Characterization Of Chimeric Surface Submentalis EMG Activity During Hypopneas In Obstructive Sleep Apnea Patients

MAK A. Daulatzai, Ahsan H. Khandoker, Chandan K. Karmakar, Marimuthu Palaniswami
Sleep Disorder Group, Dept. of EEE
The University of Melbourne
Melbourne, Australia
makd@unimelb.edu.au

Neela Khan
Faculty of Life and Social Sciences
Swinburne University
Melbourne, Australia

Abstract— **Polysomnogram (PSG) is the standard diagnostic test for the evaluation of sleep disorders. The current rules require surface (s) electromyography (EMG) of the submentalis muscle (SM) in order to document atonia during REM sleep. The sSM EMG signals reflect contracting motor units; the firing of the latter is a function of intrinsic neuromuscular characteristics of its component muscle fibers, and indeed forms the basis for the spectral properties. Here we have studied OSA patients with apnea-hypopnea index (AHI) of <5, 5-10, 30-35, and 60+, and document, for the first time, a "Chimeric" sSM EMG activity phenotype during hypopneas in Non-REM sleep. This unique pattern characteristically displays contiguous tonic-phasic segments of high activity and low activity or vice versa. We have analyzed the total duration, and other attributes of these hybrids in comparison with the normal awake and apnea/hypopnea-free sleep periods. We document an inherent heterogeneity between hypopneas, and between heterogeneous segments of the chimeras in OSA patients of varying AHI. This study emphasizes that rectified and filtered sSM EMG activity signals provide a novel, valid and useful metric in PSG evaluation which may be of clinical significance in sleep-related and other pathological conditions.**

Keywords- polysomnogram, surface electromyography, submentalis muscle, apnea-hypopnea index, Chimeras, hybrid activity, novel metric, sleep diseases

I. INTRODUCTION

Obstructive sleep apnea (OSA) is a major risk factor for a number of clinical conditions. These include cardiovascular conditions including hypertension [1-3], myocardial infarction [4, 5], neurocognitive impairment [6], stroke and sudden death [7, 8]. It is also linked to various other diseases such as memory perturbations, depression, and poor cognition performance [9]. Sleep disordered breathing ranges from snoring through increased airway resistance and reduction in airflow (hypopnea) to periods of breathing cessation and airway collapse (apnea). Apnea-hypopnea index (AHI) is the average number of apnea and hypopnea per hour of sleep. The AHI number is taken to characterize the severity of OSA. An AHI of >5 is generally regarded as abnormal. Mild disease is reflected by 5-15 AHI, moderate by 15-30, and severe by an AHI greater than 30 per hour. UA negative pressure is the critical factor, and the UA occlusion during sleep is caused by the subatmospheric pharyngeal pressure during respiration, and reduced UA dilator muscle activity [10-13]. OSA causes hypoxemia, multiple arousals (resulting in daytime sleepiness) increased respiratory effort, sleep fragmentation, and various pathophysiological sequelae [14].

The classical epidemiological data have characterized hypopnea utilizing thermisters and/or inductance plethysmography in association with a 4% oxygen desaturation. However, more recently nasal pressure transducers are used in scoring hypopnea. There are several clinical definitions of hypopnea in use, and hence different labs use different criteria owing to a lack of consensus on this issue [15]. Although hypopnea and apnea are not equal and differ significantly, the physiological outcome of hypopneas have been considered in various studies to be similar to that of apnea. Despite the fact that consequences of hypopnea in low AHI subjects may seem not to translate in significant pathology, in the long run however, they are devastating since it is the progression in quality and quantity of hypopneas that eventually results in the genesis of apnea and OSA-associated co-morbidities. As such studies that may throw any light on different facets of hypopnea are called for.

An important component of polysomnograms (PSG) is surface submental electromyography (sSM EMG). This is a non-invasive method that depicts electrical activity from submental as well as from the muscles in its close proximity. sEMG sensors are placed in and around the submental area between the mandible and the hyoid bone, and as such measures muscles of the mouth floor [16]. Although sSM EMG has been extensively studied in dysphagic patients, there

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are very few detailed studies on the characteristic features of sSM EMG activity during specific breathing events in OSA patients. Therefore, we recently studied the qualitative and quantitative characteristics of the submentalis sEMG activity signals and its related parameter, with emphasis on phenotypic sSM EMG activity patterns during hypopneas in PSG of patients from varying AHI groups [17]. We have documented in our above mentioned paper an inherent heterogeneity of sSM EMG activity pattern in hypopneas, in that some hypopneas showed a higher tonic-phasic, or predominantly phasic activity, while some showed a much lower activity, yet others displayed a rhythmic pattern of activity oscillation. However, there was yet another variety of hypopneas that were characterized by a segment each of high and low tonic-phasic activity, within the same hypopneic event. We termed this variety of combined activity pattern "chimeric" or "hybrid". Here we have focused on the characteristic hypopnea variety that displays this particular chimeric pattern in OSA patients from different AHI groups, ranging from very low to very high AHI. This study is optimistic and anticipates that rectified and filtered sSM EMG activity signal should be studied as a novel metric in routinely collected PSG data in order to gain additional insight in sleep-related and other disorders.

II. Material and Methods

A total of 18 subjects were studied in this study. There were 13 males and 5 females. The mean age was 18 to 66. The range of age of the patients placed in the four AHI groups, of <5, 5-10, 30-34, and 60-80 was 35.30, 49.60, 49.80, and 52.60 (%) years respectively. There were no subjects beyond 76 years of age. This study conducted a full polysomnographic (PSG) diagnostic in-laboratory study on the patients during the latter part of 2008. All patients were studied for clinical confirmation of OSA by PSG. The subjects did not suffer from respiratory failure, nor was any one of them on supplemental oxygen.

The nocturnal PSG recording data were collected from patients suffering from snoring, hypopnea and OSA. They were otherwise fit and took no CNS drugs and refrained from coffee and wine the day before PSG to avoid any interfere with their sleep. The subjects fell asleep in less than 30 minutes, slept for six and a half hours, and their usual occasional nocturnal awakening were never prolonged. They first familiarized themselves with the sleep laboratory and the technique of PSG recordings to be used. The PSG study was done in a partially soundproof recording area in a standard sleep laboratory setting in order to avoid non-physiological arousals and any environmental stimuli. All subjects were monitored by personnel experienced in sleep disorders, and video cameras. The PSG signals were recorded continuously from each subject, and this included measurements of :- air flow (nasal pressure), oxygen saturation (finger pulse oximetry), transcutaneous carbon dioxide values, movements of thoracic and abdominal excursion (inductance plethysmography), eye movements (electrooculogram), heart rate (electrocardiogram), sSM EMG, lower limb (right and left tibialis anterior) movement (piezoelectric signals), and electroencephalogram (EEG) (C3/A2). Oximetry was carried out using a Nellcore N-595 (Nellcor Inc. boulder, Colorado, USA) set to shortest averaging time (2-4 seconds) and sampled at 5Hz. PSGs were recorded using compumedics E-series equipment. All signals were recorded in digital form on a magnetic tape. The chart record was annotated at 10 second intervals by the PC with time from the very start of data acquisition; this allowed the chart records to be synchronized with the corresponding digitized signals. The analysis of conventional sleep stages, hypopnea, apnea, arousals, and delta waves was based on the central EEG derivation, as per the ASDA guidelines [18] in standard 30 second epochs. On the basis of their AHI (i.e. number of apnea/hypopnea per hour), the subjects were allocated to four groups: <5, 5-8, 30-34, and 60-80. A total of 2732 epochs were studied and particular emphasis was placed on the arousals, quantitative analysis plus qualitative analysis of tonic-phasic configuration of sSM EMG activity during hypopneas in non-REM sleep stages 1 through 4; REM sleep was not considered. Two experienced sleep scientists scored the data manually for sleep stages, sleep EEG signals, hypopnea and OSA. Apnea was defined as the cessation of oro-nasal airflow of a minimal duration of 10 s, while a lack of persistent thoraco-abdominal excursions during apnea rendered them obstructive. The following criteria were used for an event to be labelled as hypopnea: 1. substantial reduction in airflow, i.e. 50% or more, 2. moderate reduction in airflow, i.e. less than 50% associated with >3% desaturation, and 3. moderate reduction in airflow, i.e. less than 50% associated with EEG evidence of arousal [18]. Sleep was staged according to standard criteria [18]. For purposes of analysis presented here, care was taken not to include any hypopnea that immediately followed or preceded awakening, arousal or delta wave, since EEG associated with these is considered to be suggestive of an awake sate.

We have used the standard median filter for eliminating the ECG artifacts while preserving the EMG content in the original signal, as much as possible. Using median filter this has been achieved by taking advantage of the quasi-periodic characteristics of the ECG signal, and this kind of template subtracting has proved to be a good way to remove the ECG artifacts, without sacrificing sections of the EMG signal [19]. We used the median filter with window length-9 for formulating the ECG template, and then subtracting the template from the EMG signal. All statistical features were calculated using statistics toolbox of MATLAB 2008a.

III. Results

Our observations indicate that either an increased or decreased tonic-phasic sSM EMG activity pattern exists during different hypopneas in all N–REM sleep stages, although not in the same patient (Figs. 1, 2, 4). The hypopneas possessing the chimeric activity pattern (Fig. 4) were minimal in the PSGs of subjects having <5 AHI. These were present only occasionally in patients having 5 to 10 AHI. However, the PSGs of patients in the AHI 30 to 34 range were replete with hypopneas of chimeric pattern. The latter was minimal in the hypopneas of AHI 60 to 80, where predominantly phasic variety of "varicosity" activity pattern (Fig.3) was present. Duration of the chimeric hypopneas differed significantly – from very brief to very long. Although the chimeric hypopneas were present in all sleep stages, they were quite common in stage 2. The two

segments of the hybrid hypopneas spatially were either High followed by low, or low followed by high activity signal. Occasionally, the above activity patterns were tripartite, in that some hypopnease had segments of "High, low, and high again", or "Low, high, and low again". Not uncommonly, one segment of either high or low activity was present in one sleep stage (e.g. in stage 2), and the reciprocal second segment was located in another sleep stage (e.g. in stage 3).

It was of interest to note a higher variability in the sSM EMG activity in awake subjects of AHI <5 or 5-10 (Figs. 5, 6); a lesser variability existed in patients of AHI 30 and higher. The so-called normal sleep of the patients (i.e. sleep period without adverse breathing events of hypopnea and apnea), exhibited least activity variability in subjects of the three AHI groups (5-10, 30-35, 60+) studied. During the entire duration of hypopnea with chimera, the activity displayed lesser variability- hence the data were consistent in both lower AHI 5-10, and 60+. However, any variability noticed was a function of age of the patients from the AHI group 30-35. Those aged 40 and below had twice as much inherent variation in activity compared with those aged 50 and higher. While the sSM EMG activity in the low activity segment of chimera (whether it was the first or the second of the two segments) was consistently low and uniform in all AHI and age groups; however, the higher activity segment in the chimeric hypopnea was the most variable (Figs. 7, 8). In comparison with AHI 5-10 subjects, patients in AHI 30-35 and 60+ groups had twice as much activity. However, again the activity variability was age-related, in that a 29 year-old patient displayed slightly more (0.7) activity than those from the AHI 5-10 group (0.5).

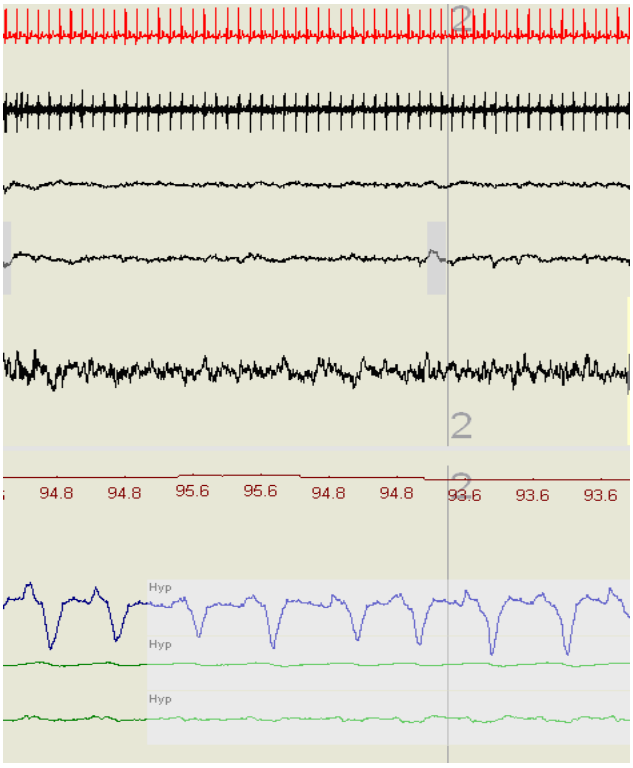

Figure 2. Polysomnogram. Showing a second pattern of surface submentalis complex EMG activity during hypopnea. Note the low activity, compare with Figs. 1, 3 and 4.

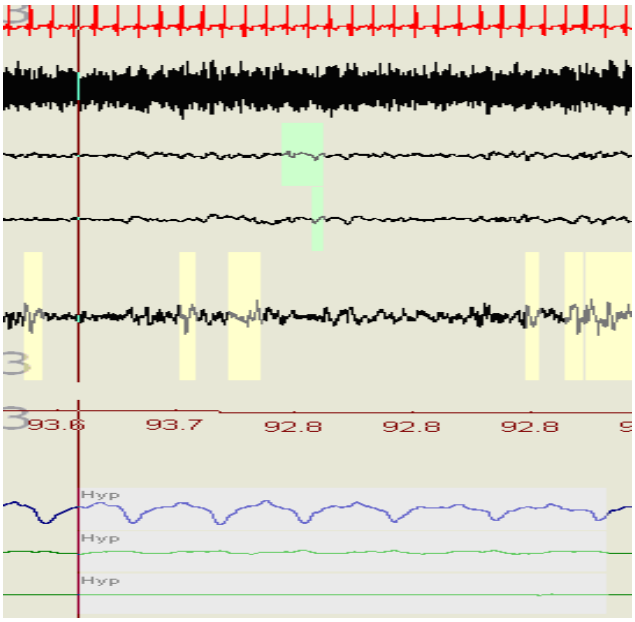

Figure 1. Polysomnogram. Showing a pattern of surface submentalis complex EMG activity during hypopnea. Note the higher activity, compare with Figs. 2-4. Traces from top to bottom are: ECG, EMG, 2 traces of EOG, EEG, Plethysmogram, Nasal pressure, Thoracic activity, Abdominal activity. The order of traces is identical in Figs. 2-4.

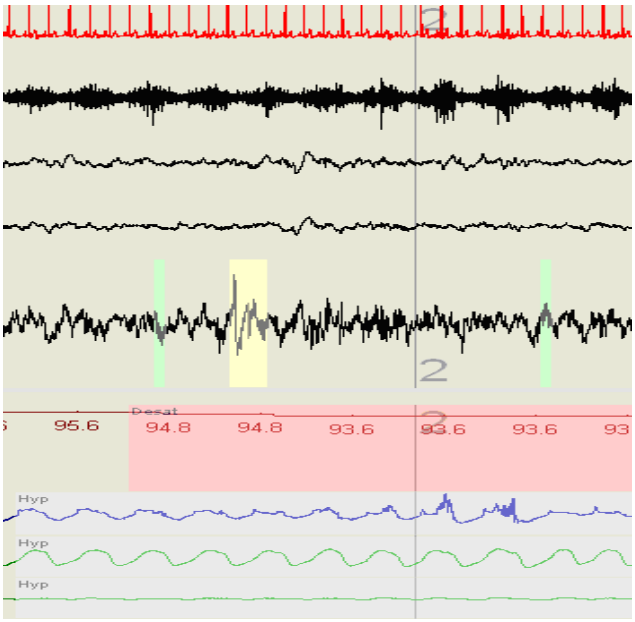

Figure 3. Polysomnogram. Showing a third variety of surface submentalis complex EMG activity during hypopnea. Note the rhythmic oscillating beaded pattern of activity, compare with Figs. 1, 2 and 4.

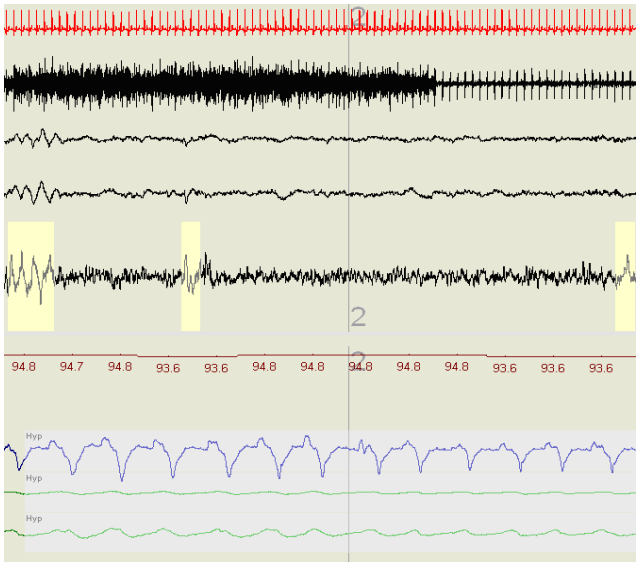

Figure 4. Polysomnogram. Showing surface submentalis complex EMG activity pattern termed "Chimeric or Hybrid". Note both high and low activity components in the same hypopnea. Compare with Figs. 1-3.

IV. Discussion

This study emphasizes that the sSM EMG activity is not quiescent and uniform, in fact it is dynamic, heterogeneous and in a state of flux. It has phases of higher and lower activity that oscillate regularly; accordingly the group of epochs that display such activity patterns alternate. Further, epochs possessing higher or lower sSM EMG activity signals also contained hypopneas that mimic similar activity. However, the variability noted in activity during awake period in low AHI subjects reflects possible phasic and tonic contractility in different floor-of-mouth muscles. Such disparate firing of motor units seems to be minimal in patients of higher AHI. Importantly, regardless of AHI or age in a given higher AHI group, all patients appear to demonstrate a similarly depressed variability in terms of activity heterogeneity. Thus, sleep plus a higher AHI have a conjoint dampening effect on the muscles responsible for the sSM EMG activity signals. Our assumption was that during sleep devoid of respiratory events (apnea-hypopnea), subjects of lower AHI (5-10) and particularly those of younger age would possess invariably sustained higher activity levels, but this was not the case. This was noticed during the high activity epochs and high activity chimeric segments, but not in the low activity epochs or low activity chimeric segments of hypopneas. This is possibly due to an attempt by the mouth floor muscles to supplement GG activity to keep the upper airway (UA) patent; however, such an effort was only ephemeral, and presumably the muscular fatigue in conjunction with other physiological factors results in activity depression seen in the low activity epochs and hybrid segments [20-22]. At the end of lower activity epochs or segment, there appears to be a higher efferent output from the higher centers and the higher activity epochs then recommence.

The sleep architecture changes in a number of ways due to hypopnea, apnea, and the process of aging [23, 24]. These changes may include increases in sleep latency, in stages 1 and 2, and duration of awake period after sleep onset; there are however, decreases in total sleep time, sleep efficiency, the percentages of slow wave and REM sleep. The prevalence of OSA is about three times higher in older (≥ 65 yr) compared with 30-64 yr old (middle aged) persons [25]. Thus analogously, it is not unexpected that the younger subjects in this study possess higher sSM EMG activity variability attribute than the older ones. The pathophysiological causes as to why the sSM EMG activity vary in younger and lower AHI subjects, but not in the older subjects with severe disease (very high AHI) as depicted here, are possibly related to propensity and capability of dilatory muscles to restore airflow without arousal. Other important factor(s) producing notable decreases in sSM EMG activity variability in older patients, particularly those with higher AHI, may be correlated with the their dysfunctional sensory-motor UA neuromuscular reflex. The latter has been shown repeatedly to cause pharyngeal occlusion and respiratory depression during sleep. Of course, other state-related UA and lower airway changes are expected to play a possible role also in influencing the contractile physiological traits of motor units in SM muscle complex of these patients.

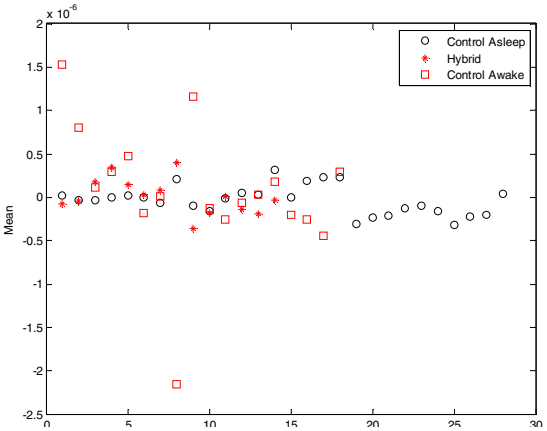

Figure 5. Mean surface submentalis complex EMG activity for Control awake, control asleep, and chimeric hypopneic total period.

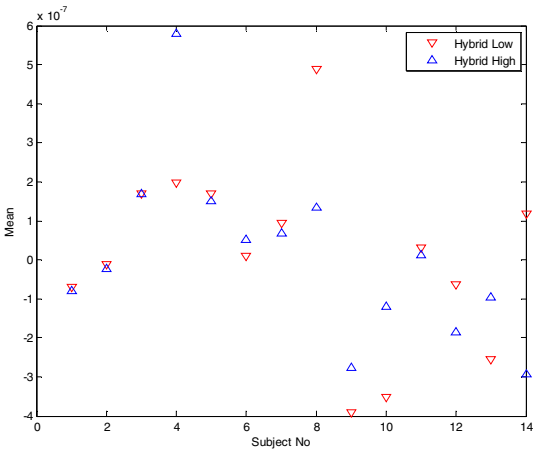

Figure 6. Mean surface submentalis complex EMG activity for the individual high or low activity segments during the chimeric hypopneic period.

EMG signals are detected by placing electrodes either intramuscularly or on the skin surface near the muscle of interest. The bioelectrical conduction of skeletal muscle function occurs through surrounding soft tissues between its source and the recording electrode, and this invariably impacts on the spatial and temporal attributes of the sEMG [26, 27]. Further, sEMG signals arise not only from the muscle of interest but also from muscles located in close proximity of the muscle and electrode. Thus, sEMG reflects an estimate of the conjoint activity of muscles located in region of the electrode. Accordingly, the sEMG recorded from SM region is considered to reflect the differing activity from various muscles located at the mouth floor. Specifically, these include - the mylohyoid, geniohyoid, and digastric (anterior belly) muscles. These muscles have been shown to help advance the mandible, and position the tongue more anteriorly, thus increasing the occlusal vertical dimension, and resulting in opening of the pharyngeal lumen [11, 29]. Consequently, the latter reduces UA resistance keeping the airway patent during sleep.

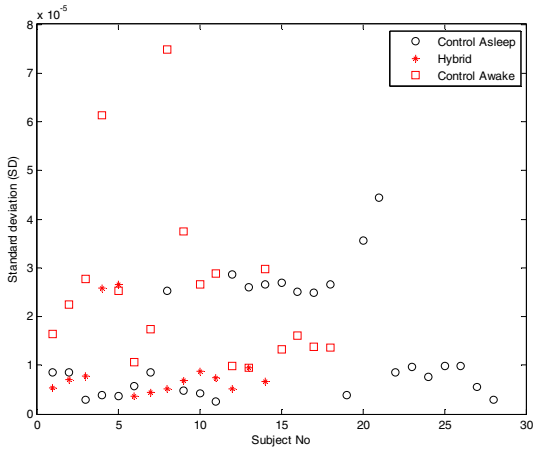

Figure 7. Standard Deviation (SD) of surface submentalis complex EMG activity for Control awake, control asleep, and chimeric hypopneic total period.

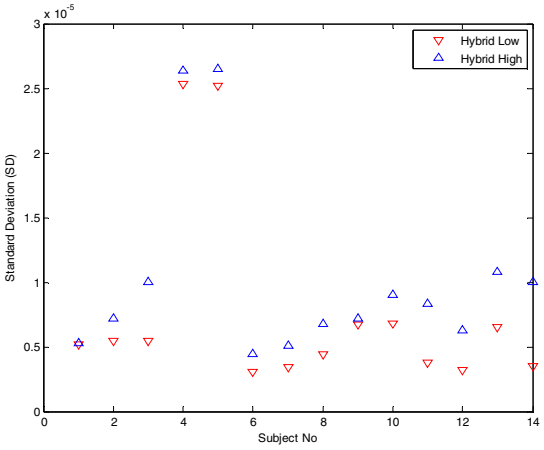

Figure 8. Standard Deviation (SD) of surface submentalis complex EMG activity for the individual high or low activity segments during the chimeric hypopneic period.

UA reflexes play an important role in mediating tonic-phasic activity in UA dilator muscles [20-22]. Further, negative pressure alterations in UA, as noted in OSA, can inhibit inspiratory pump muscles. When dilator activity of GG does not keep pace with the pharyngeal collapsing forces at sleep commencement, it is not unreasonable to assume that other dilators such as muscles of the floor-of-mouth, may participate in patenting the collapsing pharynx, and this is manifested in the higher sSM EMG activity signal noted in many OSA patients. Thus the balance of power may shift from GG to these compensatory dilators, and the afferent input stimulation by the pharyngeal collapse may enhance the efferent output to the bottom-of mouth muscles also, as a compensatory mechanism in order to supplement the dilatory function in an effort to overcome any ongoing pharyngeal collapse. Leiter et al. (1992) [28] posit that depending on the nature of airflow, the pharynx may not always reflexly activate the GG. Thus different hyoid muscles including the submentalis muscle complex that are involved in protruding mandible, plus tensor veli palitini, may increase pharyngeal pressure as dilators as well [11, 29]. It is important to consider that a central efferent output to these muscles conceivably enhances their tonic-phasic activity in order to maintain pharyngeal patency. Both UA receptors and the afferents from these muscles conceivably convey afferent inputs. To the extent that this argument is true, it would mean that given any paucity in dilatory activity of GG, stimulation of other relevant muscles can provide reflex compensatory function in order to dilate and stiffen the pharynx.

There is increased magnitude and duration of the sSM EMG signals whenever an increase in pharyngeal function occurs [30]. A similar relationship is understandable between the requirements of occluding pharynx to remain patent and the increase in sSM EMG activity signals. In previous studies, sSM EMG activity recording has shown primary muscle contribution from mylohyoid, digastric (anterior belly), and the geniohyoid muscles, with only minor contribution from platysma and GG. A subject-specific pattern was found, in that a major contribution was noted from one of the three main muscles, and a minor contribution from the remaining two [15, 31]. In the hybrid pattern of sSM EMG activity in hypopnea, one does not know the relative contribution of these muscles in segments of either high or low activity. The variability seen in activity of the chimeras must reflect the variability in the spatiotemporal activity pattern of mouth floor muscles. Further research should address this question in order to estimate a relative contribution of individual muscle of this complex in different varieties of sSM EMG activityincluding the chimera.

It is worth emphasizing that one of the attractive features of the current morphological plus quantitative delineation of sSM EMG activity is the ease of availability from any conventional PSG. While acknowledging however the problem of small sample size, yet the current study clearly documents a new metric in PSG evaluation, specifically involving the sSM EMG activity signals. Such an evaluation, however, requires a careful epoch-by-epoch, and event-by-event analysis. Initially the detection of heterogeneous morphological pattern of activity in epochs and hypopneas is done visually, and then by quantitation. Any chances of misclassification are minimal,

since the phenotypes of sSM EMG activity are robust and clear. The information thus collected would not be trivial, since it basically reflects the neuromuscular contractility level of motor units in the SM muscle complex. Further, this could then be correlated with other PSG signals/traces during different sleep stages and events. In OSA and other sleep disorders, PSG measures the indicators of disease, and its severity, we believe the sSM EMG activity would add further robustness to this clinical evaluation and extrapolation.

Many important questions and criteria should be debated and approved by the research community. The question whether the variety of hypopnea showing chimeric sSM EMG activity we noted herald a significant feature, are significant physiologically remains to be answered. There needs to be discussion and further studies on aspects, such as what sort of control be used? Should the sSM EMG activity be compared with one's own awake, and/or event-free configurational data during sleep. Further, there is a need for formulating a normogram (different age-sex-AHI groups) from available pooled PSG data. This study emphasizes that both visual phenotypic sSM EMG activity signal, and rectified plus filtered data may provide a novel, valid, and useful metric in routinely collected PSGs. Such an evaluation may be of clinical significance in sleep-related and other pathological conditions.

REFERENCES

[1] D. Brooks, R.L. Horner, L.F. Kozar, C.L. Render-Teixeira and E.A. Phillipson, "Obstructive sleep apnoea as a cause of systemic hypertension.", J Clin Invest, vol. 99, pp. 106-109, 1997.

[2] P.E. Peppard, T. Young, M. Palta, and J. Skatrud, "Prospective study of the association between sleep-disordered breathing andhypertension." N Engl J Med, vol. 342, pp. 1378-84, 2000.

[3] J.C. Pepperell, S. Ramdassingh-Dow, N. Crosthwaite, R. Mullins, C. Jenkinson, J.R. Stradling, and R.J. Davie, "Ambulatory blood pressure after therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnea. a randomized parallel trial." Lancet, vol. 359, pp. 204-210, 2002.

[4] L.S. Doherty, J.L. Kiely, V. Swan, and W.T. McNichols, "Long term effects of nasal continuous positive airway pressure therapy on on cardiovascular outcome in sleep apnoea syndrome." Chest, vol. 127, pp. 2076-84, 2005.

[5] J.M. Marin, S.J, Carrizo, E, Vicente, and E, Agusti, "Long-term cardiovascular outcomes in men with obstructive sleep apnea-hypopnea with or without treatment with continuous positive airway pressure; an observational study." Lancet, vol. 365, pp. 1046-53, 2005.

[6] H.C. Kim, T. Young, C.G. Mathews, S.M. Weber, A.R. Woodard, and M. Palta, "Sleep-disordered breathing and neuropsychological deficits. A population-based study." Am J Respir Crit Care Med, vol. 156, pp. 1813-1819, 1997.

[7] T. Arzt, T, Young, L. Finn, J.B. and Skatrud, T.D. Bradley, "Association of Sleep-disordered breathing and the occurrence of stroke." Am J Respir Crit Care Med, vol. 172, pp. 1447-51, 2005

[8] J. Yaggi, J. Concato, W.N. Kernan, J.H. Lichtman, L.M. Brass, and V. Mohsenin, "Obstructive sleep apnea as a risk factor for stroke and death." N Engl J Med, vol. 353, pp. 2034-41.

[9] S. Lis, S. Kreiger, D. Henning, C. Roder, P. Kirsch, W. Seeger, B. Gallhofer, and R. Schulz, "Executive functions and cognitive subprocesses in patients with obstructive sleep apnea." J. Sleep. Res, vol. 17, pp. 271-280, 2008.

[10] R.B. Fogel, J. Trinder, D.P. White, and A. Malhotra, "Within-breath control of genioglossus muscle activation in humans: Effect of sleep-wake state." J Physiol, vol. 550, pp. 899-910, 2003.

[11] R.L. Horner J.A. Innes, M.J. Morrell, S.A. Shea, and A. Guz, "The effect of sleep on reflex genioglossus muscle activation by stimuli of negative airway pressure in humans." J Physiol, vol. 476, pp. 141–151, 1994.

[12] J.R, Wheatley, W.S. Mezzanotte, and D.J. Tangel, "Influence of sleep on genioglossus muscle activation by negative pressure in normal men." Am Rev Respir Dis, vol. 148, pp. 597-605, 1993a.

[13] J.R, Wheatley, D.J. Tangel, W.S Mezzanotte, and D.P. White, "Influence of sleep on response to negative airway pressure of tensor palatini muscle and retropalatal airway." J Appl Physiol, vol. 75, pp. 2117–2124, 1993b.

[14] R.B. Fogel, A. Malhotra, and D.P.White, "Sleep. 2: Pathophysiology of obstructive sleep apnoea/hypopnoea syndrome." Thorax, vol. 59, pp. 159–163, 2004.

[15] W.R. Ruehland, P.D. Rochford, F.J. O'Donoghue, R.J. Pierce, P. Singh, and A.T., "Thornton, The new AASM criteria for scoring hypopneas: Impact on the Apnea Hypopnea Index." Sleep, vol. 32, pp. 150-157, 2009.

[16] P.M. Palmer, E.S. Luschei, D. Jaffe, and T.M. McCulloch, "Contribution of individual muscles to the submental elctromyogram during swallowing." J Speech Lang Hearing Res, vol. 42, pp. 1378-1391, 1999.

[17] M.A. Daulatzai, A.H. Khandoker, C. K. Karmakar, N., Khan, and M. Palaniswamy, "The phenotypic characteristics of surface submentalis EMG activity. Activity patterns-how many and what type?" Submitted.

[18] A. Rechtshaffen, and A. Kales, "A Manual of Standardized Terminology, Techniques and Scoring System for Sleep States of Human Subjects. Washington, DC: Public Health Service, US Government Printing Office; 1968. EEG Arousals: Scoring rules and examples: A preliminary report from the sleep disorders task force of the American Sleep Disorders Association." Sleep, vol. 15, pp. 173-184, 1992.

[19] A. Bartolo, R. R. Dzwonczyk, C. Roberts and E. Goldman, "Description and validation of a technique for the removal of ECG contamination from diaphragmatic EMG signal." Med. Biol. Eng, Comput. vol. 34, 76–8, 1996.

[20] A. Brancatisano, P., Davis, and T. Van der Touw, « Effect of upper airway negative pressure on proprioceptive afferents from the tongue." J Appl Physiol, vol. 86, pp. 1396-1401, 1999.

[21] P.R. Eastwood, A.K. Curran, and A.K, Smith, "Effect of upper airway negative pressure on isnspiratory drive during sleep." J Appl Physiol, vol. 84, pp. 1063-1075 1998.

[22] P.R. Eastwood, M. Satoh, C.A. Curran, and A.K. Smith, " Inhibition of isnspiratory motor output by high-frequency low-pressure oscillation in the upper airway of sleeping dogs." J. Physiol, vol. 517, 259-271, 1999.

[23] D.L. Bliwise, "Sleep in a nonagenarian: N. Kleitman." Arch Ital Biol, vol. 139, pp. 19-21, 2001.

[24] M.M. Ohayon, "Sleep and the elderly." J Psychosom Res, vol. 56, 463-4, 2004 .

[25] Bixler, E.O., A.N, Vgontzas, T., Ten Have, K., Tyson, A. Kales, "Effects of age on sleep apnea in men. 1. prevalence and severity." Am J Respir Crit Care Med, Vol. 157, pp. 144-148, 1998.

[26] J.H. Blok, D.F. Stegeman, and A. van Oosterom, "Three layer volume conductor model and software package for application in surface electromyography." Annals Biomed Eng, vol. 30, pp. 566-577, 2002.

[27] K. Roeleveld, J.H. Blok, D.F. Stegeman, A. van Oosterom, "Volume conduction models for surface EMG, confrontations with measurements." J. Electromyogr. Kinesiol, vol. 7, pp. 221-232, 2007.

[28] J.C. Leiter, S.L. Knuth, and D. Bartlett Jr, "Dependency of pharyngeal resistance on genioglossal EMG activity, nasal resistance, and airflow." J. Appl. Physiol, Vol.73, 584-590, 1992.

[29] J.H. Sherrey, M.J. Pollard, and D. Megirian, "Respiratory functions of the inferior pharyngeal constrictor and sternohyoid muscles during sleep." Exp Neurol, vol. 92, pp. 267-77 1986.

[30] R.O. Dantas, and W.J. Dodds, "Effect of bolus volume and consistency on swallow-induced submental and infra-hyoid electromyographic activity." Braz J. Med. Biol. Res, Vol. 23, pp. 37-44, 1990.

[31] P.M. Palmer, A.L. Perlman, T.M. McCulloch. D.J, Vandaele, and E.S. Luschei, "The effect of bolus volume on electromyography of select oral, laryngeal and pharyngeal muscles." Dysphagia, vol. 10, 139, 1995.