

A Study of REM Behavior Disorder (RBD) in a subgroup of subjects with Craniomandibular Disorders (CMDs) and Bruxing Behavior (BB).

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Abstract

Introduction: REM sleep behavior disorder (RBD) is a neurological alteration occurring during REM sleep and characterized by loss of normal skeletal muscle atonia. Little is known about this disorder in Craniomandibular Disorder subjects with Bruxing Behavior. **Goals:** Evaluate frequency of REM sleep Behavior Disorder (RBD) in Craniomandibular Disorder with Bruxing behavior subjects and in no CMDs with/without bruxing behavior, assess the frequency RBD related behaviors, evaluate the frequency of bruxing behavior in pooled RBD subjects and in pooled no RBD subjects. **Methods:** Subjects recently and consecutively referred to a University based facility and to a private practice clinic for diagnosis and treatment of Craniomandibular Disorders and Facial Pain (n=29) were evaluated comprehensively and compared to a control no Craniomandibular Disorder subgroup (n=28). Information from the chief complaint, palpation of joint and muscles, self-reported questionnaires for Bruxism, pain, headache, evaluation of jaw movements, biomechanical tests for internal derangements of the temporomandibular joints and from the REM sleep behavior disorder screening questionnaire was used to gather diagnostic data and compare the dysfunctional (CMDs) with the normal control (No CMDs) subgroup. Accepted criteria for bruxing behavior and Craniomandibular disorders were also used. Data were analyzed using Mann-Whitney statistics and Fisher's exact test, significance was accepted if $p < 0.05$. **Outcome:** REM Behavior Disorder was diagnosed in 37,9% of Craniomandibular Disorders subjects and in 35,7% of the Control Subgroup (Fisher's exact test $p = 1,000$). Mean characteristics or behaviors indicating RBD was about 3,2 (SD=2,8, range=0-10) in the Craniomandibular Disorder subgroup and 2,6 (SD=2,3, range=0-6) in the Control subgroup (Mann-Whitney statistics $p = 0.5$). The frequency of bruxing behavior in the Craniomandibular Disorder subgroup was about 93,1% as compared to 28,6% in the Control subgroup (Fisher's exact test $p < 0,0001$). Pooled RBD subjects with or without Craniomandibular Disorders (n=21) demonstrated a frequency of 76,2% bruxing behavior as compared to 58,3% in the Control subgroup but the difference was statistically nonsignificant: Fisher's exact test $p = 0,25$.

Conclusion: The frequency of RBD was high and practically equivalent in both the CMDs (experimental) and non CMDs (control) subgroups. Subjects in the experimental subgroup did not demonstrate a higher frequency of RBD. The frequency of bruxing behavior was very high in the Craniomandibular Disorders subgroup and lower in the Control subgroup with no Craniomandibular Disorders. The frequency of bruxing behavior in the pooled subgroup of RBD subjects with or without Craniomandibular Disorders was higher than the Control subgroup but the difference was not statistically significant. REM behavior disorder was observed with a moderate frequency in both the experimental and control subgroups.

Key Words: Bruxism. REM Behavior Disorder. Craniomandibular Disorders. REM sleep.

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I. Introduction

Craniomandibular Disorders (CMDs) constitute a heterogeneous subgroup of clinical disorders affecting the Temporomandibular Joints (TMJs), masticatory muscles, ligaments, tendons and adjacent anatomic structures of the face, head, and neck, usually of musculoskeletal origin. CMDs signs and symptoms include a

complaint of pain, restriction of jaw movements, tenderness to palpation of muscles and joints, joint noises, and headaches of musculoskeletal origin^[1]. Sleep Bruxing Behavior (SB) is defined as a chronic or acute act of grinding the teeth at night that causes serious lesions and pain in many if not all the components of the masticatory system^[2]. Such signs and symptoms include headache, tooth wear, tooth fracture, failed restorations, difficulties to perform normal jaw movements, muscle and joint pain^[2]. Other clinical signs and symptoms include jaw muscle discomfort, stiffness, and fatigue of the jaw elevators (temporal and masseter muscles)^[3]. Sleep is a stereotyped behavior in human beings characterized by the presence of different and characteristic stages occurring at different moments during the night. A simple definition of sleep would be “a sleep behavior characterized by changes in the level of mobility, movement and awareness”^[4]. REM sleep is one of various sleep stages characterized by loss of EEG synchronization, rapid eye movements episodes, muscle relaxation (muscle atonia=significant reduction of muscle tone), activation of the autonomous system, changes in heart and respiratory rates, and mental activity in a paralyzed body^[4].

REM behavior disorder (RBD) is a parasomnia involving dream reenactment behavior associated with loss of normal atonia during REM sleep^[5]. This disturbance can also be defined as a motor alteration occurring during REM sleep^[6] and characterized by desynchronization of motor centers in the brainstem^[7]. RBD may also be defined as a common polysomnographic observation during REM sleep. Common signs and symptoms of RBD include sweating, wide opening the eyes, increased motor behavior, waking up suddenly, looking fearful, increased motor activity of the legs and feet, shouting, and confusion^[8]. Other clinical manifestations of RBD include nightmares, nocturnal leg cramps, sleep-related bruxism and sleep talking^[9]. RBD does not occur frequently and can be caused by many factors including the use of fluoxetine, sertraline, venlafaxine and tricyclic antidepressants and disorders of the CNS. According to recent studies, fluoxetine (a selective serotonin reuptake inhibitor= SSRI antidepressant), shares with tricyclic antidepressants, the capacity to induce signs and symptoms of RBD^[10]. The use of fluoxetine and other SSRI drugs (venlafaxine, sertraline, duloxetine), is reported frequently by CMDs patients with severe sleep BB and CMDs signs and symptoms. Because RBD is a severe clinical disorder but the relationship between sleep BB, CMDs and RBD is still poorly understood, this clinical investigation was designed to:

1. Compare age in the experimental and control subgroup and discuss age differences with other study of groups demonstrating characteristics of RBD;
2. Evaluate the frequency of RBD in patients with signs and symptoms of CMDs and BB as compared to the frequency in the control no CMDs subgroup with/without BB;
3. Evaluate frequency of characteristics of RBD in the experimental (CMDs) and in the Control (no CMDs) subgroup.
4. Assess the frequency of BB in one subgroup of pooled individuals with RBD (with/ without CMDs, n=21) as compared to another subgroup of subjects without RBD (n=36) and with/without CMDs.

II. Methods

To undertake this investigation, all subjects that were consecutively referred to an Orofacial Pain Unit in a private practice setting and those referred to a Department of Orofacial Pain at UNIRG University for diagnosis and treatment in the last six months were consecutively and comprehensively evaluated by a specialist in the field (OFM). The chief pain complaint was evaluated regarding anatomic location, quality, frequency, intensity, pattern of radiation and severity of the pain. The TMJs and masticatory muscles were assessed using gentle palpation and jaw movements, biomechanical tests during jaw movements were carried out to diagnose the type of TMJ-IDs. The diagnosis of CMDs was carried out using the presence of signs and symptoms including a complaint of pain, TMJ noises, and tenderness to palpation of major masticatory muscles. Twenty-nine CMDs and BB subjects were evaluated consecutively during four months and were compared to a similar group of non CMDs dental students evaluated in the same period of time. Patients and controls were carefully assessed, they were informed about the nature of the investigation, absence of injury or lesion during the procedure, the fact that the subject could withdraw at any moment during the evaluation, anonymity and the importance of the procedure for the advancement of sciences. Patients and controls agreed to the use of their clinical material for future studies and anonymity was guaranteed for all those evaluated in the same period of four months.

Inclusion criteria for CMDs: Patients were included in the CMDs subgroup based on the presence of the classical signs and symptoms of CMDs including a complaint of pain in the masticatory structures and of musculoskeletal origin, presence of joint noises, tenderness to palpation, difficulties to perform jaw movements and headaches.

Inclusion criteria for sleep BB: Patient's self-report of catching himself or herself clenching or grinding the teeth at night, a friend or relative report of having observed the patient grinding or clenching the teeth at

night, patient's report of morning awakening with facial, TMJ or headache, and patient's self-report of difficulties to opening the jaw early in the morning.

Inclusion criteria for RBD: Patients were accepted in the experimental group if using self-report, they reported the presence of at least 5 signs, symptoms or behaviors based on the use of the REM Sleep Behavior Disorder Screening Questionnaire^[11]

Exclusion criteria: Subjects demonstrating the presence of severe psychological and psychiatric disorders, those with cognitive impairment, patients presenting with signs and symptoms of any motor disorder including Parkinson Disease, and those with incomplete data and absence of a comprehensive evaluation, were excluded from this clinical investigation

III. Measures

The REM Sleep Behavior Disorder Screening Questionnaire is a novel self-reported instrument used to assess RBD in the medical setting^[11]. The questionnaire includes 10 yes/no questions to assess signs, symptoms or behaviors including vivid dreams, aggressive or action-packed content dreams, abnormal body movements, harm to the patient or others during sleep, excessive and vigorous body movements and awakening during sleep, disturbed sleep, and other behaviors. A cut off point of 5 determines the presence of the disorder.

IV. Statistical Analysis

Mann and Whitney statistics was used to analyze age differences and frequency of characteristics of RBD in the CMDs subgroup (n=29) as compared to the subgroup (n=28) of no CMDs subjects with or without BB. Fisher's exact test was used to evaluate statistically significant differences when comparing the frequency of RBD in the experimental and in the control subgroups. The same test was used to compare the frequency of BB in a subgroup of RBD subjects with or without CMDs to another subgroup of subjects with no RBD with or without CMDs. Significance was accepted if $p < 0,05$.

V. Outcome

This preliminary investigation evaluated a subgroup of CMDs subjects (n=29) and a comparison subgroup of 28 subjects with no CMDs signs and symptoms referred for diagnosis and treatment in the same period. Mean age in the CMDs subgroup was about 34,0 (SD=12,4, range=18-63) and 21,4 (SD=2,9, range=17-32) in the control no CMDs subgroup. There were 26 females and 3 males in the CMDs subgroup as compared to 23 females and 5 males in the control one. There was a statistically and significant difference when age was compared in the two subgroups (Mann-Whitney statistics $p < 0,0001$). See Table 1, for additional details.

Using the Stiasny-Kolster and associates^[11] criteria for the presence of RBD in which a minimum of 5 self-reported characteristics indicates RBD according to the screening questionnaire, 11/29= 37,9% CMDs subjects and 10/28=35,7%no CMDs subjects demonstrated the presence of RBD. The difference in the frequency of RBD comparing the experimental CMDs and the control subgroup was not statistically significant (Fisher's exact test, $p = 1,000$). See Table 2, for further information.

Mean of characteristics or behaviors of RBD in the CMDs subgroup with RBD (n=29) was about 3,2 (SD=2,8, range=0-10) as compared to 2,6 (SD=2,3, range=0-6) in the Control no CMDs subgroup (n=28), Mann-Whitney statistics ($p = 0,5$). See Table 3, for further information.

Regarding the frequency of BB, 27/29=93,1% subjects in the CMDs subgroup demonstrated signs and symptoms of BB in different intensities as compared to 8/28=28,6% subjects in the Control no CMDs subgroup. Consequently, the frequency of BB was higher and statistically significant in the CMDs subgroup as compared to the Control one (Fisher's exact test, $p < 0,0001$). See Table 4 for further details. Because there were only 11 subjects with RBD in the CMDs subgroup and 10 subjects in the Control one, the severity of BB in those subjects was not compared.

When subjects with RBD independent of the presence of CMDs signs and symptoms were pooled (n=21) and compared to those with no RBD independent of the presence of CMDs, signs and symptoms (n=36), regarding the presence of BB, the frequency was about 16/21=76,2% in the first group and 21/36=58,3% in the second group. Fisher's exact test ($p = 0,25$, a nonsignificant difference). Consequently, there was not a statistically and significant difference in the frequency of BB in the RBD subgroup as compared to the non RBD one. Such data indicate that BB may occur in subjects with or without RBD. See Table 5 for further details.

VI. Discussion

1. Age, Gender and RBD

In the current investigation, we assessed an experimental subgroup of CMDs and BB subjects most of them "young adults" and another subgroup (control subgroup) of very young individuals with a predominance of females. Because the prevalence of RBD in the CMDs and Control subgroup was relatively high, the outcome of this investigation is in accordance with one study^[7] indicating that "RBD can affect any gender and can

emerge at virtually any age, even in infancy". On the other hand, the outcome in the current research is not in line with one study^[12] stating that " RBD is commonly regarded as a strongly male-predominant disease". Such discrepancy may be explained by the selection method of the experimental subgroup, for instance, researchers more frequently evaluate subjects with neurological^[13] and/or psychiatric disorders, who are usually older. Further, RBD is a neurological disorder, thus, researchers are more likely to evaluate patients in neurological and/or psychiatric facilities. This is so true, that the prevalence of RBD in the general population is reported to be 0,3-2,1%.^[14] The predominance of females in the experimental and control subgroups can be explained by the fact that it is a common observation that more females seek consultations for diagnosis and treatment in the Orofacial Pain and CMDs centers. The current investigation also evaluated 21 subjects from the experimental (n=11) and control subgroup (n=10), presenting with features of RBD in which many of them were young, older or in their middle age. Thus, this outcome is in part echoed by one investigation^[15] asserting that "the typical profile of chronic RBD consists of middle-aged or older men with aggressive dream-enacting behavior that causes repeated injury to themselves".

2.Frequency of RBD in the Experimental (n=29) and in the Control Subgroup (n=28).

In the current study the frequency of RBD in the experimental subgroup of 29 CMDs subjects was about 37,9% and 35,7% in the control non CMDs subgroup. Thus, this frequency is not in line with one study^[13] reporting a frequency of 9,04% in a subgroup of 365 patients evaluated in the neurology department. Because patients evaluated in such facility were referred from the neurology, pulmonary and psychiatric departments, the heterogeneity of such populations combined with a different method to assess the presence of RBD may account for the differences in frequencies. Because RBD can occur in other patient populations, criteria or cut off point to determine the presence of RBD and other methodological differences may account for different in frequencies observed across many studies. Thus, further studies are needed to elucidate differences in frequencies. The high frequency of RBD observed in the current study may in some way be related to the fact that there was a high prevalence of bruxing behavior in both the experimental and control subgroups. In this regard noteworthy to mention is the fact that both BB and RBD are considered neurological and movement disorders indicating closer interrelationships, mechanisms, and probably etiologic factors, thus influencing the frequency of RBD. Because this assumption is highly speculative, further studies are needed to elucidate this issue. Frequencies of 37,9% and 35,7% were observed in the experimental (CMDs subjects) and controls (health science students), respectively in the current investigation. Regarding the experimental CMDs subgroup (RBD=37,9%), this outcome is to a certain extent similar to the frequency of 46,3% observed in one investigation^[16] in young health sciences students in Ethiopia using a RBD screening questionnaire and a cut off point of 5. It is likely that the frequency of RBD varies in different populations as the disease can be observed in patients with motor, neurological, toxic or metabolic disorders^[6]. In this regard, one investigation^[17] evaluated the frequency of RBD in subjects with migraine, headache disability and sleep disorders. Researchers reported a frequency of 24,2% in the experimental subgroup. This difference in frequency (24,2%) as compared to the experimental subgroup (37,9%) in the current investigation may be related to differences in the characteristics of the samples being investigated (CMDs and BB subjects versus migraine non CMD subjects). This comparison is necessary and extremely informative. For instance, CMDs and BB subjects are considered psychosomatic, anxious, depressed individuals prone to react "psychosomatically" in the presence of stress, tension, and pressure, which in some way may influence and inflate RBD frequency.

CMDs and BB individuals are those with strong somatization tendencies prone to depression and thus are more likely to use antidepressants including selective serotonin reuptake inhibitors. CMDs and BB individuals differ from the classical samples of older individuals in whom high frequencies of RBD have been reported. Such high frequencies in neurological and psychiatric subgroups may be attributed in part to the high frequency of neurological and motor disorders which inflate the prevalence of RBD. On the other hand, CMDs no RBD samples are constituted by middle age or young adult individuals in whom anxiety, somatization and depression predominate. Many of these individuals take antidepressants (more frequently SSRIs) to reduce depression. Because most SSRIs alter cerebral neurochemistry, a series of reports indicates that SSRIs are involved in the development of RBD. This discussion emphasizes different samples with different mechanisms leading to the same disorder. Here we are discerning about neurologically or neuropsychiatry induced RBD versus antidepressants induced RBD. Further, RBD induced by antidepressants may be observed more frequently in CMDs subjects with chronic depression and intense pain and/or in young adults with severe depression independent of the presence or absence of signs and symptoms. Strongly supporting these considerations one investigation^[17] asserts that various medications including SSRIs and other antidepressants are known to induce RBD. Further, the incidence of SSRIs use is increasing as it is the frequency of RBD in young depressed individuals. Sertraline, another SSRI type, may induce or exacerbate RSWA and prolong REM latency^[18]. The aforementioned consideration are also in line with one study^[19] indicating that serotonin reuptake inhibitors and tricyclic antidepressants are frequently the etiological factors of medication induced RBD. It has been demonstrated that antidepressants increase muscle tone during REM sleep in subjects without

RBD^[19]. Further, in psychiatric patients, the frequency of RBD-like disorders is about 6% and among patients taking SSRIs, the prevalence of RBD-like disorders is 5% whereas a large-scale study^[20] found that 12,2% of patients taking antidepressants demonstrated behaviors and characteristics of REM sleep without atonia but the frequency of RBD was very small. This investigation highlights the fact that there are different populations presenting with RBD, the causes and mechanisms are multifactorial and the relationship between SSRIs, tricyclic antidepressants and RBD is very strong. From a different perspective, CMDs and BB subjects may present a high prevalence of RBD associated with somatization, high frequency of depression and dissociative trends whereas in young individuals both males and girls the high frequency of RBD is mostly correlated with depression and intake of various types of antidepressants. This observation is congruent with one investigation asserting that predisposing factors that increase the likelihood for the development of RBD include elderly age, male sex, neurological disorders, and antidepressant use^[5].

3. Frequency of BB in RBD and no RBD subjects with / without CMDs.

RBD subjects with or without signs/symptoms of CMDs were pooled (n=21) and compared with pooled subjects without RBD and with/without signs and symptoms of CMDs (n=36) regarding the presence of signs and symptoms of BB. The frequency of BB was about 16/21=76,2% in the RBD subgroup and 21/36=58,3% in the no RBD subgroup. Because Fisher's exact test yielded a p value=0,25, we can state that the frequency of BB was not higher in the subgroup with RBD as compared to the non RBD subgroup. These findings indicate that even though bruxism may be a concomitant of RBD, not all subjects with RBD demonstrate signs and symptoms of BB. On the other hand, bruxism may also be present in no RBD subjects. It may be that sleep bruxism is present in some subjects with RBD but is absent in others. This means that BB may be observed in RBD subjects but is not a sufficient disorder to cause BB in all individuals. Because BB was observed in non RBD subjects other factors including antidepressant use, neurological disorders, a general arousal disorder without the presence of RBD may cause bruxism. Supporting in part this point of view, one investigation^[21] evaluated a small and selected subgroup of destructive bruxers and asserted that sleep bruxism could be a sign of a general arousal disorder. Repeated periods of arousals occurring together with sleep BB may lead to a complain of insomnia or excessive daytime sleepiness. In one investigation using EMG and PSG^[22], RBD patients had significantly higher index of repetitive masseter muscle activity than control subjects during sleep. However, this observation does not mean that all RBD subjects demonstrate a higher masseter muscle activity that ultimately results in BB. There may be a gradient of severity in both RBD and BB which is likely to be dependent on the degree of inhibition of neurons in the pontine tegmentum and medial medulla that control skeletal muscle atonia. In some cases of insufficient inhibition of skeletal muscle atonia, there may be BB during REM sleep and incomplete RBD. Congruent with this line of reasoning, one investigation^[6] reported one case presenting with RWA, a preserved proper NREM-REM cycle and increased REM density indicating subclinical RBD. Tachibana and associates^[6] used all night PSG instrumentation to assess a group of 21 consecutive patients with subclinical RBD. Even though the frequency of teeth clenching was very high, not all subjects demonstrated sleep BB, thus providing some support to findings in the current study demonstrating that not all CMDs or Non CMDs subjects with RBD, demonstrate signs and symptoms of BB. The higher prevalence of sleep BB (90,5%) in the group evaluated by Tachibana and associates^[6] as compared to 76,2% found in the current investigation is explained by the fact that all-night PSG is probably more accurate in the determination of BB occurring at night.

VII. Conclusion

Based on data analyzed to carried out the current study and the observations of the current literature, it is concluded that signs, symptoms, or behaviors indicating RBD can be observed with a moderate frequency in subjects with and without CMDs. Signs and symptoms of BB can be observed more frequently in CMDs as compared to Controls no CMD individuals. Even though the literature is replete with information relating BB with RBD, BB is not necessarily present in many cases of RBD. More studies are needed to elucidate and examine carefully, the etiology and types of RBD, and the possibility that RBD occur in populations with different age, health status and social characteristics. Interesting to note is that RBD was found with some frequency in subjects without CMDs. More studies with larger samples with well-defined criteria for BB, CMDs and RBD should be undertaken to elucidate many questions related to the interactions between sleep bruxism and CMDs, sleep bruxism and RBD and RBD and CMDs.

Table 1: Social and Demographic data in the experimental (n=29) and in the Control subgroups (n=28).

Experimental Subgroup CMDs + BB=29	Control no CMDs Subgroup n=28	
AGE		
Mean	34,0	21,4*
SD	12,4	3,9
Range	18—63	17—32
GENRE		
Females	26=89,7%	23=82,1%
Males	3 = 10,3%	5 =17,9%
Total	29=100%	28=100%

*Mann-Whitney statistics $p < 0,0001$ (A statistically significant difference).

Table 2: Frequency of RBD, RBD related behaviors, and BB in pooled RBD and no RBD subjects with and without CMDs.

RBD frequency	CMDs + BB Subgroup n=29	Control no CMDs Subgroup n=28
Yes	11=37,9%	10=35,7% **
No	18=62,1%	18=64,3%
Totals	29=100%	28=100%
Frequency of RBD related behaviors		
Mean	3,2	2,6 ***
SD	2,8	2,3
Range	0—10	0--6
Frequency of BB		
Yes	27=93,1%	8=28,6% ****
No	2 =6,9%	20=71,4%
Totals	29=100%	28=100%
Frequency of BB	Pooled RBD subjects n=21	Pooled no RBD subjects n=36
Yes	16/21=76,2%	21/36=58,3% *****
No	5/21 =23,8%	15/36=41,7%
Totals	21 =100%	36=100%

**Fisher' s exact test $p = 1,000$ (A statistically nonsignificant difference)

***Mann-Whitney statistics $p = 0,5$ (a statistically nonsignificant difference)

****Fisher' s exact test $p < 0,0001$ (an extremely statistically significant difference)

*****Fisher' s exact test $p = 0,25$ (a nonsignificant statistical difference)

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