA must reach > 1 and be twice greater than the average of the movement values during the related event to be considered as significant SMM. Some body position could influence the amplitude of the mandible movement and affect hypopnoea recognition with MMAA, whilst

respiratory arousals being more consistently identified on hypnogram by the polysomnographic scorer.

It is important to recognize a severe disease that is accessible to an efficient and easy treatment. Therefore, the improvement in sensitivity by the added MMAA is interesting. Moreover, in this population (AHI ≥ 30/h), positive likelihood ratios were excellent for both studied methods with an overlap in confidence intervals. Despite this improvement by adding MMAA, Se was lower than 80 %. This lack of Se could be overcome by associating an anthropomorphic questionnaire with high Se. The high number of false positive cases associated with this first step could potentially be balanced by the high Sp (99 %) of the PM with added MMAA. Moreover, the selection of sleep apnoea patients in the recruitment process, frequently occurring in sleep laboratory, would improve the pre-test probability having OSAS. Compared to other studies with PM, moderate to severe SA prevalence is not very high in our population (AHI ≥ 15/h : n = 307; 54 %) which could have interacted with predictive values, a higher prevalence leading to higher percentage of positive test.

The present study has several limitations. First, the software version used did not comprise a sleep/wake assessment since it was not available at the time of the recordings.

The important difference between TDT and TST is probably due to the fact that our population is composed of patients with complaints of bad sleep and submitted to "first night effect". In the future, MMAA has the potential to be used as an actigraphy and to give an indirect sleep/wake assessment as described in the publication of F. Senny et al.[12] Another prospective and multicentre study would give more powerful data to the PM, showing a wider spectrum of analysis.

Second, the addition of the MMAA to a simple PM resulted in a poorer Sp albeit an improved Se when considering a cut-off of AHI ≥ 5/h. Therefore, as recommended in guidelines on portable monitoring, screening device has to be

confronted to the pre-test clinical complaints (pre-test probabilities of having the disease).[13,14]

A third limitation is the restricted in-lab assessment, particularly for a screening method dedicated to in-home use.

The population of the study included 9 adolescents (between 13 and 16 year-old). They were referred to sleep study to exclude narcolepsy. Sleep and respiratory events definitions used were identical as those for the entire population. None of them were outliers of the general Bland & Altman plots.

The occurrence of abnormal repetitive mandible movement such as bruxism, chewing has not been studied but seemed to occur rather rarely in our sample. It has been registered in 4 patients (0.7 %), as based on the visual PSG scoring. In our study, this was not the subject and we did not process the analysis by searching bruxism. Nevertheless, as mentioned previously, bruxism has another pattern than SMM, occurs with closed mouth and is repetitive. It has been described in association with sleep respiratory disorders by T.T. Sjöholm et al. with a high incidence which is questioning for us.[3] We think that masseter contraction should not be regarded as bruxism unless rhythmic and repetitive. This kind of behaviour does not correspond to the definition of SMM used in the automated analysis.

CONCLUSION

In conclusion, in a population with high prevalence of respiratory disorder, the addition of MMAA significantly improves the accuracy for the detection of respiratory events with a mean underestimation RDI of 5/h. This portable monitoring is an interesting screening method for moderate to severe sleep apnoea. Even if, in this study, the method is less accurate for very low AHI, this is a promising way to detect severe disease requiring a treatment which is accessible.

Chapter 2 - Part 2
Added value of a Mandible Movement Automated Analysis in the screening of Obstructive Sleep Apnoea : is there a gender influence ?

Expanded from J Sleep Dis Treat Care 2013, 2:3

SUMMARY

In the first part of this second chapter, we have demonstrated the added value of mandible movement automated analysis (MMAA) to a portable device for the screening of obstructive sleep apnoea syndrome (OSAS). In the present study, we aimed at investigating its respective value in the two genders. Several sleep monitoring equipments have been developed for the screening of OSAS but few have been assessed in the female population. In a Systematic Review of the literature on portable devices published in 2003, the authors recommend that studies include more diversified populations, among them women.

We prospectively compared in-laboratory polysomnography to simultaneous recording with a portable device with MMAA in 570 patients. The portable device included 3 signals : SpO_2, NAF and MMAA. Two respiratory disorder indexes (RDI) were automatically calculated in each gender : RDI (without MMAA) and SMM-RDI (with MMAA). The added value of the MM study was assessed in each group and compared to each other.

Correlations between apnoea hypopnoea index (AHI) derived from PSG and SMM-RDI were excellent both in men ($r : 0.95$; $p < 0.001$) and women ($r : 0.94$; $p < 0.001$) and better ($p < 0.001$ for both) than AHI with RDI (respectively $r : 0.93$; $p < 0.001$ and $r : 0.91$; $p < 0.001$). By adding the MMAA, the sensitivity improved significantly in both genders. The sensitivity of SMM-RDI was lower in women

for the detection of both mild to severe (AHI ≥ 5/h) ($p = 0.005$) and moderate to severe (AHI ≥ 15/h) disease ($p < 0.001$). These differences disappeared for severe disease.

This study demonstrated a significant added value of MMAA to a portable device in the screening of OSAS in both genders, although the SMM-RDI had a lower sensitivity in women for the diagnosis of mild to moderate OSAS.

INTRODUCTION

Obstructive sleep apnoea syndrome (OSAS) is a frequent disease associated with multiple co-morbidities. Assessing the severity of the disease relies on the calculation of the apnoea hypopnoea index (AHI) which is the number of apnoeas and hypopnoeas per hour of sleep time. OSAS is highly prevalent in the general population of western countries but largely more so in men than women. In 2001, Bixler et al. published an OSAS (AHI $\geq$ 10/h and daytime symptoms) prevalence of 3.9 % in men and 1.2 % in women.[15] A large number of patients with OSAS remain undiagnosed. Several less elaborate sleep monitoring equipments have been developed for the diagnosis of OSAS but few have been assessed in the female population. In a Systematic Review of the literature on portable devices endorsed by the American Academy of Sleep Medicine, American College of Chest Physicians and American Thoracic Society published in 2003, the authors recommend that studies include more diversified populations, among them women.[16]

OSAS was initially considered to be highly prevalent in men, occurring in later life and presenting differently in women. Due to this idea and the lack of understanding of gender differences in clinical presentation, referral bias probably explains the poor representation of women in previous studies on portable devices. Later, gender-differences have been identified including a greater predominance of rapid eye movement- associated sleep abnormalities in women[17-19] and a lower mean AHI[18-20] contributing to under-diagnosis of OSAS in women. More and more attention is being paid to these gender specificities.

Studies on portable monitoring assessments in the diagnosis of OSAS in women are rare, mostly performed in mixed populations with a small number of women. These do not allow drawing a clear picture on the value of the portable devices in the female gender. To our knowledge, only one recent study assessed a visual analysis of a portable home monitoring in a selected women population.[21]

The mandible movement study assessed here has been described in the first part of this chapter analysing a cohort including a high percentage of women (33%). The method is based on the better detection of hypopnoea thanks to the associated SMM as described by Senny et al.[4] According to the definition used for hypopnoea in this study, SMM is considered as an arousal marker.

Data are now studied in each gender group to describe, first, the added value of the mandible movement automated analysis (MMAA) to a portable screening device in both genders and, secondly, to assess the gender influence on the accuracy of this method.

MATERIAL AND METHODS

1. Setting

The sleep laboratory of the Centre Hospitalier Universitaire of Liège. This laboratory is linked to a neurological unit.

2. Participants

We prospectively included 629 consecutive subjects referred for diagnostic PSG who had a recording in one of the rooms of the sleep laboratory of the CHU Liège between January 2006 and March 2010, without any selection according to gender. There was no intentional selection for assignment of the patients in this particular room. The only exclusion criterion was ongoing Continuous Positive Airway Pressure (CPAP) treatment.

Methods have been described in details in the first part of this chapter.

3. Recordings

We compared attended full PSG with 2 methods combining nasal airflow (NAF) and pulse oximetry (SpO_2) recordings, with (SMM – RDI) or without MMAA (RDI). In order to avoid divergences of sensors, NAF and SpO2 signals were common for the portable device and the PSG.

4. Analysis

The analysis has been detailed previously. The added value of MMAA is analyzed according to the gender, as well as the characteristics of the two groups. The first step was to describe the improvement gained by the MMAA in each gender : this new portable screening device was compared to RDI (without MMAA) and to the gold standard test (PSG). The second step was to compare the results between both genders.

Both RDI and SMM-RDI were calculated for both genders.

The PSG scorer was blinded to the automated analysis and mandible movement signal.The mean SpO_2 and the time below 90 % SpO_2 during sleep were computed in the PSG analysis.

5. Statistical analysis

This statistical method has been described in the first part of this chapter, section 5.

RESULTS

1. Whole population

Data were collected in 629 patients consecutively and randomly admitted in one room of the sleep laboratory, and 570 were considered for the analysis. Fifty nine patients were excluded for the analysis as depicted before. Most frequent main diagnoses were OSAS (IAH ≥ 5/h; n = 344; 60 %), insomnia/ anxiety/ depression (n = 75; 13 %) and upper airway resistance syndrome (n = 25; 4 %).

Table 1 : Patient's characteristics			
	Women	**Men**	
N	189	381	
AHI PSG §	15.5 ± 19.0/h	28.6 ± 24.0/h	< 0.001
AHI ≥ 5 h^{-1} #	123 (65)	337 (89)	< 0.001
AHI ≥ 15 h^{-1} #	64 (34)	243 (64)	< 0.001
AHI ≥ 30 h^{-1} #	24 (13)	145 (38)	< 0.001
RDI §	7.5 ± 13.0	17.7 ± 19.6	< 0.001
SMM-RDI §	12.1 ± 14.4	22.8 ± 19.4	< 0.001
Age §	49 ± 13	50 ± 13	NS
BMI (kg/m²) §	27 ± 6	30 ± 6	< 0.001
Complaints #			
- Snoring	48(25)	156(41)	< 0.001
- sleepiness	61(32)	114(30)	NS
- apnoea (witness)	12(6)	99(26)	< 0.001
- tiredness	40(21)	60(16)	NS
- lack of sleep	35(18)	18(5)	< 0.001
- not refreshing sleep	9(5)	15(4)	NS
- frequent awakenings	7(4)	5(1)	NS (0.063)
- gasping	1(0.5)	8(2)	NS
Epworth Sleepiness Score §	11 ± 10	10 ± 5	NS
Known smoking habits # (Current/Former / Non smoker)	179 49(27)/22(12)/108(60)	360 85(24)/81(22)/194(54)	NS NS
Current BzD use #	35(18)	55(14)	NS
HTA #	55(31)	137(36)	NS (0.091)
Chronic respiratory disease # Asthma COPD Others*	21(12) 14 4 3	37(10) 11 20 6	NS 0.014 NS (0.077) NS
Cardiovascular disease #	11(6)	53(14)	< 0.005
Related psychiatric disorder #	52(27)	42(11)	< 0.001
Neurological disease # Ischemic event/ MS/ Epilepsy/others**	45(24) 4(9)/4(9)/2(4)/35(78)	68(18) 17(25)/33(48)/7(10)/11(16)	NS
Nose & Throat disease # Uvulo-palatal surgery	38(21) 3(2)	73(19) 12(3)	NS NS
Surgical mandible treatment #	3(2)	6(2)	NS

Patients characteristics : § : mean ± SD; # : n (%); BMI : Boby Mass Index. Complaints are those related by the patients, sometimes in association which is not mentioned. BzD : benzodiazepine; HTA : hypertension; COPD : chronic obstructive pulmonary disease. MS : multiple sclerosis. *bronchiectasis and restrictive lung disease; ** muscular dystrophy, traumatic injury, headache

The population studied was divided in 2 groups according to gender. The men-to-women ratio was 2:1 (381 men and 189 women). The characteristics of the patients are described in table 1. Age was similar in both genders but both BMI and AHI were higher in men than women. Significantly more men (n : 145; 38 %) than women (n : 24; 13 %) had severe OSA (AHI ≥ 30/h; $p < 0.001$). The prevalence of asthma and psychiatric disorders was higher in women whilst the prevalence of cardiovascular co-morbidities was higher in men.

2. Added value of the MMAA in each gender

Correlations between SMM-RDI and AHI were excellent both in men (r : 0.95) and women (r : 0.94) and better than those between RDI and AHI : respectively r : 0.93 ($p < 0.001$ for comparison between correlation coefficient of each methods) and r : 0.91 ($p < 0.001$ for comparison between correlation coefficient of each methods).

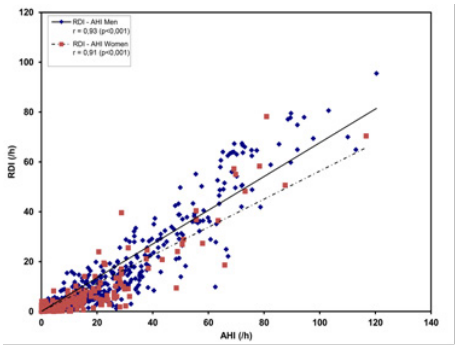


Figure 1 : Correlations of RDI method with the AHI-PSG in Men (diamond; continuous line) and Women (square; dotted line). Correlations between RDI with AHI were linear and excellent in both men (r : 0.93; $p < 0.001$) and women (r : 0.91; $p < 0.001$).

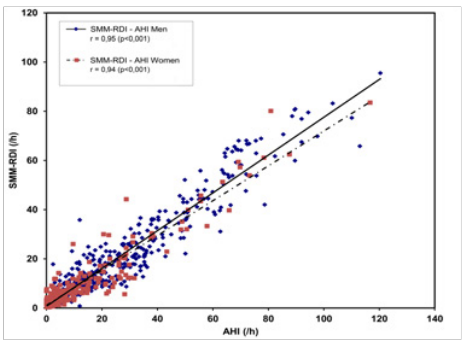
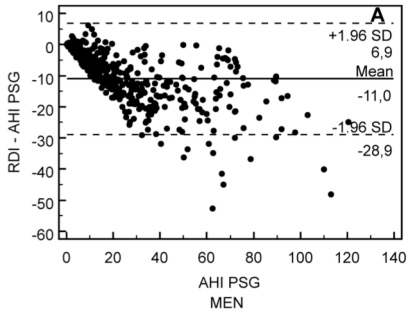


Figure 2 : Correlations of the SMM-RDI method with the AHI-PSG in Men (diamond; continuous line) and Women (square; dotted line). Correlations between SMM-RDI and AHI were linear and excellent in both men (r : 0.95; $p < 0.001$) and women (r : 0.94; $p < 0.001$).

A Bland & Altman plot corroborated the analysis. Whilst RDI underestimated AHI, this was improved by adding MMAA. In women, mean underestimation with RDI was -8.0 ± 9.1/h but only -3.4 ± 7.4/h with SMM-RDI ($p < 0.001$). Limits of agreement were [9.8; -26.0] for RDI-AHI and [11.1; -18.0] for SMM-RDI - AHI in women. In men, mean underestimation with RDI was -11.0 ± 9.1/h but -6.0 ± 8.2/h with SMM-RDI ($p < 0.001$). Limits of agreement were [6.9; -28.9] for RDI-AHI and [10.2; -22.0] for SMM-RDI - AHI in men.



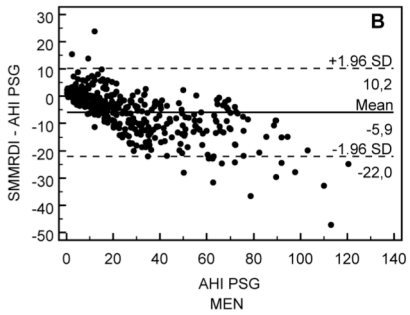
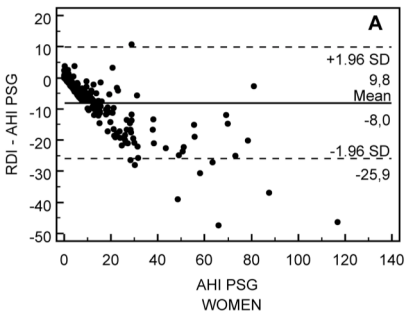


Figure 3A : Bland & Altman graphs in Men RDI-AHI.
Figure 3B : Bland & Altman graphs in Men SMM RDI-AHI. The mean underestimation with RDI was significantly higher than SMM-RDI ($p<0.001$).



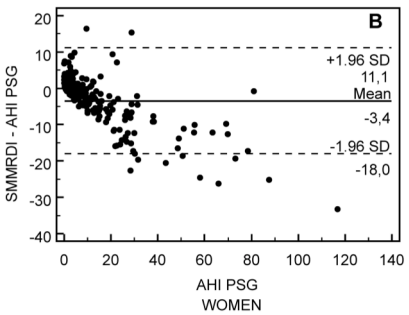


Figure 4A : Bland & Altman graphs in Women RDI-AHI.
Figure 4B : Bland & Altman graphs in Women SMM RDI-AHI. The mean underestimation with RDI was significantly higher than SMM-RDI ($p<0.001$).

In this second part, Bland & Altman plots are different from those from the first part of this chapter.

To insist on the understimation with both RDI, the difference has been inversed on the Y axis whereas the reference "AHI-PSG" is on the X axis.

Respectively 337 (89 %), 243 (64 %) and 145 (38 %) men had an AHI ≥ 5/h, ≥ 15/h and ≥ 30/h. Respectively 123 (65 %), 64 (34 %) and 24 (13 %) women had an AHI ≥ 5/h, ≥ 15/h and ≥ 30/h. Significantly more men had moderate or severe OSA ($p < 0.001$). Accuracy characteristics of the method with or without MMAA for the different AHI cut-offs are described in table 2. We found a statistically significant improvement in sensitivity with the addition of MMAA (SMM-RDI) in both male and female at the three different AHI thresholds.

The values of Sp for moderate to severe and severe AHI were excellent for the automated methods with or without MMAA, both above 90 % in both genders. For severe disease (AHI≥ 30/h), the addition of MMAA to simple RDI significantly improved Se (respectively 42 % for RDI; 71 % for SMM-RDI in women ($p < 0.001$) and 54 % for RDI; 68 % for SMM-RDI in men ($p < 0.05$). This occurred without a significant loss of Sp (table 2 - A&B).

Positive and negative likelihood ratios were similar for the 2 methods in both genders however LR seemed to improve with the AHI severity. Used in the screening of moderate to severe (AHI ≥ 15/h) and severe (AHI ≥ 30/h) disease, a positive test will clearly increase the likelihood of a disease and a negative test will markedly decrease the likelihood of disease.

Table 2A : Sensitivity, specificity and likelihood ratios derived from the 2 methods and compared to simultaneous polysomnography in women									
WOMEN	**AHI ≥ 5/h**			**AHI ≥ 15/h**			**AHI ≥ 30/h**		
	RDI	**SMM-RDI**	**p**	**RDI**	**SMM-RDI**	**p**	**RDI**	**SMM-RDI**	**p**
Se (% - CI 95 %)	51 [42-60]	88 [82-93]	< 0.001	41 [29-54]	59 [46-71]	< 0.001	42 [22-63]	71 [49-87]	< 0.05
Sp (% - CI 95 %)	98 [92-100]	75 [63-84]	< 0.001	100 [97-100]	99 [96-100]	< 0.001	99 [97-100]	99 [96-100]	NS
LR + (% - CI 95 %)	34.32 [4.87-242]	3.46 [2.28-5.25]			74.81 [10.5-533]		69.17 [9.26-516.53]	58.79 [14.48-238.72]	
LR - (% - CI 95 %)	0.50 [0.41-0.59]	0.16 [0.10-0.27]		0.59 [0.48-0.73]	0.41 [0.3-0.55]		0.59 [0.42-0.82]	0.30 [0.16-0.55]	

Sensitivity, specificity and likelihood ratios derived from the 2 methods and compared to simultaneous polysomnography in women and men. AHI : apnoea hypopnoea index (provided by the PSG). RDI : respiratory disturbance index (nasal airflow and SpO_2). SMM-RDI : respiratory disturbance index based on nasal airflow, SpO_2 and MMAA. Se : sensitivity; Sp : specificity; LR + : positive likelihood ratio; LR - : negative likelihood ratio. Exact confidence intervals are based on F distribution. NS : Not Significant

Table 2B : Sensitivity, specificity and likelihood ratios derived from the 2 methods and compared to simultaneous polysomnography in men									
MEN	**AHI ≥ 5/h**			**AHI ≥ 15/h**			**AHI ≥ 30/h**		
	RDI	**SMM-RDI**	**p**	**RDI**	**SMM-RDI**	**p**	**RDI**	**SMM-RDI**	**p**
Se (% - CI 95 %)	76 [71-81]	95 [92-97]	< 0.001	58 [52-64]	79 [74-84]	< 0.001	54 [45-62]	68 [59-75]	< 0.001
Sp (% - CI 95 %)	93 [81-98]	67 [51-81]	< 0.001	98 [94-100]	92 [86-96]	< 0.01	100 [98-100]	100 [98-100]	NS
LR + (% - CI 95 %)	10.93 [3.66-32.61]	2.93 [1.90-4.50]		26.5 [8.61-81.56]	9.89 [5.60-17.50]			158.83 [22.39-1126.52]	
LR - (% - CI 95 %)	0.26 [0.21-0.31]	0.07 [0.04-0.12]		0.43 [0.37-0.50]	0.22 [0.17-0.29]		0.46 [0.39-0.55]	0.33 [0.26-0.41]	

Sensitivity, specificity and likelihood ratios derived from the 2 methods and compared to simultaneous polysomnography in women and men. AHI : apnoea hypopnoea index (provided by the PSG). RDI : respiratory disturbance index (nasal airflow and SpO_2). SMM-RDI : respiratory disturbance index based on nasal airflow, SpO_2 and MMAA. Se : sensitivity; Sp : specificity; LR + : positive likelihood ratio; LR - : negative likelihood ratio. Exact confidence intervals are based on F distribution. NS : Not Significant.

3. Gender specificities and comparison between men and women

Snoring and apnoea were significantly more frequently related by men (respectively 41 % versus 25 %; $p < 0.001$ and 26 % versus 6 %; $p < 0.001$). Men had more cardiovascular co-morbidities (14 % versus 6 % ; $p < 0.005$) but not hypertension (36 % men and 31 % women; p : 0.091). Lack of sleep (reported difficulties initiating or maintaining sleep) was more frequently related by women (18 % versus 5 %; $p < 0.001$) but this did not translate into more frequent use of benzodiazepines (18 % in women versus 14 % in men; p : NS). Epworth Sleepiness Score (ESS) was not statistically different in men (10 ± 5) and women (11 ± 10; p : NS). In both groups, for the three sub-groups defined by the three different AHI thresholds (≥ 5/h; ≥ 15/h; ≥ 30/h), ESS was not significantly correlated with AHI.

There were significant gender differences in non-vascular co-morbidities such as asthma and psychiatric disorder (mainly depression). In both men and women, the correlation between AHI and BMI was statistically significant ($p < 0.001$). Multiple regression showed that AHI was independently influenced by BMI ($p < 0.001$), age ($p < 0.001$) and gender ($p < 0.001$).

Mean SpO_2 was significantly lower in men (94.0 ± 5.2 %) than in women (95.2 ± 6.7 % ; $p < 0.001$) and the time spent below 90 % SpO_2 during sleep was significantly higher in men (36.8 ± 76.2 min) than in women (14.8 ± 56.3 min; $p < 0.001$).

Men had a significantly higher mean RDI (17.7 ± 19.6/h), and SMM-RDI (22.8 ± 19.4/h) compared with women RDI (7.5 ± 13.0/h) and SMM-RDI (12.1 ± 14.4/h; $p < 0.001$ for both). TST and TDT were not statistically different between genders, respectively 416 ± 94 and 549 ± 88 minutes in men, and 426 ± 107 and 562 ± 94 minutes in women.

The correlation coefficient of the relationship between AHI and RDI in women and men (respectively 0.91 and 0.93) and between AHI and SMM-RDI (respectively 0.94 and 0.95) did not significantly differ (table 3).

Table 3 : Correlations, Bland & Altman difference and limits of agreement in each gender which are compared to each other			
	WOMEN (189)	**MEN (381)**	**Comparison between the 2 groups**
AHI (h^{-1})	15.5 ± 19	28.6 ± 24.0	< 0.001
TST	426 ± 107	416 ± 94	NS
TDT	562 ± 94	549 ± 88	NS
RDI (h^{-1})	7.5 ± 13.0	17.7 ± 19.6	< 0.001
Dif RDI-AHI	- 8.0 ± 9.1	- 11.0 ± 9.1	< 0.001
B&A Limits of agreement	[9.8; -25.9]	[6.9; -28.9]	
Pearson correlation r	0.91	0.93	NS
SMM-RDI (h^{-1})	12.1 ± 14.4	22.8 ± 19.4	< 0.001
Dif SMM-RDI - AHI	- 3.4 ± 7.4	- 6.0 ± 8.2	< 0.001
B&A Limits of agreement	[11.1; -18]	[10.2; -22]	
Pearson correlation r	0.94	0.95	NS

AHI : apnoea hypopnoea index (provided by the PSG).TST : total sleep time. TDT : total dark time. RDI : respiratory disturbance index (nasal airflow and SpO_2). Dif RDI-AHI : the difference between AHI and RDI. B&A : Bland & Altman. SMM-RDI : respiratory disturbance index based on nasal airflow, SpO_2 and MMAA. Dif SMM-RDI - AHI : the difference between AHI and SMM-RDI. NS : not significant. All the data are Mean ± SD except limits of agreement and r Pearson correlation with AHI.

Se of both automated methods was significantly lower in the women than in the men for the detection of both mild to severe (AHI ≥ 5/h) ($p < 0.001$ for RDI and p : 0.005 for SMM-RDI) and moderate to severe (AHI ≥ 15/h) OSA ($p < 0.05$ for RDI and $p < 0.001$ for SMM-RDI). Moreover, Sp of SMM-RDI for the detection of moderate to severe disease (AHI ≥ 15/h) was significantly higher in female (p : 0.005) whilst remaining above 90 % in both genders. However, the Se (table 4) and Sp (table 5) of both automated methods did not significantly differ between genders for the detection of severe OSA (AHI > 30/h).

Table 4 : Comparisons of AHI-RDI and AHI-SMM-RDI sensitivities between women and men

Sensitivity	Women	Men	P
RDI			
≥ 5 h^{-1}	51	76	< 0.001
≥ 15 h^{-1}	41	58	< 0.05
≥ 30 h^{-1}	42	54	NS
SMM-RDI			
≥ 5 h^{-1}	88	95	0.005
≥ 15 h^{-1}	59	79	< 0.001
≥ 30 h^{-1}	71	68	NS

Table 5 : Comparisons of AHI-RDI and AHI-SMM-RDI specificities between women and men

Specificity	Women	Men	P
RDI			
≥ 5 h^{-1}	98	93	NS
≥ 15 h^{-1}	100	98	NS
≥ 30 h^{-1}	99	100	NS
SMM-RDI			
≥ 5 h^{-1}	75	67	NS
≥ 15 h^{-1}	99	92	0.005
≥ 30 h^{-1}	99	100	NS

DISCUSSION

In this prospective study, we compared attended polysomnography to 2 automated methods, with or without MMAA provided by a distance meter and added to airflow and oxygen saturation analysis for the detection of respiratory events in 381 men and 189 women. A comparison between genders was performed. In both genders, correlations between RDI and AHI as well as Se were improved significantly by adding the MMAA (SMM-RDI).

In patients with severe disease (AHI ≥ 30/h) SMM-RDI Se and Sp were similar in both genders. The comparison of the two automated methods between genders showed that the Se of both RDI and SMM-RDI was significantly lower in women for mild to severe (AHI ≥ 5/h) and moderate to severe (AHI ≥ 15/h) diseases. The analysis of the mean SpO_2 during sleep showed a significantly lower value in men ($p < 0.001$). This was most probably explained by a significantly higher BMI in men. Accordingly, the higher Se observed of both automated methods in men for the diagnosis of both mild to severe and moderate to severe disease could be explained by a better detection of hypopnoea associated with oxygen desaturation in this gender. Indeed, due to the curvilinear shape of the oxyhemoglobin dissociation curve, a hypopnoea of similar duration is more likely to induce a significant desaturation if the initial SpO_2 is lower. Moreover, as functional residual capacity is inversely correlated to BMI, a similar decrease in ventilation will be associated with a higher drop in PaO_2 in more obese subjects. This could explain why the difference of Se between genders was observed with the RDI as well as the SMM-RDI. In men and women patients with severe disease (AHI ≥ 30/h) SMM-RDI sensitivities are not significantly different because apnoeas and hypopnoeas are more frequent and probably longer, leading to desaturation or typical SMM. Moreover, for the SMM-RDI,

another reason could be evoked for the gender differences in Se : the smaller amplitude of the mandible oscillations linked to respiratory effort in women. In our study, this movement which is thought to be a surrogate for cortical arousal, is used in hypopnoea recognition not defined by the presence of desaturation. The MMAA deals with absolute values and not values expressed as a percentage of the maximal amplitude of the voluntary mandible movement used for calibration. A SMM was considered as a relevant arousal for hypopnoea definition if its maximal value was greater or equal to 1 (which corresponds to a movement of an absolute amplitude around 1mm) and two times greater than the average of the movement values during the related event. As described by Lewis et al., there are sex differences in mandibular opening distances which appear to be due to the combined effects of mandibular length and mandibular rotation.[22] The amplitude of the oscillatory movements of the mandible and the distance linked to the elevation of the mandible could differ in men and women. Accordingly, an adapted definition for SMM might be needed in women. In addition, a higher resolution of the signal to detect mandible oscillation could be necessary in women with mild and moderate disease. For patients suffering from severe disease (AHI $\geq$ 30/h), the movements could have more amplitude, thus reducing the differences between genders in predictive parameters.

As we believe that the mandible movement occurs passively, secondary to respiratory efforts[23], the REM sleep atonia may induce a reduction of respiratory effort[24] and mandible movement. Since REM AHI is recognized as being higher in women than men[17-19] this might also explain a reduced sensitivity of the SMM-RDI for diagnosing OSA in women.

The mean underestimation SMM-RDI - AHI was -3.4 ± 7.4 in women and -6.0 ± 8.2 in men. This difference was in proportion to the difference in AHI between the 2 genders (15.5 ± 19.0/h in women and 28.6 ± 24.0/h

in men). There was also a significant difference in BMI between genders. The link between OSAS and obesity has been frequently related in prospective cohort study and is unquestionable.[25] A multiple regression analysis showed that BMI, age and gender independently influenced AHI. In our cohort, the correlations between the three indexes were not significantly different between genders.

Recent studies showed other gender differences in complaints, co-morbidities and polysomnographic features in OSAS.[15,26-27] In the present study, the complaint of "lack of sleep" was more frequent in women without more frequent use of benzodiazepines than in men or significant differences in TST between genders measured on the PSG. The TST observed in the present population is in the expected range for age and gender. [28]

There could be a link between related psychiatric disorder reported by 27 % women and 11 % male ($p < 0.001$) (mainly depression) and the complaint of lack of sleep in women (18 % of her and 5 % in men). Insomnia due to mental disorder is more prevalent in women than in men. The main final diagnosis was insomnia/anxiety/depression in 75 patients (13 %) among them 45 women (8 %). But Shepertycky et al. found that women had a significantly higher incidence of depression (OR = 4.6) and complaints of insomnia in case of sleep disordered breathing.[27] We did not use questionnaires to assess functional status and mood disturbance at baseline. This has been related in the medical history and based on history taking : it is difficult to distinguish, in this study, how these gender characteristics differences in complaints are linked to the identified dyssomnia.

The prevalence of hypertension is similar in both groups and not higher in men despite higher OSA severity index and prevalence. The reason is probably that hypertension is recognized as an indication for polysomnographic exploration and in this way, causes a selection bias.

As mentioned in the first part of this chapter, the present study has several limitations. Despite the specific complaint of women, TST and TDT do not differ significantly between the genders and so do not contribute to the gender differences of indexes issued from automated analysis.

Despite these anatomic and sleep related differences between genders, correlation of the SMM-RDI with AHI and the added value of MMAA to a simple portable device were excellent in both men and women.

CONCLUSION

In the field of apnoeas and hypopnoeas screening devices, few data regarding women are currently available.

In our cohort including a large proportion of women, SMM-RDI correlations with PSG were excellent in both genders. The addition of MMAA to NAF and oxygen saturation analysis significantly improved the accuracy for the detection of respiratory events in both men and women. This added value occurred in both genders.

To improve the sensitivity of SMM-RDI in women, a specific SMM definition may be required.

REFERENCES

1. Miyamoto K, Özbek M.M., Lowe A.A. et al. Mandibular posture during sleep in healthy adults. Arch. Oral Biol. 1998; 43 : 269-275.
2. Miyamoto K., Özbek M.M., Lowe A.A. et al. Mandibular posture during sleep in patients with obstructive sleep apnoea. Arch. Oral Biol. 1999; 44 : 657-664.
3. Sjöholm T.T., Lowe A.A., Miyamoto K., Fleetham J.A., Ryan C.F. Sleep bruxism in patients with sleep-disordered breathing. Arch. Oral Biol.; 2000, 45 : 889-896.
4. Senny F., Destiné J., Poirrier R. Midsagittal jaw movement analysis for the scoring of sleep apnoeas and hypopnoeas. IEEE Trans. Biomed. Eng. 2008; 55(1) : 87-95.
5. Rechtschaffen A., Kales A. A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. National Institutes of Health. Washington, DC, 1968.
6. ASDA (American Sleep Disorders Association and Sleep Research Society) Atlas task Force. EEG arousals : Scoring rules and examples. Sleep 1992; 15 : 173–84.
7. Cohen A. Comparison of correlated correlations. Stat. Med. 1989; 8 : 1485-1495.
8. Masa, J.F., Corral, J., Pereira, R. et al. Effectiveness of home respiratory polygraphy for the diagnosis of sleep apnoea and hypopoea syndrome. Thorax, 2011, 66 : 567-573.
9. Meoli A.L., Casey K.R., Clark R.W. et al. Clinical Practice Review Committee. Hypopnoea in sleep disordered breathing in adults. Sleep 2001; 24(4) : 469-470.

10. Centers for Medicare and Medicaid Services. National Coverage Determination for Continuous Positive Airway Pressure (CPAP) Therapy for Obstructive Sleep Apnoea (OSA). NCD#240.4.2005[cited 2008 22 september]; available from : http://www.cms.hhs.gov.
11. Ruehland W.R., Rochford P.R., O'Donoghue F.J., Pierce R.L., Singh P., Thornton A.T. The new AASM criteria for scoring hypopnoeas : impact on the apnoea hypopnoea index. Sleep 2009, 32(2):150-157.
12. Senny F., Maury G., Cambron L., Leroux A, Destiné J., Poirrier R. The sleep/wake state scoring from mandible movement signal. Sleep Breath. 2012 ; 16(2) : 535-542.
13. Flemons W.W., Littner M.R., Rowley J.A. et al. Home diagnosis of Sleep Apnoea : a systematic review of the literature. Chest 2003; 124 : 1543-1579.
14. Flemons W.W., Littner M.R. Measuring agreement between diagnostic devices. Chest 2003; 124 : 1535-1542.
15. Bixler E.O., Vgontzas A.N., Lin H.M., Ten Have T., Rein J. et al. Prevalence of sleep-disordered breathing in women : effects of gender. Am J Respir Crit Care Med 2001; 163 (3Pt1) : 608-613.
16. American Academy of Sleep Medicine. The international classification of sleep disorders revised. Diagnostic and coding manual. Chicago, Illinois, 2005.
17. Ye L, Pien G.W., Ratcliffe S., Weaver T.E. Gender differences in obstructive sleep apnoea and treatment response to continuous positive airway pressure. J Clin Sleep Med 2009; 5 : 512-518.
18. O'Connor C., Thornley K.S., Hanly P.J. Gender differences in the polysomnographic features of obstructive sleep apnoea. Am J Respir Crit Care Med 2000; 161 : 1465-1472.

19. Vagiakis E., Kapsimalis F., Lagogianni I., Perraki H., Minaritzoglou A. et al. Gender differences on polysomnographic findings in Greek subjects with obstructive sleep apnoea syndrome. Sleep Medicine 2006; 7 : 424-430.
20. Ware J.C., McBrayer R.H., Scott J.A. Influence of sex and age on duration and frequency of sleep apnoea events. Sleep 2000; 23:165-170.
21. Gjevre J.A. Taylor-Gjevre R.M, Skomro R., Reid J., Fenton M. et al. Comparison of polysomnographic and portable home monitoring assessments of obstructive sleep apnoea in Saskatchewan women. Can respir J 2011; 18 : 271-274.
22. Lewis R.P., Buschang P.H., Throckmorton G.S. Sex differences in mandibular movements during opening and closing. Am. J. Orthod. Dentofacial Orthop. 2001; 120 : 294-303.
23. Van de Graaff W.B. Thoracic influence on upper airway patency. J.Appl.Physiol 1988; 65 : 2124-2131.
24. Krieger J., Sforza E., Boudewijns A., Zamagnie M., Petiau C. Respiratory effort during obstructive sleep apnoea. Chest 1997; 112 : 875-849.
25. Peppard P.E., Young T., Palta M., Dempsey J., Skatrud J. Longitudinal study of moderate weight change and sleep-disordered breathing. JAMA 2000; 284 : 3015-3021.
26. Gillin J.C., Duncan W.C., Murphy D.L., Post R.M., Wehr T.A. et al. Age-related changes in sleep in depressed and normal subjects. Psychiatry Research 1981; 4 : 73-78.
27. Shepertycky M.R., Banno K., Kryger M.H. Differences between men and women in the clinical presentation of patients diagnosed with obstructive sleep apnoea syndrome. Sleep 2005; 28 : 309-314.

28. Ohayon M.M., Carskadon M.A., Guilleminault C., Vitiello M.V. Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals : developing normative sleep values across the human lifespan. Sleep 2004; 27 : 1255-1273.