[Original article]

Association of masticatory muscle activity with sleep arousal and other concomitant movements during sleep

Abbreviated title: Concomitant movement in sleep bruxism and arousal

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ABSTRACT

Objective: This study aims to verify the associations among sleep bruxism (SB), sleep arousal (SA), and concurrent body movements.

Material and Methods: Subjects underwent a standard overnight polysomnography test and audio-video recordings. Sleep quality was evaluated according to the Rechtschaffen and Kales criteria, while SA was determined as per the American Sleep Disorders Association criteria. Analyses were performed by an external institution after masking of the subjects' information. SB was assessed based on the presence/absence of rhythmic masticatory muscle activity (RMMA) episodes, which were identified by using electromyography of the masseter muscle. The observed simultaneous movements included lower leg movement (LLM), swallowing, face scratching, head movement, body movement, eye blinking, coughing, licking, sighing, body scratching, lip sucking, somniloquy, and yawning. The LLM was determined visually, as well as through an increase in the tibialis electromyogram signal. Other movements were visually assessed using audio-video recordings. The incidences of all the simultaneous movements were compared between RMMA with intercurrent SA (SAwRMMA; RMMA episode derived from a masseter electromyogram showing more than 10% of maximum voluntary contraction) and SA without RMMA (SAw/oRMMA).

Results: Fourteen subjects were included in this study (females/males: 4/10, mean age: 31.5 ± 5.7 years). Among these, LLM, swallowing, body movement, licking, body scratching, and lip sucking were frequently observed in SAwRMMA episodes than in SAw/oRMMA episodes, significantly. However, the non-specific simultaneous movements were higher observed in SAw/oRMMA episodes than that in SAwRMMA.

Conclusion: Our results suggest that SB is concurrently activated with LLM in relation to arousal.

Key words:

concomitant movement

sleep arousal

sleep bruxism

polysomnography assessment

rhythmic masticatory muscle activity (RMMA)

non-specific simultaneous movements

1. Introduction

Sleep bruxism (SB) is widely recognized as a risk factor for poor prognoses of dental prostheses and periodontal tissue conditions (particularly pathological conditions), teeth damage, and for the exacerbation of masticatory muscle and temporomandibular joint diseases.[1-4] Currently, several therapeutic approaches have been applied to reduce the frequency and/or intensity of SB. However, none of these approaches are based on precipitating and/or perpetuating factors of SB, and therefore can only be considered symptomatic therapies. Thus, understanding the etiological aspects of SB is necessary for the development of novel approaches to etiology-based treatment.

SB typically presents as a repetitive jaw-muscle activity characterized by clenching or grinding of the teeth and/or by bracing or thrusting of the mandible.[5] These movements are similar to chewing movements of approximately 1 Hz, and SB episodes constitute a rhythmic masticatory muscle activity (RMMA). According to the International Classification of Sleep Disorders Third Edition (ICSD-3), SB has also been defined as a sleep-related movement disorder. Currently, periodic limb movement disorder (PLMD) is described as a periodic, repetitive, and stereotyped limb movement that occurs during sleep; hence, it is also categorized as a sleep-related movement disorder. Interestingly, there are numerous aspects that are similar between SB and PLMD, apart from the conspicuous repetitive involuntary movement during

sleep. First, the prevalence of SB is estimated at 12.8 ± 3.1% in the general adult population[6], which is similar to that of PLMD with a prevalence of approximately 4-11% in the general adult population.[7, 8] Furthermore, both SB and PLMD show a close association with electroencephalographic (EEG) arousals. Specifically, a majority of the RMMA/SB episodes (87.3%) have been shown to occur during phase A of the cyclic alternating pattern (CAP).[9] CAP is an EEG arousal pattern, in which phase A is linked with heightened EEG, and muscle, and autonomic activity.[10-12] In response, RMMA in SB patients was clearly preceded by cortical EEG signal changes. Most RMMA episodes, in both SB patients and normal subjects, were also associated with motor activity. The arousal is a primary factor in the initiation of RMMA during sleep; thus, SB can be considered a form of oromotor activation secondary to micro-arousal.[13]

PLMD was frequently observed before and after EEG arousal (66.8%); however, PLMD was not primary to arousal; it was a phenomenon underlying arousal, since these occurrences were not simultaneous.[14] Furthermore, it has been reported that PLMD induces arousal in both brain and autonomic activation.[15]

Considering prior evidence, the occurrence of arousals may be temporally related to both RMMA and PLMD events, but these associations have not been fully elucidated. There have been, however, a few studies evaluating the association between RMMA and PLMD. For instance, one study found that

60–80% of SB events were associated with increased leg muscle activity[16-18], although the presence of arousal was not mentioned. Zaag et al., examined the association between SB/PLMD and EEG arousals and found that they all commonly occurred during sleep in a time-linked manner.[19] However, this study merely indicated that the number of SB/PLMD episodes associated with EEG arousal was significantly higher than those not associated with EEG arousal. Furthermore, there is no clear evidence regarding the association between SB and other simultaneous movements, such as swallowing, scratching, and lip sucking.

Thus, this study aimed to 1) investigate the association between the simultaneous occurrence of RMMA, body movement, and arousals; and 2) evaluate other possible simultaneous movements during arousal and RMMA. Our null hypothesis for the current study predicted no systematic association between head/body movements, and RMMA and SA in the recording series.

2. Materials and Methods

2.1. Subjects

Subjects were recruited from among the faculty members and post-graduate students of the Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences and Okayama

University Hospital. Subjects were excluded from the study if they 1) were receiving orthodontic treatments; 2) had been taking psychotropic and/or hypnotic medication, muscle relaxants, or antidepressants within the past 6 months; 3) had been diagnosed with a cutaneous disease (e.g. atopic dermatitis); 4) had more than two missing posterior teeth, not including the third molars; 5) consumed alcohol and/or tobacco at any point during the experiment; or 6) demonstrated insufficient sleep efficiency (less than 80%). Clinical examination with respect to the TMD, such as jaw opening dimension, joint noise during jaw movement, presence of palpation pain on TMJ and masticatory muscles, and pain in the TMD and masticatory muscles during jaw movement were assessed before the initiation of the study. For information on SB, we considered the individual's self-assessment of SB. To obtain a wide range of RMMA frequencies within the sample, subjects were not subjected to rigorous selection criteria related to SB frequency. Prior to experimentation, all subjects were asked to sign a consent form. This study protocol was approved by the Ethical committee of Okayama University Graduate school of Medicine, Dentistry and Pharmaceutical Science (# 602).

2.2. Nocturnal polysomnography test

Each subject underwent a polysomnography (PSG) in an audio-visually monitored, dark,

partially soundproof, and temperature-controlled recording room. The single-night PSG recording was performed at an accredited sleep laboratory (Okayama University Hospital, Okayama, JAPAN). The following parameters were recorded continuously: EEG signal (C3-A2, C4-A1, O1-A2, O2-A1); electrooculogram (EOG) signal; electromyogram (EMG) signal of the bilateral masseter, chin/suprahyoid, and anterior tibial muscle; heart rate; electrocardiogram (ECG); respiration (nose thermostat, nose cannular sensor, and thoracis sensor); and blood oxygen saturation level. Audio and video recordings of the facial region were performed simultaneously to distinguish RMMA/SB events from non-specific orofacial activities (e.g. coughing, somniloquy, grimacing). All other amplified physiological signals were digitized at a sampling frequency of 200 Hz and stored for off-line analysis by PSG software in an associated computer drive. All test preparations were performed by a nationally accredited sleep laboratory technician.

2.3. Sleep stage, sleep arousal and apnea hypopnea analysis

Conventional sleep stage was determined according to the International Standard Criteria.[20] Total sleep time, sleep efficiency, and sleep latency were calculated based on EEG data, EOG data, and EMG data of the bilateral chin/ suprahyoid regions. Sleep and micro-arousal responses were analyzed based on the criteria laid out by the American Academy of Sleep Medicine. In this study, an arousal index was

applied to the total number of micro-arousals and awakenings. A micro-arousal was defined as an abrupt EEG frequency shift (greater than 3 seconds but less than 15 seconds) without complete awakening, and an awakening was defined as an abrupt EEG frequency shift longer than 15 seconds. Apnea and hypopnea index were assessed by the PSG data based on the AASM-ICSD criteria (2014)[21, 22]. Analyses and diagnoses were completed at the Sleep Apnea Syndrome health examination support center with masking of the subjects' information (Niigata, JAPAN).

2.4. Assessment of RMMA episodes

The recording period for the PSG examination was set from the time the subject moved into the bed to the time the subject woke up in the morning. The original waveform of the bilateral masseter EMG was converted to a time-constant 60-ms root mean square process, and then analyzed to obtain the percentage of the maximum voluntary clenching (%MVC). This process was performed automatically by the software program, and outsourced to the Department of Stomatognathic Function and Occlusal Reconstruction, Graduate School of Biomedical Sciences, Tokushima University, and analysts were unaware of the subjects' individual information. Then, RMMA episodes were automatically identified according to the criteria described by Lavigne et al. (10% of MVC criteria)[23] using a software manufactured

by the University of Tokushima. Among the hyper masticatory muscle activities that showed more than 10% MVC and more than a 0.25-s burst or sustained activity lasting more than 2 s, ineligible muscle activities resulting from orofacial motion were excluded based on visual assessment of the video recording data. These ineligible muscle activities were due to the motion artifact of scratching, body/head movement, coughing, and somniloquy.

2.5. Assessment criteria for simultaneous movements

Movements that were considered simultaneous movements included lower limb movement (LLM), swallowing, face/body scratching, head/body movement, eye blinking, coughing, licking, sighing, lip sucking, somniloquy, and yawning. LLM was assessed visually as well as based on an increase in the EMG signal of the tibialis.[24] Swallowing was assessed based on an audible swallowing sound in the audio-video recording and an elevated laryngeal response in the EMG recording. Rubbing movement and other orofacial activities were assessed visually, by one examiner, based on the video recordings. Body movement and head movement were assessed based on the presence/absence of movement as detected by the position sensor.

Simultaneous movements were considered to have occurred concomitantly with arousal and

RMMA when the movement occurred during the sequential arousal and RMMA duration previously diagnosed outside the facility. These assessments of co-occurrence-association were performed visually based on the PSG monitor screen that displayed the sequential data of EEG, EOG, masseter EMG, tibialis EMG, laryngeal EMG, and response of the position sensor simultaneously. All assessments were conducted twice by one examiner, and only data that remained consistent across both the assessments were treated as positive simultaneous events.

Simultaneous movements were classified into those that occurred during the period of sleep arousal or those that occurred independently. These movements were then further classified into those that occurred simultaneously with RMMA or those that did not. Finally, simultaneous movements were classified into those with/without sleep arousals and those with/without RMMA. The differences in incidences were then compared.

2.6. Statistical analysis

We compared the ratio of the presence/absence of total simultaneous movement variables between those occurring with arousal or and those not occurring with arousal using a 2 x 2 table. We also compared the ratio of the presence/absence of total simultaneous movements between those occurring with

RMMA and those occurring without RMMA. Additionally, we compared the total simultaneous movements occurring with arousal and RMMA and those occurring with arousal but without RMMA.

Finally, we compared the incidence of simultaneous movements in arousal with RMMA and simultaneous movements in arousal without RMMA for each candidate's simultaneous movement. Significance level for all comparisons was set at $p < 0.05$.

3. Results

3.1. Demographic data

A total of 17 subjects (male/female: 11/6; mean age = 31.5 ± 5.2 years) underwent PSG examination concomitantly with audio-video recordings. Six subjects were re-examined due to video recording failure (n = 2), waking up during examination (n = 2), and a displaced electrode (n = 2). Additionally, three subjects were excluded due to insufficient sleep efficiency (< 80%). Consequently, the final sample consisted of 14 subjects (male/female: 4/10 males; mean age = 31.5 ± 5.7 years).

3.2. Sleep quality

Total sleep time, mean sleep efficiency, and sleep latency of the final 14 subjects were 421.6 ±

26.8 min, 93.2 ± 4.46 %, and 7.7 ± 10.8 min, respectively. Among the sleep stages, Stage 2 (63.4 ± 6.6%) was most frequently observed; however, the distribution of sleep stage was within the normal range. RMMA Index, mean number of awakenings, micro-arousals and PLM index were 1.6 ± 1.13, 5.0 ± 3.0, 10.3 ± 3.1, and 0.5 ± 1.5 times/hour, respectively. The mean apnea and hypopnea index (AHI) was 4.8 ± 3.3, and the AHI was more than 5 in four subjects. (Table 1).

3.3. Relationship among sleep arousal, simultaneous movements, and RMMA episodes

The total number of sleep arousal episodes across all subjects was 1435 episodes, of which 1031 episodes were associated with simultaneous movements, and 404 episodes were not associated with simultaneous movements. However, only a small number of episodes (43 episodes) exhibited simultaneous movements without arousal (Table 2). All RMMA episodes occurred concurrently with sleep arousal. The mean incidence of sleep arousal events with concomitant RMMA (SAwRMMA) was 10.6 ± 7.63 time/ hour. This was significantly lower than the number of sleep arousal events without RMMA (SAw/oRMMA) (91.9 ± 36.2 times/hour) (*t-test*, $p < 0.01$) (Table 3).

Out of a total of 1435 sleep arousal events, 146 events (10.2%) occurred concomitantly with both movements and RMMA, whereas merely three events (0.2%) occurred simultaneously with an RMMA

event alone. Additionally, 885 sleep arousal events (61.7%) occurred concomitantly with movements, and 401 sleep arousal events (27.9%) occurred without movements or RMMA. These findings indicate that the ratio exhibiting movements was significantly higher in episodes with RMMA than in episodes without RMMA ($p < 0.01$, Chi-square test, Table 4).

3.4. Description of individual movements and their incidence with/without RMMA

The mean number per hour during sleep arousal is shown in Table 5. Our results show that LLM was observed more frequently than the other simultaneous movements. Furthermore, simultaneous movements were observed more frequently in SAwRMMA than in SAw/oRMMA. Of all the movements, LLM was the most frequently observed both in SAwRMMA and SAw/oRMMA episodes. In addition, LLM, swallowing, body movement, licking, body scratching, and lip sucking were frequently observed during SAwRMMA episodes (paired *t-test*, $p < 0.01$, < 0.01, 0.03, 0.02, 0.04, < 0.01, respectively) than during the SAw/oRMMA episodes. The number of occurrences of LLM, swallowing, body movement, licking, body scratching and lip sucking not related to RMMA, called the non-specific simultaneous movements, were higher in episodes SAw/oRMMA than those in SAwRMMA.

4. Discussion

This study evaluated in detail the tripartite association among the occurrences of RMMA episodes, sleep arousal, and body movements on PSG along with audio-visual assessments. Our findings indicate a possible association between the RMMA and LLM, swallowing, body movement, licking, body scratching, and lip sucking. Furthermore, these movements tend to show high incidence during episodes with RMMA rather than in episodes without RMMA. However, the number of occurrences of these non-specific simultaneous movements was higher in episodes without RMMA than that in with RMMA. Thus, it might appear that these non-specific movements were treated as muscle hyperactivities associated with SB with an RMMA event only in the case of an EMG-based assessment system. These informative findings may be helpful in developing novel diagnostic procedures for EMG-based RMMA/SB assessment.

To date, only a few studies have focused on the association between arousal and SB episodes[13, 25, 26], or arousal and body movements[27]; however, rarely has a study investigated the tripartite and temporal associations among RMMA occurrence, body movement, and SA by means of a PSG and audio-visual assessment. Therefore, the presence of non-specific orofacial movements unrelated to RMMA would be important aspect to elucidate the novel diagnostic system of SB. Previously, Dutra et al., and Yamaguchi et al., reported the weak points of a single EMG-based SB assessment.[28, 29] Both of these studies indicated

that sleep motor activities can be observed in normal and SB subjects. In the absence of audio-video signal recordings, the discrimination of various types of orofacial activities was difficult to achieve and might have lead to erroneous estimation of SB-related activities. Therefore, false positive orofacial movements could be the cause of mis assessment of SB in case of single EMG examination. This study further revealed the detail of these false positive orofacial movement that was not simultaneous with RMMA.

In addition, several reports have revealed the association between RMMA/SB events and cortical arousal.[13, 26, 30, 31] In conjunction with the temporal association of RMMA/SB with cortical arousal, the physiological mechanisms preceding SB are also arousal related. Specifically, arousals are normally characterized by tachycardia, often followed by bradycardia[32], and can occur with or without EEG desynchronization (cortical or subcortical arousal). These events are similar to the physiological sequences involved in RMMA/SB, and these physiological sequences have also been observed in other sleep movement disorders, especially in PLMD. PLMD was also associated with arousal and indicated by the tachycardia/bradycardia pattern.[27] Furthermore, in patients with obstructive sleep apnea syndrome, contractions of the masseter and anterior tibialis muscles after respiratory events can be nonspecific motor phenomena dependent on the duration of arousals, rather than the occurrence of respiratory events.[33] In light of this finding, it is possible that both SB and LLM might be regulated by arousal and related

sympathetic activity.

This study applied several procedures and methods in order to avoid bias. First, this study assessed data using a sleep quality-related analysis, masseter muscle activity-related analysis, and video-recording-based visual analysis, while masking patients' information and results of analysis. Consequently, we were able to limit bias and obtain highly validated results, by performing a strictly independent analysis.

There were several limitations, which should be noted to avoid misleading interpretations or extrapolations. One limitation was the single-night PSG test that was used in this study. Generally, the first-night effect in the sleep laboratory is reported to influence several recorded sleep variables, and thus, in clinical research settings, PSG recordings obtained during the first night of a study are generally excluded from the analysis to avoid the first-night effect.[34] However, it has been reported that both micro-arousal index and RMMA episode index do not differ between the first and second nights in young healthy subjects.[35] The subjects in this study were young and healthy, and given that this study focused on the associations among SA, RMMA, and orofacial/body movements, it would be unlikely that the first-night effect would significantly impact the validity of this study. Another limitation was that the subjects who participated in this study were relatively healthy and had only mild SB. Consequently, individuals with severe SB were not recruited and thus, it was impossible to verify the SB severity-dependent relationship

between the incidence of SB and body movements. Furthermore, inclusion of dental students in this study may have reduced the capacity to extrapolate the findings. However, the nocturnal unconscious phenomenon will be unlikely to be affected by the subjects' knowledge and education level. Therefore, there was a potential sampling bias in this study; however, we believe that it would be not reduce the validity of the results. Therefore, further studies are required to verify our findings with a larger sample size that includes a range of SB severity in non-dental student subjects. In addition, four apnea subjects participated in this study. Thus, their sleep arousal might not be identical to that of non-apnea subjects, which may again affect the validity of our results. Despite this limitation, the prevalence of mild SB in subjects in this study was nearly similar to that of the general population (4), and the subjects with apnea had mild cases of apnea (mean AHI ± S.D.: 8.4 ± 3.6); thus, the validity our findings should be within the acceptable range.

Based on our results, the total number of simultaneous movements during episodes without RMMA was higher than that during episodes with RMMA. Furthermore, these SAw/oRMMA-related simultaneous movements included numerous oral-facial-related movements that affected the EMG data. Therefore, in the absence of PSG and/or audio-video recordings, it seems that the use of a single EMG test may not allow accurate distinction of actual SB events from pseudo-RMMA episodes, and may lead to an overestimation of the number of RMMA/SB events. Thus, it would be strongly advised that multi-modal

evaluation systems and/or novel diagnostic algorithms be developed to assess SB severity. In order to realize this hypothesis, future studies would need to clarify the difference between the true SB-related muscle hyper activities and non-specific movements based on EMG assessment. Such investigations would provide meaningful evidence that contributes to a valid diagnostic algorism of SB.

5. Conclusion

This study investigated the concomitant occurrence of simultaneous body movement with arousal and SB, and provided detailed description and incidences of each movement. Among these, lower leg movement was observed more frequently in concomitance with arousal and SB than in arousal without SB. Our results, therefore, have important implications for SB etiology, and suggest that SB is concurrently activated with lower leg movement in relation to arousal.

In addition, the non-specific simultaneous movements were higher in SAw/oRMMA episodes than in SAwRMMA episodes. These results suggest that non-RMMA-related movement should also be considered in any analysis, especially when a single channel EMG source is used for data collection.

Compliance with Ethical Standards:

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Conflict of Interest: The authors declare that they have no conflict of interest.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

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