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Authors: Gizem Yilmaz, Christopher Laine, Neslihan Tinastepe, M. Gorkem Ozyurt, Kemal S. T*ü*rker

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PERIODONTAL MECHANORECEPTORS AND BRUXISM AT LOW BITE FORCES

SHORT TITLE: PERIODONTAL MECHANORECEPTORS AND BRUXISM

GIZEM YILMAZ[1], CHRISTOPHER LAINE[2], NESLIHAN TINASTEPE[3], M. GORKEM OZYURT[1], KEMAL S. TÜRKER[1*]

[1] Koç University School of Medicine, Istanbul, Turkey

[2] Division of Biokinesiology and Physical Therapy, University of Southern California, Los Angeles, California

[3] Private Dentist, Istanbul, Turkey

[*]CORRESPONDING AUTHOR:

Kemal S. Türker, BDS, PhD
Professor of Physiology
Koc University School of Medicine
Rumelifeneri Yolu, 34450, Sariyer
Istanbul, Turkey
kTürker@ku.edu.tr
http://medicine.ku.edu.tr/faculty
Tel: +902123381174
Fax: +902123381168

HIGHLIGHTS

- Previously, patients with sleep bruxism showed abnormal jaw tremor during production of a constant bite force.
- With low-level bite force, tremor in 6-9 Hz band for bruxists was not significantly different compared to controls.
- Jaw tremor in bruxism displays different characteristics under different conditions.

ABSTRACT

Objective: In this study, we examined if 6-9 Hz jaw tremor, an indirect indicator of Periodontal Mechanoreceptor (PMR) activity, is different in bruxists compared to healthy participants during production of a low-level constant bite force.

Methods: Bite force and surface EMG from the masseter muscle were recorded simultaneously as participants (13 patients, 15 controls) held a force transducer between the upper and lower incisors very gently.

Results: Tremor in 6-9 Hz band for bruxists was greater on average compared to controls, but the difference was not significant, both for force recordings and EMG activity.

Conclusions: The low effect sizes measured with the current protocol contrast highly with those of our previous study, where larger, dynamic bite forces were used, and where jaw tremor was markedly different in bruxists compared with controls.

Significance: We have now gained important insight into the conditions under which abnormal jaw tremor can be elicited in bruxism. From a scientific standpoint, this is critical for understanding the 'abnormality' of PMR feedback in bruxism. From a clinical perspective, our results represent progress towards the development of an optimal protocol in which jaw tremor can serve as a biological marker of bruxism.

Keywords: Tremor, Jaw, Bruxism, Periodontal mechanoreceptors, Bite force

1. Introduction

Bruxism is a malfunction of masticatory apparatus that appears with "clenching or grinding of the teeth and/or bracing or thrusting of the mandible" which can occur during sleep (sleep bruxism) or during wakefulness (awake bruxism) (Lobbezoo et al., 2013). The unconscious jaw muscle activity of patients with bruxism may cause temporomandibular disorder which can result in headaches and severe damage to the teeth (Lavigne et al., 2008). The gold

standard for evaluating bruxism is the recording of electromyography (EMG) activity during sleep (polysomnography), although the condition is typically diagnosed through questionnaires and/or clinical examination.

The exact physiological mechanism of bruxism is not known, however, several lines of evidence indicate a sensorimotor deficit related to the control of jaw force, particularly in the acquisition of afferent feedback. For example, compared with healthy individuals, bruxism patients overestimate the level of bite force required for a precise task (Mäntyvaara et al., 1999) and they have lower interoccusal tactile thresholds due to hypersensitive periodontal mechanoreceptors (PMRs) (Suganuma et al., 2007). Feedback from these receptors causes an ~8 Hz jaw tremor in healthy participants during bite force tracking (Sowman et al., 2006, 2007, 2008) and periodontal anesthetization eliminates this tremor (Sowman et al., 2006, 2007). Moreover, the ~8 Hz jaw tremor is higher during decreasing force ramp contractions in healthy subjects relative to the increasing ramp (Sowman et al., 2008). In bruxism, there is evidence that this tremor-generating circuit is abnormal. Specifically, during a triangular bite-force task, bruxists show greater jaw tremor at ~8 Hz relative to controls (Laine et al., 2015). Accordingly, jaw tremor may provide a physiological marker of neural dysfunction in bruxism, and may provide insight into the neural origins of the condition.

However, previous studies have shown that the emergence of jaw tremor can depend on many factors, including the specific protocol of bite force production (e.g. Sowman et al., 2008), and these issues have not been systematically evaluated in the context of bruxism. An important disadvantage of using force ramps, as in Laine et al., 2015, is that the adaptation of PMR activity depends on the dynamics of bite force production (Schoo et al., 1983; Sowman et al., 2008) as well as the force magnitude. Using dynamic force ramps makes it difficult to disambiguate potential causes of bruxism-related changes in jaw tremor, such as altered firing thresholds, saturation levels, or response dynamics. A helpful simplification may be to use constant forces when assessing bruxism-related changes in jaw tremor. Also, PMRs are most sensitive at forces less than 1N for anterior and 4N for posterior teeth (Trulsson, 2006). Beyond this point, the firing rates of about 80% of PMRs saturate and discharge rate follows steady state response for all force levels above the limit. Therefore, to investigate the role of PMRs in bruxism, it may be of benefit to study PMR-related tremor at extremely low forces in which PMRs are most sensitive, rather than the moderate forces used previously.

In this study, we aimed to test if ~8 Hz jaw tremor is altered in bruxism patients when the bite-force production protocol was optimized to 1) reduce receptor-saturation, 2) avoid issues related to dynamic responsiveness, and 3) maximize the force-sensitivity of PMR by using a very low level bite force task. We hypothesized that the bruxism patients would have greater magnitude of tremor at 8 Hz compared to the control group.

2. Methods

The protocol was approved by the Human Ethics Committee of Koç University and all procedures conformed to the Declaration of Helsinki. All subjects provided informed, written consent prior to participation, and were encouraged to interrupt or stop the experiment should they feel any discomfort or pain.

Experiments were performed on 28 healthy volunteers (16 females, 12 males). Participants were required to: 1) have complete dentition and 2) be between 20 and 30 years of age. Exclusion criteria included medication for any type of psychological problem or neuromuscular disorder, and those with ongoing neck/head pain.

2.1. Bruxism Assessment

Bruxism and symptom severity was assessed by a clinician in our research group based on stiff/painful jaw muscles and dental examination.

Assessment of sleep bruxism was made by using a questionnaire (Yes/No questions) and a clinical dental examination. The diagnostic criteria for sleep bruxism determined by the American Academy of Sleep Medicine (AASM) were used to diagnose sleep bruxism. (American Academy of Sleep Medicine, 2005.)

The patient was defined as having active sleep bruxism, if they reported tooth-grinding or tooth clenching during sleep, and/or showed clinically abnormal wear of the teeth (level 2 according to Lobezzoo & Naeije (2001), and in addition exhibited one or more of the following signs: report of morning jaw locking and / or jaw muscle discomfort, masseter muscle discomfort upon voluntary clenching in maximal intercuspation. As result of the examination, 13 of 28 subjects were diagnosed with bruxism and 15 of 28 did not show signs of bruxism therefore they are used as control.

2.2. Experimental Task

Participants sat upright in a dental chair facing the bite-bar carrying the force transducer. The bite-bar consisted of two stainless-steel bite bars where strain gauges were mounted. The position of bite bar was adjusted according to subjects' body height via an adjustable arm to allow a comfortable and stable position. In each trial, participants were instructed to hold the force transducer between the upper and lower incisors for about one minute very gently as if the teeth were only touching on the surface of the bite bar. The same procedure was repeated 3 times for each subject.

2.3. Data Recording

Bite force was measured using a custom apparatus in which a force transducer (Kyowa (KFG-5-120-C1-11) strain gauge) was fitted to a bite bar. The surface of bite plates was kept uncoated and plane. Surface EMG electrodes were placed over the right masseter muscle in a bipolar configuration grounded at the lip. Force and EMG signals were amplified using CED 1902 amplifiers and acquired at 2000Hz using CED power 1401 data acquisition board along with Spike 2 software (Cambridge Electronic Design, Cambridge, UK). Data analysis conducted offline using Spike 2 and custom Matlab (The Mathworks, Inc, Natick, MA, USA) scripts.

2.4. Analysis

Each subject had 3 trials of gentle bite bar hold which lasted for a minute. From each trial, we selected 30 seconds of continuous signal (force and EMG simultaneous) during which force fluctuations were minimal. Raw EMG signals were band pass filtered in 1-500 Hz range and rectified. Raw force signals were also band pass filtered in 1-50 Hz range. The filtered and rectified EMG signals were concatenated to form 90 seconds of continuous data. Similarly the filtered Force signals were also concatenated to form 90 seconds of continuous data for further power spectrum analysis. The contact area of bite bar included six teeth (2 upper and 4 lower incisors) and the mean overall bite force was 4.4 N. Thus each tooth was subjected to about 0.7 N± 0.5, which is below the level at which PMR firing activity saturates for these teeth.

2.5. Power Spectrum and Coherence

Power spectra of EMG and force signals were estimated with "Welch's periodogram" in Matlab, using a 4096 points Hamming window with 50% overlap. The frequency resolution was 0.49 Hz (≈ 0.5 Hz). For the uniformity of EMG and Force spectra, only the spectral values in frequency range of 2-50 Hz were selected for relative power calculation. The spectral values in this range constituted the absolute power. Then, the value of absolute power spectra at each frequency was divided by the total power in 2-50Hz range to obtain the relative power spectral values of EMG and Force respectively, as percentage of absolute power.

The median and median absolute deviation (MAD) values of relative EMG spectra and relative Force spectra were calculated at each frequency, across participants and plotted separately for EMG and force fluctuations.

In addition, the maximal value of relative power between 6 and 9 Hz was calculated for each participant, to facilitate comparisons of tremor magnitude across groups.

2.6. Statistical Analysis

Differences between the power spectrum of bruxists and controls were tested using a two-sided Wilcoxon rank sum test and p values were calculated at each frequency sample. This comparison was aimed to explore the full range of any spectral differences across groups. To test our initial hypothesis, the maximum tremor values in 6-9 Hz range were statistically compared using two-sided Wilcoxon rank sum test. The confidence interval was selected as 95% and p values smaller than 0.05 was evaluated as significant. Similarly, the difference of maximum relative power between 6 and 9 Hz between bruxists and controls was calculated using two-sided Wilcoxon rank sum test. The confidence interval was selected as 95% and p values smaller than 0.05 was evaluated as significant.

3. Results

The relative force spectra during gentle bite bar hold was obtained for bruxists and controls to compare the force fluctuations in the 6-9 Hz tremor band (Fig.1). The median relative force power +/- 1 MAD for bruxists and controls are shown (Fig.1.A). There was a clear trend for greater tremor in the 6-9 Hz band for bruxists compared to controls when p values were calculated at each frequency. The differences observed in Figure 1.A did not achieve statistical significance, although the trend towards higher tremor in bruxists was again clear (Fig.1.B). When the median and inter-quartile range for the maximum power in the 6-9 Hz

range across individuals in each group was compared (Fig.1.C), despite a visible trend, the statistical difference was not significant between bruxists and controls (p=0.0724).

Similarly, the fluctuations in relative EMG spectra were obtained for bruxists and controls. The median relative EMG powers +/- 1 MAD are shown for each group (Fig2.A). The statistical difference between groups at each frequency was calculated and plotted (Fig.2.B). The trend appears again, as in Fig.1, but the differences were not statistically significant between groups. When the median and inter-quartile ranges of maximum 6-9 Hz tremor amplitudes were compared across individuals within each group, there was no significant difference in 6-9 Hz EMG power across groups (p = 0.2494) (Fig.2C).

4. Discussion

In this study, we investigated if 6-9 Hz jaw tremor differed in bruxists compared to healthy participants when low, constant bite forces were produced. We found that bruxists tended to have greater jaw tremor, but the difference was not statistically significant in terms of force or muscle activity. The contrast between these results and our previous study (Laine et al., 2015) demonstrates that tremor generation in bruxism is only significantly abnormal under certain bite-force conditions. Avoiding receptor saturation by keeping forces under 1N did not accentuate differences in jaw tremor between bruxists and controls, but actually accomplished the opposite. Most likely, PMR activity becomes most 'abnormal' in bruxism, at least in terms of tremor generation, at higher forces, or during dynamic bite force production. This implies that bruxism may alter the normal saturation curve of PMRs in addition to any changes in their initial firing thresholds, or that the ~20% of PMRs which do not saturate (and are hardly active at low forces) (Trulsson, 2006) are particularly important for generating the increased jaw-tremor associated with bruxism.

4.1. The role of PMRs in physiological tremor of the jaw

In nearly all muscles, physiological tremor appears in the frequency range of 6–12 Hz (McAuley & Marsden, 2000). In general, physiological tremor has been discussed in terms of rhythmic central drives (Gross et al., 2000, 2002; Farmer et al. 1993; Farmer, 1999; McAuley & Marsden, 2000; Wessberg & Kakuda, 1999) and/or proprioceptive feedback loops (Cresswell & Loscher, 2000; Durbaba et al., 2005; Fisher et al., 2002; Jacks et al., 1988; Joyce & Rack, 1974; Joyce et al., 1974; Matthews & Muir, 1980; Prochazka & Trend, 1988; Sowman & Türker, 2007). The human masticatory system is no different (Jaberzadeh et al.,

2003; Junge et al., 1998; McFarland et al., 1986; Sowman & Türker, 2005), however, the mechanism of tremor generation is unique in that it relies heavily on the integrity of the periodontal mechanoreceptors rather than the muscle spindles (Sowman & Türker, 2005). In the last decade, numerous studies have demonstrated a critical role for exteroceptive input from PMRs in generating ~8 Hz physiological jaw tremor (Sowman & Türker, 2005; Sowman et al., 2006, 2007, 2008). For example, jaw tremor during isometric biting tasks (up to 10% MVC) was decreased or abolished after the application of local anesthetics in periodontium (Sowman et al., 2006, 2007) as the PMR input to masseter motor neurons was impaired after anesthetization.

4.2. Functional and Clinical Implications

Feedback from PMRs is functionally important for sensing and regulating the level of force applied to the teeth while contributing to the development of strong and effective masticatory forces, the teeth and supporting tissues are protected. Patients who were treated with dental bridges supported by implants display approximately the same pattern of muscle activity during the whole masticatory sequence compared to the bite-to-bite variation in muscle activity of healthy subjects (Türker et al., 2007). Moreover, in anaesthetized or edentulous subjects who lost their PMRs force is increased during the hold please of the 'hold-and-split' task and bite force is reduced indicating an impaired perception of bite force. (Trulsson & Gunne, 1998; Trulsson, 2006). On the other hand, people with bruxism overestimate the amount of bite force required to hold a given load (Mäntyvaara et al., 1999) and exhibit higher periodontal sensation compared to healthy individuals (Sagunama et al., 2007). It is not clear if these specific effects are critical for initiating/maintaining the behaviours associated with bruxism, whether these effects relate to PMR activity directly, or if they relate to abnormal CNS handling of PMR output instead.

Because PMR activity is critical for the generation of 8 Hz jaw tremor, alteration of PMR activity within bruxism may be studied through changes in tremor rather than invasive nerve recordings. The study of Laine et al. (2015) demonstrated markedly high 8 Hz tremor amplitudes in bruxists during dynamic bite force production with ascending and descending force trajectories kept between %5 and %35 of MVC. The possibility that oversensitive PMRs may have been responsible was proposed.

Trulsson (2006) detailed that almost 80% of PMRs in anterior teeth are most sensitive to changes in force below 1 N, after which their firing rates plateau. Therefore, we hypothesized

that PMR-related tremor should be most sensitive to the effects of bruxism at low force levels, where the receptors have not yet saturated. However, as depicted in Figure 1 and Figure 2, we found the opposite to be true. Although bruxists had a tendency to show more pronounced jaw tremor than controls, there was no statistical difference between these groups.

One possibility is that PMR oversensitivity in bruxists may not explain the accentuated tremor observed in Laine et al., 2015, at least if oversensitivity relates only to a decreased threshold for firing. Instead, sleep bruxism might impair the saturation characteristics of PMR feedback. In this scenario, it may actually be hypersensitivity to forces higher than 1N and/or a lack of saturation that explains previous findings of increased tremor. In order to test this hypothesis, an experimental design with different bite force levels would be necessary. An alternative explanation could be that the 20% of PMRs which do not saturate are important for tremor generation. These receptors are not very active at low forces but hyperactivity in these receptors could help explain the fact that jaw tremor is sensitive to specific dynamics of force production in experiments where forces exceed the level at which most PMRs saturate.

One last point to discuss is the sensitivity of the diagnostic criteria for sleep bruxism might have an effect on the grouping of participants. As AASM criteria and the grading system for bruxism diagnosis which was propped by the international consensus (Lobbezoo et al.,2013) are both used for clinical and research purpose on diagnosis of the bruxism, neither of them can reach the high diagnosing success of the current gold standard of Polysomnography (PSG). However, when compared with other methods, AASM criteria displays strong diagnostic capabilities as a screening tool to identify sleep bruxism (Palinkas et al., 2015) and we believe our grouping of bruxists and controls was coherent with clinical practice although a diagnosis step via PSG might be able to strengthen the difference between groups.

5. Conclusion

Our results demonstrate that the abnormal jaw tremor previously associated with bruxism is critically dependent upon the specific parameters of bite force generation. We found that bruxists tended to have greater jaw tremor, but the difference was not statistically significant at very low bite forces in contrast to our previous study (Laine et al., 2015) where bruxists had significantly higher tremor during dynamic force task. Most likely, PMR activity becomes most ‘abnormal’ in bruxism, at least in terms of tremor generation, at higher forces, or during dynamic bite force production. Accordingly, the study of jaw tremor under different

experimental conditions could lead to a better understanding of exactly which features of PMR activity are altered in bruxism. Further, the use of jaw tremor as a non-invasive metric of PMR circuit activity holds potential as an informative tool for scientific/clinical evaluation. Our findings contribute to this effort in that we have now established that PMR sensitivity (in terms of responsiveness to low forces) is not a critical factor in generating the abnormal jaw tremor associated with bruxism. Our results suggest that the measurement of tremor in bruxism may require higher rather than lower forces, with careful attention paid to the dynamics of bite force production.

7. Conflict of interest

None of the authors have potential conflicts of interest to be disclosed

6. Acknowledgements

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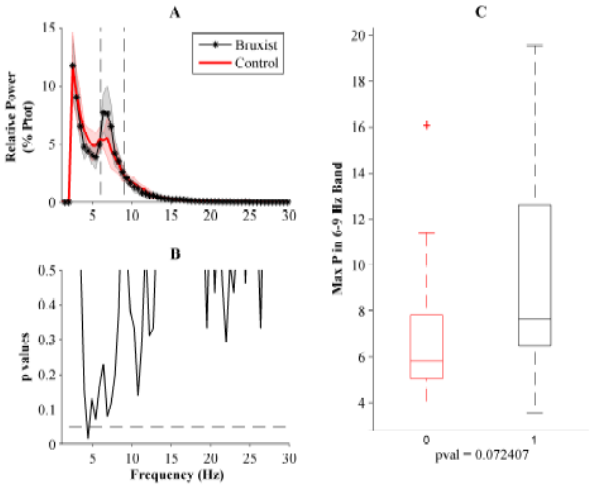

Fig.1: Power spectra of force fluctuations for bruxists and non-bruxists. **A.** Median of relative power at each frequency as percentage of total power (P tot) was shown for controls (red curve) and bruxists (black line with asterisk) with each groups' +/- MAD values (shaded region). **B.** The statistical comparison of tremor amplitudes in terms of power spectra of force at each frequency between bruxists and controls are shown as p values which did not achieve statistical significance in 6-9 Hz band ($p>0.05$ for 6-9 Hz). The x-axis in A and B are both Frequency (Hz). **C.** Box plot shows the median and inter-quartile range for the maximum power (Max P) in the 6-9 Hz range across individuals in each group. The difference was not significant between bruxists and controls ($p=0.0724$).

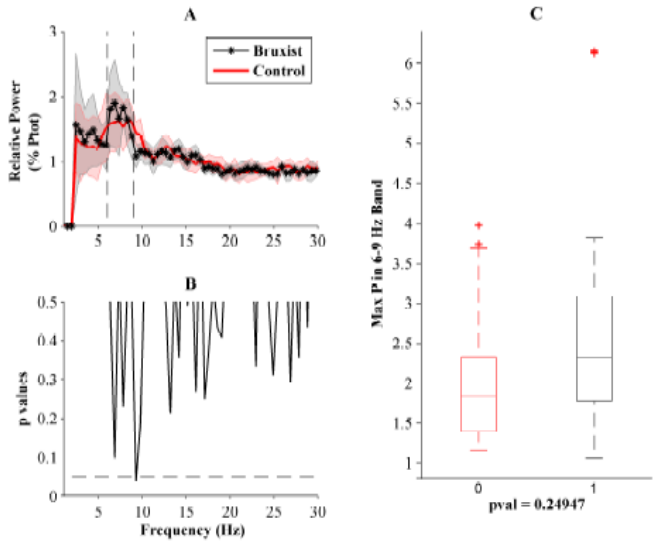

Fig. 2: Power spectra of EMG fluctuations for bruxists and non-bruxists. **A.** Median of relative power at each frequency as percentage of total power (P tot) was shown for controls (red curve) and bruxists (black line with asterisk) with each groups' +/- MAD values (shaded region). **B.** The statistical comparison of tremor amplitudes in terms of power spectra of EMG at each frequency between bruxists and controls are shown as p values which did not achieve statistical significance in 6-9 Hz band ($p>0.05$ for 6-9 Hz). The x-axis in A and B are both Frequency (Hz). **C.** Box plot shows the median and inter-quartile range for the maximum power (Max P) in the 6-9 Hz range across individuals in each group. The difference was not significant between bruxists and controls ($p=0.2494$).