OROFACIAL PAIN, BRUXISM, AND SLEEP

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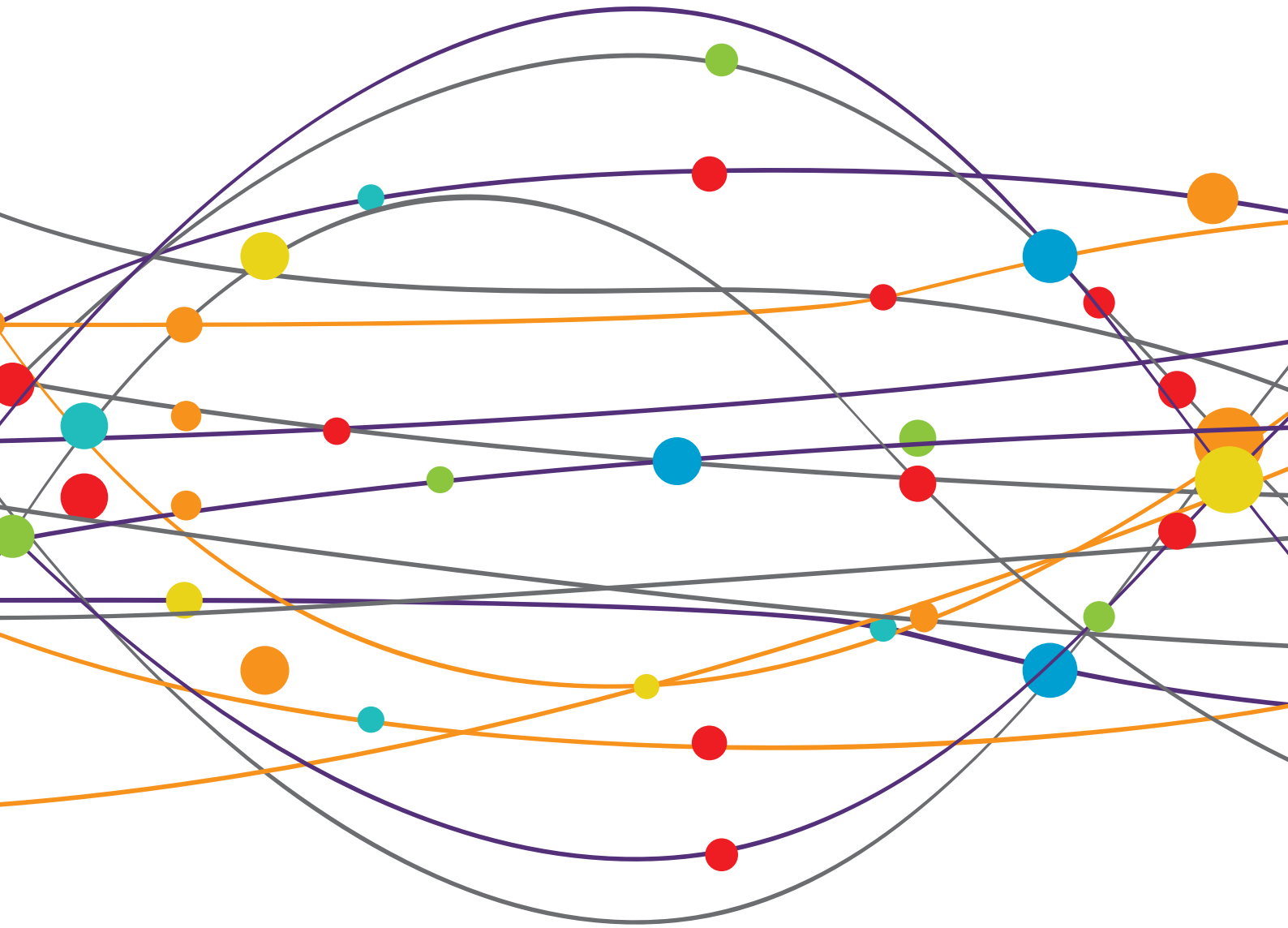

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OROFACIAL PAIN, BRUXISM, AND SLEEP

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EDITORIAL
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Editorial: Orofacial Pain, Bruxism, and Sleep

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Keywords: orofacial pain, sleep bruxism, awake bruxism, sleep, temporomandibular disorders

Editorial on the Research Topic

Orofacial Pain, Bruxism, and Sleep

The task force on taxonomy of the International Association for the Study of Pain (IASP) defines pain as "An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (1). Furthermore, IASP says that orofacial pain is a frequent form of pain perceived in the face and/or oral cavity. It may be caused by diseases or disorders of regional structures, dysfunction of the nervous system, or through referral from distant sources. The orofacial pain is a serious global problem which affects ∼20% of human population each year. According to the current approach (2), bruxism is considered as two different behaviors observed during sleep and wakefulness, respectively, and the single definition for bruxism has been replaced by two separate definitions: (1) Sleep bruxism is a masticatory muscle activity during sleep that is characterized as rhythmic (phasic) or non-rhythmic (tonic) and is not a movement disorder or a sleep disorder in otherwise healthy individuals. (2) Awake bruxism is a masticatory muscle activity during wakefulness that is characterized by repetitive or sustained tooth contact and/or by bracing or thrusting of the mandible and is not a movement disorder in otherwise healthy individuals.

Even though the etiopathogenesis of bruxism is not fully understood, many different factors are believed to be associated with this muscular activity. An increasing number of evidence suggests a relationship between bruxism and other disorders, conditions or systemic diseases, including sleep breathing disorders, uncontrolled limbs movements during sleep, reflux disease, neurological disorders and orofacial pain (3, 4). This Research Topic aimed to determine the nature of sleep bruxism and its types, as well as investigate the relationship between sleep bruxism and orofacial pain as well as different general health diseases, conditions and disorders.

Nine articles had been included in this Research Topic.

Three published articles are concerning: the prevalence of orofacial and general pain related to muscular temporomandibular disorders (Kuć et al.), and prevalence of insomnia among patients with orofacial pain (Cruz et al.), and epidemiology of awake and sleep bruxism among adolscents (Winocur et al.).

Three articles are related to diagnostic methods in a group of people with increased activity of masticatory muscles (Osiewicz et al.; Szyszka-Sommerfeld et al.; Zani et al.). Furthermore, it should be emphasized that two from mentioned three papers describe the new diagnostic method of awake bruxism i.e., ecological momentary assessment and intervention principles for the study of awake bruxism behaviors. Next two papers assessed relationship between sleep bruxism and headache (Martynowicz et al.), as well as sleep bruxism and TMD-related pain (Smardz et al.).

A single article describes the nociceptive effect of platelet-rich plasma intramuscular injections in myofascial pain of masseter muscles (Nitecka-Buchta et al.).

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Published articles confirm how difficult clinical issues are related to impaired function of the orofacial structures. At the same time, the described studies indicate that the etiology of complaints reported by patients can be very compound. Thus, it requires an objective diagnostic approach and personalized therapeutic strategies. Therefore, the approach to sufferers should be holistic based on broad evidence-based knowledge from various fields of medicine.

Editors strongly encourage potential readers to look at the articles.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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ORIGINAL RESEARCH
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Ecological Momentary Assessment and Intervention Principles for the Study of Awake Bruxism Behaviors, Part 1: General Principles and Preliminary Data on Healthy Young Italian Adults

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Background: Awake bruxism (AB) is an oral condition that has some uncertainties concerning the epidemiology, also due to the different diagnostic strategies that have been adopted to address it in the research setting. The recent new definition of AB suggests that an ecological momentary assessment (EMA), which enables real-time reporting of the condition under study, can implement knowledge on the topic.

Objectives: This article will discuss the general principles of EMA and EMI (Ecological Momentary Intervention) and comment on a preliminary dataset gathered with a smartphone application in a population of Italian young adults.

Materials and Methods: A dedicated smartphone application has been used (BruxApp®) on a sample of 30 University students (mean age 24 ± 3.5 years) to record real time report on five specific oral conditions (relaxed jaw muscles, tooth contact, teeth clenching, teeth grinding, mandible bracing) that are related with the spectrum of AB activities. Data were recorded over a 7-day period for two times, with a 1-month interval between the two observation periods. The purpose of collecting data over a second week, 1-month later, was to monitor AB behaviors over time, and test for potential "EMI" effects.

Results: Over the first 7 days (T1), the average frequency of relaxed jaw muscles reports at the population level was 62%. Teeth contact (20%) and mandible bracing (14%) were the most frequent AB behaviors. No significant gender differences were detected. One month later, during the second week of data collection (T2), the frequency of the conditions was as follows: relaxed jaw muscles 74%, teeth contact 11% and mandible bracing 13%.

Conclusions: These data recorded do not allow any generalization due the unrepresentativeness of the study population. On the other hand, they can be used as templates for future comparisons to get deeper into the study of natural fluctuations of

AB behaviors as well as into the potential biofeedback effect of an ecological momentary assessment/intervention. It is important to recognize that the use of smartphone technology may help to set range of values for AB frequency in otherwise healthy individuals, in order to stand as comparisons for selected populations with risk or associated factors.

Keywords: awake bruxism, ecological momentary assessment, ecological momentary intervention, bruxism, smartphone, awake bruxism behaviors

INTRODUCTION

Bruxism is an oral condition that is attracting interest from researchers and clinicians of several medical disciplines, such as neurologists, psychologists, dentists, physicians, and orofacial pain experts. The constantly evolving knowledge and the diverging approaches by the different specialties is reflected in the number of different bruxism definitions that has been provided over the past decades (1, 2).

In March 2017, a panel of invited experts took part to an International Consensus Meeting that provided separate definitions for sleep bruxism (SB) and awake bruxism (AB) and revisited the diagnostic grading that was previously proposed in 2013 by the same panel. The introduction of a specific definition for AB is of particular interest, especially considering the paucity of epidemiological data. AB has been defined as "a masticatory muscle activity during wakefulness that is characterized by repetitive or sustained tooth contact and/or by bracing or thrusting of the mandible and is not a movement disorder in otherwise healthy individuals" (3).

Such definition has implications concerning the diagnosis, especially in the light of the influence that the adoption of different diagnostic strategies may have on the prevalence data reported for both adults (4) and children/adolescents (5). In short, the consensus paper suggests that bruxism should be considered as a jaw-muscle behavior that must be measured in its continuum to achieve a definite diagnosis. As such, the muscle behavior should be measured at best with continuous electromyographic (EMG) recordings during wakefulness (6). On the other hand, it should be recognized that acquiring hour-long EMG recordings while awake is difficult for obvious technical reasons as well as the discomfort for the patients. For this reason, an alternative option to AB assessment, viz., the Ecological Momentary Assessment (EMA), has been suggested.

EMA refers to real time report of a behavior, a feeling, or whichever condition under study (7). It was developed in the 1980 s as a way of addressing the limitation of traditional quantitative methods in psychological science (8). In short, over a time frame within the course of his/her daily affairs, an individual is prompted at fixed or random time points to answer questions about what he/she is currently doing and/or experiencing. Doing so, multiple recording points during the day, close in time to the experience in the natural environment, are allowed (9). The fact that data are collected in the everyday ("real world") environment, as subjects go about their lives, increases their representativeness and this ecological aspect allows generalization to an individual's real life. Several studies on the natural course of AB could be performed using EMA strategies as an instrument to investigate the day-to-day variability of behaviors over multiple observation periods (e.g., during stressful periods that may have an influence on the individuals' current psychological wellbeing).

Based on the definition of AB provided in the consensus paper, using EMA in the bruxism field will help achieving a better description of AB epidemiology, both at the general population level and in selected group of individuals with purported risk factors for additive AB and with possible clinical consequences. Within these premises, this two-part article will discuss the general principles of EMA and comment on a preliminary dataset gathered in Italian young adults with a dedicated smartphone application (part 1), and will describe the translational efforts into Polish language as part of an ongoing multicenter research on AB epidemiology (part 2).

CURRENT APPLICATION OF EMA PRINCIPLES

EMA strategies are being used to study the prevalence of a wide spectrum of conditions in behavioral medicine [e.g., smoking cessation, alcohol consumption, eating disorders (7)]. In addition, they are useful to conduct specific studies on daily habits to monitor a behavior over time, such as in the case of a mobile app supported by the American Sleep Apnea Association to study the correlation between sleep habits and some illnesses (e.g., diabetes, heart pathologies, obesity, depression) (10). As far as oral behaviors are concerned, EMA has already proven reliable in the research setting (11), but it should be remarked that EMA-based data on AB are fragmental and limited to a few investigations on selected behaviors, such as tooth clenching and tooth contact habits (9, 12). The simplest EMA strategy is the daily diary, which is still commonly used in several clinical medical fields and has also been used to gather the few data available on AB so far. However, with the widespread development of mobile electronic technologies, new ways to approach EMA in the research and clinical settings have become available. Interestingly, the use of technology has introduced a new possible way for clinicians to engage patients from a therapeutic viewpoint as well [i.e., Ecological Momentary Intervention (EMI)] (8). In other words, the progressive adaptation of EMA techniques to the technological progress has *de facto* opened a new era for EMA (9) and created more therapeutic opportunities (i.e., EMI).

Over the past few years, the most commonly used devices were palmtop computers and mobile phones (7), but today there is no doubt that smartphones offer the best potential in terms of customized applications and internet access. Smartphones diffusion is widespread in all age groups, so they are useful to capture real-time experiences in potentially huge study samples. EMA protocols based on smartphones typically require participants to complete assessments at predetermined time intervals or windows, either in response to specific states or events or in response to an auditory signal programmed by the researchers. Thus, smartphones provide an ideal platform for real-time reports at multiple daily recording points over multiple-day spans.

There are only few studies on the application of EMA principles in the dental field. In the field of orofacial pain, the only available findings suggest that non-functional tooth contact (i.e., tooth contact during activities that are not associated with normal function, such as reading books, watching television, working, etc.), recorded at 20-min intervals for 10 days, are more prevalent in patients with temporomandibular disorders (TMDs) than in healthy subjects (12).

With the purpose to get deeper into the knowledge on awake bruxism, an application (form here on abbreviated as "app") based on EMA principles was recently developed (BruxApp®, BruxApp Team, Pontedera, Italy). The app sends alert sounds at random times during the day. The smartphone user must answer in real time by tapping on the display icon that refers to the current condition of the jaw muscles or teeth position: relaxed jaw muscles, tooth contact, tooth clenching, tooth grinding or jaw clenching [without tooth contact (i.e., mandible bracing)]. Such behaviors were selected as they that are part of the AB spectrum. For further details on the software, readers are referred to the original publication (13, 14).

PRELIMINARY SMARTPHONE-BASED EMA REPORT ON AB AND DATA DISCUSSION

A preliminary study on AB using BruxApp has been performed in a population of undergraduate University students, on a sample of 30 otherwise healthy young adults (9 males, 21 females; mean age 24 ± 3.5 years) during the period from October 2015 to March 2016. All subjects were undergraduate students attending different University courses (e.g., school of Dentistry, Medicine and Surgery, Law, and school of Engineering). Data were recorded over a 7-day period for two times, with a one-month interval between the two observation periods. Data were collected by the leading author of this manuscript (A.Z.) and stored in an excel database. The study was approved by the Institutional Review Board of the University of Padova, Italy, and all participants signed a written consent to take part to the study.

This set of preliminary data is an example of two potentially separate investigations. During the first week, smartphone-based EMA has been used to get an overview of the frequency of each oral condition (i.e., relaxed jaw muscles, mandible bracing, teeth clenching, tooth contact, teeth grinding). On the other hand, it has been theorized that being asked about a behavior in close contextual and temporal proximity to its occurrence draws one individual's attention toward the behavior, thereby promoting self-awareness and potentially inducing positive changes with respect to the capability to self-recognize and avoid the behavior (i.e., EMI-biofeedback) (15). Thus, the purpose of collecting data over a second week, one-month later, was twofold, viz., (1) to monitor AB behaviors over time, and (2) to test for potential "EMI" effects. The app was programed to send 15 alerts per day during the 8.00–22.00 h span, with individually set breaks during lunchtimes. In order to reduce the possibility that individuals may modify their behavior based on the expectation of receiving the alert at predetermined time intervals or hours, alerts were randomly generated by the app. Over the first seven days, the average frequency of relaxed jaw muscles reports at the study population level was 62%. Teeth contact (20%) and mandible bracing (14%) were the most frequent AB behaviors. No significant gender differences were detected. One month later, during the second week of data collection, the frequency of the conditions was as follows: relaxed jaw muscles 74%, teeth contact 11% and mandible bracing 13%. (**Table 1**)

Data collected during the second week suggested an increase in the frequency of relaxed jaw muscles' condition and a decrease in teeth contact habit, thus indicating a certain degree of variability of AB behaviors over time on one hand, but also potentially supporting an EMI effectiveness on the other hand. These preliminary ideas and dataset recorded in a small, selected population of university students do not allow any generalization. Nonetheless, they can be used as templates for future comparisons to get deeper into the study of natural fluctuations of AB behaviors as well as into the potential biofeedback effect of an ecological momentary assessment approach to patients with clinically relevant bruxism.

DISCUSSION

Until now, most available data on AB prevalence have been obtained by means of retrospective self-reporting at a single observation point (4). Such approach requires the participants to recall to their minds the frequency of a habit over the timespan covered by the report (e.g., days, weeks, months, and years) and give a generic answer. The resulting answers can be biased due

TABLE 1 | Mean values of frequency data of positive observations (standard deviations in parenthesis) expressed in percentage for the different AB behaviors over the 7-day observation period (T1) and the second period of observation after a month (T2).

Activity	T1	T2
Relaxed	62 (34.9)%	74 (30.0)%
Teeth clenching	3 (9.5)%	2 (5.8)%
Teeth contact	20 (22.5)%	11 (19.5)%
Teeth grinding	1 (0.4)%	1 (0.6)%
Mandible bracing	14 (20.1)%	13 (26.0)%

Data refer to a study population-level average.

to reporting errors (16, 17). Such shortcoming can easily be overcome with EMA, which requires participants to report close on time with the current experience. Moreover, EMA occurs in natural settings, thus offering a potential advantage in terms of generalizability and ecological validity of findings with respect to hour-long EMG recordings during wakefulness.

The above-outlined general framework can be refined and the EMA usefulness can be maximized by using smartphones apps, which are so diffused that they generally do not even require an explanation on how to use them thanks to a user-friendly interface (18, 19). Smartphone apps provide a pre-programmed or randomly generated auditory signal that recalls the patient's attention to the behavior under investigation several times per day. An additional advantage is that apps allow tracking compliance rate. All in all, this means that the outcome variable can be assessed multiple times and researchers are enabled to collect huge amounts of information on the epidemiological features, risk factors, and clinical consequences of the condition under study (6, 20).

As for awake bruxism, a basic premise to understand the potential usefulness of smartphone-based EMA is that the 2018 definition highlights two important aspects. First, focus has been definitively shifted to the muscle activity, specifying that bruxism does not necessarily involve tooth contact (21). Second, it must be remarked that in "otherwise healthy people," bruxism is not a pathological condition. From an etiological viewpoint, bruxism can be a sign of a disorder [e.g., obstructive sleep apnea, psychological or neurological disorders (22)]. From a clinical perspective, it may be a risk factor for negative consequences (e.g., tooth wear, muscle fatigue and pain, failures of dental restorations) or even a factor associated with positive health outcomes [e.g., reducing the risk of detrimental chemical tooth wear by increasing salivation in patients with gastro-esophageal reflux (23)].

The above considerations suggests the need to re-conceptualize bruxism as a spectrum of behaviors, which need to be more extensively studied from an epidemiological perspective than in the past. As for AB, the basic requirement is to gather information on the frequency of all conditions of the behavioral spectrum (i.e., tooth contact habits, tooth clenching, tooth grinding, mandible bracing) and to possibly identify a range of "normal values" for AB in healthy individuals in a natural environment. The second step should be to collect data in selected groups of subjects with associated conditions and risk factors for additive AB (e.g., stress sensitivity, anxiety).

Currently, knowledge on AB is very limited as far as prevalence or frequency data on healthy individuals are concerned. In particular, there is an almost complete lack of information on mandible bracing. Within this framework, the development of a smartphone app to definitively introduce EMA into the field of AB research (EMA/AB) is a much required strategy to implement knowledge on the epidemiological features of AB by studying the natural course and fluctuations of signs, symptoms, and exposure to etiological factors.

An app-based EMA approach is also suitable for collecting consistent data across different investigations and within multiple observation points of the same study, thus making it a promising option to perform longitudinal and multicenter researches. The ultimate goal is to approximate the "definite" assessment of AB in the clinical setting.

Using a smartphone app (i.e., BruxApp) in a population of healthy young adults has allowed to gather preliminary data on the average frequency for the different AB behaviors (i.e., tooth contact, mandible bracing, tooth clenching, tooth grinding) over two 7-day observation periods. Tooth contact habits and jaw clenching were the most frequently reported conditions, with an average frequency for the "relaxed jaw muscles" answer of 62% at the study population level. One month later, data gathered over a second observation week showed a 74% frequency, potentially showing both natural fluctuation and a self-awareness effect. The paucity and inconsistency of the available literature on this topic makes it impossible to compare these findings with previous studies.

In an effort to standardize all the investigations performed with BruxApp, a Research Version has thus been developed. It has a pre-set number of alerts programmed per day (viz., 20) as well as the possibility to access the raw application data, without any filters to automatically discard "low-compliance" days. Thus, it can be easily hypothesized that these findings, which show the potential of smartphone-based EMA in the research setting, will soon be part of a wide international dataset on the frequency of AB.

In the clinical setting, the app has a potential usefulness beyond the scope of gathering epidemiological data for research purposes. Indeed, an individual's awareness, behavior, and experience are altered when he/she are knowingly being assessed (13). Smartphone-based EMA can minimize this potential bias, since it allows the patient to focus his/her attention to the focal behavior only at random moments and in the natural environment, thus avoiding any laboratory setting biases. Nonetheless, focusing repeatedly on a specific behavior might enable the patient to improve self-awareness, which is responsible in promoting more control and cognitive change (24) (i.e., biofeedback/EMI). Thus, the app may have a rationale for use as a potential therapeutic strategy in myofascial pain patients with a self-reported history of awake bruxism.

The term EMI provides a framework for treatments characterized by the delivery of interventions when people go about their daily lives (25, 26). In other words, the treatment setting is the real world. Smartphone-based apps open the possibility to perform EMI treatments in many forms, ranging from basic clinical recommendation and counseling to more formalized and structured interventions. (27) EMI benefits of extending the treatment beyond the standard context, providing support in patients' daily routine. Thus, the potential for the use of smartphone/EMA approach as a strategy to implement cognitive-behavioral management of AB is worth an assessment within the framework of multimodal conservative treatment (28).

Such an app-based cognitive-behavioral approach is also interesting as for the amount of information on awake bruxism and its possible consequences that can be conveyed to the patients via the smartphone display. This could implement an individual's understanding of the need to keep the jaw muscles relaxed. Thus, there are enough elements to hypothesize that an app that

instructs patients on the various consequences of bruxism, with an alert biofeedback function such as sound pulses at random times that remind patients about keeping their jaw muscles relaxed, may have interesting clinical potential. Support to this suggestion comes from encouraging literature findings on other conditions. Indeed, EMI based on the biofeedback mechanism has already been used effectively in people who show potentially dangerous behaviors as a strategy to recognize and modify it. Within the last several years, interventions have been delivered to patients with a variety of conditions and health behaviors, such as eating and anxiety disorders (10), smoking habits (7, 29, 30), and psychological distress (31), and have been even used to facilitate prevention behavior amongst HIV-infected individuals (32, 33).

As for the indications, it must be recognized that, at the moment, there are no specific recommendations on when and how to prescribe the use of EMA method in clinical practice. On the other hand, it can be suggested that a twofold strategy of prescription should be refined: (1) to assess the frequency of AB behavior (i.e., EMA), and (2) to implement the control of AB in patients with potential clinical consequences (i.e., EMI). The two prescriptions are consequential, based on the logical diagnosis-to-treatment pathway, and can be equally adopted in both the research setting and the clinical setting. On the other hand, research findings gathered over the next few years will be fundamental to design treatment-need algorithms based on the frequency of AB behaviors in patients with clinical signs and symptoms. Amongst those, myofascial pain patients with stress sensitivity and anxiety personality are the theoretical best-fitting targets of app-based EMI due to the potential influence on emotion-related mandible bracing.

Considering the above, BruxApp has been translated into several languages to ease consistency of cross-cultural investigations, and it is currently used in an international multicenter research project on the epidemiology of awake bruxism. The project involves more than 20 countries worldwide, and its description is one of the topics of the second part of this manuscript.

CONCLUSIONS

This article discussed the possible application of ecological momentary assessment and intervention principles to the study of awake bruxism behaviors by adopting smartphone technology. Among the possible EMA strategies, the development of smartphone-based applications seems a promising strategy to get deeper into the evaluation of several epidemiological, etiological, and management issues concerning AB.

Future EMA researches on the frequency of AB activities (e.g., teeth clenching, mandible bracing, teeth grinding, teeth contact) in healthy individuals and on their additive frequency in selected populations with comorbid conditions (e.g., psychological and social impairment, orofacial pain, sleep disorders) will shed light onto these behaviors and will contribute to a better understanding of this complex topic.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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The Diagnostic Value of Electromyography in Identifying Patients With Pain-Related Temporomandibular Disorders

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Introduction: Orofacial pain disorders can be divided into several subgroups. One of them is temporomandibular disorders (TMD) with recognizable signs such as joint noises, limitations in the range of motion, or mandibular deviation during function and symptoms—pain in the muscles or joint. Surface electromyography (sEMG) is a diagnostic tool that ensures reliable and valid evaluation of muscle activity. sEMG detects electrical potentials and on this account may conceivably be employed in the TMD recognition. The aim of this study was to assess the sensitivity, specificity, and accuracy of electromyography in diagnosing subjects with temporomandibular disorders, including pain-free TMD and pain-related TMD.

Methods: The sample comprised 88 patients with cleft lip and palate and mixed dentition. TMD has been recognized on the grounds of Axis I of the Research Diagnostic Criteria for TMD (RDC/TMD). To evaluate the electrical activity of the temporal and masseter muscles in the rest position and during maximum voluntary contraction, a DAB-Bluetooth Instrument (Zebris Medical GmbH, Germany) was used. The analysis of the receiver operating characteristic (ROC) curve gave information about accuracy, cut-off point value, sensitivity and specificity of the normalized sEMG data.

Results: The highest diagnostic efficiency of sEMG in terms of identifying subjects with TMD and pain-related TMD was observed for the mean values of temporal and masseter muscle activity as well as the Asymmetry Index of the masseter muscles in a rest position. A moderate degree of EMG accuracy in differentiating between pain-related TMD and non-TMD children was observed for the mean values of masseter muscle activity and the Asymmetry Index of the masseter muscles at rest.

Conclusion: An evaluation of electromyography exhibits its diagnostic usability in recognition of patients with pain-related TMD and it could be used as an adjunctive tool in the identification of this disorder.

Clinical Trial Registration: This clinical research was registered in the ClinicalTrials.gov database under the number NCT03308266.

Keywords: orofacial pain, temporomandibular disorders, pain-related temporomandibular disorders, surface electromyography, cleft lip and palate

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INTRODUCTION

Orofacial pain disorders can be divided into several subgroups. One of them are temporomandibular disorders (TMD) with recognizable signs such as joint noises, limitations in the range of motion, or mandibular deviation during function and symptoms—pain in the muscles or joint (1, 2). The multifactorial etiology of this condition hinders the precise diagnosis and requires many tools and activities to draw correct conclusion (3–6). An accurate medical history and standardized tests and examinations are considered to be the standard reference point. In clinical evaluations of many TMD cases to provide valid quantitative data it is advisable to collect additional information by using electronic devices (6–11).

The one of the most current and useful tool for TMD assessment are the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) (2, 12). The criteria provide a holistic approach to the TMD identification by diagnosing both physical and psychosocial aspects and therefore ensuring standardized procedures for epidemiological studies, and a comparison with the results of other similar studies (2, 13, 14). An accurate recognition of TMD is especially important in the case of children, as early identification of TMD in childhood could be useful when minimizing the risk of developing chronic pain and preventing persistent or severe TMD problems during adolescence (15). Children with congenital abnormalities, such as cleft lip and palate (CLP) are potentially at risk of developing TMD due to psychosocial burdens, as well as malocclusions predisposing them to this condition (16, 17). The signs and symptoms of TMD occur more frequently in children with CLP than in children and adolescents in the general population (15–21).

One of the only diagnostic tool that allows an evaluation of muscle function and efficiency by directly and objectively detecting their electrical potentials is electromyography (22). This method has been widely used for the diagnosis of patients with general muscle disorders, neuromuscular diseases or diseases affecting neuromuscular performance (23, 24). Surface electromyography (sEMG) as global electromyography, in contrary to the quantitative intramuscular electromyography that uses intramuscular needle electrodes, "uses surface electrodes and detects superimposed motor unit action potentials from many fibers, as opposed to the single ones recorded by the intramuscular type" (23). Wherefore the analysis of the sEMG findings is limited to three main subjects: "general muscle activity, the cooperation of different muscles, and the variability of their activity over time" (23). The most important advantage of sEMG is its non-invasiveness (23). It is a painless and innocuous method for evaluating muscle function that may conceivably be used in the TMD identification (6, 25). Nevertheless, its application in the recognition of this disorder remains disputable due to significant variability in the results described in the literature (6, 26). A systematic review gained no attestation to support the efficacy of surface electromyography as a diagnostic tool for TMD (2, 27). On the other hand, a more recent study presented the moderate accuracy of sEMG values for masticatory muscles when assessing TMD in adults (6).

The most dominant TMD conditions are pain-related temporomandibular disorders (TMD-P) (28). The primary manifestation of TMD-P is a persistent, recurring, or chronic pain that affects jaw muscles, the temporomandibular joint (TMJ), and/or adjacent structures (13, 29). Subjects diagnosed with TMD-P modify a tension of their masticatory muscles. Pain induces adaptations by reworking muscle activity in order to shield the masticatory motor system from possible trauma (30, 31). During muscle contraction pain can cause greater alteration in electromyographical activity, which in turn may affect the accuracy of this equipment (6, 32).

As the assessment of subjects with TMD by using the sEMG remains disputable and there have been no previous studies assessing the efficacy of EMG in diagnosing TMD, including pain-related TMD in CLP children, it is important that we undertake research in this field. Electromyographic study of masticatory muscle activity in cleft lip and palate subjects with a TMD-pain diagnosis have previously been completed (15).

The aim of the present study was to assess the sensitivity, specificity, and accuracy of electromyography in diagnosing TMD, including both pain-free TMD (TMD-PF) and pain-related TMD (TMD-P) in cleft lip and palate patients. We hypothesized the diagnostic inefficiency of electromyography in identifying CLP patients with TMD.

METHODS

This clinical research was registered in the ClinicalTrials.gov database as number NCT03308266. The protocol was approved by the Local Bioethics Committee of the Pomeranian Medical University (number KB-0012/08/15). The children's parents were notified about the test procedures and gave written informed consent to all the performers' procedures in accordance with the Declaration of Helsinki.

The sample comprised 88 patients with cleft lip and palate and mixed dentition. Following an evaluation based on algorithms for Axis I of the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) (13), children diagnosed with pain-free TMD were included in the non-pain TMD group (Group 1), subjects diagnosed with pain-related TMD were included in the TMD-pain group (Group 2) and patients with no TMD diagnosis comprised the non-TMD group (Group 3). Participants were selected from the group of 100 patients who had been referred to Orthodontic Cleft Care Center in Poland. After adaptation of the exclusion criteria there were 88 patients qualified for further examination left. Group 1 comprised 25 children (12 girls and 13 boys) with a mean age of 9.4 $\pm$ 1.7 with CLP and a pain-free TMD diagnosis. Group 2 included 30 CLP subjects (14 girls and 16 boys) with a mean age of 9.1 $\pm$ 1.5 with a TMD-P diagnosis. Group 3 comprised 33 CLP subjects (16 girls and 17 boys) with a mean age of 8.9 $\pm$ 1.5 with no TMD. The exclusion criteria for all groups included the following: the presence of a cleft lip and palate with other congenital abnormalities, the presence of systemic or rheumatologic diseases, a history of cervical spine or TMJ

surgery, trauma or deformities, as well as completed orthodontic or masticatory motor system dysfunction treatment.

The function of the masticatory motor system was evaluated by taking into consideration a clinical and electromyographic the analysis. The general medical histories of the patients were taken, which provided information on the patients' masticatory motor systems, including subjective TMD symptoms, such as jaw pain during function, frequent headaches, jaw stiffness/fatigue, difficulty of mouth opening in normal plane, teeth gnashing, and TMJ sounds (33). Axis I scoring of the Research Diagnostic Criteria for TMD (RDC/TMD) (13) was used to assess children for the presence of temporomandibular disorders with the same trained examiner. The RDC/TMD was used as the gold standard. The temporomandibular disorder was recognized when the clinical signs fulfilled the criteria of RDC/TMD such as "pain on palpation, mandibular range of motion, associated pain (jaw opening pattern, unassisted opening, maximum assisted opening, mandibular excursive and protrusive movements), sounds coming from the TMJ, and tenderness induced by muscle and joint palpation" (34).

To take electromyographical recordings a DAB-Bluetooth Instrument (Zebris Medical GmbH, Germany) was used by a single experienced researcher. We followed the methods previously described by Szyszka-Sommerfeld et al. (15, 22). In the process of recordings, the head was unsupported, in natural head position (NHP) (35, 36). The masseter and temporal anterior muscles were examined with disposable silver/silver chloride (Ag/AgCl), self-adhesive, bipolar surface electrodes at an interelectrode distance of 20 mm (Noraxon Dual Electrode, Noraxon, USA) positioned on the muscle bellies parallel to the muscle fibers ("temporal anterior: vertically along the anterior muscular margin, around the coronal suture; masseter: parallel to the muscle fibers, with the upper pole of the electrode at the intersection between the tragus-labial commissure and the exocanthion-gonion lines") (37, 38). Reference electrodes were applied in positions "inferior and posterior to the right ear" (39).

The main hindrance of the examination could be the skin impedance. The obstacle was withdrawn by cleaning the skin surface with 70% ethyl alcohol and dried prior to the placement of the electrode (39). The proper preparation was proven by carrying an impedance test that was performed with Metex P-10 a measuring device (Metex Instruments Corporation, Korea). If the test produced a positive result showing low skin tissue impedance, further examinations would be conducted (22). The EMG assessments were performed 5 min later. EMG activity was then recorded during three different tasks, in the same way as was previously described by Szyszka-Sommerfeld et al. (22):

1. Rest activity of the masticatory muscles was performed "in the clinical rest position."
2. Maximum voluntary clench (MVC)—was performed "in the intercuspal position and the subject was asked to clench as hard as possible for 5 s."
3. Maximum voluntary clench (MVC)—was performed "with two 10-mm thick cotton rolls positioned on the mandibular second premolars and molars, or on the mandibular second milk molars and the first permanent molars and the subject was asked to clench as hard as possible for 5 s."

The movements were repeated at least three times to ascertain stability. Between each of every recording 5 min of rest was granted a permission to avoid any effects of fatigue.

The EMG signals after the registration were processed by amplification, digitization and digital filtration. The DAB-Bluetooth Instrument was ported to a computer, which enabled the data graphical presentation and further quantitative and qualitative analyses. The analysis encompassed mainly the normalization process as the essential procedure for the initial processing of raw data to ensure reliable further analysis. The EMG recordings ought to be mutually likened to the electrical muscle activity detected during certain standardization recordings, such as MVC. The electrical potentials collected in maximum voluntary clenching are reported to have the highest repeatability. Amidst the various protocols, MVC on cotton rolls is reported to vary inter-individually in the smallest extent and on that account a method based on this standardization is now regularly used (37, 40, 41). On the grounds, normalization included referring the raw results (the mean values of the electrical potentials) to the data acquired from each patient after clenching on cotton rolls (reference values) in accordance with the following formula: "mean values (μV) during rest position or MVC / mean values (μV) during MVC with two 10-mm cotton rolls × 100%" (22). EMG potentials of every analyzed muscle were submitted as a percentage of the maximum voluntary clenching value with cotton rolls (unit μV/μV%). Regularly, normalized EMG data will implement information about the impact of "teeth contact on neuromuscular activity, while avoiding individual variability (anatomical variations, physiological and psychological status, etc.) and technical variations (muscle cross-talk, electrode position, skin, and electrode impedance, etc.)" (15, 41).

Finally, the Asymmetry Index (As, unit %) was recorded to assess asymmetry concerning the activity of the left and right masticatory muscles using the following formula:

$$\mathrm{As} = \sum_{i=1}^{N} |R_i - L_i| \,/\, \sum_{i=1}^{N} (R_i + L_i) \times 100$$

This ranges from 0% (total symmetry) to 100% (total asymmetry) (42).

In order to achieve a proper statistical result, the Levene test was used to evaluate homogeneity of variance and the Kolmogorov-Smirnov test was used to assess normality. To verify the research hypotheses toward the presence or absence of differences between the mean values of the independent variables the Student t-test and the Mann-Whitney U test were applied. The level of significance was set at $p = 0.05$. The area under the curve (AUC) was determined by the receiver operating characteristic (ROC) curve. It gave information about accuracy, cut-off point value, sensitivity (Se) and specificity (Sp) of the normalized sEMG data. The classification of the AUC was as follows: "0.5, result due to chance; >0.5–0.7, low accuracy; >0.7–0.9, moderate accuracy; >0.9–<1.0, high accuracy; and 1.0, a perfect test" (6, 43, 44).

RESULTS

Table 1 shows the diagnostic efficiency of EMG in identifying CLP subjects with TMD (pain-free TMD and pain-related TMD; Group 1 and Group 2 vs. Group 3). The analysis of the ROC curve demonstrated that the diagnostic efficiency of electromyography in distinguishing between TMD and non-TMD children was highest in the case of estimators of distribution of variables, such as the mean values of temporal and masseter muscle activity in a rest position (temporal: AUC = 0.664, the standard error of mean [SEM] = 0.058, $p = 0.0110$; cut-off point = 6.45 μV/μV%, Se = 63%, 1–Sp = 38%; masseter: AUC = 0.662, SEM = 0.062, $p = 0.0120$, cut-off point = 3.80 μV/μV%, Se = 77%, 1–Sp = 50%), as well as the Asymmetry Index for the masseter muscles at rest (AUC = 0.647, SEM = 0.063, $p = 0.0220$, cut-off point = 4.47%, Se = 48%, 1–Sp = 22%).

Table 2 presents the diagnostic value of EMG in identifying CLP children with pain-related TMD (Group 2 vs. Group 3). The highest diagnostic efficiency of EMG in discriminating between TMD-P and non-TMD subjects was observed for the mean values of temporal and masseter muscle rest activity (for temporal muscle AUC = 0.655, SEM = 0.069, $p = 0.0342$, cut-off point = 6.45 μV/μV%, Se = 68%, 1–Sp = 38%; for masseter muscle: AUC = 0.728, SEM = 0.064, $p = 0.0018$, cut-off point = 3.80 μV/μV%, Se = 90%, 1–Sp = 50%), as well as the Asymmetry Index for the masseter muscles at rest (AUC = 0.723, SEM = 0.064, p = 0.024, cut-off point = 10.12%, Se = 87%, 1–Sp = 50%). A moderate degree of EMG accuracy in terms of differentiating between TMD-P and non-TMD children was observed for the mean values of masseter muscle activity and the Asymmetry Index of the masseter muscles at rest position (**Table 2**).

The results showed that the highest diagnostic efficiency of EMG in identifying pain-free TMD children (Group 1 vs. Group 3) was achieved in the case of the mean values of temporal muscle activity in the mandibular rest position (AUC = 0.658, SEM = 0.076, $p = 0.0427$, cut-off point = 7.43 μV/μV%, Se = 52%, 1–Sp = 19%, **Table 3**).

The efficiency of the normalized EMG data for all variables during rest and MVC was higher in assessments of TMD-P than in diagnoses of TMD and TMD-PF subjects (**Tables 1**–**3**).

DISCUSSION

In this research we evaluated the diagnostic value of surface electromyography as a technique for identifying temporomandibular disorders in cleft lip and palate children. The non-pain TMD and pain-related TMD groups were compared with a control group with no TMD. An analysis of the results demonstrated that the highest diagnostic efficiency for EMG in identifying subjects with TMD (TMD-PF and TMD-P) and patients with TMD-P was achieved for such variables as the mean values of temporal and masseter muscle activity and the Asymmetry Index of the masseter muscles in the rest position, as well as for the mean values of temporal muscle rest activity to diagnose children with pain-free TMD. A moderate degree of EMG accuracy in differentiating between pain-related TMD and no TMD patients was observed in the case of the mean masseter muscle activity values and the Asymmetry Index of the masseter muscles at rest position.

As mentioned earlier, surface electromyography (sEMG) by dint of detecting electrical potentials is the most reliable and valid method for assessing muscle function and efficiency (39). The EMG method is harmless, painless and innocuous which is an utmost importance when conducting studies involving children (22, 23). In our study there were no difficulties with reference to the cooperation of the children during EMG recordings. The diagnostic value of EMG in identifying pain-related TMD in children, has yet to be agreed in the literature. The present study provides the first ever data on the accuracy, sensitivity and specificity of normalized sEMG values in the recognition of pain-related TMD in CLP children in the rest position and during MVC. The data analysis encompassed mainly the normalization process. This scheme was essential for the initial processing of raw data to ensure interindividual comparisons (22, 37). EMG potentials of every analyzed muscle were submitted as a percentage of the MVC value using cotton rolls. In order for the research to be objective, any variability arising from skin and electrode impedance, electrode positioning or relative muscular hypo- or hypertrophy should be obviated (37–46).

The previous study concerning masticatory muscle EMG activity in CLP children diagnosed with TMD-P based on the RDC/TMD criteria confirmed that in comparison to non-TMD patients subjects diagnosed with pain-related TMD have altered temporal and masseter muscle activity. It was noted that altered muscle electrical activity in subjects with TMD-P can affect muscle fatigue, and can, as a consequence, have an impact on every function they perform in the stomatognathic system (15).

The diagnostic effectiveness of selected non-invasive methods of instrumental diagnostics to identify temporomandibular disorders have previously been discussed. The authors demonstrated considerable variability in the diagnosis of this disorder (32, 47–49). The assessment of patients with TMD by using the sEMG remains disputable. The diagnostic accurateness of surface electromyography and kinesiography devices in the diagnosis of individuals with myofascial pain of masticatory muscles was assessed by Manfredini et al. (32). The authors reported an unacceptable efficiency of sEMG at rest in discriminating between myogenous TMD-pain and asymptomatic subjects (AUC = 0.28–0.48) and fair to excellent degree of EMG accuracy during clenching tasks (AUC > 0.7). It has been also promulgated and should be emphasized that the use of EMG indices in the diagnosis of myogenous TMD should be used attentively, rarely if ever, due to the potential risk of false-positive results (6, 32). Contrarily, De Felício et al. (50) remarked a positive correlation between sEMG indices and TMD-signs and symptoms, implying potential sEMG efficiency in distinguishing between myogenous TMD plus disc displacement with reduction and normal subjects. Castroflorio et al. (51) and Lauriti et al. (9) found that sEMG indices of the masticatory muscles are reproducible in identifying TMD and non-TMD patients at rest position and during MVC on parafilm (9).

TABLE 1 | Data of the area under ROC curve, best cut-off value, sensitivity and specificity of EMG in identifying children with TMD (Group 1 and 2) and non-TMD subjects (Group 3).

Activity	Region	Variable	AUC (95% CI)	SEM	*P*-value	Cut-off value	Se [%]	1–Sp [%]
Rest	TA	EA [μV/μV%]	0.664 (0.550–0.777)	0.058	0.0110*	6.45	63.0	38.0
		As [%]	0.616 (0.485–0.746)	0.067	0.0726	18.43	86.0	56.0
	MM	EA [μV/μV%]	0.662 (0.540–0.783)	0.062	0.0120*	3.80	77.0	50.0
		As [%]	0.647 (0.524–0.770)	0.063	0.0220*	4.74	48.0	22.0
MVC	TA	EA [μV/μV%]	0.595 (0.474–0.717)	0.062	0.1380	103.89	52.0	31.0
		As [%]	0.552 (0.431–0.673)	0.062	0.4198	9.38	41.0	25.0
	MM	EA [μV/μV%]	0.537 (0.413–0.660)	0.063	0.5699	77.94	32.0	16.0
		As [%]	0.612 (0.489–0.736)	0.063	0.0805	6.32	59.0	34.0

*MVC, maximum voluntary contraction; TA, anterior temporal muscle; MM, masseter muscle; EA, electrical activity; As, asymmetry index; AUC, area under ROC curve; SEM, standard error of mean; Se, sensitivity; Sp, specificity; *Statistically significant difference.*

TABLE 2 | Data of the area under ROC curve, best cut-off value, sensitivity and specificity of EMG in identifying children with TMD-P (Group 2) and non-TMD subjects (Group 3).

Activity	Region	Variable	AUC (95% CI)	SEM	*P*-value	Cut-off value	Se [%]	1–Sp [%]
Rest	TA	EA [μV/μV%]	0.655 (0.521–0.790)	0.069	0.0342*	6.45	68.0	38.0
		As [%]	0.620 (0.468–0.705)	0.073	0.1018	17.57	94.0	56.0
	MM	EA [μV/μV%]	0.728 (0.604–0.853)	0.064	0.0018*	3.80	90.0	50.0
		As [%]	0.723 (0.597–0.848)	0.064	0.0024*	10.12	87.0	50.0
MVC	TA	EA [μV/μV%]	0.607 (0.466–0.748)	0.072	0.1450	109.58	65.0	41.0
		As [%]	0.580 (0.437–0.722)	0.073	0.2774	8.97	48.0	28.0
	MM	EA [μV/μV%]	0.593 (0.451–0.734)	0.072	0.2059	104.63	71.0	47.0
		As [%]	0.630 (0.489–0.771)	0.072	0.0761	6.59	65.0	34.0

*MVC, maximum voluntary contraction; TA, anterior temporal muscle; MM, masseter muscle; EA, electrical activity; As, asymmetry index; AUC, area under ROC curve; SEM, standard error of mean; Se, sensitivity; Sp, specificity; *Statistically significant difference.*

TABLE 3 | Data of the area under ROC curve, best cut-off value, sensitivity and specificity of EMG in identifying children with TMD-PF (Group 1) and non-TMD subjects (Group 3).

Activity	Region	Variable	AUC (95% CI)	SEM	*P*-value	Cut-off value	Se [%]	1–Sp [%]
Rest	TA	EA [μV/μV%]	0.658 (0.509–0.806)	0.076	0.0427*	7.43	52.0	19.0
		As [%]	0.610 (0.463–0.757)	0.075	0.1570	22.16	92.0	66.0
	MM	EA [μV/μV%]	0.556 (0.400–0.711)	0.079	0.4742	5.00	52.0	28.0
		As [%]	0.554 (0.403–0.705)	0.077	0.4892	4.68	40.0	22.0
MVC	TA	EA [μV/μV%]	0.535 (0.380–0.690)	0.079	0.6525	113.88	59.0	40.0
		As [%]	0.518 (0.360–0.675)	0.081	0.8219	13.11	28.0	13.0
	MM	EA [μV/μV%]	0.533 (0.373–0.693)	0.082	0.6700	119.31	78.0	52.0
		As [%]	0.591 (0.441–0.740)	0.076	0.2436	4.12	76.0	50.0

*MVC, maximum voluntary contraction; TA, anterior temporal muscle; MM, masseter muscle; EA, electrical activity; As, asymmetry index; AUC, area under ROC curve; SEM, standard error of mean; Se, sensitivity; Sp, specificity; *Statistically significant difference.*

The efficacy of the sEMG in identifying TMD patients was also confirmed by Woźniak (52). It has been stated that the most significant recordings were those of temporal muscles in maximum voluntary clenching (AUC = 0.918) and changes in the mean power frequency (MPF%) of the masseter muscle during a 10-s maximum voluntary clenching in an intercuspal position (AUC = 0.911).

Santana-Mora et al. (53) determined the diagnostic value of EMG in distinguishing between TMD and non-TMD patients. They reported a moderate effectiveness of sEMG at rest position in discriminating between patients without TMD and those with TMD (Se = 0.547, Sp = 0.842) only in the left temporal muscle (AUC = 0.660). Glaros et al. (54) observed the diagnostic efficiency for EMG in differentiating between the TMD and control groups (Se = 68.5, Sp = 66.8), specifically in the case of the left anterior temporal and left masseter muscles.

A study performed by Berni et al. (6) confirmed the findings of Santana-Mora et al. (53) and Glaros et al. (54). Berni et al. (6) analyzed the accuracy, sensitivity and specificity of the anterior temporal, masseter and suprahyoid EMG muscle activity in the diagnosis of myogenous TMD in women at rest position and during maximum voluntary clenching on parafilm. In all examined muscles, with reference to the diagnosis of TMD at rest and in the suprahyoid muscles during MVC on parafilm, a

moderate degree of sEMG accuracy was detected (AUC = 0.747–0.848, Se = 71.3–80%, Sp = 60.5–76.6%). Contrarily, the authors observed unacceptable degrees of accuracy for masseter and temporal muscles during maximum voluntary clenching with parafilm (AUC < 0.5). It was confirmed that the sEMG is an auxiliary tool in the identification of the myogenous TMD.

Our study also corroborates these results, since a moderate degree of EMG accuracy was observed for masseter muscle rest activity and the Asymmetry Index for the masseter muscles at rest and low accuracy for all variables during MVC in differentiating between pain-related TMD and non-TMD patients. These findings suggested that EMG studies could be used as an adjunctive tool in evaluating of this disorder.

The study limitations were as follows: the relatively small number of subjects involved, along with a heterogenous group due to comparatively wide age range of patients. Hence some differences between individuals may result from variations in neuromuscular system development which can vary according to the age. It should also be noted that the TMD groups included both joint- and muscle-related disorders, while EMG activity may vary in these subgroups of patients. On that account, a further study would be necessary to substantiate the study results.

CONCLUSIONS

The findings and limitations of this study lead to the conclusion that an evaluation of electromyography is diagnostically useful in identifying patients with pain-related TMD. It could be used as an auxiliary and additional tool in the recognition of this disorder. Most essential in this regard were the EMG recordings of the masseter muscle rest activity and the Asymmetry Index for the masseter muscles in the rest position.

DATA AVAILABILITY

All datasets generated for this study are included in the manuscript and/or the supplementary files.

AUTHOR CONTRIBUTIONS

LS-S prepared the conception and design of the study. LS-S and KW collected the data. LS-S analyzed the data. ML performed the statistical analysis. LS-S and MM prepared the manuscript. All authors revised, read, and approved the submitted version.

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Ecological Momentary Assessment and Intervention Principles for the Study of Awake Bruxism Behaviors, Part 2: Development of a Smartphone Application for a Multicenter Investigation and Chronological Translation for the Polish Version

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Objectives: The aim is to describe the process of translating the smartphone application *BruxApp* into Polish within the context of an ongoing multicenter project on awake bruxism (AB) epidemiology.

Material and Methods: An ongoing cooperation involving 11 universities is based on the adoption of the smartphone-based EMA protocol to collect real time report of AB behaviors in the natural environment. The English version of *BruxApp* is adopted as a template for the multi-language translation, according to a step-by-step procedure led by mother-tongue experts in the field. A dedicated web platform for translation (viz., *POEditor*) is used. The process of translation into Polish is here described as an example.

Results: There are two software versions available, viz., *BruxApp* and *BruxApp Research*. For both versions, back translation from Polish to English was performed to verify the accuracy of the translation procedure. The validity of the translation has been confirmed by the perfect agreement between the original and back-translated English versions, and the Polish version of *BruxApp* can thus be introduced in the clinical and research setting to get deeper into the study of AB epidemiology in Poland.

Conclusions: As far as clinical studies are concerned, the described strategy to record data can be very useful—patients can acknowledge their habits, monitor changes over time, and implement remedial measures. In the field of research, *BruxApp* makes it

possible to collect and store a huge amount of data about the epidemiology of different forms of awake bruxism, both at the individual level and at the population level.

Keywords: awake bruxism, bruxism, translation, ecological momentary assessment, smartphone, diagnosis

INTRODUCTION

Awake bruxism (AB) is a masticatory muscle activity during wakefulness that is characterized by repetitive or sustained tooth contact and/or by bracing or thrusting of the mandible and is not a movement disorder in otherwise healthy individuals (1). The expert consensus panel that provided the above definition also suggested a diagnostic grading to assess both sleep and awake bruxism as "possible," "probable," and "definite." In addition, the panel recognized that most research so far has focused on sleep bruxism (SB), so that knowledge on AB is fragmental due the incomplete description of its epidemiology.

The recent expert consensus paper suggested that a definite diagnosis of AB should be based on electromyographic (EMG) recordings or, as an alternative due to the compliance limitations to perform hour-long EMG recordings of jaw muscles' activity during wakefulness, could rely on Ecological Momentary Assessment (EMA). EMA is a simple method to collect data on patients' self-reported AB. Its introduction in the research setting could allow getting a better understanding of the condition's epidemiology as well as of the condition's relationship with various forms of bruxism, masticatory muscle pain, and temporomandibular joint (TMJ) pain (2). Comparison of data across studies would be implemented by the adoption of a standardized EMA approach and, as discussed in the previous paper, taking advantage of smartphone technology seems to be a rational approach.

Based on the above, this manuscript describes in more detail a software application that is now available to report AB behaviors close in time with the experience (*BruxApp*, BruxApp Team, Pontedera, Italy) (3). As a secondary aim, the paper also introduces an ongoing multicenter cooperation involving, for now, 11 universities on the adoption of a smartphone-based EMA protocol to collect real time report of AB behaviors in the natural environment. For this purpose, the application has been formally translated into more than 20 languages, and a standardized procedure for translations (i.e., using the so-called forward and back translation procedure via web platforms) has been adopted. So far, no formal Polish translation was performed. Hence, the final aim of this article is to present the Polish version of the application *BruxApp,* and to describe the process of its official translation from English into Polish and all other languages.

BruxApp

The BruxApp introduced the EMA principles in the field of AB by the use of smartphone technology. The idea of EMA was formulated in the eighties as a strategy to overcome the limitations of the traditional quantitative methods used in various psychological studies (4). The common principle of many EMA techniques is that the patient reports in real time the outcome variable under investigation, as in the case of AB behaviors. Such reports can be obtained repeatedly for prolonged periods of observation (5), and the use of a smartphone app fits perfectly with the need for maximizing compliance and simplicity (6). Moreover, smartphone-based EMA approaches could also be implemented in an interventional strategy (i.e., EMI) to educate patients about a behavior that may be negative for their health.

Within these premises, the *BruxApp* application aims to re-educate the patient by reminding him/her to relax his/her muscles and to avoid teeth contact. The application is based on a very simple principle of data recording. Thanks to the sound emitted by the app, the patient is alerted to focus his/her attention on jaw muscles and teeth position at random times during the day to allow a real time report. This enables monitoring the patient's oral behaviors in his/her natural environment.

When the patient receives the alert, he/she has to identify the current condition from among five options: relaxed jaw muscles, mandible bracing, teeth contact, teeth clenching, or teeth grinding. An additional answer to an item on the presence of facial pain is also required. After that, the patient has to tap on the display and give a real time feedback (**Figures 1**–**4**). The application has a very simple and intuitive interface, which can be personalized according to the individual needs and expectations. The default mode provides a 7-day monitoring, which can be extended or/and repeated to collect data for longer periods. Alert sounds are generated at a random frequency, with no predefined time intervals. There are several options designed to allow for the individualization of the alarm setting, such as the number of observation days, the start and end time of the report during the day, and the number of alarms per day.

Importantly, the application also includes an information section on bruxism and an explanation of the objectives of *BruxApp*. As a result, pain in the jaw muscles and/or the temporomandibular joint could be managed within a cognitive-behavioral framework.

Multicenter Research

The potential number of *BruxApp* users is impressive. According to the data reviewed in 2013 by Manfredini et al. sleep bruxism affects 12% of the general population, whereas awake bruxism occurs in approximately 22–30% of people (7). The latest estimates show that in economically well-developed regions, approximately 35% of people have mobile phones with an application download feature (iOS and Android). There are no exact data on the number of downloads for medical applications, but if one assumes that approximately 10% of patients who are affected by bruxism and who own a smartphone would be willing to download *BruxApp* on their phones, the potential of the application for epidemiological research will be enormous at a worldwide level.

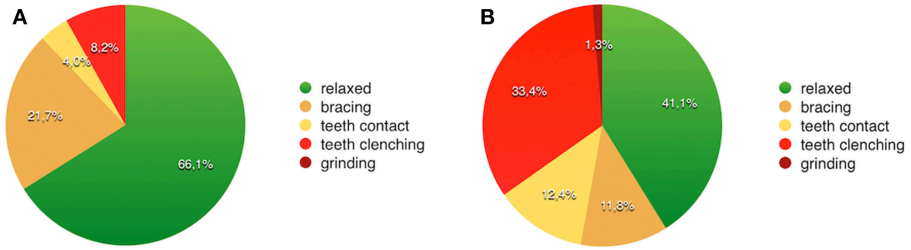

FIGURE 1 | Examples of screenshots of individual AB activities recorded using the BruxApp over 1 week. In the example patient **(A)**, muscles were relaxed in 66.1% of the recorded time, while in in the patient **(B)**, the frequency of relaxed answers was 41.1%. The most frequent AB behaviors are teeth clenching (33.4%) and teeth contact (12.4%).

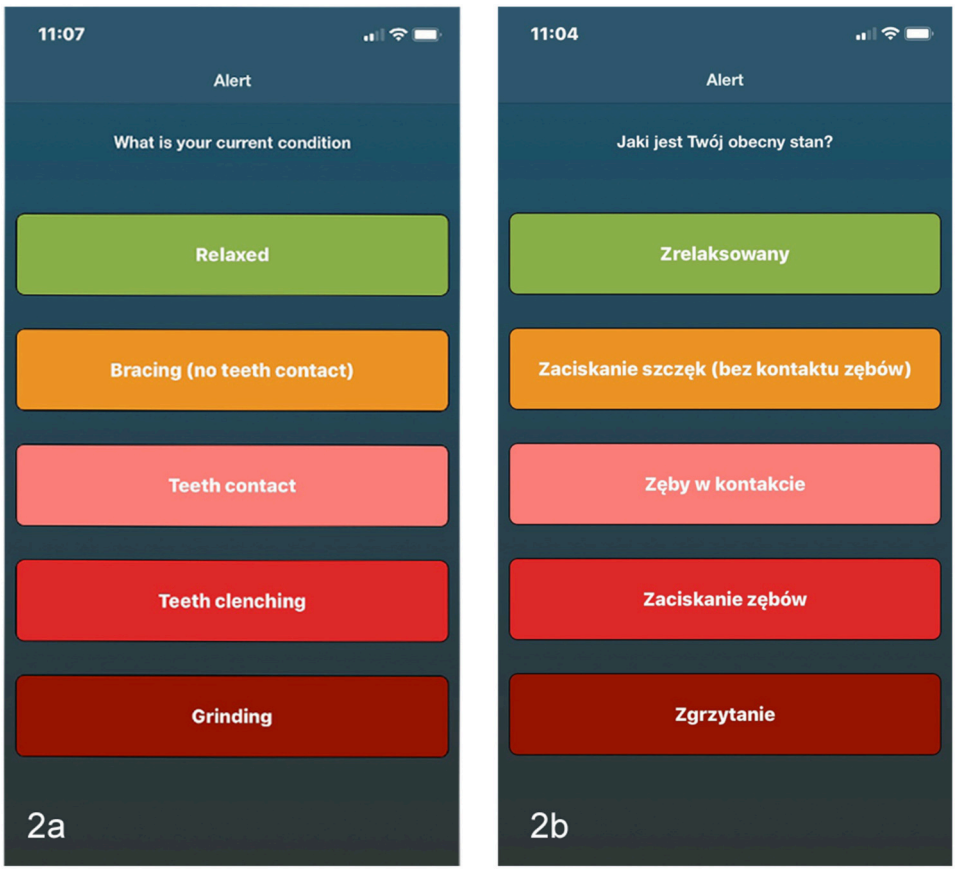

FIGURE 2 | Screenshots of the *BruxApp* application. Comparison of the original English version **(a)** and the Polish one **(b)**, as an example of the translational procedures.

As a result of this impressive potential, an ongoing multicenter cooperation involving 11 universities is currently performed with the adoption of a specific smartphone-based EMA protocol (*BruxApp Research*). Experts and leaders on the topic are coordinating data collection in various languages. *BruxApp* is currently available in the Bosnian, Brazilian, Chinese, Croatian, Dutch, English, Finnish, French, German, Greek, Hebrew, Italian, Japanese, Lithuanian, Polish, Portuguese, and Spanish language. About ten other translations are currently performed, based on the procedure described below.

Training sessions for the leading researchers are organized under the supervision of the main coordinator, who is an expert in primary research and clinical management of bruxism (D.M.). In short, the critical issue is to maximize internal validity of findings, and careful instructions to the patients have to be conveyed as for the recognition of the following five conditions:

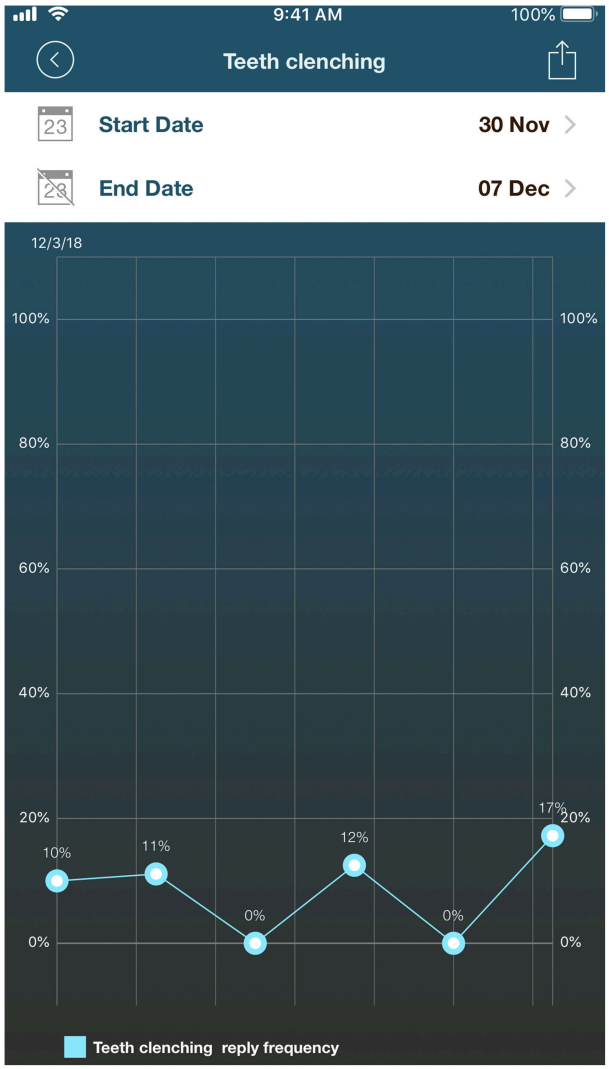

FIGURE 3 | Screenshot of Individual results for the behavior "teeth clenching" recorded using the English version of *BruxApp* for 1 week.

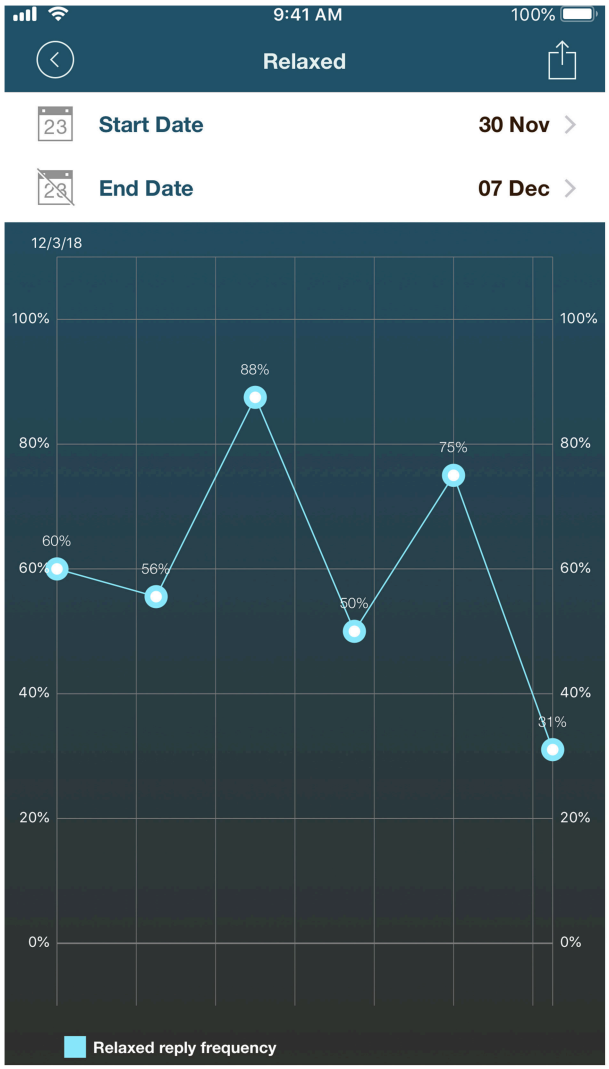

FIGURE 4 | Screenshot of individual results for the "relaxed" answer recorded using the English version of *BruxApp* for 1 week.

- Relaxed jaw muscles: condition of perceived relaxation of jaw muscles, with the jaws kept apart;
- Teeth contact: condition of slight teeth contact like the teeth contact that the subject perceives when a 40 μ articulating paper is put between the dental arches and he/she is asked to slightly keep the teeth in contact to retain it on site. In short, this condition is defined as light touching of teeth when the mouth is closed;
- Teeth clenching: all conditions in which teeth contacts are more marked than the above, and jaw muscles are kept tense;
- Teeth grinding: condition in which the opposite teeth are gnashed or ground, independently of the intensity and direction of antagonist teeth contacts;
- Jaw clenching (without teeth contact): condition of jaw-muscle stiffness or tension like teeth clenching, but with teeth kept apart (i.e., mandible bracing).

The standardization of this message is fundamental to overcome the shortcomings due to the self-reported nature of the gathered data and to implement the comparability of data across different investigations. The ultimate goal of the large-scale multicenter cooperation is to enhance research on AB with the creation of international databases for data storage and consultation. A multi-language platform for multicenter research coordination and implementation of cross-cultural and ethnic comparisons has thus been created, and the translational process is described below.

Translation Into Polish

The English version of *BruxApp* is adopted as a template for the multi-language translation, according to a step-by-step procedure led by mother-tongue experts in the field. As a first step, the Polish bruxism expert (M.O.) was trained by

the supervisors of the smartphone—EMA project adopting the software *BruxApp (AB; DM)*. Then, the application was tested by the same expert for the next 2 weeks, before translating the files into Polish. The files describe the objectives and functioning of the application, and contain the *BruxApp* manual. The next step was to translate *strings,* which means sequences of alphanumeric texts in computer programming, which are extremely important for the functioning of the application. All translation procedures were done on a special platform (viz., *POEditor)*, on which English is the reference language. Before the translation was done, the translator had to get acquainted with the *POEditor* manual.

As part of the cultural adaptation process, two bilingual Polish mother-tongue translators translated the original text independently. One translator was a professional in the bruxism field, while the other translator was naïve to this field. In general, when creating an instrument, the selection of two translators who have different knowledge helps in reducing bias and enhancing a more general understanding of the item content. The two independent translations were assessed for differences by the Polish project coordinator (MO), who created a single forward translation. The so-derived Polish forward translation, was sent to an independent bilingual back translator whose native language is English. The back translator was naïve to the source text but had some basic knowledge of the bruxism field.

A reviewer who was a contributing author of the original version of *BruxApp* (AB) compared the back translation to the original version. A document describing all discrepancies between the back translation and the source (English) version was created in order to identify areas of concern in the Polish translation. The forward and back translation steps were then repeated for the discrepant items, followed by an independent review. In the next stage, a committee consisting of a Polish language specialist and two laypersons (one of whom did not know the English language, and one of whom was Polish-English bilingual) reviewed the Polish version of *BruxApp*. The task of the committee was to review the translation with regard to four types of equivalences (somatic, idiomatic, experiential, and conceptual) of the document as to validate it cross-culturally.

The validity of the English-to-Polish translation was confirmed by the perfect agreement between the original and back-translated English versions. This means that the Polish version of *BruxApp* can be introduced in the clinical and research setting to get deeper into the study of AB epidemiology in Poland.

DISCUSSION

The *BruxApp* was conceptualized based on the idea that bruxism may be considered one of civilization's "phenomena of the new millennium." In the clinical setting, there are some empirical observations that awake bruxism, exerted in the form of keeping the jaw muscles in a prolonged tension or in the form of repeated teeth contact habit, may be associated with fatigue and pain (8). Cognitive behavioral approaches, which help patients understanding their need to maintain relaxed mastication muscles, are likely the best first-step therapeutic solution. In addition, they could be seen as important strategies to strengthen the positive long-term effects of other treatment protocols.

Therefore, along with the usefulness as an assessment tool, the application may educate the patient to understand the possible consequences of bruxism and may serve as a *biofeedback* strategy with a large clinical potential. Repeated alerts at random intervals are potentially useful as an educational strategy to acquire awareness and reverse the awake bruxism behaviors in patients with TMD pain. When the patient receives an alert, he/she must pay attention to the position of the teeth and the condition of the mastication muscles; doing so, the patient can react properly, for example by relaxing the jaw muscles.

Clinical research protocols should be established to assess the effectiveness of this approach, and it is plausible that the clinical outcomes largely depend on the patient's self-discipline to use the application. Notwithstanding the latter, the data collected with the application are useful, both individually and at the general population level. For instance, at the individual level, the immediate return of the information makes it possible to have a fruitful doctor-to-patient relationship. At the population level, investigators of the various research centers can achieve a clearer picture of the prevalence, incidence, and risk factors of AB. Therefore, using officially translated and culturally adapted versions of *BruxApp* can be helpful for a consistent communication among dental professionals. On this purpose, EMA/AB data gathered in otherwise healthy individuals will provide a dataset for a range of average frequency values of AB behaviors as a function of the different populations in different countries. From there, comparative studies can be performed in selected study samples, also taking into account the time-related variability of the specific AB activities.

CONCLUSIONS

BruxApp makes it possible to collect data on awake bruxism behaviors for both clinical and research purposes. In the clinical setting, the data can be useful to help patients acquiring awareness of their habits, monitoring changes over time, and implementing appropriate corrective measures. In the research setting, using an officially translated and culturally adapted version of *BruxApp* provides opportunities to collect a large amount of data about the epidemiology of different forms of awake bruxism, both at the individual and at the population level.

AUTHOR CONTRIBUTIONS

MO designed the study, performed the study, wrote, and revised the article. DM supervised and critically revised the article. FL, AB, JA, and JP-P critically revised the article.

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Sleep Bruxism and Occurrence of Temporomandibular Disorders-Related Pain: A Polysomnographic Study

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Introduction: The diagnosis of sleep bruxism is challenging due to the difficulties involved. Sleep bruxism can lead to clinical consequences, including pain in masticatory muscles, limitation of jaw mobility, headache, and the spectrum of symptoms associated with damage to the teeth and oral mucosa. Currently, only video-polysomnography can definitely diagnose sleep bruxism. Due to the risk of painful temporomandibular disorders (TMD) in sleep bruxers, early diagnosis of pain in the temporomandibular region using questionnaires is recommended. Therefore, this study aimed to assess the relationship between the intensity of sleep bruxism and the occurrence of pain related to TMD.

Materials and Methods: This study was conducted on the patients of the Clinic of Prosthetic Dentistry operating at the Department of Prosthetic Dentistry at the Wroclaw Medical University. Based on a positive medical history, a thorough examination for the diagnosis of probable sleep bruxism was carried out in the enrolled patients. Eligible patients were then subjected to a video-polysomnographic study. Each patient was asked to complete the TMD Pain Screener questionnaire to assess the occurrence of pain in jaw and temple area.

Results: The results of the study showed that increased bruxism episode index (BEI) was statistically significantly correlated with increase of all types of bruxism episodes—phasic, tonic, and mixed—in all the studied patients; a significant correlation was also found with respect to division of patients into studied and control groups. The study also showed that there was no statistically significant difference between BEI values and scores of TMD Pain Screener. In all the studied patients, a higher BEI was not found to be correlated with the occurrence of TMD-related pain assessed by TMD Pain Screener; similarly, no correlation was found with respect to division of patients into studied and control groups.

Conclusions: The occurrence of TMD-related pain is not related to the intensity of sleep bruxism. TMD Pain Screener may be used as an auxiliary tool in the diagnosis or risk of occurrence of TMD-related pain, whereas in the case of sleep bruxism, it has only limited diagnostic value.

Clinical Trial Registration: www.ClinicalTrials.gov, identifier NCT03083405

Keywords: sleep bruxism, pain, temporomandibular disorders, polysomnography, TMD pain screener

INTRODUCTION

Bruxism is a common phenomenon, and is estimated to occur in 8−31% of the population without division into subtypes and without significant variation in relation to gender (1). Awake bruxism (AB) occurs in 22–31% and sleep bruxism (SB) in approximately 13% of adults (1, 2). The occurrence of bruxism decreases with age. Currently, in adults, bruxism is not considered as a disorder, but as a risk factor for other clinical consequences (1–5). In children, the unambiguous classification of symptoms commonly associated with bruxism is difficult. While bruxism occurring during sleep may be a physiological element of the natural maturation of the central nervous system, it may also be considered as a response to excessive stress, be caused by certain independent psychological and social factors, or constitute a protective mechanism in patients with sleep disorders (2, 3, 6, 7).

The origin of bruxism is multifactorial (1–3). It is now believed that bruxism may be caused by three groups of factors. The first group are biological factors, which include neurotransmitters, in particular dopamine, genetic factors, and cortical arousals. The second group are psychological factors, which include sensitivity to stress, individual character traits, and anxiety, among others. Both adults and children with bruxism have been shown to present higher scores on scales examining the intensity of stress, anxiety, and mental disorders compared to the control group. The third and a more popular group of factors causing bruxism are those of exogenous origin: nicotine, caffeine, alcohol, drugs, and some medications (3). There are also scientific reports indicating the comorbidity of bruxism with systemic disorders, including thyroid diseases, disorders of the digestive system, sleep disorders, and cardiovascular diseases (1–3, 6–8).

The widely accepted definition of bruxism was created in 2013 in an international consensus (1). Bruxism is defined as a repetitive activity of the jaw muscles, characterized by clenching or grinding of the teeth and/or bracing or thrusting of the mandible. This activity of jaw muscles may appear while wake (awake bruxism—AB) or during sleep (sleep bruxism—SB) (1, 3). The above definition formed the basis for the description of bruxism in the fourth edition of the guidelines for the evaluation, diagnosis, and treatment of orofacial pain of the American Academy of Orofacial Pain (2, 8) and the third edition of the International Classification of Sleep Disorders (2, 6). Although this definition was quickly and widely accepted due to its pragmatism, according to the latest suggestions, it requires verification, considering the hypothesis that bruxism occurring during wakefulness and the one occurring during sleep are separate phenomena and therefore require separate definitions (2). In 2018, as a part of the next international consensus, Lobbezoo et al. (2) proposed two separate definitions. According to these authors, SB can be defined as the activity of masticatory muscles during sleep, which can be rhythmic (phasic) or nonrhythmic (tonic), and should not be considered as a movement disorder or a sleep disorder in otherwise healthy individuals. On the other hand, AB is defined as an activity of the masticatory muscles during wakefulness which is characterized by repetitive or sustained tooth contact and/or by bracing or thrusting of the mandible and should not be considered as a movement disorder in otherwise healthy individuals. In both the definitions, the key phrase is "activity of the masticatory muscles," indicating the potential clinical consequences of both the types of bruxism (2). Currently, bruxism is not considered as a disorder but referred to as a behavior that can act as a risk factor for detrimental disorders, or in contrast a protective factor for others (2, 7, 9).

Due to the difficulties involved, diagnosis of SB is challenging. SB can lead to clinical consequences, including pain in the masticatory muscles, limitation of jaw mobility, orofacial pain, headache in the temporal region, and the spectrum of symptoms associated with damage to the teeth and oral mucosa. Currently, only video-polysomnography can efficiently diagnose SB. According to the guidelines of the International Classification of Diseases-10-Clinical Modification (ICD-10-CM), during sleep, repeated contractions of the masticatory muscles occur in patients with SB are called as a rhythmic masticatory muscle activity (10). During electromyographic recording, these contractions can manifest as a series of repetitive activities (phasic contractions) lasting for 0.25–2 s or as isolated, long-lasting jaw clenching (tonic contractions) lasting over 2 s. A third type of contractions is also observed, which is a combination of phasic and tonic contractions, called mixed contractions (10, 11).

Due to the risk of pain related to temporomandibular disorders (TMD) in sleep bruxers, early diagnosis of pain in the temple and jaw area using questionnaires is recommended. One of the questionnaires used for diagnosis is TMD Pain Screener (12). This study aimed to assess the relationship between the intensity of SB and occurrence of pain related to TMD using the TMD Pain Screener.

MATERIALS AND METHODS

Participants

The study population consisted of patients of the Prosthetic Dentistry Clinic operating at the Department of Prosthetic Dentistry at the Wroclaw Medical University. Based on a positive medical history and thorough examination following the guidelines of the ICD-10-CM of the American Academy of Sleep Medicine, probable SB was diagnosed in the patients.

This study was approved by the Ethical Committee of the Wroclaw Medical University (ID KB-195/2017). Written informed consent was obtained from all the participants of this study.

Selection of Participants for Video-Polysomnography

The selection of patients for video-polysomnography was based on a medical interview with particular emphasis on the presence of severe systemic diseases and psychoemotional disorders, physical examination for the presence of TMD, and interview and physical examination for the presence of sleep disorders with particular emphasis on grinding of teeth at night and, if possible, confirmed by partner. In addition, each patient was subjected to physical extra- and intraoral examination for an accurate assessment of the condition of teeth and oral mucosa in terms of symptoms indicating the presence of bruxism and with the use of Tooth Wear Index developed by Smith and Knight. After verification of the identified symptoms in accordance with the guidelines of ICD-10-CM, the diagnosis of bruxism was carried out.

Inclusion Criteria

Criteria for inclusion of a patient for further examination were as follows: age above 18 years, lack of severe systemic (including genetic) diseases, lack of severe mental illness and significant mental (including genetic) disabilities, positive diagnosis of SB based on the criteria of ICD-10-CM, lack of contraindications for polysomnographic examination, and consent to participate in the study.

Exclusion Criteria

The exclusion criteria except inverse to inclusion included: the presence of SB caused by a diagnosed disorder or as a side effect to intake of a drug or medication; use of medicines that significantly affect the function of the nervous and muscular systems.

Video-Polysomnography

A one-night polysomnographic examination with video recording was carried out in each of the included patients using Nox A1 (Nox Medical, Iceland) in the Sleep Laboratory at the Wroclaw Medical University. Examination took place between 10.00 p.m. and 6.00 a.m., taking into account the preferences and sleeping habits of the patient. Before the tests, the electrodes were arranged in a standard manner as recommended by the manufacturer. A modification relative to the standard distribution of electrodes included placing only bipolar leads for electromyographic recording from the masseter muscles. In agreement with the manufacturer's recommendations, a modification was made by placing the electromyographic electrodes on both sides of the origin and insertion of masseter muscles.

Each of the polysomnography examinations included electroencephalography, electrocardiography, electrooculography, and electromyography from the chin area and bilaterally from the regions of the masseter muscles, motion recording of abdominal and thoracic breathing activity, assessment of body position, as well as audio and video recording. An additional recording tool, NONIN WristOx2 3150 pulse oximeter (Nonin Medical, Inc., USA), was used which enabled the recording of the level of saturation, pulse, and plethysmographic data. The restoration of the full polysomnographic record was possible, thanks to the device Noxturnal developed for sleep recording and analysis (Nox Medical, Iceland).

Bruxism was assessed according to the ICD-10-CM guidelines based on the electromyographic recording of masseter muscles and audio and video recordings. Episodes of rhythmic activity of masseter muscles, which were often accompanied by grinding sounds and characteristic movements in the orofacial region occurring after a minimum of 3 s break from the last muscle activity, were qualified as episodes of bruxism. Based on the types of contractions, episodes were classified as phasic (lasting 0.25–2 s), tonic (lasting more than 2 s), or mixed (**Figure 1**).

The participants were divided into study group (bruxers—bruxism episode index (BEI) $\geq$ 2) and control group (non-bruxers—BEI $<$ 2) according to the BEI (6).

TMD Pain Screener

Each of the qualified participants was asked to fill in TMD Pain Screener. This questionnaire has been validated by the International Network for Orofacial Pain and Related Disorders Methodology (https://ubwp.buffalo.edu/rdc-tmdinternationa). It allows an easy assessment of the occurrence of pain in the temporomandibular area in patients over the last month. The survey consists of three questions. Questions 1, 2, and 3a are called as "short screener," while questions 3b—3d are called as "long screener". Answers are scored as follows: "a"—0 point, "b"—1 point, and "c"—2 points. The maximum number of points given for a "short screener" is 4, while for a "long screener" it is 7. The questionnaire also allows screening of pain associated with TMD.

Database

After obtaining data from extra- and intraoral examination, polysomnography, laboratory tests, and questionnaires, a database was created in Excel (Microsoft Office, USA). Selected elements of the database were then subjected to statistical analysis.

Statistical Analysis

A statistical analysis of the obtained data was carried out using the statistic program Statistica 13.1 (Statsoft, Poland). The level

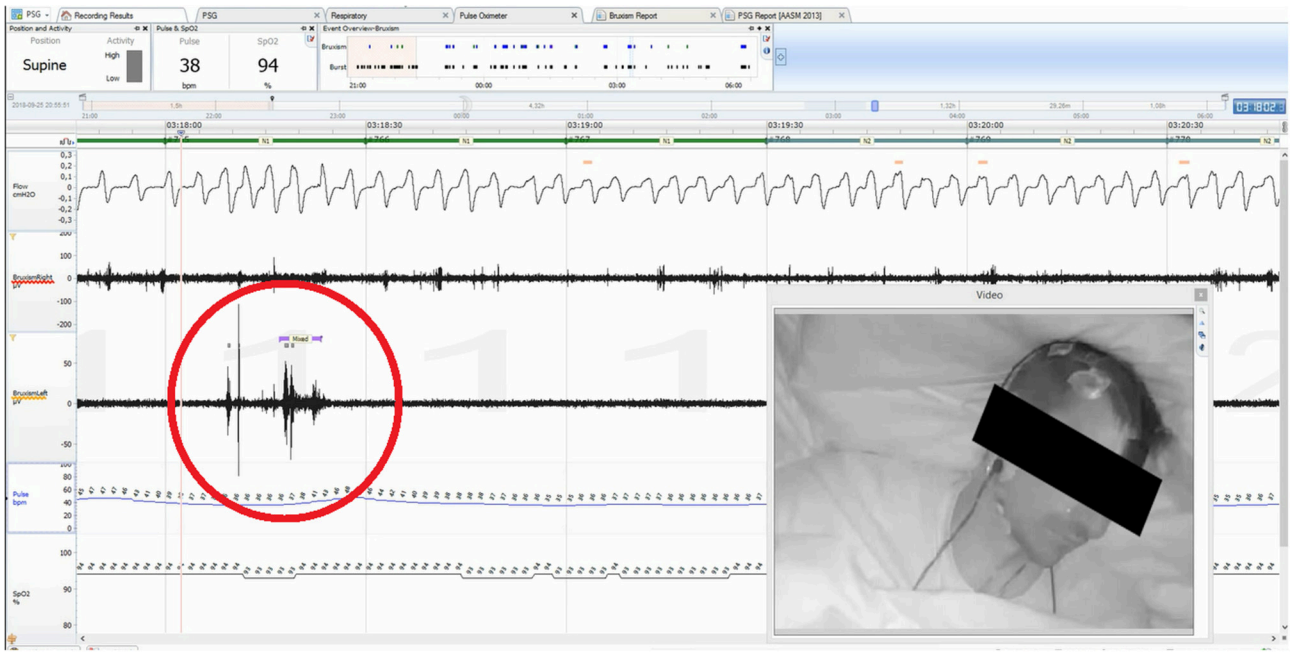

FIGURE 1 | Noxturnal interface, mixed bruxism episode indicated with red circle.

of statistical significance was assumed at $\alpha = 0.05$, i.e., the results of statistical tests that appeared with a probability of $p < 0.05$ were considered statistically significant. The shapes of the data distributions and deviations from the shape of the normal distribution were analyzed with the Shapiro–Wilk test.

The following principle was adopted in the analyses: first, the use of parametric methods was preferred. If the data did not meet the assumptions of the parametric methods (e.g., due to the shapes of the distribution), they were further transformed. If the data met the assumptions after the transformation, parametric methods were used for the analyses. If the data still did not meet the assumptions after the transformation, non-parametric methods were used for the analyses, and the analyses were performed on the original (untransformed) data.

In additional analyses, the determined BEI was divided into two groups: BEI value up to 2 ("<2") and BEI value of 2 and above ("2+"), corresponding to the control and test group, respectively. The preferred analytical approach for the study of differences between the groups was Student's *t*-test for unrelated samples. This test verifies the hypothesis that there are no differences between means in the compared groups.

The assumptions of Student's *t*-test are as follows:

i) distributions of data in the compared populations are normal, and
ii) in both the compared populations, there is the same variance (variances are homogeneous).

If the assumption regarding homogeneity of variance was not met, the analysis of significance of differences between means in both the groups was carried out using Cochran–Cox test. In the case of a significant breach of the assumption about the normality of the data distribution, the Mann–Whitney *U* test was used to analyze the differences between groups. This test is a non-parametric equivalent of the Student's *t*-test and verifies the hypothesis that the medians in both the compared groups are not equal or, in other words, that two randomly selected samples come from the same population. For some comparisons, the size of groups differed from the size of the starting study and control group due to incorrect or incomplete filling of the questionnaires by the patients.

RESULTS

Sample Characteristics

There were 77 patients included in the study (56 women and 21 men). All the patients subjected to polysomnography were Caucasians, aged 18–63 (mean age 34.8 ± 10.8). Of the 77 patients, 58 were included in the studied group and 17 in the control group.

BEI and Type of Electromyographic Pathway

Phasic Episodes

The distribution of BEI data deviated from the normal distribution ($W = 0.8745$, $p < 0.0001$). Therefore, the BEI values were subjected to a logarithmic transformation, after which the data distribution was not found to differ significantly from the normal distribution ($W = 0.9728$, $p = 0.10$). Similarly, the distribution of data of phase contraction differed statistically significantly from the normal distribution ($W = 0.7021$, $p < 0.0001$). However, even after applying the logarithmic

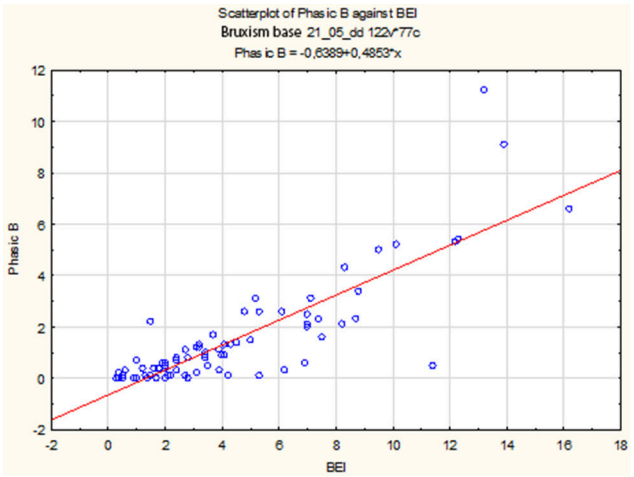

FIGURE 2 | Relationship between BEI values and the number of phasic episodes.

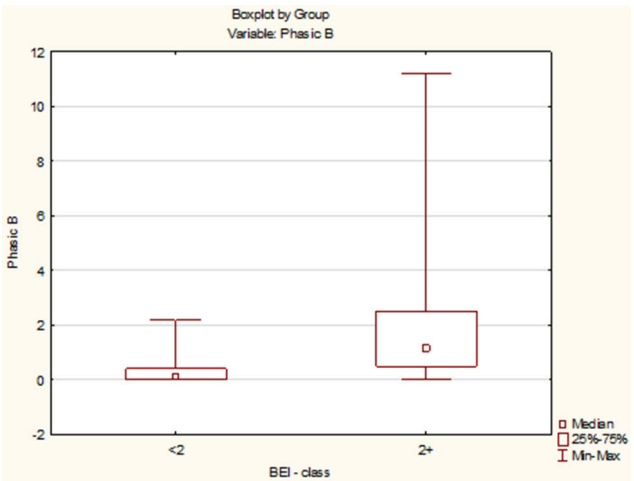

FIGURE 3 | Comparison of the number of phasic episodes in the studied and control group.

TABLE 1 | Descriptive statistics for phasic episodes in studied and control group.

	Phasic episodes					
	Number	**Average**	**Median**	**Minimum**	**Maximum**	**Standard deviation**
BEI <2	19	0.29	0.10	0	2.2	0.513
BEI 2+	58	1.90	1.15	0	11.2	2.214

transformation, the data distribution was found to deviate from the normal distribution ($W = 0.7759$, $p < 0.0001$).

The non-parametric Spearman rank correlation test was used to analyze the strength and significance of the BEI and the number of phasic episodes. The analysis showed a statistically significant relationship between BEI and the number of phasic episodes [$rs_{(77)} = 0.79$, $p < 0.00001$]. The increase in BEI was accompanied by an increase in the number of phasic episodes (**Figure 2**).

Descriptive statistics for phasic episodes are presented in **Table 1**.

The distribution of data of phasic episodes in the "BEI < 2" group deviated from the normal distribution ($W = 0.5933$, $p < 0.0001$). Similarly, the distribution of data of phasic episodes in the "BEI 2+" group differed statistically significantly from the normal distribution ($W = 0.7470$, $p < 0.0001$).

Due to the violation of the assumption about the normality of the data distribution in the groups "BEI < 2" and "BEI 2+", the Mann–Whitney U test was used for analysis. The analysis showed that both the groups differed significantly in terms of phasic episodes ($U = 149.5$, $p < 0.0001$), and the number of phasic episodes was statistically significantly higher in the "BEI 2+" group (**Figure 3**).

Tonic Episodes

The distribution of BEI data deviated from the normal distribution ($W = 0.8745$, $p < 0.0001$). Therefore, the BEI values were subjected to a logarithmic transformation, after which the data distribution was not found to differ significantly from the normal distribution ($W = 0.9728$, $p = 0.10$). Similarly, the distribution of data of tonic episodes differed statistically significantly from the normal distribution ($W = 0.8858$, $p < 0.0001$). However, even after applying the logarithmic

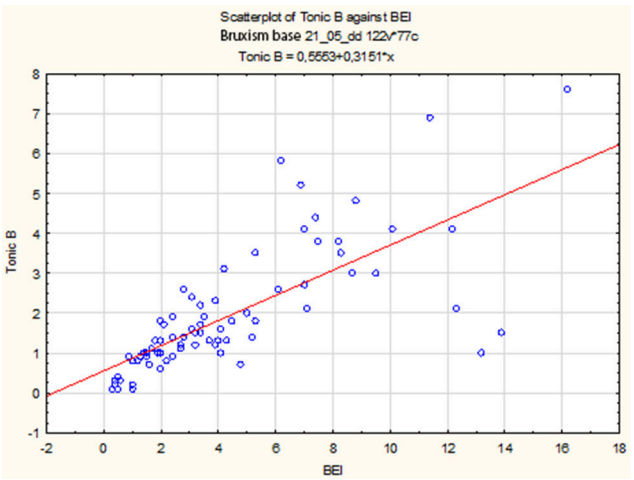

FIGURE 4 | Relationship between BEI values and the number of tonic episodes.

TABLE 2 | Descriptive statistics for tonic episodes in studied and control group.

	Tonic episodes					
	Number	**Average**	**Median**	**Minimum**	**Maximum**	**Standard deviation**
BEI <2	19	0.64	0.80	0.10	1.30	0.398
BEI 2+	58	2.38	1.80	0.60	7.60	1.521

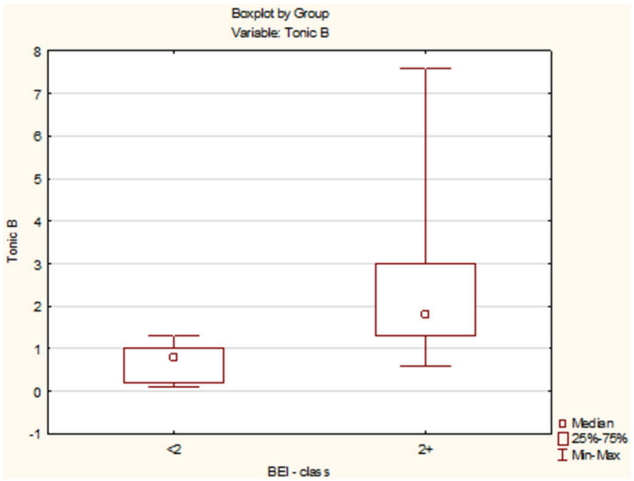

FIGURE 5 | Comparison of the number of tonic episodes in the studied and control group.

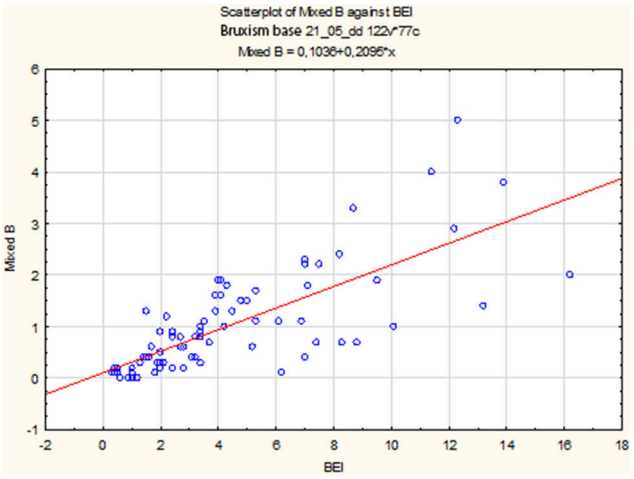

FIGURE 6 | Relationship between BEI values and the number of mixed episodes.

transformation, the data distribution was found to deviate from the normal distribution ($W = 0.9293$, $p = 0.0004$).

The non-parametric Spearman rank correlation test was used to analyze the strength and significance of the BEI and the number of tonic episodes. The analysis showed a statistically significant relationship between BEI and the number of tonic episodes [$rs_{(77)} = 0.81$, $p < 0.00001$]. The increase in BEI was accompanied by an increase in the number of tonic episodes (**Figure 4**).

Descriptive statistics for tonic episodes are presented in **Table 2**.

The distribution of data of tonic episodes in the "BEI < 2" group deviated from the normal distribution ($W = 0.8916$, $p = 0.03$). Similarly, the distribution of data of tonic episodes in the "BEI 2+" group differed statistically significantly from the normal distribution ($W = 0.8463$, $p < 0.0001$).

Due to the violation of the assumption about the normality of the data distribution in the groups "BEI < 2" and "BEI 2+", the Mann–Whitney *U* test was used for analysis. The analysis showed that both the groups differed significantly in terms of tonic episodes ($U = 54.5$, $p < 0.0001$), and the number of tonic episodes was statistically significantly higher in the "BEI 2+" group (**Figure 5**).

Mixed Episodes

The distribution of BEI data deviated from the normal distribution ($W = 0.8745$, $p < 0.0001$). Therefore, the BEI values were subjected to a logarithmic transformation, after which the data distribution was not found to differ significantly from the normal distribution ($W = 0.9728$, $p = 0.10$). Similarly, the distribution of data of mixed episodes differed statistically significantly from the normal distribution ($W = 0.8386$, $p < 0.0001$). However, even after applying the logarithmic transformation, the data distribution was found to deviate from the normal distribution ($W = 0.8722$, $p < 0.0001$).

TABLE 3 | Descriptive statistics for mixed episodes in studied and control group.

	Mixed episodes					
	Number	**Average**	**Median**	**Minumum**	**Maximum**	**Standard deviation**
BEI <2	19	0.253	0.20	0	1.30	0.304
BEI 2+	58	1.283	1.00	0.10	5.00	1.008

The non-parametric Spearman rank correlation test was used to analyze the strength and significance of the BEI and the number of mixed episodes. The analysis showed a statistically significant relationship between BEI and the number of mixed contractions [$rs_{(77)} = 0.77$, $p < 0.00001$]. The increase in BEI was accompanied by an increase in the number of mixed episodes (**Figure 6**).

Descriptive statistics for mixed episodes are shown in **Table 3**.

The distribution of data of mixed episodes in the "BEI < 2" group deviated from the normal distribution ($W = 0.7339$, $p = 0.0002$). Similarly, the distribution of data of mixed episodes in the "BEI 2+" group differed statistically significantly from the normal distribution ($W = 0.8589$, $p = 0.00001$).

Due to the violation of the assumption about the normality of the data distribution in the group "BEI < 2" and "BEI 2+", the Mann–Whitney *U* test was used for analysis. The analysis showed that both the groups differed statistically significantly in terms of the number of mixed episodes ($U = 102.5$, $p < 0.0001$), and the number of mixed episodes was statistically significantly higher in the "BEI 2+" group (**Figure 7**).

BEI and TMD Pain Screener

The distribution of BEI data deviated from the normal distribution ($W = 0.8745$, $p < 0.0001$). Therefore, the BEI values were subjected to a logarithmic transformation, after which the data distribution was not found to differ significantly from the normal distribution ($W = 0.9728$, $p = 0.10$).

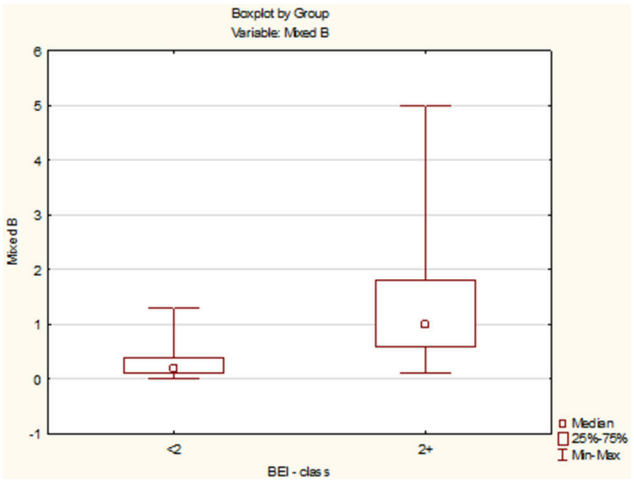

FIGURE 7 | Comparison of the number of mixed episodes in the studied and control group.

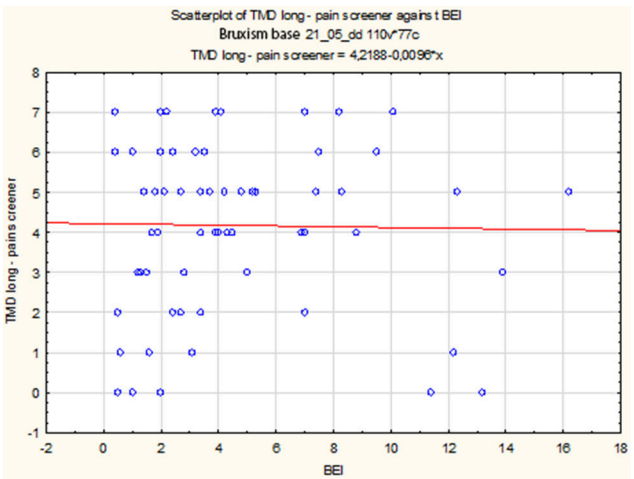

FIGURE 8 | Relationship between BEI and scores of TMD Pain Screener.

TABLE 4 | Descriptive statistics for TMD pain screener in studied and control group.

	TMD pain screener					
	Number	**Average**	**Median**	**Minimum**	**Maximum**	**Standard deviation**
BEI <2	15	3.33	3.00	0	7	2.23
BEI 2+	48	4.44	5.00	0	7	1.98

The data distribution of TMD Pain Screener differed from the normal distribution ($W = 0.9196$, $p = 0.0005$). Therefore, the data of TMD Pain Screener were subjected to a second-degree power transformation. Due to the fact that the raw data of TMD Pain Screener contained 0 values, each value was increased by a fixed value 10 before the data were raised to power. However, even after applying the transformation, the data distribution

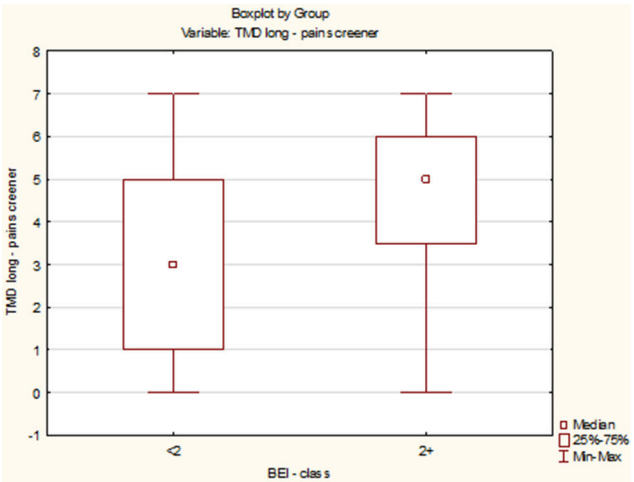

FIGURE 9 | Comparison of the scores of TMD Pain Screener in studied and control group.

was found to significantly deviate from the normal distribution ($W = 0.9345$, $p = 0.002$). The non-parametric Spearman rank correlation test was used to analyze the strength and significance of the BEI and the scores of TMD Pain Screener. The analysis showed no significant relationship between BEI and TMD Pain Screener [$rs_{(63)} = 0.08$, $p = 0.55$] (**Figure 8**).

Descriptive statistics for the scores of TMD Pain Screener, in patients divided into studied group and control group, are presented in the **Table 4**.

The distribution of data of TMD Pain Screener in the "BEI < 2" group did not differ from the normal distribution ($W = 0.9521$, $p = 0.56$). In contrast, the distribution of data of TMD Pain Screener in the "BEI 2+" group differed statistically significantly from the normal distribution ($W = 0.9090$, $p = 0.001$). Due to the violation of the assumption about the normality of the data distribution in the "BEI 2+" group, the Mann–Whitney U test was used for analysis. The analysis showed that both the groups did not differ significantly in terms of the results of TMD Pain Screener ($U = 253.0$, $p = 0.08$) (**Figure 9**).

DISCUSSION

Presented study showed that increase in BEI is associated with increased number of all types of muscle contractions. The number of phasic, tonic and mixed episodes was statistically significantly higher in bruxers than non-bruxers. Authors used TMD Pain Screener to assess the relationship between the intensity of SB and occurrence of pain related to TMD. Analysis showed no statistically significant relationship between intensity of SB and TMD Pain Screener scores taking into account all studied material and when dividing it into studied and control group. Summarizing, study showed that intensity of bruxism is associated to muscle activity, but not to pain related to TMD.

Bruxism during sleep is inextricably linked to the function of the masticatory muscles in two ways: it is caused by

the increased activity of muscles, or it acts as a possible important risk factor for the occurrence and severity of pain related to TMD, the essential component of which are the disorders of muscle origin. The consequences of bruxism during sleep related to muscle pain are very common and sometimes severe (1–3, 13–16).

Lobbezoo et al. indicate that the possible negative clinical implications of bruxism are often related to the type of electromyographic activity, and not the number of episodes (2). Other authors also indicate this assertion (17). BEI represents only the number of bruxism episodes per hour of sleep without taking into account their duration and strength, what can be crucial for development of serious clinical consequences. In this case, the BEI may turn out to be an unreliable factor, and therefore, we should consider not only the intensification of muscle activity but also its character. It may be useful in this case to look at the type of dominating episode. However, it should be remembered that an increase in the number of episodes of bruxism per hour of sleep is always accompanied by an increase in the number of overall contractions, as well as an increase in each type of contractions separately.

In the present study, the authors verified the activity of masticatory muscles during sleep both quantitatively and qualitatively. BEI was used in the quantitative assessment, and the classification of episodes as phasic, tonic, and mixed was applied in qualitative assessment. The analysis showed that the increase of BEI was statistically significantly correlated with increase in the number of all types of electromyographic pathways, and thus, the types of episodes. This result suggests that increase in specific type of muscle activity could be associated with more frequent conditions contributing to pain related to TMD.

Many scientific teams have investigated the relationship between the comorbidity of TMD and bruxism. Blanco Aguilera et al. attempted to determine the correlation between SB and pain in temporomandibular region based on the sensitivity, age, and gender of patients and clinical subtypes of TMD. They reported that the occurrence of bruxism during sleep correlated positively with age below 60, female sex, more intensification of pain symptoms, and muscular as well as articular TMD. The study supports the hypothesis of bruxism as a risk factor for more frequent TMD. However, the study does not indicate a more frequent occurrence of the muscular disorders than the articular disorders (18). In a clinical trial of the coexistence of bruxism and TMD, Kapusevska et al. found that proper management of bruxism leads to a significant reduction in the number and intensity of symptoms of both the joint component and the muscular TMD (19). In addition, in a clinical trial determining the role of bruxism as a risk factor in the formation and exacerbation of TMD, Sierwald et al. observed almost the same share of SB and AB. They also found a significant increase in the risk of occurrence of TMD in the case of patients with both types of bruxism (20). Raphael et al. aimed to evaluate sleep background electromyographic activity remaining after activity attributable to SB with removing other orofacial activity, other oromotor activity and movement artifacts in women suffering from chronic myofascial TMD. Results of this study indicated that background electromyographic activity during non-sleep bruxism event periods was higher in women with myofascial TMD. Background electromyographic activity in contrast to sleep bruxism event-related activity was also associated with pain intensity. This study indicates the need for a broader view of muscle activity during sleep (21).

In the present work, to examine the relationship between the intensity of SB and the occurrence of pain caused by TMD, TMD Pain Screener, a questionnaire validated by the International Network for Orofacial Pain and Related Disorders Methodology, was used (12). TMD Pain Screener is used to examine the occurrence of pain in the jaw and temple area (22). Statistical analysis showed that higher values of BEI did not correlate with higher scores of the TMD Pain Screener. In addition, more severe bruxism was not found to correlate with more severe pain in temporomandibular area, even if increased number of all types of muscular activities was taken into account. This observation may be due to the inaccuracy of diagnostic methods which are based only on patients' observations, and in all conditions, they should be compared with the results of the clinical examination. TMD Pain Screener could be of great diagnostic significance as a tool for assessing pain associated with TMD, but maybe not in the context of pain associated with TMD caused by SB because this relationship was not supported in this study.

Berger et al. conducted a study analyzing the association between TMD-related pain and specific diagnoses of bruxism, both based on questionnaires. Patients were asked to fill an anonymous questionnaire, consisting of three questions, to verify the presence of TMD-related pain and the two forms of bruxism. In this study, the authors also showed that there was no statistically significant association between SB and TMD-related pain (23). A major limitation of this study was that the diagnosis of both bruxism and pain was based only on questionnaires. Also, van Selms et al. investigated whether pain related to TMD is caused by an interaction between psychological factors and self-reported bruxism activities. Patients were diagnosed with TMD-related pain according to the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD). The authors also found that there were no significant interactions between any of the psychological factors and bruxism with respect to the clinical presence of TMD-related pain (24). A strength of this study was the application of DC/TMD to determine pain, but bruxism was diagnosed only on the basis of a questionnaire, which makes it impossible to arrive at a conclusion. On the other hand, Reissmann et al. conducted a study exploring whether self-reported awake and SB interact in their associations with painful TMD (assessed in accordance with DC/TMD) and whether the interaction is multiplicative or additive. The authors found that awake and SB are associated with an increased presence of painful TMD, and that both types of bruxism are not independently associated, but interact additively (25). Again, a limitation of the study was the use of self-reporting to determine the occurrence of bruxism. It should also be noted that some studies consider both awake and SB. In the light of the latest, separate definitions of these behaviors, it is possible that only the coexistence of both types of bruxism has an effect on the appearance of

pain symptoms. However, this assumption should be studied more thoroughly.

The limitation of the study was lack of adaptive night and providing only one-night polysomnography. The study was conducted in such way due to the lack of foundation of the adaptive night by the Polish National Health Service.

CONCLUSIONS

The occurrence of TMD-related pain is not related to the intensity of SB. TMD Pain Screener may be used as an auxiliary tool in the diagnosis or risk of occurrence of pain related to TMD, whereas in the case of SB, it has only limited diagnostic value.

AUTHOR CONTRIBUTIONS

JS analyzed the data and wrote the manuscript. HM and MW created the research concept, edited the manuscript, and finally revised it before submission. MM-Z recruited patients for the study and collected data. AW collected the references. GM and EW finally revised the manuscript before submission. All authors read and approved the final manuscript.

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Platelet-Rich Plasma Intramuscular Injections — Antinociceptive Therapy in Myofascial Pain Within Masseter Muscles in Temporomandibular Disorders Patients: A Pilot Study

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Background and Objective: The objective of this study was to explore the nociceptive effect of platelet-rich plasma (PRP) intramuscular injections in myofascial pain of masseter muscles in patients with TMD.

Methods: Patients diagnosed with myofascial pain were assessed for eligibility for the study. Masticatory muscle disorder was diagnosed based on the Research Diagnostic Criteria for Temporomandibular Disorders (Ia and Ib). A total of 80 patients were enrolled in the study; 58 of them (21 male and 37 female, 29.4 ± 6.53 years old) met the inclusion criteria and were randomized to one of the two groups: Group I ($n = 29$) and Group II ($n = 29$). The first group received injections with PRP and the second group received injections with isotonic saline as the control group (0.9% NaCl). The Visual Analog Scale (VAS) was used to determine the pain intensity changes during follow-up visit**s** in each group.

Results: A significant improvement in pain intensity in VAS scale was observed, with 58% reduction in the experimental group and 10.38% in the control placebo group, 5 days after the injections (Day 5). The pain intensity reduction (VAS) 14 days after the injections (Day 14) in experimental group was 47.16 and 4.62% in control group, according to the baseline values (Day 0).

Conclusions: Intramuscular injection of PRP was a successful method for reducing myofascial pain within masseter muscles in temporomandibular disorders patients. However, the use of PRP for the treatment of myofascial pain within masticatory muscles requires further, clinical trials evaluation.

Clinical Trial Registration: Bioethical Commission at the Silesian Medical Chamber in Katowice, Poland 44/2017 as well as at ClinicalTrials.gov NCT03323567 (December 13, 2017).

Keywords: platelet-rich plasma, myofascial pain, masseter muscle, intramuscular injection, muscle regeneration

INTRODUCTION

Platelets are cytoplasmic fragments of megakaryocytes ∼2 μm in diameter, which are formed in the human bone marrow. They produce adhesion molecules: fibrine, fibronectin, and vitronectin. Degranulation of platelets causes secretion and protein binding to target cells: osteoblasts, fibroblasts, and mesenchymal cells. As the result of cellular proliferation, synthesis of collagen, and production of extracellular matrix occurs. All products of degranulation are secreted approximately for 1 h (1). Dhurat et al. found that for optimal concentration of platelets of 1.25 × 106−1.5 × 106 per mL of PRP provides proliferation of endothelial cells and angiogenesis (1). There is an average level of 200,000 ± 75,000/μL blood platelet count in human blood (2). The therapeutic PRP counts up to 1 million platelets per 1 mL (1). Platelet concentration 2.5 times higher than in the whole blood concentration seems to be as effective as optimal platelet concentration (3). The goal of PRP in healing process is to concentrate the main growth factors from native blood and to reintroduce them in the injured tissue. Many different techniques are available for PRP preparation and it is difficult to get the same product with different protocols and technical conditions. The most popular and well-known form of blood-derived products for severe thrombopenia treatment is a concentrate for transfusion that contains 0.5×10^{11} platelets per unit (one unit is 1 dose for an adult, with 0.5×10^{11} platelets suspended in 45–65 ml of plasma) (3). PRP contains many growth factors such as: vascular endothelial growth factor, platelet-derived growth factor, and transforming growth factor-β1 (TGFβ-1). These are very important factors for angiogenesis, extracellular matrix changes, and cell production (3). PRP has been used in medicine since 1970s. Pihut et al. and Lin et al. have used them in the temporomandibular disorders (TMD) therapy (4, 5). Reurink et al. have used PRP in the therapy of skeletal muscles injuries (6). To the best of our knowledge there were no studies concerning intramuscular application of PRP in masticatory muscles.

Polish version of Research diagnostic criteria for temporomandibular disorders (RDC/TMD) was used in the study (7). Myofascial pain of masseter muscles can be a difficult issue for differential diagnosis in TMD patients. In most cases it is related to parafunctional activity during sleep, classified as sleep bruxism (8, 9). Bruxism leads to an excessive effort in masticatory muscles and consequently, to anaerobic metabolism and to muscle pain. According to Osiewicz et al. the frequency of muscle disorders in polish patients suffering from TMD was 56.9% (10). Different methods could be used for myofascial pain treatment as occlusal appliances, biofeedback or pharmacotherapy, but they are not always fully effective. Antinociception has a priority in the treatment of masticatory muscle disorder. The longer the muscle pain persists, the harder it is to overcome it. PRP intramuscular injections as a minimally invasive treatment is an additional therapy and can be used only in selected patients with myofascial pain, when other conservative methods do not bring relief.

Muscle regeneration and myogenesis are closely related to growth factors such as insulin-like growth factor-1, fibroblast growth factor-2, hepatocyte growth factor, transforming growth factor beta 1(TGFβ-1), tumor necrosis factor-α, platelet-derived growth factor, and prostaglandins. These factors stimulate proliferation, and differentiation of myoblasts (11). Hepatocyte growth factor activates satellite cells from which myoblasts develop. The level of TGFβ-1 and prostaglandins E-2 has to be balanced to prevent muscle fibrosis and scar tissue formation. PRP can not only promote muscle healing but also decrease pro-inflammatory and apoptotic cells, reducing inflammation (11, 12). PRP is a concentrate of these factors, it promotes muscle healing after intramuscular injection in painful muscles, but is also used in therapy of other diseases, such as: tendonitis, arthritis, osteoarthritis, wound healing, ophthalmology and tissue engineering.

The aim of this study was to explore the nociceptive effect of platelet-rich plasma (PRP) intramuscular injections in selected patients with myofascial pain of masseter muscles.

MATERIALS AND METHODS

Study Participants

Eighty adult patients were selected from the population of subjects referred to the Department of Temporomandibular Disorders. Fifty nine subjects (38 female and 21 male, mean age 29.35 ± 6.61) suffering from myofascial pain of the masseter muscles were found eligible and enrolled to the study.
The inclusion criteria were:

1) Age ≥18 and ≤80.
2) Presence of myofascial pain within masseter muscles according to the RDC/TMD (Ia and Ib) (7).
3) Patient's agreement for participation in this study.

The exclusion criteria were:

1) Patients being treated with or addicted to analgesic drugs and/or drugs that affect muscle function.
2) Patients with neurological disorders, and/or neuropathic pain, and/or headache.
3) History of the head or neck trauma in preceding the enrollment 2 years.
4) Edentulous patients.
5) Patients after radiotherapy.
6) Presence of mental disorders.
7) Pregnancy or lactation.
8) Pain of dental origin.
9) Diagnosis of malignancy.
10) Drug and/or alcohol addiction.
11) Patients with needle phobia.

This study was approved by the Bioethical Commission at the Silesian Medical Chamber in Katowice, Poland (number 44/2017), and retrospectively registered at ClinicalTrials.gov (NCT03371888). The study was performed in accordance with the Declaration of Helsinki as well as the International Conference on Harmonization: Guidelines for Good Clinical Practice. All included patients gave their consent to participate in

the study and received verbal and written information describing the trial.

Study Protocol

This randomized, controlled, double-blind, two-arm trial followed the consolidated standards of reporting trial statement (12) and was performed between December 7, 2017 and December 24, 2018 in the Department of TMD. The patients (n = 59), of both genders were randomized into one of two groups: experimental (Group I, n = 29), and control (Group II, n = 29) (**Figure 1**). Patients were randomized by choosing the number from a closed envelope. Groups were structured as follows: Group I: n = 29, 17 female, 12 male, mean age 28.9 ± 6.23 years and Group II: n = 29, 20 female, 9 male, mean age 29.8 ± 6.99 years. Patients were blinded to the substance injected during the procedure. Only the study coordinator, knew what substance was prepared in the disposable syringe. Another research team member was not informed to which group the patients were allocated during the follow-up visits (Day 5 and Day 14) while checking the pain level in Visual Analog Scale (VAS). PRP was prepared for both groups: I and II before the injection on Day 0. PRP in controls was prepared and frozen at −20°C for the future use (13).

Pain intensity was measured with VAS scale (0 = no pain, 10 = the worst pain that one can imagine) before (Day 0), during (Day 5), and after (Day 14) of the therapy with PRP injections.

The trial consisted of three visits:

1) Baseline visit: injection of study substances—Day 0
2) Control no. 1 after 5 days–Day 5
3) Control no. 2 after 14 days–Day 14

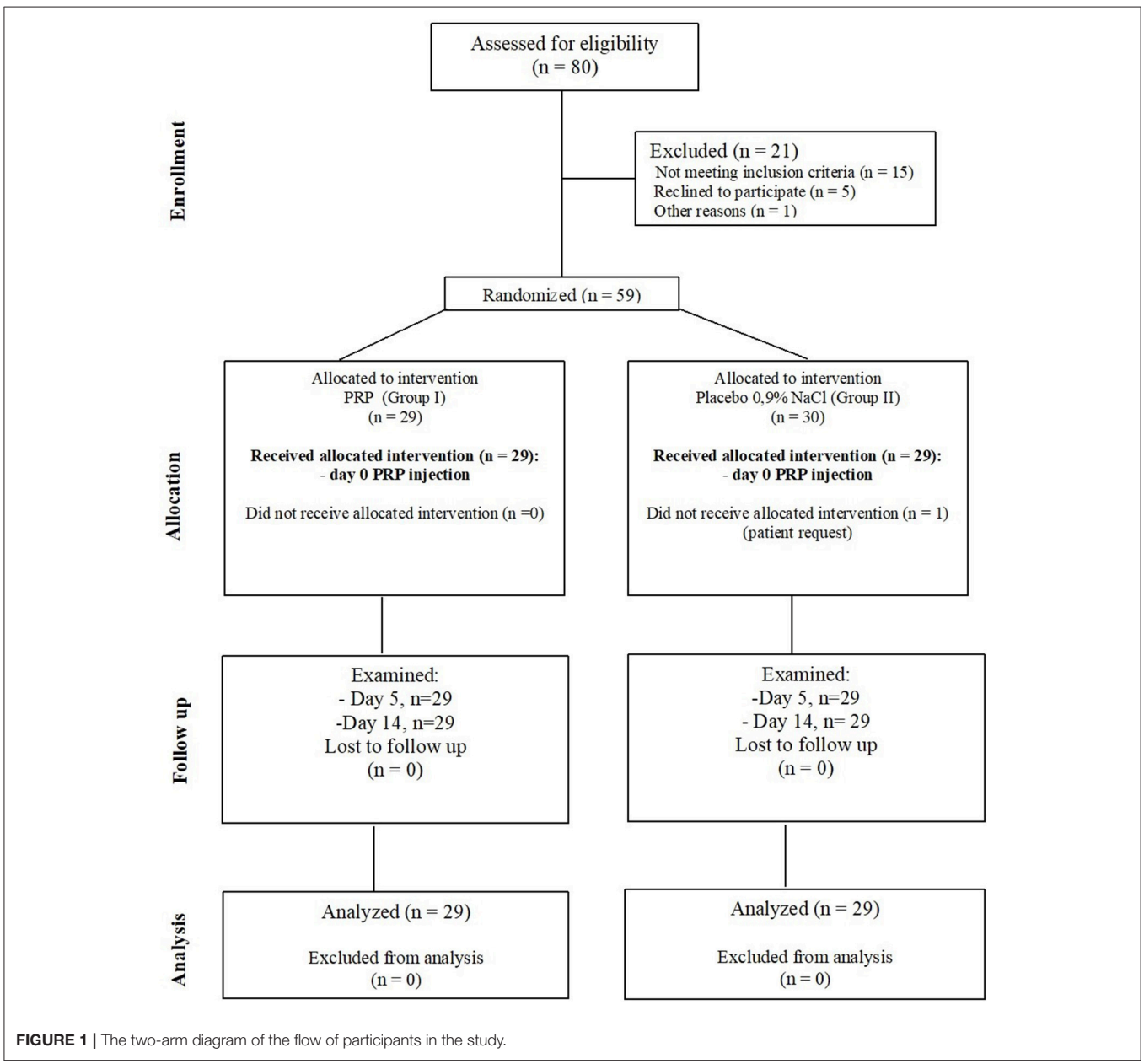

FIGURE 1 | The two-arm diagram of the flow of participants in the study.

The activities undertaken by the investigators during the trial are presented in **Table 1**.

PRP Preparation Protocol

Approximately 40 mL of venous blood was harvested from the cubital vein in four anticoagulant vacutainer tubes (Vacuette 9 mL, sodium citrate 3.2%, Greiner Bio-One, Austria), with a dedicated large-bore needle (butterfly valve fitted to a syringe with long adapter BD Vacutainer Safety-Lok blood collection set with pre-attached holder 21G, 19 mm). The blood was mixed (5 times to prevent micro bunches creation) with an anticoagulant (3.2% sodium citrate). Pure-PRP was prepared as described by Ehrenfest (3). Manual PRP protocol with double spin centrifugation process was used with the centrifuge Zenithlab80–2C. First step of centrifugation: a "soft" spin was performed with an anticoagulant at 1,500 rpm for 5 min (14, 15). Three typical layers of whole blood were found: red blood cells, platelet poor plasma, and a PRP layer between them. Platelet poor plasma and PRP were collected as supernatants over the red blood cells from the tube and transferred into another sterile tube. The temperature during centrifugation was room temperature: 21°C. The second step was a "hard" spin at 3,200 rpm for 15 min. In this process about 6 mL of pure-PRP was obtained. There were no leucocytes or low-density fibrine network in the produced PRP. There was no blood chilling before centrifugation and blood was immediately processed with a low force.

Treatment

During the intervention, painful muscle parts within the masseter muscles were identified with palpation of the masseter muscle and in each group the same amount of the appropriate substance was injected. In all groups, disposable syringes (5 mL) and needles (BD Microlance, 0.3 × 13 mm) were used for injections. Group I PRP and in Group II isotonic saline (0.9% NaCl) were injected bilaterally into the right and left masseter muscles at 3 painful points at each site (6 × 0.5 mL = 3 mL) near the origin, under the zygomatic arch. Injections were deposited 0.5–1.0 cm under the skin surface.

TABLE 1 | Activities of investigators during the trial Visual Analog Scale (VAS I.1, VAS, Group I, first measurement, Day 0).

Visit	1 (Screening and inclusion)	2 (Baseline)	3 (Control 1)	4 (Control 2)
Day of the study	–	Day 0	Day 5	Day 14
Injection PRP or Placebo	–	+	–	–
Measure VAS	–	+	+	+

TABLE 2 | Baseline characteristics of 58 patients included in the study.

	Group I	Group II
n Male/Female	12/17	9/20
Age (years)	28.9 ± 6.23	29.8 ± 6.99

Treatment Outcome Measures

For measuring a treatment outcome, VAS scale was used at Day 5 and Day 14 follow-up visits.

Sample Size Estimation

The minimum sample size necessary to achieve the presumed accuracy of the estimation is determined by the two-stage Stein method.

Statistical Analysis

For the statistical analysis the Statistica software, version 13.1. by Statsoft Polska was used.

To demonstrate the effect of the applied treatment on the level of pain, the following parametric tests were used for two independent tests (experimental group, Group I and control group, Group II:

- *t*-test for two means;
- tests for two variances (F test, Levene test, and Brown-Forsythe test).

In the *t*-Student test, the null (test) hypothesis H_0 was the equality of the corresponding means in the experimental Group I and the control Group II; for variance tests, it was the equality of the corresponding variances.

At the end, we will verify the null hypothesis about the equality of the distribution of pain levels in both groups of patients, using

- Wald-Wolfowitz runs test;
- U Mann-Whitney test.

RESULTS

There were no statistically significant differences in age or gender between the groups ($p > 0.05$) (**Table 2**). There was a 58% reduction in pain intensity in Group I, 5 Days after PRP injection in masseter muscles. In the control group II, after isotonic saline injection, there was 10.24% reduction in pain intensity (**Figures 2–4**).

Descriptive Measures and Confidence Intervals

In the case of the experimental group I (PRP), the values of key descriptive statistics and the limits of confidence intervals for the mean and standard deviation of pain level at the confidence level of 0.95 (or 95%) were as in **Table 3**. In the case of PRP application, after 5 days, the pain decreased substantially (considering the average level of the variables, from ∼5.28 to ∼2.21, average reduction 58.15%). After 2 weeks (Day 14), the average pain level increased slightly (to ∼2.79, average reduction 47.16%). It is worth considering a significant decrease in the median of the examined feature: from the value of 5 to the value of 2 at Day 5. Thus, immediately after PRP application, 50% of patients experienced pain at the level of 5 or higher; after 5 days, 50% of patients experienced pain at the level of at least 2, but at the same time at 50% at the level of at most 2. An

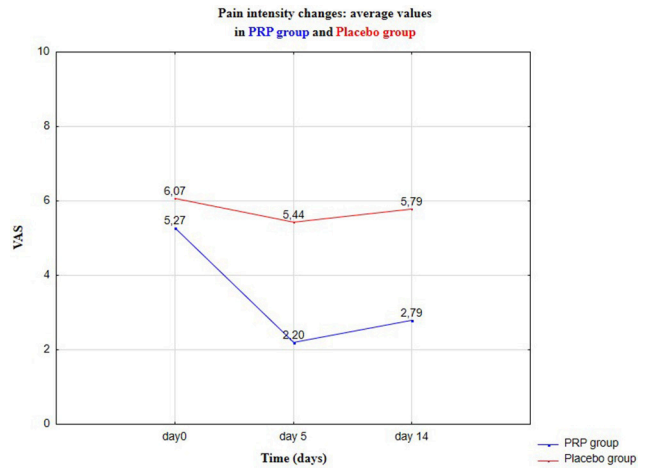

FIGURE 2 | Pain intensity changes in VAS—average values: baseline visit (Day 0), control 1 (Day 5), and control 2 (Day 14).

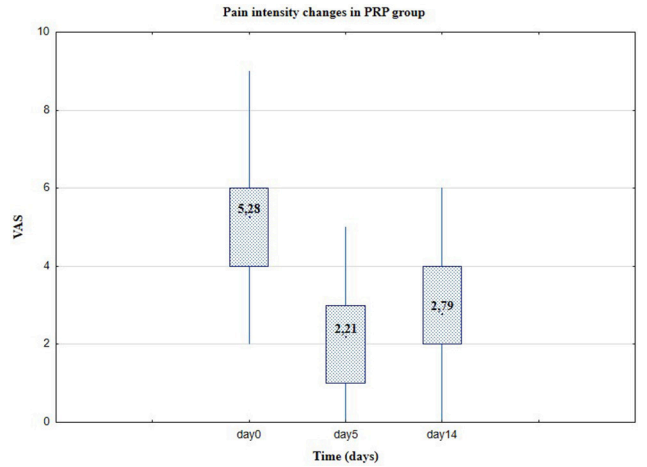

FIGURE 3 | Pain level in VAS, Group I-platelet-rich plasma (Day 0, 5, and 14).

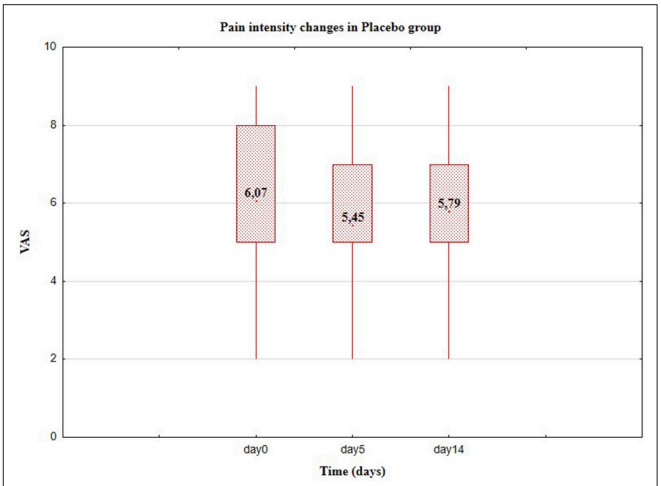

FIGURE 4 | Pain level in VAS, Group II-placebo (Day 0, 5, and 14).

TABLE 3 | Descriptive measures and confidence intervals in experimental group (Group I).

Characteristic	Day 0 (Baseline)	Day 5 (Control 1)	Day 14 (Control 2)
Mean	5.27	2.20	2.79
Median	5.00	2.00	3.00
Range	7.00	7.00	6.00
SD	1.79	1.56	1.69
CV	33.94%	71%	60.80%
Confidence interval for mean (95%)	(4.59, 5.95)	(1.61, 2.80)	(2.14, 3.43)
Confidence interval for SD (95%)	(1.42)	(1.24)	(1.34)

increase in the coefficient of variability in subsequent follow-up tests is characteristic. This is due to a decrease in the average level of pain with only a slight change in the standard deviation: therefore, the average level of pain is significantly reduced, but the degree of dispersion of the results is not significantly changed (differences in the level of symptoms in different patients).

For control experiments, the confidence intervals for the mean and standard deviation at the confidence level $1-\alpha = 0.95$ were constructed.

Relevant results for Group I are represented in **Table 4**. The average level of pain does not change significantly, also the standard deviation remains at almost the same level; similarly for median, range, and coefficient of variation. Pain reduction in the control Group II was observed from the average level of the variables: from ∼6.07 to ∼5.44 (reduction 10.38%) after 5 days and after 14 days to ∼5.79 (reduction to 4.62%). Compared with the results in **Table 2**, this indicates a significant effect of the PRP therapy, on the pain level of patients. Pain levels in VAS in the experimental (Group I) and control (Group II) are presented in **Figures 2**, **3**, respectively.

Parametric Tests

For both control visits: after 5 days and after 14 days, we have rejected the null hypothesis about the equality of the average level of pain in the experimental and control groups. The tests confirm the earlier observation that the level of pain in the experimental group, Group I, is significantly lower than the corresponding level in the control group, Group II, both after 5 and after 14 days. The tests results are given in **Table 5**.

Non-parametric Tests

Non-parametric tests confirm the thesis that the level of pain in Group I is significantly lower than the analogous level in Group II, both after 5 and after 14 days. The results are given in **Table 6**.

Adverse Effects

After the injection of PRP or isotonic saline in the masseter muscle, three patients in Group I, and one

TABLE 4 | Descriptive measures and confidence intervals in the control group (Group II).

Characteristic	Day 0 (Baseline)	Day 5 (Control 1)	Day 14 (Control 2)
Mean	6.06	5.44	5.79
Median	6.00	6.00	6.00
Range	7.00	8.00	7.00
SD	2.01	2.14	1.93
CV	33.22%	39.42%	33.38%
Confidence interval for mean (95%)	(5.30, 6.83)	(4.63, 6.26)	(5.05, 6.52)
Confidence interval for SD (95%)	(1.60, 2.72)	(1.70, 2.90)	(1.53, 2.61)

TABLE 5 | Parametric tests results for the baseline, control 1, control 2 visit.

	Day 0 (Baseline)	Day 5 (Control 1)	Day 14 (Control 2)
Test	***p*-value**	***p*-value**	***p*-value**
T	0.11	0.00	0.00
F	0.53	0.10	0.49
Levene	0.47	0.05	0.84
Brown-Forsythe	0.47	0.06	1.00

TABLE 6 | Non-parametric tests results for the baseline, control 1, control 2 visit.

	Day 0 (Baseline)	Day 5 (Control 1)	Day 14 (Control 2)
Test	***p*-value**	***p*-value**	***p*-value**
Wald-Wolfowitz	0.50	0.00	0.00
U Mann-Whitney	0.09	0.00	0.00

patient in Group II, reported edema and muscle pain. Seven patients had an adverse side effect: bruising, as a result of blood harvesting procedure from the blood vessel. These symptoms were only temporary and completely reversible. There were no serious adverse effects during the trial.

DISCUSSION

The 58% reduction in pain intensity, 5 days after PRP injection in masseter muscles was achieved, comparing to the control group, where the 10.24% reduction in pain intensity was observed. An intramuscular administration of PRP is being used more frequently as a popular treatment for skeletal muscle injuries in athletes (5, 15). Better healing effects of muscle injuries after intramuscular injections are observed and potential benefits of PRP in myofascial pain treatment have been demonstrated in many studies but these studies are not related to orofacial muscle pain. Most studies analyze the impact of PRP intra-articular injections on the function and condition of the temporomandibular joint (4, 5).

In patients suffering from TMD it is important to stop the pain in the first place and after pain relief other types of therapies should be included, such as treatment with intraoral occlusal appliances, anti-inflammatory treatment, and muscle tension-pharmacotherapy, psychotherapy: parafunction prevention, and treatment of bruxism (9).

The use of PRP is an innovative method. It carries almost no risk of complications and although not all authors agree with its high effectiveness of action, according to this research study it is an effective treatment for masseter muscle myofascial pain (5, 16, 17). Martinez-Zapata et al. in his clinical trial obtained a shortening of healing time from 38 days in the control group to 31 days in the study group with PRP intramuscular injection (18). In addition, he also obtained fewer relapses: 7 people in the control group and only 1 person in the study group. He did not find any significant improvement in the duration of healing. In the case of masseter muscle myofascial pain, the possibility of obtaining such results would be a very promising treatment method.

In Franchini meta-analysis, the author has proved the lack of effectiveness of the PRP in orthopedics (16). According to the authors of the mentioned study, the therapeutic effect is clear, however short-term (up to 14 days). Based on the literature data, the best muscle healing was observed 2–10 days after injection (19), probably because of the platelet half-life time, which *in vivo* is ∼7–10 days (2). The effect of PRP found in this study is not long-lasting and the injections should be repeated, more or less after 14 days, when the level of pain is slightly increased. Hammond et al. reported a significant functional improvement in muscle function at Day 3 to Day 14 after intramuscular injection of PRP in rats (20). According to the authors, PRP injections in masseter muscles should be repeated until a satisfactory therapeutic effect is obtained, often as a supportive treatment for other therapies used in TMD. Ineffective therapies using PRP may result from different protocols of PRP preparation, differences in the methodology of administration, and specificity of the disease entity. Intramuscular injection of PRP into masseter muscles in myofascial pain resulted in best antinociceptive results. The pain level reduction in placebo Group II, was probably due to therapeutic injections of isotonic saline, to some extent similar to acupuncture. Despite the satisfactory results and an innovative contribution to myofascial pain research, this study has some limitations: a small study group and a short follow-up observation.

CONCLUSIONS

In selected patients with TMD, suffering from myofascial pain, the intramuscular injection of PRP could be considered as additional, successful therapy in pain relief, when other conservative methods do not bring relief. The further investigation on safety and efficacy of the method are needed.

DATA AVAILABILITY

The datasets supporting the conclusions of this article are included within the article. Access to these data will be considered by the corresponding author upon request.

AUTHOR CONTRIBUTIONS

AN-B created trial concept, performed intramuscular injections of PRP and wrote and edited the manuscript. KW-D collected information concerning pain intensity changes using VAS. SB conducted the randomization and edited the manuscript. Statistical calculations were carried out by WK. All authors read and approved the final manuscript.

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Awake and Sleep Bruxism Among Israeli Adolescents

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Introduction: Sleep and awake bruxism are potential risk factors for oral hard tissue damage, failure of dental restorations and/or temporomandibular disorders. Identifying the determinants of sleep and awake bruxism among adolescents will enable development of preventive interventions for those at risk.

Objectives: To determine emotional, behavioral and physiological associations of sleep and awake bruxism among Israeli adolescents.

Methods: Two thousand nine hundred ninety-three Israeli high school students, from five different high schools in Israel, were approached in the classroom and requested to complete online questionnaires on sleep and awake bruxism, emotional aspects, smoking, alcohol consumption, oral habits, facial pain, and masticatory disturbances. The final study sample concerning awake and sleep bruxism included 2,347 participants.

Results: 1,019 (43.4%) participants reported not experiencing any form of bruxism (neither sleep nor awake), 809 (34.5%) reported awake bruxism, 348 (14.8%) reported sleep bruxism and 171 (7.3%) reported both sleep and awake bruxism. Multivariate analyses (Generalized Linear Model with a binary logistic dependent variable) showed that one of the prominent variables affecting the occurrence of sleep bruxism was anxiety (mild, moderate and severe anxiety, Odds Ratios (OR) of 1.38, 2.08, and 2.35, respectively). Other variables associated with sleep bruxism were stress (each point in the stress scale increased the risk of SB by 3.2%), temporomandibular symptoms (OR = 2.17) and chewing difficulties (OR = 2.35). Neck pain showed a negative association (OR = 0.086). Multivariate analyses for awake bruxism showed an effect of moderate anxiety (OR = 1.6). Other variables associated with awake bruxism were stress (each point in stress scale increased the risk of AB by 3.3%), high and low levels of facial pain (OR = 2.94 and 1.53, respectively), creaks (OR = 1.85) and oral habits (OR = 1.36). Sleep bruxism was found to be a predictor for awake bruxism, and vice versa. In both cases ORs were 8.14.

Conclusions: Among adolescents, sleep and awake bruxism are associated with emotional aspects as well as with facial pain symptoms and/or masticatory system disturbances. Awareness is recommended to decrease potential risks to teeth, dental restorations, and the masticatory system.

Keywords: awake bruxism, sleep bruxism, adolescents, anxiety, stress, oral habits, alcohol consumption, TMD symptoms

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INTRODUCTION

Definition of bruxism has been under debate for some time. In 2013 (1), an international group of bruxism experts issued a consensus proposal based on the concept that bruxism is "a repetitive jaw activity" which can occur during sleep (sleep bruxism- SB) or during wakefulness (awake bruxism–AB). In 2018, it was argued that AB is a masticatory-muscle activity which occurs during wakefulness and is characterized by repetitive or sustained tooth contact and /or by bracing or thrusting of the mandible (2). Such behavior does not necessarily include other behaviors that people engage during the day, such as lip biting, pen biting etc. Those are rather referred to as oral habits. SB is a masticatory-muscle activity during sleep, characterized as rhythmic (phasic) or non-rhythmic (tonic). Neither of the bruxism forms is defined as a movement disorder or a sleep disorder in otherwise healthy individuals (2).

According to both definitions (1, 2), bruxism is characterized by clenching or grinding of the teeth and/or by bracing or thrusting of the mandible. Bracing could be interpreted as forcefully maintaining a certain mandibular position; and thrusting as forcefully moving the mandible in a forward or lateral direction. Both activities are performed without the necessary presence of tooth contact. This addition to "classical" bruxism activities (viz. clenching or grinding of the teeth) accords with the current view that bruxism is not caused by anatomical factors such as certain characteristics of the occlusion, and with the emerging consensus that bruxism involves more than tooth contact (1). Thus, bruxism should not be considered as a disorder, but as a behavior that can be a risk (and/or protective) factor for certain clinical consequences (2).

It was suggested that sleep and awake bruxism are positively associated, whereby, individuals reporting sleep bruxism have a higher probability of also reporting awake bruxism than individuals not reporting sleep bruxism (3, 4). However, these findings should be considered with care. Since sleep bruxism occurs during sleep, the report may reflect false negative proportion due to poor sensitivity of the assessment question(s).

Furthermore, a possible association between bruxism (sleep and/or awake) and temporomandibular signs and symptoms, especially pain, has been suggested. A generally accepted theory claims that masticatory muscle pain results from awake activity, rather than from sleep activity, while it is muscle stiffness when waking up in the morning, which may be associated with sleep bruxism (5).

Uncertainty exists concerning the causes, mechanisms and effects of bruxism. Even the reported prevalence of bruxing activities has a very large range (2.7–57.3% for awake bruxism, 4.1–59.2% for sleep bruxism) (6). According to Manfredini et al. (6), an accurate estimation of bruxism is problematic due to different diagnostic strategies, non-representative populations and comorbid conditions that may act as confounding variables. Additionally, dentally-based diagnosis of treatment and/or prevention demanding bruxism is not accurate in the absence of control for other potential causes of tooth wear (e.g., functional, endogenous, or exogenous factors).

The influence of stress and psychological factors in the etiology of bruxism is also controversial. Some (7) claim that awake bruxism is influenced by psychological factors, with no evidence to such relation with sleep bruxism. Others (8) are of the opinion that anxiety and stress are risk factors for sleep bruxism. Even the association of bruxism with demographic, behavioral and psychological risk factors is under dispute (7, 8).

It is, however, important to acknowledge that bruxism (sleep and awake) can pose a potential risk factor for negative oral health consequences such as painful temporomandibular disorders (TMD), mechanical tooth wear, prosthodontic complications, and others (3, 9).

The present study aimed to identify some of the factors that are associated with bruxism in general (not necessarily demanding treatment and/or prevention), among Israeli adolescents.

METHODS

The Chief Investigator of the Israeli Ministry of Education gave the ethical approval for the study and allowed its performance among students of five high Schools in Israel, located in different cities/areas.

Following coordination with the schools' administration, all students were met in the classroom by one of the researchers (T.M.). The researcher had no personal acquaintance with any of the students, nor access to their personal data.

Students received a full explanation about the study's aims and importance and were encouraged to participate. They were assured that the study was completely anonymous and that they were free not to participate without any consequences to their studies. Following the explanation, the school authorities sent a link to the students' mobile phones or personal computers, through which they could download the online questionnaire. At this point, students who chose to participate signed up an informed consent form and completed the questionnaires online using their mobile devices. To assure anonymity responses were automatically collected into a single database that did not enable tracing of the individual source.

Questionnaire

The questions included in the final questionnaire were derived from the following sources:

- The official Hebrew version of the DC/TMD (10) (https://ubwp.buffalo.edu/rdc-tmdinternational/tmd-assessmentdiagnosis/dc-tmd/).
- Oral habits and temporomandibular noises were derived from a study by van Selms et al. performed among Dutch adolescents (9). The Dutch team tested the reliability of the questionnaire. The questionnaire was translated from Dutch to Hebrew and backwards and used in a previous study performed among Israeli population (4). The questions were multiple-choice and referred to the last month (9)
- The General Anxiety Disorder-7 (GAD-7) questionnaire (11)
- The Perceived Stress Scale-10 (PSS) questionnaire (12)

The studied variables were as follows:

1. **Facial pain symptoms and/or masticatory system disturbances** (during the past month **(TM symptoms**), were evaluated through the official Hebrew version of the DC/TMD (10) (https://ubwp.buffalo.edu/rdc-tmdinternational/tmd-assessmentdiagnosis/dc-tmd/). One was considered as suffering from TM symptoms when s/he gave a positive reply (a "yes" response) to at least one of the following questions:
   - Do you suffer from pain in your face, jaws, the front of an ear, or inside the ear**? (Facial pain).**
   - Have you had pain in your neck? (**Neck Pain**)
   - Do you experience any difficulty in chewing? (**Chewing difficulties**)
2. **Bruxism** was assessed by the following questions (3, 9):
   - Sleep bruxism (**SB**)—"Have you been told, or did you notice by yourself, that you grind your teeth or clench your jaws when you are asleep?" (Yes, no, don't know)
   - Awake bruxism (**AB**)—"Have you been aware that you are clenching or grinding your teeth in wakefulness?" (Yes, no, don't know or unaware)
3. **Smoking** (3, 9) was assessed by the question: "Do you smoke cigarettes at present?" (Never, Occasionally, Regularly, Often, or Daily). For the purpose of this study, one was considered a smoker (a "yes" response) when one marked at least a regular smoking frequency (namely, marked one of the following responses: Regularly, Often, or Daily).
4. **Alcohol Consumption** (3, 9) was measured using the question "Do you drink alcohol at present?" (Never, Occasionally, Regularly, Often, or Daily). Alcohol consumption was considered positive (a "yes" response) when one marked at least a regular consumption (namely, marked one of the following responses: Regularly, Often, or Daily).
5. **Oral Habits** (3, 9) were evaluated by questions about various activities (Never, Occasionally, Regularly, Often, or Daily). A habit was considered positive when the activity was marked as either–Regularly, Often, or Daily.
6. **Temporomandibular joint noises** (3, 9) **(Joint Noise)** while opening/closing the mouth, or while chewing was considered positive when a positive reply was given to at least one of the following questions:
   - Does your jaw make a clicking or popping sound when you open or close your mouth, or while chewing?'
   - Does your jaw make a scraping or grating sound when you open or close your mouth, or while chewing?'
7. **Anxiety**- the GAD-7 questionnaire (11), was used to classify and rate general anxiety disorder and assesses its severity in clinical practice and research. The questionnaire was initially developed, following DSM criteria, to screen generalized anxiety disorder and measure the severity of symptoms, *in the last 6 months*. GAD-7 is a 7-item measure that can be self-completed or administrated by an interviewer. Participants are asked how often over the past 2 weeks they have been bothered by each one of the seven cores items (e.g., worrying too much about different things; feeling afraid as if something awful might happen; not being able to stop or control worrying). Each item is assessed on a 1 to 4 Likert scale from (1 = not at all, to 4 = nearly every day). The cutoffs were adjusted to adolescents by Mossman et al. (13). Answers were scored by the index and divided into four severity levels: 0 = *None* (no anxiety whatsoever), 1 = *Mild anxiety*, 2 = *Moderate anxiety*, and 3 = *Severe anxiety*.
8. **Stress** – The PSS-10 questionnaire (12) was used to measure participants' perception of stress. The scale has been used with both adolescents and adults (14). Participants were asked to mention how regularly they experience stress, or a specific feeling, following different incidents in the last month. Each item is rated on a 5-point scale of 0–4 ("*Never*," "*Almost Never*," "*Sometimes*," "*Fairly Often*" and "*Very Often*"). The total score ranges from 0 to 40. The scale was analyzed as a continuous variable.

Statistical Analysis

Descriptive statistics followed by univariate Chi (2) or Fishers' Exact Test and *T*-Test analyses for PSS associated with AB and SB. The significance level was set to $\alpha = 0.05$. For multiple comparisons of column proportions, the Bonferroni method for adjusted *p*-value was calculated. Regression results were also corrected using Bonferonni.

Significant results from the univariate analyses were used for further multivariate analyses using General Linear Model (GLM) with binary logistic dependent variables SB and AB. The reference group was non-bruxing participants (reporting neither AB nor SB). The reference group for GAD-7 score adapted for adolescent's independent variable was "No anxiety whatsoever." Odds Ratio compared to the reference level in each categorical independent variable where the study groups SB or AB respectively, set as the risk category (of having either AB or SB). A Receiver Operating Characteristic (ROC) analysis was followed by Youden's J statistics to capture the maximum sensitivity and specificity performance of a dichotomous diagnostic test for PSS cut points predicting SB and AB.

The data were analyzed using IBM SPSS statistics version 23.0. (SPSS, Inc., Chicago, IL USA).

RESULTS

Overall 2,993 adolescents were approached, with a response rate of 88%. The initial study population included 2,634 students from five different high schools in Israel, as detailed in **Table 1** (1,344 girls, 1,255 boys and 35 who did not specify their sex). The average age of participants was 15.7 years (with a Standard Deviation of 1.1 years).

Of the sample, 287 participants either did not respond to the questions regarding bruxism ($n = 37$) or indicated not knowing of any form of bruxism (neither sleep nor awake, $n = 250$), and were excluded from the analysis. The final study sample was 2,347, of whom 1,019 (43.4%) reported not experiencing any form of bruxism (neither sleep nor awake). This group was set as the reference group. 171 (7.3%) participants reported experiencing both AB and SB; 809 participants (34.5%)

reported experiencing AB and 348 participants (14.8%) reported experiencing SB (**Figure 1**).

Since no significant differences were found between individuals who indicated not knowing of any form of bruxism, $n = 250$) and the final study sample ($n = 2{,}347$) regarding sex ($p = 0.133$), and age ($p = 0.076$), no adjustments for sex and age were introduced in the analyses of the final study sample.

Initially, participants who had undergone orthodontic treatment in the past, or were undergoing such treatment at the time of the study (45.9% of the final study sample), were analyzed as a separate group. As no significant differences were found among participants with and without orthodontic experience, the groups were aggregated and analyzed as one.

The most frequent symptoms associated with dysfunction of the masticatory system were neck pain (46.6%), followed by orofacial pain (28.2%), joint noises (21.2%). Pain and difficulties in chewing were less common (8.4%).

Table 2 presents frequencies of oral habits among the final study sample. Ninety percent of the participants reported chewing gum, with about 22% doing it very often. In addition, there was a high frequency of nail biting, pen chewing, and lip/cheek biting. The frequencies of alcohol consumption and smoking on at least a regularly base, were 8.5 and 5%, respectively.

At least 60% of the participants (final study sample) reported different degrees of anxiety and stress. Severe anxiety was found in 10.3% of the participants; moderate anxiety in 15.9% of the participants and mild anxiety among 32.7% of the participants.

A univariate analysis of associations between SB and the study variables is presented in **Table 3**. SB was associated significantly with the following variables: sex, joint noise, masticatory system symptoms, anxiety, oral habits, neck pain, difficulties in chewing, joint noises, and stress. Most of the variables, which showed a significant result for SB, showed also a significant result for AB (**Table 4**).

TABLE 1 | Final sample by age, sex, and school.

School num.	School location*	*n***	Average age ± SD***	Sex		
				Girls	Boys	Un-specified
1	South	369	16.2 ± 1.0	195	169	5
2	Center1	1,046	15.4 ± 1.2	543	491	12
3	Center2	423	15.3 ± 1.0	191	224	8
4	East	451	15.6 ± 0.9	250	197	4
5	North	345	16.1 ± 0.9	165	174	6
Total		2,634	15.7 ± 1.1	1,344	1,255	35

**School location: South – next to Gaza strip; Center1- Ramat Gan; Center 2-Tel Aviv; East- Jerusalem; North- Kibutz Yagur. **n, Number of students observed; ***SD, Standard Deviation.*

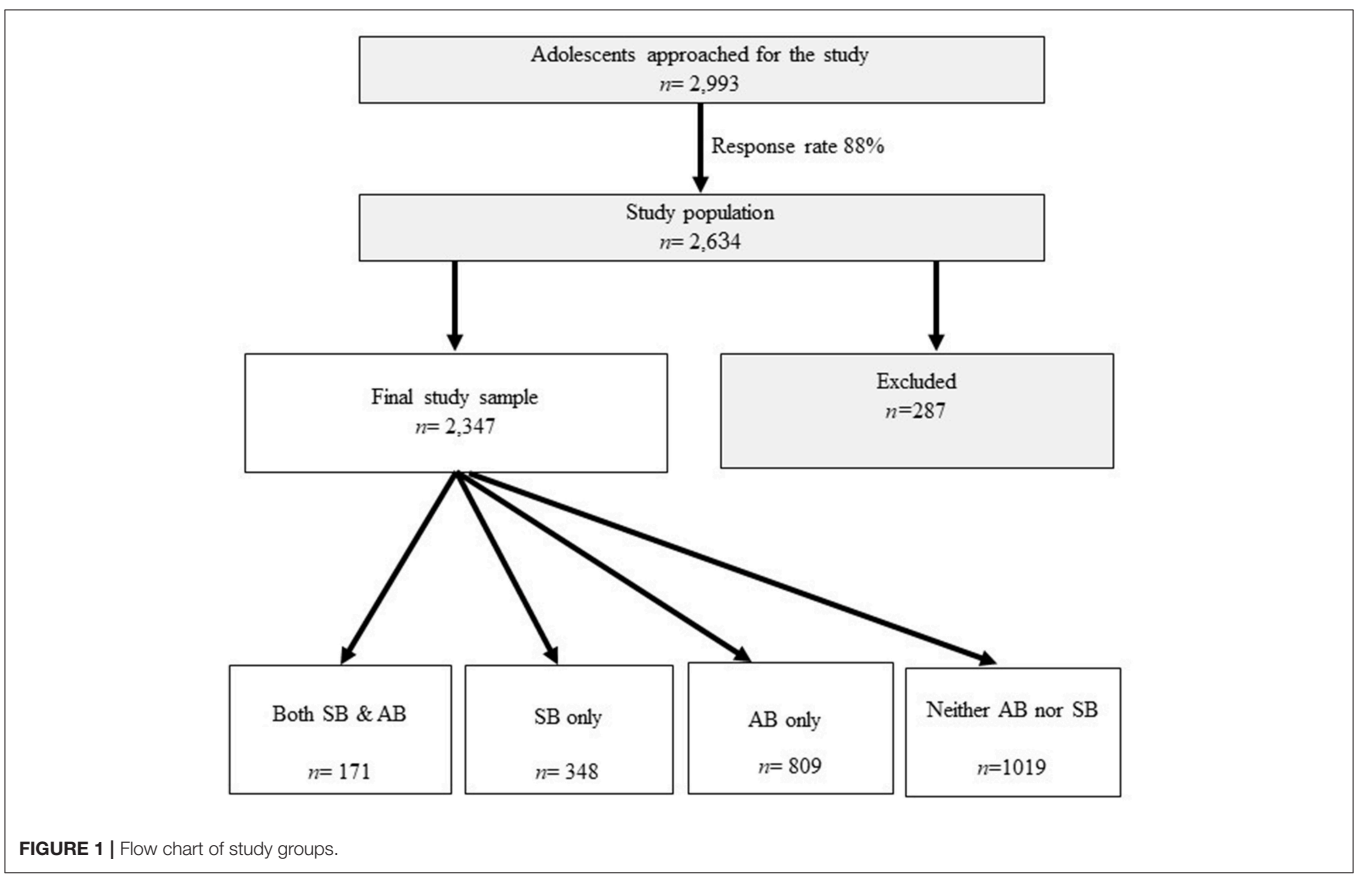

FIGURE 1 | Flow chart of study groups.

TABLE 2 | Frequencies of SB, AB, oral habits, smoking and alcohol consumption, by sex.

	n	Total	Girls	Boys
SB				
No	1,312	80.0%	75.9%	84.6%
Yes	327	20.3%	24.1%	15.4%
AB				
No	1,501	68.9%	67.9%	69.9%
Yes	678	31.1%	32.1%	30.1%
Chewing gum				
Never	284	10.8%	8.4%	13.2%
Sometimes	953	36.3%	27.5%	45.6%
Regularly	216	8.2%	10.4%	5.9%
Often	590	22.5%	24.0%	21.2%
Very often	579	22.1%	29.7%	14.0%
Total	2,622			
Nails biting				
Never	1144	43.6%	47.2%	40.0%
Sometimes	701	26.7%	29.8%	23.4%
Regularly	183	7%	4.9%	9.2%
Often	296	11.3%	8.5%	14.1%
Very often	297	11.3%	9.6%	13.3%
Total	2,621			
Pen biting				
Never	1602	61.2%	53.8%	68.9%
Sometimes	646	24.7%	29.9%	19.0%
Regularly	98	3.7%	3.7%	3.9%
Often	140	5.3%	6.8%	3.8%
Very often	132	5.0%	5.7%	4.4%
Total	2,618			
Cheek/lip biting				
Never	571	21.8%	14.7%	29.7%
Sometimes	1129	43.2%	42.1%	44.3%
Regularly	240	9.2 %	10.3%	7.9%
Often	405	15.5 %	19.6%	11.0%
Very often	269	10.3%	13.3%	7.1%
Total	2,614			
Smoking				
Never	2380	90.8%	92.8%	88.7%
Sometimes	141	5.4%	4.5%	6.4%
Regularly	28	1.1%	0.6%	1.5%
Often	31	1.2%	1.0%	1.4%
Very often	41	1.6%	1.1%	2.1%
Total	2,621			
Alcohol consumption				
Never	1,628	62.3%	65.1%	59.0%
Sometimes	784	30.3%	28.6%	31.5%
Regularly	81	3.1%	1.9%	4.5%
Often	105	4.0%	4.1%	3.9%
Very often	17	0.7%	0.3%	1.0%
Total	2,615			

Table 5 presents *t*-tests univariate analysis of PSS for awake and sleep bruxism. The Reliability Statistics Cronbach's Alpha for PSS was 0.82 without need to delete any item. A Receiver Operating Characteristic (ROC) analysis captured a cut point of PSS $\geq$ 18.645 for SB, and a cut point of PSS $\geq$ 16.805 for AB (**Figures 2**, **3**).

TABLE 3 | Chi^2 univariate analysis for SB by sex, age, and study variables.

Independent variable	Category	*n*	Percent	*P**
Sex	Boys	790	15.4[b]	<0.001
	Girls	849	24.1[a]	
Age	14	263	19.4[a]	ns
	15	405	19.3[a]	
	16	487	21.8[a]	
	17	401	19.2[a]	
	18	83	15.7[a]	
Joint noises	Yes	397	28.7[a]	<0.001
	No	1,255	17.1[b]	
TM Symptoms (at least one)	Yes	404	30.2[a]	<0.001
	No	1,249	16.7[b]	
Smoking	Yes	69	26.1[a]	ns
	No	1,581	19.7[a]	
Alcohol	Yes	135	22.2[a]	ns
	No	1,509	19.8[a]	
Anxiety (GAD child)	None*	731	11.5[a]	<0.001
	Mild	559	20.4[b]	
	Moderate	224	34.4[c]	
		112	43.8[c]	
	Never			
Oral habits	Yes	587	26.6[a]	<0.001
	No	1,064	16.4[b]	
Facial pain	Yes	122	38.5[a]	<0.001
	No	1,525	18.5[b]	
Neck pain	Yes	193	31.1[a]	<0.001
	No	1,436	18.5[b]	
Chewing difficulties	Yes	1,524	36.3[a]	<0.001
	No	113	18.8[b]	

anxiety whatsoever.

**Following Bonferonni correction.*

[a], [b], [c], denote a different adjusted significant of a proportion level of SB for each Independent variable.

Generalized Linear Model (GLM) With a Binary Logistic Dependent Variable

Following univariate analyses, multivariate analyses were performed to evaluate which of the variables reaching significance affect the occurrence of SB and AB. Regression results also met significant criteria with Bonferonni adjustment.

Results of the multivariate analysis for SB are presented in **Table 6**. One of the prominent variables affecting the occurrence of sleep bruxism was anxiety (mild, moderate and severe anxiety; odds ratios of 1.38, 2.08 and 2.35, respectively, relative to None) with a positive linear trend according to anxiety level. Other variables correlated with SB were stress (each point of PSS scale increases the Odds Ratio of SB by 3.2%); TM symptoms (OR = 2.17) and chewing difficulties (OR = 2.35). Neck pain showed a negative correlation with SB (OR = 0.086).

The results of multivariate analyses for AB are presented in **Table 7**. Only "moderate" level of anxiety was found to affect the

TABLE 4 | Chi^2 univariate analysis for AB by sex, age and study variables.

Independent variable	Category	*n*	Percent	*P**
Sex	Boys	1,081	30.1[a]	ns
	Girls	1,098	32.1[a]	
Age	14	377	29.2[a]	0.009
	15	557	33.8[a]	
	16	671	35.0[a]	
	17	493	27.6[a]	
	18	91	22.0[a]	
Joint noise	Yes	513	44.2[a]	<0.001
	No	1,691	27.5[b]	
TM symptoms (at least one)	Yes	604	45.5[a]	<0.001
	No	1,601	26.0[a]	
Smoking	Yes	84	38.1[a]	ns
	No	2,116	31.1[a]	
Alcohol	Yes	167	32.9[a]	ns
	No	2,028	31.3[a]	
Anxiety (GAD child)	None	913	21.4[a]	<0.001
	Mild	786	32.6[b]	
	Moderate	326	47.9[c]	
	Severe	152	51.3[c]	
Oral habits	Yes	833	39.6[a]	<0.001
	No	1,370	26.4[b]	
Facial pain	Yes	199	50.8[a]	<0.001
	No	1,999	29.4[b]	
Neck pain	Yes	286	44.4[a]	<0.001
	No	1,890	28.5[b]	
Chewing difficulties	Yes	2,003	50.5[a]	<0.001
	No	182	29.6[b]	

**Following Bonferonni correction.*
ns, non significant.
[a], [b], [c], denote a different adjusted significant of percent level of SB for each Independent variable.

TABLE 5 | *T*-Tests univariate analysis of PSS for AB and SB.

Variable	Category	*n*	Average PSS ± SD	*P*
SB	Yes	327	19.2 ± 8.4	<0.001
	No	1,310	14.8 ± 7.5	
AB	Yes	686	18.6 ± 7.8	<0.001
	No	1,500	14.9 ± 7.4	

occurrence of AB relative to the reference "*None*" (OR = 1.6). Other variables increasing the occurrence of AB were stress (each point in PSS scale increased the occurrence of AB by 3.2%). Regarding Facial Pain, high level of pain ("*Very*") increased the odds of AB by about 3 times and low level of pain ("*A little*") by about 1.5 times (compared to "*None*"). No linear pattern was found since the level of "*Moderate* pain" did not differ from the reference category. Creaks increased the odd of AB by 1.85 and oral habits by 1.36.

Sleep bruxism was found to be a predictor for awake bruxism, and vice versa. In both cases the ORs were 8.14 (95% IC = 6.12,10.83).

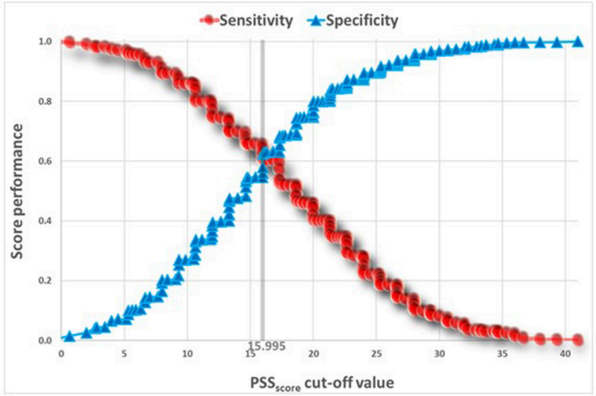

FIGURE 2 | ROC Analysis of PSS predicting AB.

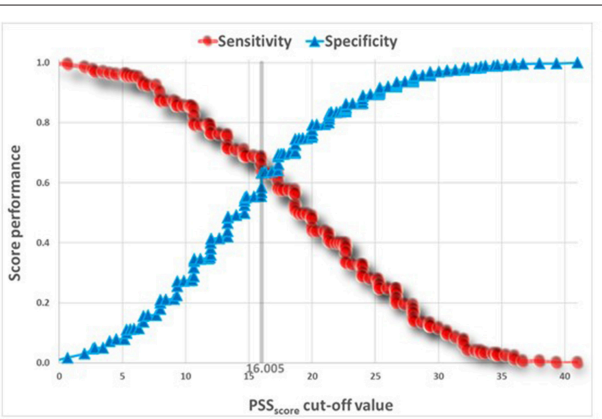

FIGURE 3 | ROC Analysis of PSS predicting SB.

DISCUSSION

Sleep and awake bruxism are muscular activities with potential deleterious effects to the maxillofacial area (2). The present study aimed to identify some of the factors that are associated with bruxism among Israeli adolescents. This was an epidemiological study and the diagnosis of bruxism was based on self-report questionnaires, representing the lower ('possible') grade of bruxism diagnosis (1, 2). To achieve a definite diagnosis, use of polysomnography (for sleep bruxism) or electromyography (for awake bruxism) are needed. Regretfully, such tests are not feasible in an epidemiological study. Self –reported questionnaires are a common tool in large population studies like the present one (3, 6, 9, 15–17). Positive associations were found between questionnaire-based diagnoses of awake bruxism and diagnoses based on history taking combined with clinical examination (18). Furthermore, a meta-analysis showed medium to high specificity for questionnaires in the diagnosis of sleep bruxism (19).

In the present study, the prevalence of sleep bruxism was 14.8%, and that of awake bruxism 34.5%. While the results regarding sleep bruxism match prior data, these of awake

TABLE 6 | General linear model with sleep bruxism as a logistic binary dependent variable.

Parameter	β	Hypothesis test	Exp(β)	95% Wald confidence interval for exp (β)	
		Sig.		Lower	Lower
(Intercept)	−2.457	0.000	0.086	0.057	0.129
GAD-7= Severe	0.855	0.006	2.352	1.278	4.331
GAD-7= Moderate	0.731	0.002	2.077	1.304	3.308
GAD-7= Mild	0.322	0.075	1.380	0.968	1.968
GADc-7= None[a]	0a	1.000	1.000	–	–
PSS	0.031	0.008	1.032	1.008	1.056
Sex	0.131	0.472	1.140	0.798	1.675
TM symptoms	0.775	0.002	2.170	1.318	1.311
Joint noises	0.242	0.082	1.274	0.970	1.686
Oral habits	−0.014	0.959	0.986	0.577	4.331
Neck pain	−2.457	0.000	0.086	0.057	0.129
Chewing diff.	0.855	0.006	2.352	1.278	4.331

[a] *Reference value.*

TABLE 7 | General linear model with awake bruxism as a logistic binary Dependent variable.

Parameter	β	Hypothesis test	Exp(β)	95% Wald confidence interval for exp (β)	
		Sig.		Lower	Lower
(Intercept)	−1.108	0.124	0.330	0.080	1.356
GAD-7 = *Severe*	0.361	0.147	1.435	0.881	2.339
GAD-7 = *Moderate*	0.467	0.010	1.595	1.120	2.272
GAD-7 = *Mild*	0.182	0.162	1.200	0.930	1.549
GADc-7 = *None*[a]	0[a]	1.000	1.000	–	–
PSS	0.032	0.000	1.033	1.015	1.051
Age	−0.055	0.224	0.947	0.866	1.034
Facial pain = *very*	1.079	0.009	2.942	1.304	6.637
Facial pain = *Moderate*	0.342	0.114	1.408	0.921	2.153
Facial pain = *A little*	0.427	0.001	1.533	1.189	1.975
Facial pain = None	*0a*	*1.000*	*1.000*	–	–
Symptoms	0.174	0.324	1.190	0.842	1.683
Joint noises	0.214	0.550	1.239	0.614	2.499
Oral habits	0.304	0.004	1.355	1.105	1.661
Neck pain	0.103	0.195	1.108	0.949	1.295
Chewing diff.	0.031	0.876	1.032	0.695	1.532

[a] *Reference values.*

bruxism are higher than previously reported in different societies (3, 6, 9, 20). The prevalence of sleep and awake bruxism were slightly higher than those reported by Manfredini et al. (6) for adults in a systematic literature review. A possible explanation for the differences may stem from the fact that adolescents in Israel reported relatively high rates of anxiety and a relatively high prevalence of oral habits (at least one type). Also, the differences among studies may origin from the assessment methods that might have led to differences in the reports of oral habits. Oral activities such as teeth clenching while awake, which are usually considered as part of AB, can sometimes be considered as oral habits and are not necessarily associated with clinical consequences.

Sleep bruxism was found to be a strong predictor for awake bruxism, and vice versa (OR 8.4). This is in accordance with a previous study (21) which showed that awake bruxism increases the odds of sleep bruxism 5-fold (and vice versa), suggesting that both entities have much in common. Manfredini and Lobbezoo (7), claimed that awake and sleep bruxism seem to be of different pathogenesis but are difficult to distinguish clinically. Possibly, participants perceive awake and sleep bruxism as a single entity a fact which unable satisfactory diagnosis through self-reported questionnaires. A large-scale investigation is warranted in an attempt to substantiate the complex relationship between sleep and awake bruxism.

Neither smoking nor alcohol consumption were associated with sleep or awake bruxism. The relation between alcohol consumption and sleep bruxism is controversial. While some studies (9) did not find an association, others (19, 22) reported associations between heavy smoking and heavy alcohol consumption and sleep bruxism. It is noteworthy that the distributions of alcohol and tobacco use in the present study were skewed. The population in the present study was young, and the number of smokers and alcohol consumers was small (only 3% reported smoking and 5% consumed alcohol often or very often). Alcohol consumption in Israel is the lowest in the OECD countries (https://www.timesofisrael.com/alcohol-consumption-in-israel-among-lowest-in-oecd-countries), so that the low percentage of alcohol consumers among the study population is not unusual. The young age of participants, together with the low percentage of smokers and alcohol consumers, may have led to the weak associations between these variables and sleep bruxism. The insufficient exposure of participants to smoking and alcohol unable reaching a meaningful conclusion.

The most prominent variables associated with sleep bruxism were anxiety and stress. The etiology of sleep bruxism seems to be centrally mediated (23). It occurs mostly during a switch from deep sleep to shallow sleep (24). It is reasonable that stress influences the quality and deepness of sleep, causing more switches between deep sleep to shallow sleep and secondarily aggravating the sleep bruxism. Additional factors increasing the risk of sleep bruxism were the presence of joint noises, facial pain symptoms, and the performance of oral habits. These symptoms are well-documented as being associated with bruxism (both sleep and awake) (25). Joint noises may be due to TMJ disc displacement with reduction caused by bruxism, based on a proposed etiology that frictional "sticking" of the disc is the cause of the disorder. In addition, the intra-capsular pressure performed during clenching may affect the joint lubrication and temporary anchorage of the disc. The energy needed to break adhesion of the disc is converted into the joint sound. For the performance of oral habits, the study suggests once again that they may be detrimental to the masticatory system (26). Another interesting finding was that sleep and awake bruxers reported significantly greater difficulties in chewing. This finding may be

due to the fact that bruxers (sleep and awake) also reported significantly more facial and neck pain. In other words the chewing difficulties are probably secondary to the pain and not directly related to the bruxing activity.

In the multivariate model, awake bruxism was associated with moderate/ high anxiety and stress. This is in accordance with the common notion of the role of psychosocial factors, especially stress, in awake bruxism (6). Awake bruxism, is often claimed to be a response to stress and anxiety (27). As expected, AB shows higher sensitivity to stress than SB.

The ROC curves (**Figures 2**, **3**) show that the discriminatory power of the PSS questionnaire is around 65% in both AB and SB, which is not a high performance. The PSS was originally intended to measure stress levels in adults. Nevertheless, it has been successfully used in previous studies to evaluate stress among adolescents (14, 28), a fact that led to its use also in the present study. Possibly, the questionnaire's adult norms are less appropriate for adolescents. Use of other measures, specifically developed for adolescents to assess stress, may have led to stronger results.

Additionally, the results show significant differences in the occurrence of SB between sexes (24.1% among girls vs. 15.4% among boys; $P < 0.0001$, Fisher's Exact Test). No such differences were found for AB (32.1 vs. 30.1%, accordingly). Sex differences in the occurrence of SB and AB are contradictory. Some studies report sex differences in the occurrence of bruxism among adolescents while others do not (3, 25, 29, 30). A systematic literature review (31) including 22 publications and accounting for more than 19,000 subjects aged 2 to 12 years, found that the prevalence of sleep bruxism in children was highly variable between the studies (3.5–40.6%), with a commonly described decrease with age and no gender differences. Thus, the findings reported above regarding sex differences in the occurrence of SB (or lack of it regarding AB) should be considered with care and need further examination.

Bruxism, both sleep and awake, can carry negative oral health consequences (e.g., severe masticatory muscle pain or temporomandibular joint pain) (1). Pain, if present, may be associated with changes in stress and anxiety. Accordingly, a vicious cycle develops. This cycle, if not interrupted promptly, may cause a neuroplasticity converting the pain into centrally mediated. Identifying factors that affect sleep and awake among adolescents will enable to better define treatment and/or prevention demanding bruxism and propose preventive interventions for subjects at risk.

Taking the findings together it can be concluded that bruxism (sleep and awake) among adolescents is associated with both emotional aspects, as well as with facial pain symptoms and/or masticatory system disturbances. Awareness to these aspects among adolescents can benefit our understanding of the bruxing behavior in order to prevent potential future negative effects.

ETHICS STATEMENT

The Chief Investigator of the Israeli Ministry of Education gave the ethical approval to the study and allowed its performance among students of five high Schools in Israel, located in different cities/areas.

AUTHOR'S NOTE

This study was undertaken in partial fulfillment of a DMD thesis at the School of Dental Medicine, Tel Aviv University, Tel Aviv, Israel.

AUTHOR CONTRIBUTIONS

EW: creation of the research concept, academic supervision of the DMD thesis, editing of the manuscript. TM: data acquisition and writing the DMD thesis. IE: academic supervision, manuscript preparation and revision, final approval of manuscript. AE-P: manuscript preparation and revision. RK: data analysis. SR: critical revision of the manuscript. PF-R: contribution to study concept design, analysis, and interpretation, drafting and critically revision of the manuscript, supervision of the DMD thesis. All authors read and approved the final manuscript.

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Evaluation of Relationship Between Sleep Bruxism and Headache Impact Test-6 (HIT-6) Scores: A Polysomnographic Study

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Sleep bruxism (SB) is a masticatory muscle activity during sleep characterized by teeth clenching or grinding and/or bracing or thrusting of the mandible. Morning headache is considered as a common symptom of SB; however, the relationship between SB and headache and its impact on patient's life is not clear. Therefore, the present study aimed to assess the relationship between SB using polysomnography with video/audio recording and Headache Impact Test-6 (HIT-6) scores. SB was evaluated in respondents by single-night diagnostic polysomnography with video/audio recording. The study found that Bruxism Episode Index was similar in the group with significant impact of headache on patient's life (HIT-6 score $\geq$ 50) and in group with little or no impact (HIT-6 score $<$ 50). A statistically significant positive correlation was observed between bruxism associated with arousal and HIT-6 score ($r = 0.51$, $p < 0.05$) and between mixed bruxism and HIT-6 score ($r = 0.58$, $p < 0.05$) in the subgroup with phasic bruxism. The results indicated the relationship between SB and impact of severity of headache on the patient's life measured by HIT-6 is only modest. It was also found that the impact of severity of headache measured by HIT-6 is altered only in those with phasic bruxism and is associated with arousal. Further research should elucidate the factors influencing the relationship between SB and headache.

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Keywords: sleep bruxism, headache, arousal, phasic bruxism, polysomnography

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INTRODUCTION

Chronic headache defined as headache occurring on 15 or more days per month for at least 3 months is a major cause of pain and disability (1). The global prevalence of headache has been estimated to be as much as 42% (2). Thus, headache has an important socioeconomic impact and is considered as a burden for society. Migraine and tension-type headache are the most common types of primary headaches, while the most common secondary headaches are those attributed to

head injury (1). Sleep and headache have a complex and extensive relationship (3). Sleep disturbances and stress are the most common headache triggers (4), and when these conditions coexist, they have an additive effect in patients with chronic headache (5). Insufficient sleep is prevalent among subjects with tension-type headache and is linked to exacerbation of symptoms (6). Poor sleep may contribute to increased sensitivity to pain, thus increasing the frequency of headache attacks. Around 15–74% of individuals with obstructive sleep apnea (OSA) suffer from morning headache (7), and morning headache are often unspecific.

SB is a masticatory muscle activity during sleep characterized by teeth clenching or grinding and/or bracing or thrusting of the mandible. ICD-10 classifies bruxism as a sleep disorder (G47.63). A recent international consensus defined SB as a masticatory muscle activity that occurs during sleep and is characterized as either rhythmic (phasic) or non-rhythmic (tonic) and suggested that SB should not be considered as a movement disorder or a sleep disorder in otherwise healthy individuals (8). The consensus also proposed that bruxism can be as graded "possible," "probable," and "definite." "Possible bruxism" is diagnosed based on a questionnaire or an interview, "probable bruxism" is diagnosed based on self-report and a clinical examination, and "definite bruxism" is diagnosed based on polysomnography (PSG) with video/audio recording (9). The American Academy of Sleep Medicine (AASM) has classified SB as a sleep-related movement disorder in the International Classification of Sleep Disorders – Third Edition (ICSD-3) (10). Most SB episodes occur in the stages N1 and N2 of sleep (called non-rapid eye movement (non-REM) sleep). SB episodes commonly occur at sleep arousal (11), with accompanying increase in heart rate and motor activity (12, 13). SB can lead to tooth wear, tooth mobility, tongue/cheek indentation, masticatory muscle hypertrophy, pain in the temporomandibular joint, and masticatory muscles, and also headache (14).

Studies focusing on the association between bruxism and headaches have shown contradictory results; while some have concluded that there is an association between bruxism and headache (15, 16), one study did not support this assertion (17). Moreover, the methods used for evaluation in many of these studies were insufficient, e.g., SB was assessed using questionnaires or by clinical examination or only with the use of a portable electromyographic device (18). These studies also had a small sample size which was a common limitation (19). Therefore, the present study aimed to assess the relationship between SB using polysomnography with video/audio recording and Headache Impact Test-6 (HIT-6) scores.

MATERIALS AND METHODS

A total of 77 adult patients hospitalized for the assessment of SB in the sleep laboratory at the Department and Clinic of Internal Medicine, Occupational Diseases, Hypertension and Clinical Oncology of Wroclaw Medical University were included in the study. The patients were enrolled between March 2017 and April 2018 by qualified dentists in Clinic of Prosthetic Dentistry operating at the Department of Prosthetic Dentistry of the Wroclaw Medical University and other clinics dealing with comprehensive dental treatment. The diagnosis of probable sleep bruxism was made on positive clinical inspection of the following symptoms: masticatory muscle hypertrophy, indentations on the tongue or lip and/or a linear alba on the inner cheek, damage to the dental hard tissues (e.g., cracked teeth), mechanical wear of the teeth (i.e., attrition), or repetitive failures of restorative work/prosthodontic constructions and/or a positive self-report

TABLE 1 | The bruxism parameters in the group with headache (HIT-6 ≥ 50) and controls (HIT-6 < 50).

	HIT-6 ≥ 50 ($n = 53$)	HIT-6 < 50 ($n = 19$)	*p*-value
BEI	4.37 ± 3.54	5.13 ± 3.69	0.43
BBI	5.20 ± 4.48	5.58 ± 6.49	0.65
apnea to bruxism index	0.88 ± 1.79	0.86 ± 1.73	0.97
arousal to bruxism index	2.14 ± 2.11	2.19 ± 2.05	0.92
Phasic bruxism index	1.43 ± 1.89	2.04 ± 2.59	0.29
Tonic bruxism index	1.89 ± 0.139	2.12 ± 1.75	0.58
Mixed bruxism index	1.10 ± 1.01	1.06 ± 0.97	0.86

BEI, bruxism episode index; BBI, bruxism burst index; HIT-6, 6-item headache impact test score.

TABLE 2 | The respiratory and sleep parameters in in the group with headaches (HIT-6 ≥ 50) and controls (HIT-6 < 50).

	HIT-6 > 50 ($n = 53$)	HIT-6 < 50 ($n = 19$)	*p*-value
AHI	5.03 ± 8.88	5.24 ± 8.00	0.93
ODI	4.38 ± 7.29	5.65 ± 8.43	0.53
Snore (%)	6.05 ± 13.29	10.52 ± 17.43	0.25
TST	416.65 ± 66.04	428.24 ± 40.39	0.48
SL	24.14 ± 23.20	22.24 ± 17.90	0.75
REML	111.59 ± 68.53	90.38 ± 35.63	0.20
WASO	36.31 ± 34.41	30.08 ± 24.68	0.47
SE	85.34 ± 11.39	87.24 ± 6.29	0.49
ArI	5.94 ± 4.52	4.69 ± 3.11	0.27
OAI	0.41 ± 2.02	0.23 ± 0.69	0.70
MAI	0.02 ± 0.10	0.01 ± 0.03	0.60
CAI	0.28 ± 0.51	0.20 ± 0.28	0.49
HI	3.76 ± 7.26	4.78 ± 7.46	0.60
C-S R	0.72 ± 2.02	0.79 ± 1.33	0.87
mean HR	62.79 ± 8.09	59.39 ± 8.06	0.13
max HR	91.23 ± 7.10	96.28 ± 5.59	0.56
min HR	49.30 ± 7.38	47.67 ± 6.00	0.40

AHI, apnea–hypopnea index; ODI, oxygen desaturation index; TST, total sleep time; SL, sleep latency; REML, REM latency; WASO, wake after sleep onset; SE, sleep efficiency; ArI, Arausal index; OAI, obstructive apnea index; MAI, mixed apnea index; CAI, central apnea index; HI, hypopnea index; C-SR, Cheyne-Stokes respiration; HR, heart rate; HIT-6, 6-item headache impact test score.

of teeth grinding, clenching, or bracing of the mandible during sleep (8).

The inclusion criteria considered were as follows: age over 18 years; diagnosis of probable SB on the basis of international consensus on the assessment of bruxism (8); absence of contraindications for PSG examination; and willingness to participate in the study. The exclusion criteria considered were as follows: severe systemic (including genetic) diseases; presence of secondary bruxism induced by systemic diseases, e.g., Parkinson's disease; use of medicines that can significantly affect the function of the nervous and muscular systems; severe mental illness and significant mental (including genetic) disorders; inability to undergo PSG, including severe mental impairment or Alzheimer's disease; presence of neurological disorders and/or neuropathic pain in the last six month; respiratory insufficiency, or active inflammation; treatment with or addicted to analgesic drugs and/or drugs that affect muscle and breath function; presence of active malignancy.

The headache impact test (HIT-6) was used to assess the impact of headache on the quality of life of the respondents. HIT-6 is a validated tool containing six questions on domains including social-role functioning, pain, emotional distress and well-being, cognitive functioning, and vitality (20). The HIT-6 scores 36–49 indicate that headache has no impact on the quality of life of the respondents, 50–55 indicate moderate impact, scores between 56 and 59 indicate a substantial impact, and scores $\geq$60 indicate a severe impact (21). For the purpose of this study, HIT-6 was translated into Polish by a native specialized in Medical English Terminology, and the questionnaire was double-checked by a physician specialized in the treatment of headaches.

For the assessment of SB, standard, multichannel, single-night diagnostic PSG was conducted using Nox-A1 (Nox Medical, Iceland) in the Sleep Laboratory at the Wroclaw Medical University. Polysomnograms were assessed in 30 s epochs according to the AASM standard criteria for sleep scoring (22). The following PSG outcome variables were assessed: sleep latency; total sleep time; sleep efficiency (%); and the percentages of N1, N2, N3, and REM sleep. Abnormal respiratory events were scored from the pressure airflow signal evaluated according to the standard criteria of the AASM Task Force (22). Electroencephalogram (frontal, central, and occipital regions), electrooculogram, electromyogram (submental), snoring, nasal pressure, rib cage, and abdominal movement by inductance plethysmography, heart rate, arterial oxygen saturation (SaO_2) by finger pulse oximetry, activity, and body position were recorded. The mean, minimum and maximum pulse rate was measured by finger pulse oximetry. Apnea was defined as the absence of airflow for $\geq$10 s, and hypopnea was defined as a reduction in the amplitude of breathing by $\geq$30% for $\geq$10 s with a $\geq$3% decline in blood oxygen saturation or an arousal.

SB was assessed by electromyography (EMG) of bilateral masseter muscles and evaluation of video and audio recordings. Bruxism episodes were scored according to the AASM standards in the following three forms: phasic, tonic, and mixed. The AASM standards specify that for confirming SB, EMG activity had to be at least twice the amplitude of the background EMG and EMG bursts should not be separated by >3 s to be considered part of the same episode. A constant burst episode sustained over 2 s in masseter EMG recording was categorized as tonic, an episode including three or more bursts over 2 s was categorized as phasic, and a combination of tonic and phasic episode was categorized as mixed (23). The Bruxism Episode Index (BEI) measures the number of bruxism episodes per hour of sleep (<2: irrelevant SB; 2–4: mild/moderate SB; >4: severe SB) (24).

The scoring of SB episodes and analysis of collected data were performed by a qualified physician (H.M.) from the Sleep Laboratory at the Wroclaw Medical University.

Statistical analyses were conducted using Dell Statistical 13 software (Dell Inc., USA). The quantitative variables were expressed as arithmetic means and standard deviations, and the distribution of these variables was verified using the Shapiro–Wilk W-test. The qualitative variables were expressed as percentages, and t-test or the Mann–Whitney U-test was used for the evaluation of the independent quantitative variables in comparative analyses. The relationships between the analyzed variables were determined by correlation analyses. Those results with $p < 0.05$ were considered statistically significant.

This study was approved by the Ethical Committee of the Wroclaw Medical University (ID KB-195/2017). The written informed consents were obtained from the participants of this study.

TABLE 3 | The HIT-6-score in bruxers (BEI > 2), non-bruxers (BEI < 2), severe bruxers (BEI > 4), and non-severe bruxers (BEI < 4).

Group (n)	HIT-6 score	p-value
BEI >2 ($n = 58$)	55.52 ± 9.95	$p = 0.99$
BEI < 2 ($n = 19$)	55.56 ± 8.30	
BEI > 4 ($n = 31$)	54.13 ± 10.14	$p = 0.30$
BEI < 4 ($n = 46$)	56.52 ± 9.03	

BEI, Bruxism Episode Index; HIT-6, 6-item headache impact test score.

RESULTS

The mean age of all the participants was 34.77 ± 10.86 years, and their mean Body Mass Index (BMI) was found to be 22.82 ± 3.89 kg/m^2. In the studied group, women accounted for 72.7%, while men accounted for 27.3%.

HIT-6 subgroups did not differ in age and BMI. In the subgroup HIT-6 $\geq$ 50 compared to the HIT-6 < 50 subgroup, there were significantly more women (83.0 vs. 52.6%, $p < 0.05$). In contrast, the HIT-6 $\geq$ 60 and HIT-6 < 60 subgroups did not differ in sex.

The mean BEI of the participants was 4.42 ± 3.55. SB (BEI > 2) was diagnosed in 75.3% ($n = 58$), mild/moderate SB in 35.0% ($n = 27$), and severe SB in 40.2% ($n = 31$) of the participants.

The mean apnea–hypopnea index (AHI) of the participants was 5.02 ± 8.37. OSA (AHI >5) was diagnosed in 23.3% ($n = 18$) of the participants, of which mild (AHI 5–15), moderate (AHI

15–30), and severe OSA (AHI > 30) were diagnosed in 14% ($n = 11$), 5.19% ($n = 4$), and 3.8% ($n = 3$), respectively.

BEI was similar in the group with significant impact of headache on patient's life (HIT-6 score ≥ 50) and in group with little or no impact (HIT-6 score < 50) (**Table 1**). No statistically significant differences in respiratory and sleep indices were found between these studied groups (**Table 2**). In addition, no statistically significant correlation was found between HIT-6 score and BEI ($r = -0.03$, $p > 0.05$) and between HIT-6 score and AHI ($r = -0.01$, $p > 0.05$).

Furthermore, no statistically significant difference was observed in HIT-6 score between the group with SB (BEI >2) and the group without SB (BEI <2) (55.52 ± 9.95 vs. 55.56 ± 8.30, $p = 0.99$). Similarly, no statistically significant difference was observed in HIT-6 score between the group with severe SB (BEI > 4) and the group with irrelevant or mild/moderate SB (BEI < 4) (54.13 ± 10.14 vs. 56.52 ± 9.03, $p = 0.30$) (**Table 3**).

The results showed a positive correlation between mean heart rate and HIT-6 score ($r = 0.30$, $p < 0.05$) (**Figure 1**), but there were no differences in mean, maximum, and minimum heart rate between the group with headache (HIT-6 score ≥ 50) and controls (HIT-6 score < 50).

There was no statistically significant difference between pulse rate in the group with significant impact of headache on patient's life (HIT-6 score ≥ 50) and in group with little or no impact (HIT-6 score < 50). However, we compared groups with severe impact of headache on the ability of subjects to function at work, school, home, and in social situations measured by HIT-6 (HIT-6 score ≥ 60) and controls (HIT-score < 60) due to fact that severe headache may increase pulse rate. In the group with severe impact of headache (HIT-6 score ≥ 60), the mean heart rate and minimum heart rate were higher compared to the control group (HIT-6 score < 60) (**Table 4**).

A positive linear correlation was observed between sleep bruxism associated with arousal and HIT-6 score ($r = 0.51$, $p < 0.05$) (**Figure 2**) and between mixed bruxism and HIT-6 score ($r = 0.58$, $p < 0.05$) (**Figure 3**) in the subgroup with phasic bruxism. In contrast, no statistically significant correlation was found between bruxism parameters and HIT-6 score in the subgroup with tonic bruxism.

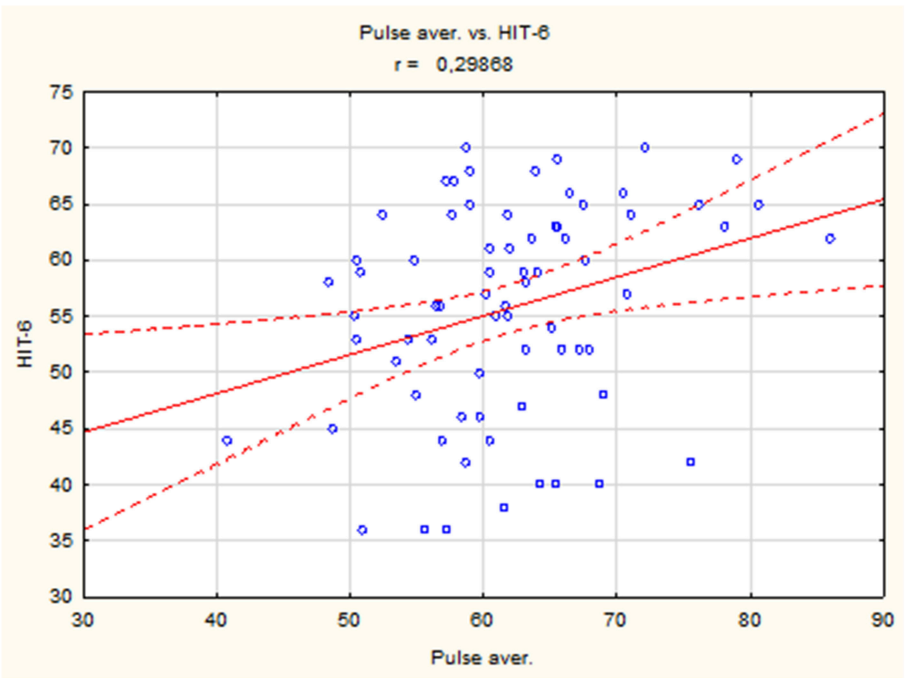

FIGURE 1 | The correlation between mean heart rate and HIT-6 score in whole studied group.

TABLE 4 | The heart rate in the group with headache (HIT-6 score ≥ 50), (HIT-6 score ≥ 60) and in controls.

	HIT-6 ≥ 50	HIT-6 < 50	*p*-value	HIT- 6 ≥ 60	HIT- 6 < 60	*p*-value
Mean HR	62.79 ± 8.09	59.39 ± 0.06	0.13	65.47 ± 8.54	59.34 ± 6.88	0.00*
Max HR	98.83 ± 17.42	96.28 ± 5.59	0.55	102.03 ± 20.87	95.28 ± 8.31	0.07
Min HR	49.30 ± 7.38	47.67 ± 6.00	0.40	51.23 ± 7.84	47.14 ± 5.95	0.02*

*Mean HR, mean heart rate; max HR, maximum heart rate; min HR, minimum heart rate; HIT-6, 6-item headache impact test score, *p < 0.05.*

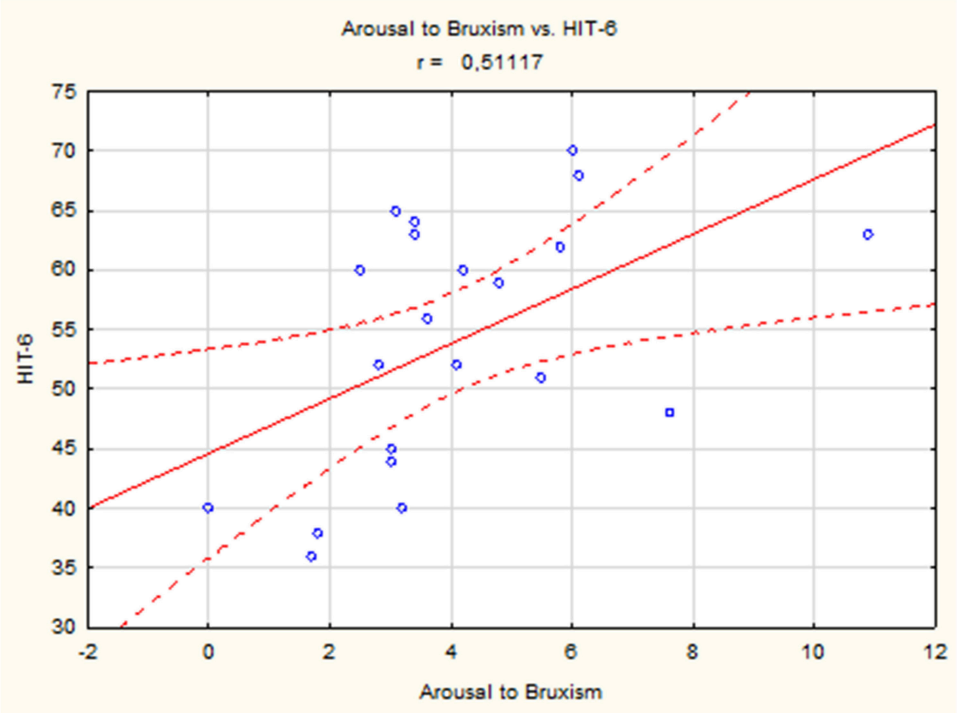

FIGURE 2 | The correlation between bruxism associated with arousal and HIT-6 score in group with phasic bruxism>2.

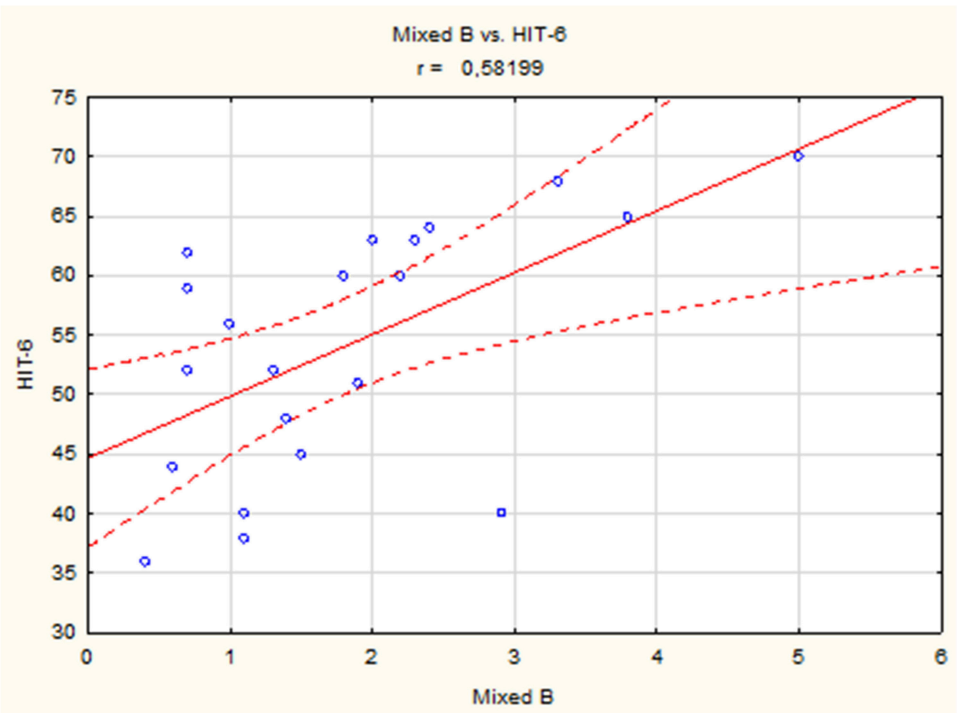

FIGURE 3 | The correlation between mixed bruxism and HIT-6 score in group with phasic bruxism>2.

DISCUSSION

All participants of the study were diagnosed with SB based on a positive physical examination and/or a positive interview (probable bruxism) (8). However, SB was confirmed only in 75% of the participants who underwent PSG with audio/video recording, and the diagnosis of SB in the remaining 25% of patients was false positive. Thus, it is worth noting that PSG with audio/video recording can serve as a gold standard for the diagnosis of SB.

HIT-6 score was higher than 49 points in bruxers (BEI $>$ 2) and non-bruxers (BEI $<$ 2), suggesting the impact of headaches on the ability of subjects to function at work, school, home, and in social situations in both the groups. The most interesting finding of this study was the absence of significant difference in HIT-6 score between bruxers (BEI $>$ 2) and non-bruxers (BEI $<$ 2) (**Table 4**). SB-related headache is described as a tension-type headache occurring in the morning or during the day (24); however, there is little evidence of any relationship between headache and bruxism (15, 16, 25). This is consistent with the findings of some case reports (26–28). Recently, a PSG study showed that SB may modestly exacerbate headache both in patients with mild brain injury and healthy controls; however, the number of bruxers included in the study was small (29). Recently, a study showed that there was no significant correlation between self-reported SB and the intensity of pain associated with temporomandibular disorders (TMDs) (30). Porporatti et al. also did not find any association between self-reported bruxism and primary headache (31) in their study. Similarly, no relationship was found between the frequency of SB diagnosed using a miniature disposable device and the prevalence of headache in an adolescent population (32). However, it was previously described that sleep bruxers with low frequencies of orofacial activities were at more risk of reporting pain (16).

SB may be associated with TMDs, and headache is often an accompanying symptom (33). Wagner et al. have showed an association between headache and TMDs ($p < 0.001$) and between headache and anxiety ($p = 0.002$), but not between headache and bruxism ($p = 0.670$) (17). Recently, it was showed that the presence of SB did not increase the risk for any type of headache, but SB coexisting with painful TMDs greatly increased the risk for episodic migraine, episodic tension-type headache, and especially for chronic migraine (34). In this study, the association between pain, bruxism, and TMDs was not investigated, and thus, the influence of TMDs on pain cannot be excluded in bruxers.

OSA was diagnosed in only 23% of the study group, and most of the cases (14 out of 18) had just mild OSA. Therefore, the impact of OSA as a compounding factor was inconsiderable.

Thus, the available scientific literature does not support the view that bruxism is a cause of pain (35, 36). This study also found no association between impact of headache on the ability of subjects to function at work, school, home, and in social situations measured by HIT-6 and severity of bruxism. However, a significant correlation was found between mixed bruxism and HIT-6 score in the subgroup with phasic bruxism. This result indicates a very modest relationship, especially for phasic bruxism. Interestingly, if bruxism was accompanied by arousal, a significant correlation with HIT-6 score was observed. This correlation may indicate the role of arousal in the etiology of headache severity impact on life in bruxers. This observation is in agreement with a previously reported association of worse sleep quality and higher intensity of headache (37).

A positive correlation between mean heart rate and HIT-6 score was observed in the study. Moreover, the mean heart rate was higher in the group with severe impact of headache on the ability of subjects to function at work, school, home, and in social situations measured by HIT-6 (HIT-6 score $>$ 60) compared to controls (HIT-6 score $<$ 60) (**Table 4**). The increased heart rate may be caused by pain in bruxers, but other factors may also be involved, e.g., increased sympathetic drive (38), inflammation, stress, anxiety (39), and stimulants like alcohol (40, 41) or caffeine (42). However, these factors were not investigated in this study.

This study has a few limitations. First of all, the clinical diagnosis of headache has not been made and the other possible causes of headache in bruxers have not been investigated. The classification of the reported headache according to the ICHD-3 has been not considered. The results for relevant subgroups could have been obfuscated. It has been showed that migraine and frequency of headache are associated with painful TMD in adolescents (43). There may be a central working mechanism overlapping TMD and headache (44). The further studies on association between bruxism, headache and TMD regarding different types of headache are needed.

CONCLUSION

The study showed the relationship between sleep bruxism and impact of severity of headache on the patient's life measured by HIT-6 is only modest. It was also found that the impact of severity of headache measured by HIT-6 is altered only in those with phasic bruxism and is associated with arousal. Further research should elucidate the factors influencing the relationship between SB and headache.

ETHICS STATEMENT

This study was approved by the Ethical Committee of the Wroclaw Medical University (ID KB-195/2017). Patients were required to sign a consent form for participating in the study.

AUTHOR CONTRIBUTIONS

HM created the research concept, analyzed the data, and wrote the manuscript. JS and MM-Z recruited patients for the study and collected data. RP and PG performed the statistical analysis. AW collected the references. GM

revised the manuscript before submission. MW created the research concept, recruited patients for the study, evaluated the content, edited the manuscript, and finally revised it before submission. All authors read and approved the final manuscript.

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Insomnia in Patients Seeking Care at an Orofacial Pain Unit

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Introduction: Orofacial pain and dysfunction include a broad range of disturbances among which pain and insomnia are some of the most common complaints. Sleep strengthens physiological and psychological resilience and is an absolute requirement for health. Insomnia is a common symptom or sleep disorder, yet data on its prevalence is sparse. Here we extracted data from the insomnia severity index which was part of the web-based interdisciplinary symptom evaluation (WISE) tool given to a large sample of patients seeking care at an orofacial pain unit for analyzing insomnia prevalence in this clinical population.

Material and methods: Anonymized data were available from 952 patients who consulted the Orofacial Pain Unit at the Center of Dental Medicine, University of Zurich, Zurich, Switzerland between January 2017 and December 2018. Prevalence data for insomnia stratified by gender and 10 age groups (decades) were calculated. The distribution of four insomnia severity grades was determined, also stratified by age and gender.

Results: 952 patients (290 men: 30.5%) with a mean age of 44.8 ± 17.4 years completed a WISE. Three hundred and fifty-two (37.0%) patients with a mean age of 45.8 ± 16.7 years positively responded to a screening question for insomnia and/or hypersomnia. Insomnia was severe in women from the 2nd to 8th decade, ranging from 4.3% (3rd decade) to 14.5% (6th decade), and moderately severe from the 2nd to 9th decade, ranging from 18.8% (6th decade) to 27.8% (2nd decade). In men, severe insomnia was present from the 3rd to 7th decade, ranging from 2.3% (7th decade) to 4.4% (4th decade) and moderately severe insomnia from the 3rd to 7th decade, ranging from 4.6% (7th decade) to 12.2% (5th decade).

Conclusions: This is the first study reporting on insomnia in a large sample of patients seeking care at an orofacial pain unit. One in three patients reported some form of sleep disturbances, which for almost half of them was moderate to severe insomnia. The gender ratio was almost equal throughout adulthood, yet younger and older women were more frequently affected and experienced higher insomnia severity than men.

Keywords: orofacial pain, sleep, insomnia, dysfunction, prevalence, insomnia severity index, sleep questionaire, epidemiology

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INTRODUCTION

Orofacial disorders can be painful or painless and with or without functional impairment. They include a broad range of disturbances with heterogeneous etiologies in dental, mucosal, musculoskeletal, and neuronal tissues. These conditions can be summarized under the umbrella term orofacial pain and dysfunction (OPD). According to community based surveys, the prevalence of OPD varies greatly, from 5 to 57% depending on the study period, population, location, and other factors (1). Chronic OPD affect women more frequently (2, 3). Impaired sleep and insomnia are commonly reported by patients with OPD (4, 5).

Healthy sleep was recently defined in a joint consensus statement of the American Academy of Sleep Medicine and Sleep Research Society as "adequate duration, good quality, appropriate timing and regularity, and the absence of sleep disturbances or disorders" (6). Sleep strengthens physiological and psychological resilience (7). Sleep regulation has a sleep-promoting, homeostatic component and a circadian component (8, 9). When a person sleeps or is awake (circadian sleep propensity) characterizes the individual chronotype. This is in part determined by genetics, and modified by age, activity, and light exposure (10–12). In the long-term, disturbed sleep is associated with multiple adverse health outcomes, including cardiovascular, metabolic, and mental health disturbances (13–16). The most common sleep disorder is insomnia, defined as "a persistent difficulty with sleep initiation, duration, consolidation, or quality that occurs despite adequate opportunity and circumstances for sleep" (17). Hence insomnia is vague term describing the phenotypes of several sleep disturbances with different underlying etiologies. Different studies of non-clinical populations worldwide assessments have reported an insomnia prevalence from 5 to 50%, mostly with a predominance in females (18–25). For insomnia evaluation, subjective assessment is considered the gold standard and has been recommended for the evaluation of patients with OPD (26–29). Numerous relatively brief self-reported questionnaires have been developed and validated to detect and quantify insomnia or sleep-related impairment in different populations (30, 31). The Patient Health Questionnaire 9 (PHQ-9) commonly used in primary care to screen for depression includes the item "trouble falling or staying asleep or sleeping too much" that screens for insomnia and/or excessive daytime sleepiness (32). In addition to screening, the insomnia severity index (ISI) also offers some quantification. (33, 34). This brief self-report questionnaire consists of seven items to be rated on a five-point Likert scale, ranging from 0 (none) to 4 (very severe). The items are difficult initiating and maintaining sleep; awaking early; dissatisfaction with current sleep patterns; sleep related impairment of quality of life (noticed by others), worries or distress, and interference with daytime functioning. Total scores range from 0 to 28,

TABLE 1 | Patient numbers (N) and distribution in the global sample stratified per decade and by gender.

	10–19		20–29		30–39		40–49		50–59		60–69		70–79		80–89		90–99		Total
	M	W	M	W	M	W	M	W	M	W	M	W	M	W	M	W	M	W	
N	20	49	36	104	64	110	60	124	53	123	35	87	19	60	3	4	0	1	952
Distribution (%)	2.1	5.1	3.8	10.9	6.7	11.6	6.3	13.0	5.6	12.9	3.7	9.1	2.0	6.3	0.3	0.4	0	0.1	100%

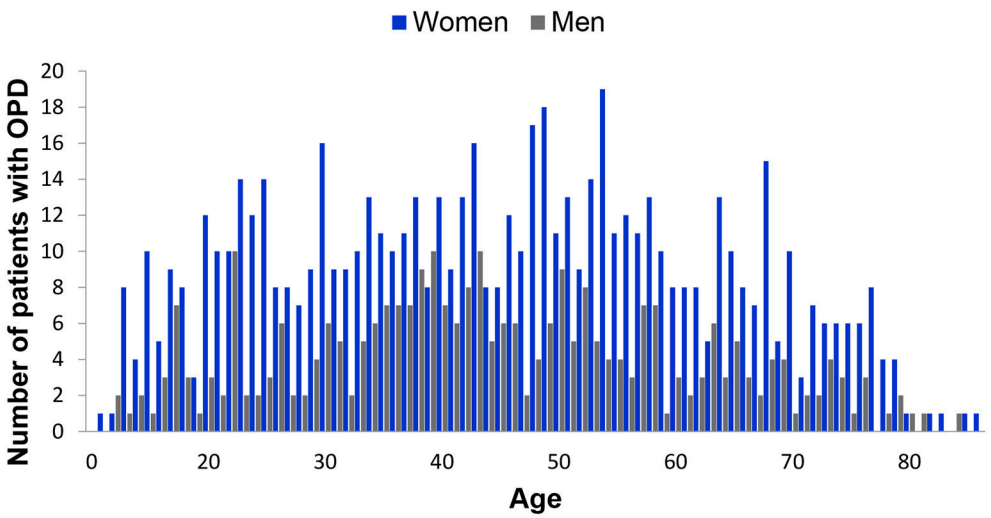

FIGURE 1 | Age and gender distribution of the global sample of 952 patients experiencing orofacial pain and dysfunction (OPD).

whereas higher scores indicate more severe insomnia. Four insomnia grades have been categorized (scores in brackets): not clinically significant (0–7), subthreshold (8–14), moderate (15–21), and severe (22–28). Moderate to severe grades are considered clinically relevant.

For this paper, we used data collected by the web-based interdisciplinary symptom evaluation (WISE) which is a new self-report instrument designed to obtain computer guided patient information related to orofacial disorders of diverse etiologies and comorbid conditions (35). The WISE combines a symptom-burden checklist with various validated psychometric in-depth questionnaires serving as case-finding instruments, one of them being the ISI. Insomnia associated with chronic pain is phenotypically similar to primary insomnia (36). Yet the interaction of sleep and pain is poorly understood (37–39). High quality prevalence data of insomnia in persons suffering from pain (including OPD) is sparse (40, 41). In this work, we aimed at identifying the prevalence of insomnia in a large sample of patients seeking care at an orofacial pain unit.

MATERIAL AND METHODS

Anonymized data were extracted from WISE completed by 952 patients who consulted the Orofacial Pain Unit at the Center of Dental Medicine, University of Zurich, Zurich, Switzerland between January 2017 and December 2018. Patients completed the WISE prior to their first appointment. The symptoms of our study population varied from painless yet burdening functional disorders to painful conditions with widely varying orofacial pain location, quality, time pattern, and related disability.

For questionnaires to be analyzed, patients must have clicked a checkbox indicating their consent that their anonymized data can be used for research. According to Swiss law, the analysis of strictly anonymized data does not require approval by an ethics committee. We compared the clinic population that completed the WISE with the clinic population that did not complete it or did not give consent to use the data for research.

Using the software SPSS version 23, we calculated prevalence data for insomnia stratified by gender and age group (decades). The distribution of four insomnia severity grades was determined stratified by age and gender. Means were compared between genders using an independent sample *t*-test with Welch's correction, since equality of variance was not assumed.

RESULTS

The population of the 952 patients completing the WISE (global sample) had a mean age of 44.8 ± 17.4 years (range: 10–90 years; 44.1 years). It consisted of 290 men (30.5%) with a mean age of 44.3 ± 16.5 years (range: 12–84 years; median 43 years) and 662 women (69.5%) of 45.0 ± 17.8 years (range: 10–90 years; median 46 years). The gender ratio therefore was 1:2.3. Mean ages between genders did not differ ($p > 0.05$) (**Table 1**; **Figures 1**, **2**).

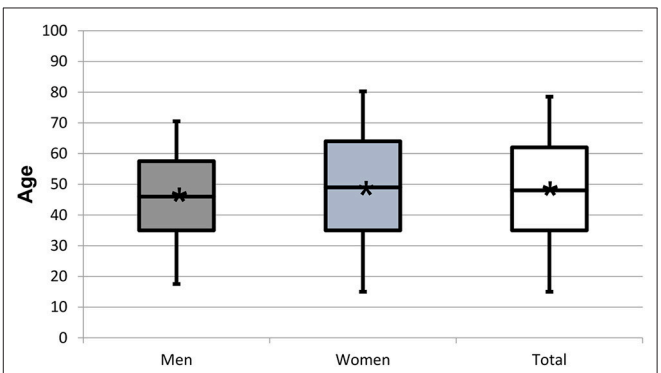

FIGURE 3 | Box plots representing the age distribution by gender of the 682 patients who did not complete the WISE or did not consent to data use. Star symbol (*) indicates mean.

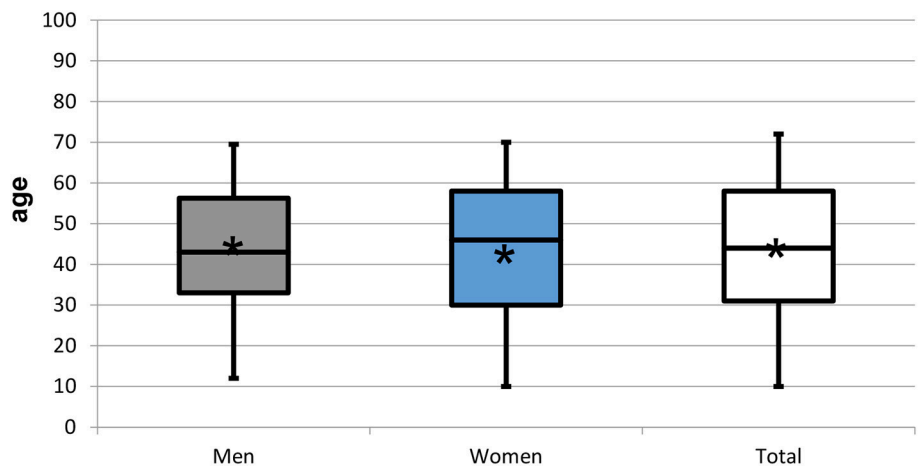

FIGURE 2 | Box plots representing the age distribution by gender of the 952 patients experiencing orofacial pain and dysfunction. Star symbol (*) indicates mean.

TABLE 2 | Patient numbers (N), distribution, proportion within gender, and prevalence of insomnia stratified by ISI categories and by gender.

	Not clinically significant				Subthreshold				Clinically relevant								Total			
									Moderate				Severe							
	M	W	T	M/W	M	W	T	M/W	M	W	T	M/W	M	W	T	M/W	M	W	T	M/W
N	17	39	56		41	105	146		29	81	110		10	30	40		97	255	352	
Distribution (%)	4.8	11.1	15.9	1:2.3	11.6	29.8	41.5	1:2.6	8.2	23	31.2	1:2.8	2.8	8.6	11.4	1:3	27.5	72.5	100	1:2.6
Proportion (%) within gender	17.5	15.3		1.1:1	42.2	41.2		1:1	29.9	31.8		1:1.1	10.3	11.8		1:1.2				
Prevalence (%) (952 pts)	1.8	4.1	5.9	1:2.8	4.3	11.0	15.3	1:2.6	3.0	8.5	11.5	1:2.8	1.1	3.2	4.3	1:2.9	10.2	26.8	37	1:2.6
Prevalence (%) within gender (290 M, 662 W)	5.9	5.9		1:1	14.1	15.9		1:1.1	10	12.2		1:1.2	3.5	4.5		1:1.3				

M/W, ratio men to women; pts, patients.

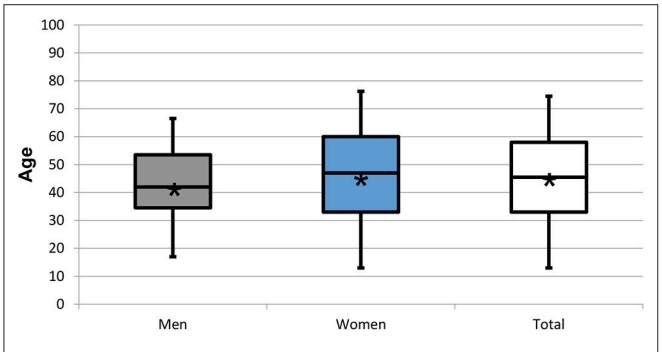

FIGURE 4 | Box plots representing the age distribution by gender of the 352 patients responding positively to the screening question on insomnia and/or hypersomnia. Star symbol (*) indicates mean.

The population of the 682 patients not completing the WISE or not giving consent had a mean age of 48.3 ± 18.3 years (range: 11–89 years; 48 years) and consisted of 213 men (31.2 %) with a mean age of 46.9 ± 17.4 years (range: 13–89 years; median 46 years) and 469 women of 48.9 ± 17.5 years (range: 11–89 years; median 49 years) (**Figure 3**). The gender ratio therefore was 1:2.2. Mean ages between the two populations did not differ ($p > 0.05$).

Three hundred and fifty-two (37.0%) patients with a mean age of 45.8 ± 16.7 years (range: 13–88 years; 45.5 years) reported "trouble falling or staying asleep or sleeping too much" on the WISE checklist and the ISI was presented to these. The 97 men (10.2%) in this group had a mean age of 43.5 ± 13.8 years (range: 17–80 years; median 42 years) and the 255 women (26.8% of global sample) of 46.7 ± 17.6 years (range: 13–88 years; median 47 years). The gender ratio therefore was 1:2.6. Neither age nor gender distribution differed between patients with insomnia and all patients ($p > 0.05$) (**Table 2**; **Figures 2**, **4**). For the four ISI categories, the distribution of men and women, the gender ratio (in round brackets), and the proportions within each gender [in square brackets] were as follows: not clinically significant 15.9% (1:2.3) [1.1:1], subthreshold 41.5% (1:2.6) [1:1], moderate 31.2% (1:2.8) [1:1.1], and severe 11.4% (1:3) [1:1.2] (**Table 2**; **Figure 5**).

The distribution of ISI scores, its gender ratios (in brackets), and its ratios within each gender [in square brackets] according to increasing severity grades were: 5.9% (1:2.8) [1:1], 15.3% (1:2.6) [1:1.1], 11.5% (1:2.8) [1:1.2] to 4.3% (1:2.9) [1:1.3] (**Table 2).** The mean ISI score was 13.8 ± 6.0 (men 13.4 ± 6.2; women 13.9 ± 6.2 (**Figure 6**).

The patients responding positively to the screening question on insomnia and/or hypersonia are listed in **Table 3**, sorted by distribution and proportion within gender per decade and by gender. This table also lists the prevalences according to all patients, to gender groups, and to gender of each decade in the global sample. The prevalence data in this table and **Figure 7** reveal that 1.9% of teenagers and adolescents experienced insomnia. Among males, insomnia was most prevalent in the 4th and 5th decade (2.7 and 2.4%, respectively) while prevalence peaked in women in the 5th and 6th decades (5.4 and 5.3%, respectively). The ratio of the prevalence within gender and within gender per decade (in brackets) was: 2nd 1:3.4 (1:3.3), 3rd 1:1 (1.2:1), 4th 1.5:1 (1.1:1), 5th 1:1 (1:1.1), 6th 1:1.2 (1:1.1), 7th 1:1.7 (1:1.6), 8th 1:3.9 (1:2.7), and 9th 1:1.7 (1:2.6) (**Table 3**; **Figure 7**).

Figure 8 shows the distributions of the three ISI categories (scores ≥ 8) per decade and by gender. The severe grade was present in women from the 2nd to 8th decade, ranging from 4.3% (3rd decade) to 14.5% (6th decade) and moderately severe from the 2nd to 9th decade, ranging from 18.8% (6th decade) to 27.8% (2nd decade). In men, severe insomnia was present from the 3rd to 7th decade, ranging from 2.3% (7th decade) to 4.4% (4th decade) and moderately severe from the 3rd to 7th decade, ranging from 4.6% (7th decade) to 12.2%(5th decade).

DISCUSSION

In this paper, we analyzed complaints of insomnia in a large sample of 952 patients seeking care at an orofacial pain unit, covering a broad age range. A first main study finding was that 37.0% of those patients reported sleep disturbance in the form of insomnia and/or excessive daytime sleepiness (hypersomnia). Secondly, women across a broader age range than men were affected by insomnia. Thirdly, when taking into consideration

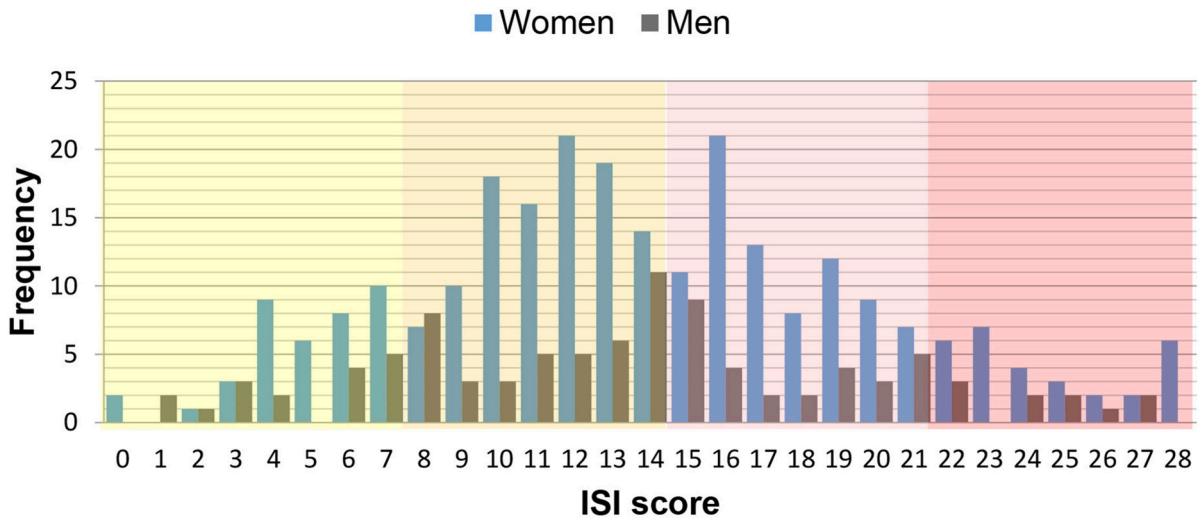

FIGURE 5 | Distribution of insomnia severity index (ISI) scores stratified by gender. Background colors reflect ISI categories: not clinically significant (yellow), subthreshold (orange), moderate (pink), severe (red).

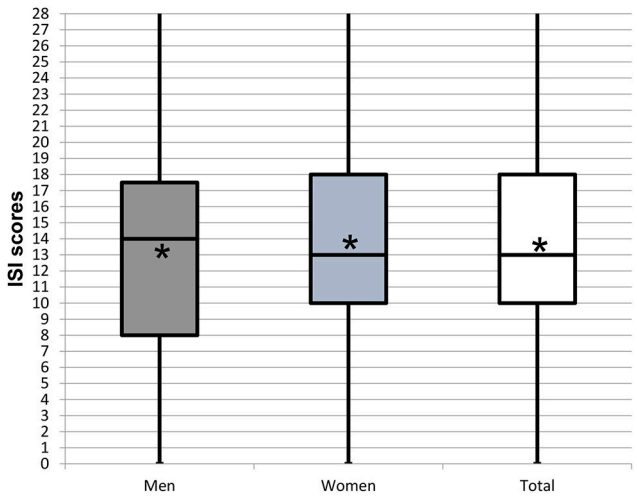

FIGURE 6 | Box plots representing the distribution of the Insomnia Severity Index (ISI) scores reported by patients experiencing insomnia by gender. Star symbol (*) indicates mean.

the proportions within gender, the ratios of insomnia between men and women were almost equal in young and middle-aged adults, yet higher in female teenagers and adolescents as well as older women.

For the three populations, namely the global sample completing the WISE, the sample that did not complete the WISE or did not consent to data use, and the patients reporting insomnia, the mean ages of 44.8 ± 17.4, 48.3 ± 18.3, and 45.8 ± 16.7 years, respectively, were not statistically different ($p > 0.05$) (**Table 1**; **Figures 1**, **2**). Also the gender ratios of 1:2.3, 1:2.2, and 1:2.6, respectively, were similar among the three populations. This mean age and the gender ratio corresponds to a patient sample of our clinic previously analyzed with a different study question (42). The unequal gender distribution of the global sample is important and can be accounted for by calculating within gender ratios for men and women. Accordingly, focusing on the ratios of the proportions within each gender in **Table 2**, they were almost equal (1:1.1 for the lower three severities and 1:1.2 for the highest severity), meaning that the proportion of men and women in all ISI categories hardly differed. Yet, with increasing severity, the prevalence of insomnia slightly increased in women compared to men (from 1.1:1 to 1.1:3), although the mean scores did not significantly differ between gender (**Figure 6**). Among all patients reporting insomnia, moderate and severe grades were reported by almost half (42.6%), representing a combined prevalence of 15.8% of these two categories. This means that one in six patients suffered from clinically relevant insomnia (**Table 2**; **Figure 5**). If the threshold criterion of an ISI score of 8 were considered, this number would double to 1 in three patients (31.1%).

The proportions within each gender had also relatively balanced ratios in the population of the 3rd, 5th, 6th, and 9th decade (**Table 3**). Men experienced proportionately more insomnia only in the 4th decade (1.5:1), whereas a reverse pattern was seen in the 2nd, 7th, and 8th decade with values of 1:3.4, 1:1.7 and 1:3.9, respectively. This means that younger and older women experienced insomnia disproportionately more than men (**Figure 7**).

The distribution of the three ISI categories (scores ≥ 8) per decade and by gender is displayed in **Figure 8**. While ISI scores in men peaked in the 4th decade and gradually declined thereafter, a reverse pattern was observed in adult women with a trend toward increasing scores with older age. In other words, with increasing age, women tended to have only slightly more insomnia yet of higher severity. Notably, severe insomnia was not reported by women in the 9th decade. On the opposite, the largest

TABLE 3 | Patient numbers (N), distribution, proportion within gender, and prevalence of patients responding positively to the screening question on insomnia and/or hypersomnia, stratified per decade and by gender.

	10–19			20–29			30–39			40–49			50–59			60–69			70–79			80–89		
	M	**W**	**T**	**M**	**W**	**T**	**M**	**W**	**T**	**M**	**W**	**T**	**M**	**W**	**T**	**M**	**W**	**T**	**M**	**W**	**T**	**M**	**W**	**T**
N	2	16	18	14	33	47	26	41	67	23	51	74	19	50	69	9	35	44	3	26	29	1	3	4
Distribution (%)	0.6	4.5	5.1	4.0	9.4	13.4	7.4	11.6	19.0	6.5	14.5	21.0	5.4	14.2	19.6	2.6	9.9	12.5	0.9	7.4	8.2	0.3	0.9	1.1
			M/W			**M/W**			**M/W**			**M/W**			**M/W**			**M/W**			**M/W**			**M/W**
Proportion (%) within gender	2.1	6.3	**1:3**	14.4	12.9	**1.1:1**	26.8	16.1	**1.7:1**	23.7	20.0	**1.2:1**	19.6	19.6	**1:1**	9.3	13.7	**1:1.5**	3.1	10.2	**1:3.3**	1.0	1.2	**1:1.2**
Global prevalence (%) (952 pts)	0.2	1.7	**1:8.5**	1.5	3.5	**1:2.3**	2.7	4.3	**1:1.6**	2.4	5.4	**1:2.3**	2.0	5.3	**1:2.7**	0.9	3.7	**1:4.1**	0.3	2.7	**1:9**	0.1	0.3	**1:3**
Prevalence (%) within gender (290 M, 662 W)	0.7	2.4	**1:3.4**	4.8	5.0	**1:1**	9.0	6.2	**1.5:1**	7.9	7.7	**1:1**	6.6	7.6	**1:1.2**	3.1	5.3	**1:1.7**	1.0	3.9	**1:3.9**	0.3	0.5	**1:1.7**
Prevalence (%) within gender per decade (**Table 1**)	10	32.7	**1:3.3**	38.9	31.7	**1.2:1**	40.6	37.3	**1.1:1**	38.3	41.1	**1:1.1**	35.9	40.7	**1:1.1**	25.7	40.2	**1:1.6**	15.8	43.3	**1:2.7**	33.3	75	**1:2.6**

M/W, ratio men to women; pts, patients. Male to female ratios are highlighted in bold.

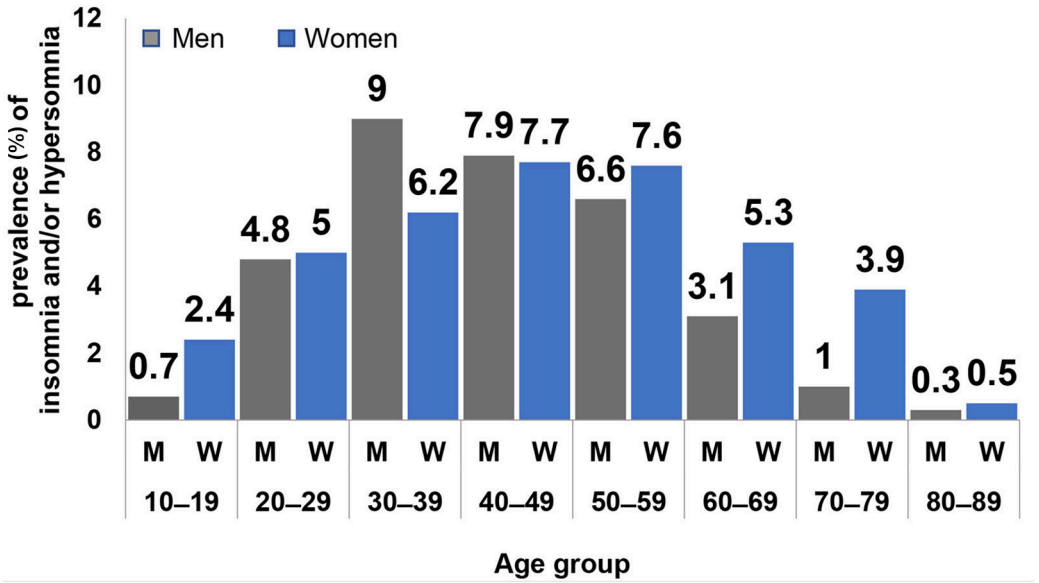

FIGURE 7 | Prevalence (%) of insomnia and/or hypersomnia, stratified by men (M), and women (W) as well as by age group (decades).

proportion of scores ≥ 8 was reported by female teenagers and adolescents, yet mainly due to the relatively high percentage of subthreshold insomnia.

Comparing our results to other studies is difficult due to the restricted use of the ISI or other validated tools for analyzing insomnia in large cohorts. We mostly identified studies using other types of self-reports that were not validated for grading insomnia severity. Hence, insomnia prevalence's ranging from 5 to 50% reported in those works have to be interpreted with caution (18–25). An exception was the report by Jank et al. who employed the ISI for analyzing insomnia in a mixed group with and without pain complaints (40). In this sample of 570 patients from Austria, insomnia prevalence was 29.1%, with 55 subjects (9.6%) complaining of clinically relevant insomnia. The mean age of this population was slightly higher (50.8 ± 18.7 years). Gender ratios were not calculated. Another study investigated insomnia in 481 Korean patients complain of low back pain (43). The mean age of the study sample was 58.2 ± 16.7 (range 20–90). The gender ratio was 1:1.5 compared to 1:2.3 in our sample. The mean ISI score was 7.5 ±7.1 and thus much lower compared to 13.8 ± 6 observed here. The distribution of insomnia among the four ISI categories compared to ours (in brackets) in ascending severity was: 57.0 (5.9), 23.0 (15.3), 14.7 (11.5), and 5.3 (4.3). Thus, the proportion of clinically relevant insomnia was similar. However, no gender ratios were provided that would allow an estimation of the gender related distribution. In 6,205 Swedish

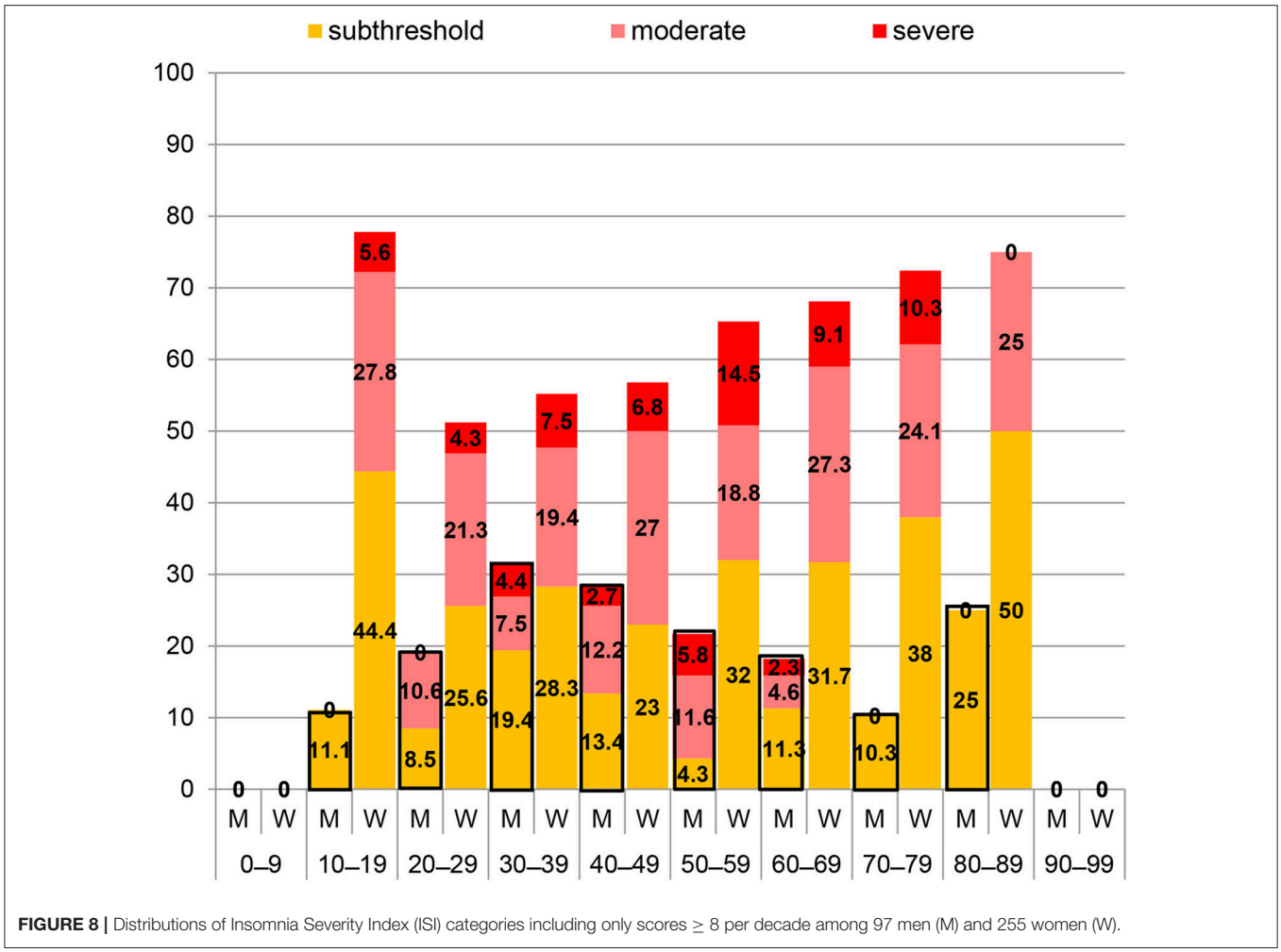

FIGURE 8 | Distributions of Insomnia Severity Index (ISI) categories including only scores ≥ 8 per decade among 97 men (M) and 255 women (W).

individuals older than 65 years with no, subacute and chronic pain, the proportion of moderate and sever insomnia was 35.1 and 4.3%, respectively (41). In this cohort, a mean ISI score of 10 was observed in the group experiencing subacute pain ($N = 510$) and 10.9 in the chronic pain group ($N = 2{,}790$), both of which are lower than the mean ISI score of 13.8 identified in our sample of OPD. None of the above-mentioned studies analyzed insomnia severity across the life span.

Our analysis has some noteworthy limitations: it is cross-sectional, i.e., insomnia was captured at one point in time. Hence, the results do not allow inferring potential time-related dynamics. As only few studies report high quality prevalence data of insomnia in persons suffering from pain (40, 41), the inclusion of age and gender paired controls would be an interesting aspect to be considered in future studies. As we aimed at reporting insomnia in a representative sample of our clinic population, we also included persons aged 10–20 years, even though the ISI is not specifically validated for this age group.

Also, no statements can be made regarding possible associations of insomnia complaints with the patients' chief complaints and/or diagnoses, co-morbidities (e.g., psychopathologies) or other confounding factors (e.g., snoring), since we did not take these aspects into account. Specifically, the assessment of somatic and/or psychological co-morbidities known to influence sleep (e.g., tinnitus, wide-spread pain, anxiety, depression, distress, catastrophic rumination, neuroticism, obsessive-compulsive, or post-traumatic stress disorder) would have offered information on possible cause-effect relationships, yet this effort was outside the scope of this work. Finally, insomnia could also be secondary to the use of medication or substance use, both of which were not controlled as a co-factor in the study.

Nonetheless, future research should focus on cross-sectional and longitudinal interactions of insomnia, psychopathology and other associated factors in patients with OPD (44).

CONCLUSIONS

This is the first study reporting on insomnia in a large sample of patients referred to an orofacial pain unit. 37.0% of patients responded positively to a screening question for insomnia and/or hypersomnia. For almost half of them, insomnia was moderate to severe. The gender ratio was almost equal throughout adulthood, yet younger and older women were more affected and experienced higher severity than men.

ETHICS STATEMENT

According to Swiss law, the analysis of strictly anonymized data does not require approval by an ethics committee.

AUTHOR CONTRIBUTIONS

MM and DE: study design, data analysis, manuscript writing. NL: data collection. BS: study design, data collection. AW: data colectivo. AG: study design.

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Evaluation of Orofacial and General Pain Location in Patients With Temporomandibular Joint Disorder—Myofascial Pain With Referral

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Introduction: Pain is an emotional experience. As a subjective feeling, it is associated with pathophysiological processes occurring in the central nervous system, which in turn may negatively affect the psychophysical function, cognitive abilities, level of functioning and quality of life.

The Aim: The aim of the study was to assess orofacial and general pain location in patients with temporomandibular joint disorder—myofascial pain with referral.

Materials and Methods: The study group consisted of 50 randomly selected, generally healthy people with complete natural dentition (37 women and 13 men) at the age of 23.36 ± 2.14 years, referred to the Department of Prosthodontics of the Medical University. All patients underwent clinical examination according to the Diagnostic Criteria for Temporomandibular Disorders (Axes I and II). The subjects were classified as people with myofascial pain with referral. The evaluation of severity of temporomandibular disorders was based on the Temporomandibular Disorder Pain Screener and the Graded Chronic Pain Scale. In order to assess orofacial and general pain location, a bodychart drawing of pain was used.

Results: The study group indicated 40 different areas of the body affected by pain. 2–3 isolated pain locations were declared by a total of six subjects. One person identified 17 affected areas. Forty four people reported pain in at least four regions of the body. 70% of patients suffered from pain within the right masseter muscle. Pain of the left masseter muscle was noted in 68% of cases. Cervical ailments were reported by 56% of people. Pain of the left temporomandibular joint was observed in 68% of patients, and of the right one in 54%.

Conclusion: The patients with myofascial pain with referral suffer from general ailments in different regions of the body. Only the frequency of pain in the right masseter muscle and right temporomandibular joint differed with respect to gender. The suggestion that the prevalence of pain in other areas of the body varies between men and women has not been confirmed. Due to a small sample size, such differences cannot be excluded. Further studies in this area are needed.

Keywords: orofacial pain, myofascial pain, referred pain, temporomandibular disorder, headache

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INTRODUCTION

Functional disorders of temporomandibular joints belong to the group of chronic facial disorders and affect about 10–15% of the total population (1). Women suffer twice as often as men (1). The most common type of dysfunction is myalgia, which intensifies during daily activities and muscle palpation. It is characterized by the occurrence of headache, referred pain, and the restriction of mandible mobility (1). A possible cause is excessive teeth clenching, which leads to disturbances in local muscle blood flow and consequently results in ischemia (1). It promotes the secretion of bradykinin, protons, serotonin, glutamate, or cytokines that sensitize nociceptors, causing muscle pain and/or allodynia (1–3). Repetitive parafunctional activity through temporal summation maintains chronic muscle pain (1, 4). An increased concentration of biomarkers such as IL-1ß, IL-6, IL-7, IL-8, IL-10, IL-13, TNF, and IL-1ra is observed (2, 5–7).

According to the definition of The International Study of Pain, pain is defined as an unpleasant sensory and emotional experience related to real or potential tissue damage or is described in terms of such damage (8, 9). Pain is a subjective feeling. Due to the unpleasant impression, it affects emotional experience (8, 9). Chronic pain lasts longer than the healing of the damaged tissue and is associated with pathophysiological processes which occurs in the central nervous system, which in turn may negatively affect the emotional state and psychophysical function, cognitive abilities, level of functioning, and quality of life. Chronic pain is defined as continuous or recurrent and lasting for more than 3–6 months (9). The options for treatment of chronic pain include pharmacological agents, surgical procedures, psychological therapies, rehabilitation, physiotherapy, as well as alternative medicine (9). Pharmacological treatment is applied in accordance with the criteria of the WHO (World Health Organization) analgesic ladder. Aspirin, non-steroidal anti-inflammatory drugs and opioids are recommended (9). Alternative therapies include massage, yoga, chiropractic, acupuncture, and magnetotherapy (9).

The aim of the study was to assess orofacial and general pain location in patients with temporomandibular joint disorder—myofascial pain with referral. The hypothesis was that the prevalence of pain in different areas of the body varies between men and women.

MATERIALS AND METHODS

The Subjects and Sample Size

The study group consisted of 50 randomly selected, generally healthy Caucasian people (37 women and 13 men) at the age of 23.36 ± 2.14 years (women: mean 23.19 ± 2.31, Me = 24; men: mean 23.85 ± 1.57, Me = 24), referred to the Department of Prosthodontics of the Medical University. All the participants were in the process of obtaining higher education, had never married and had at least good household income. The qualification criterion was the presence of pain in the cranio-facial and/or cranio-mandibular area at the level of 8 points in the VAS (Visual Analog Scale) on clinical examination. The evaluation was performed by a researcher who was also a dentist and physiotherapist. The patients represented complete natural dentition with the intercuspation corresponding to Class I, according to Angle, with no history of orthodontic treatment or retention status after its completion exceeding 3 years. Regarding the DC/TMD (Diagnostic Criteria for Temporomandibular Disorders), the subjects were classified as suffering from myofascial pain with referral pain (10–13). Sixty seven out of 100 examined temporomandibular joints had no symptoms of dysfunction with respect to the DC/TMD. In 30 cases, disc dislocation with a reduction was found, and in another three, one disc dislocation with reduction and intermittent locking was observed.

People who had previous traumas and surgical procedures in the craniofacial area were excluded from participation. Cases affected by metabolic diseases and people whose medication or possible ailments could influence the functioning of masticatory muscles were also excluded. The group did not declare a history of physiotherapeutic treatment in the cranio-facial, cranio-mandibular, and/or cranio-cervical areas.

Clinical Procedure

All patients underwent a thorough assessment. The proceedings covered:

- Clinical examination including functional evaluation of temporomandibular joints and muscles of the masticatory system according to the DC/TMD (10–13)—axis I
- TMD Pain Screener—axis I of the DC/TMD (**Supplementary Material**)
- Graded Chronic Pain Scale version 2.0—axis II of the DC/TMD (**Supplementary Material**)
- Pain drawing (Bodychart) (**Figures 1**, **2**) to assess orofacial and general pain location—axis II of the DC/TMD. The patients were asked to mark the sites of all pain in the body. In the case of localized pain, "•" mark was used. If the pain changed, then arrows were used to indicate how the pain location moved.

Statistical Analysis

Statistical analysis was carried out using Statistica 12 Software (StatSoft Power Solutions, Inc.) (14) (**Supplementary Material**). A Chi-square test of independence for 2 × 2 table was calculated comparing the frequency of pain locations in men and women. In the cases of small samples (expected number of frequencies fewer than 5), Fisher's Exact one-tailed test was additionally used. Differences in $p < 0.05$ were considered as statistically significant. With respect to Fisher's exact test, statistical post hoc power analysis was performed using G Power v. 3.1.9.4 Software (Germany). Power (1-ß) was calculated as the function of α, the population effect size and N.

Ethical Approval

The project was carried out after obtaining consent from the Bioethical Commission of the Medical University No R-I-002/322/2016. The research was performed in accordance with the Helsinki Declaration of the World Association of Physicians and the principles of Correct Clinical Trial Guidance (Guidelines for Good Clinical Practice). Participation in the project was

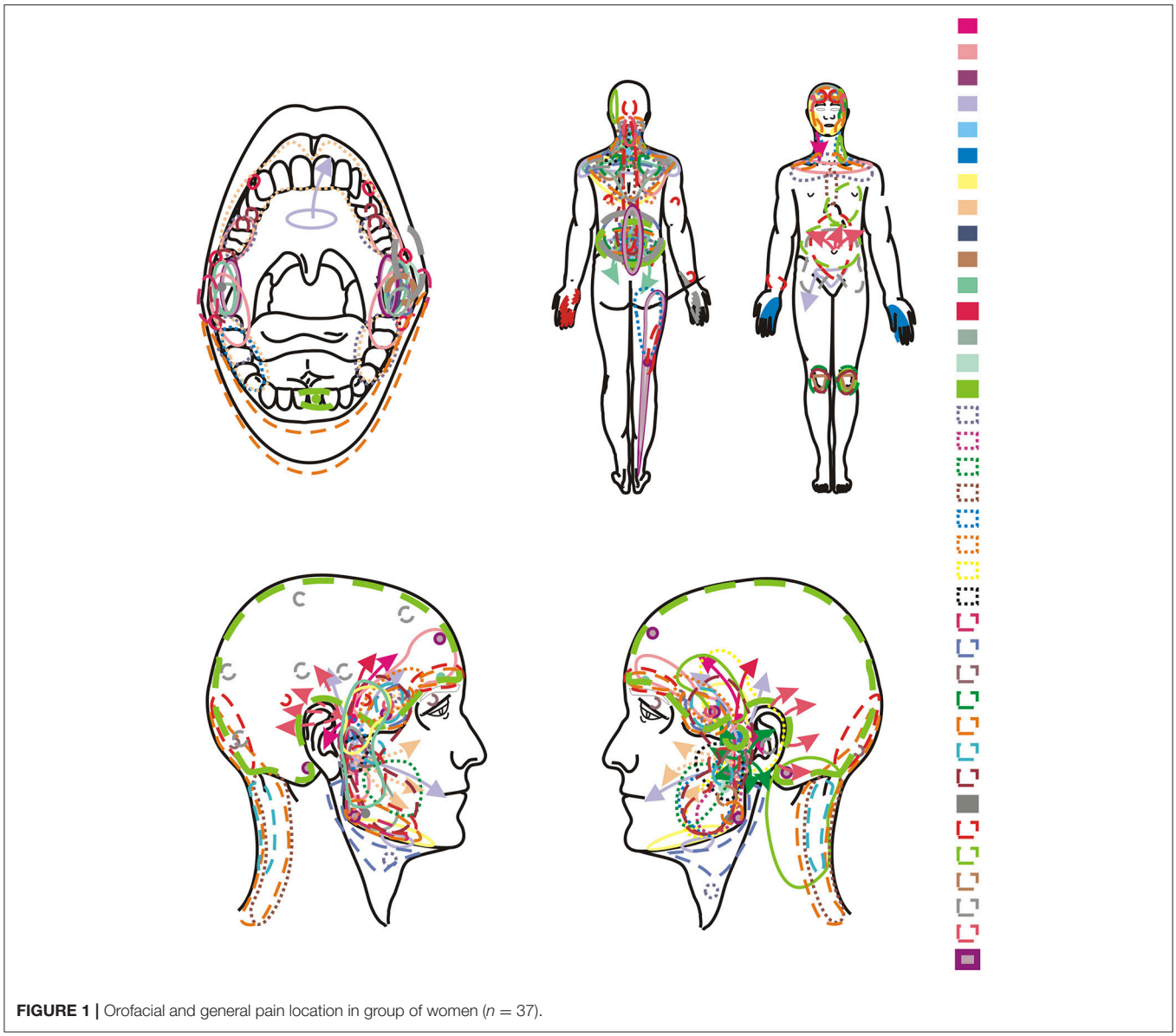

FIGURE 1 | Orofacial and general pain location in group of women ($n = 37$).

voluntary. Patients had obtained comprehensive information about the nature, scope of clinical activities and the course of the proceedings. At each stage, the respondents had the right to refuse to participate in the study, without any corresponding consequences. Participation in the study was preceded by the patient's written informed consent.

RESULTS

The study involved 50 patients, 13 men and 37 women. Seventy percent of the people reported a possible occurrence of functional disorders of temporomandibular joints (TMD-PSc = 4–6) (**Table 1**). In 15 people (TMD-PSc = 0–3), including 11 women and 4 men, the presence of dysfunction was dubious (**Table 1**). The prevalence of temporomandibular joint disorders in the group of women and men was comparable, at 70%.

In three patients from the study group, no significant chronic TMJ pain was found in the last 6 months with respect to GCPS v.2. (**Table 2**). 30 (60%) of the subjects displayed low intensity of pain without functional disorders. High intensity of pain and low disability (II°) or moderate limitation (III°), was reported by six (12%) patients. In five (10%) subjects, high disability with severe limitation was found (**Table 2**).

Seventy percent of patients suffered from pain within the right masseter muscle. Pain in the left masseter muscle was noted in 68% of cases. Cervical ailments were reported by 56% of participants. Pain of the temporomandibular joint was observed in 68% of patients on the left side and in 54% on the right side (**Table 3**).

With respect to gender, a statistically significant difference in the prevalence of pain was noted within the right masseter muscle ($\chi^2 = 4.162954$, $p = 0.04132$) (**Table 3**). Test's power

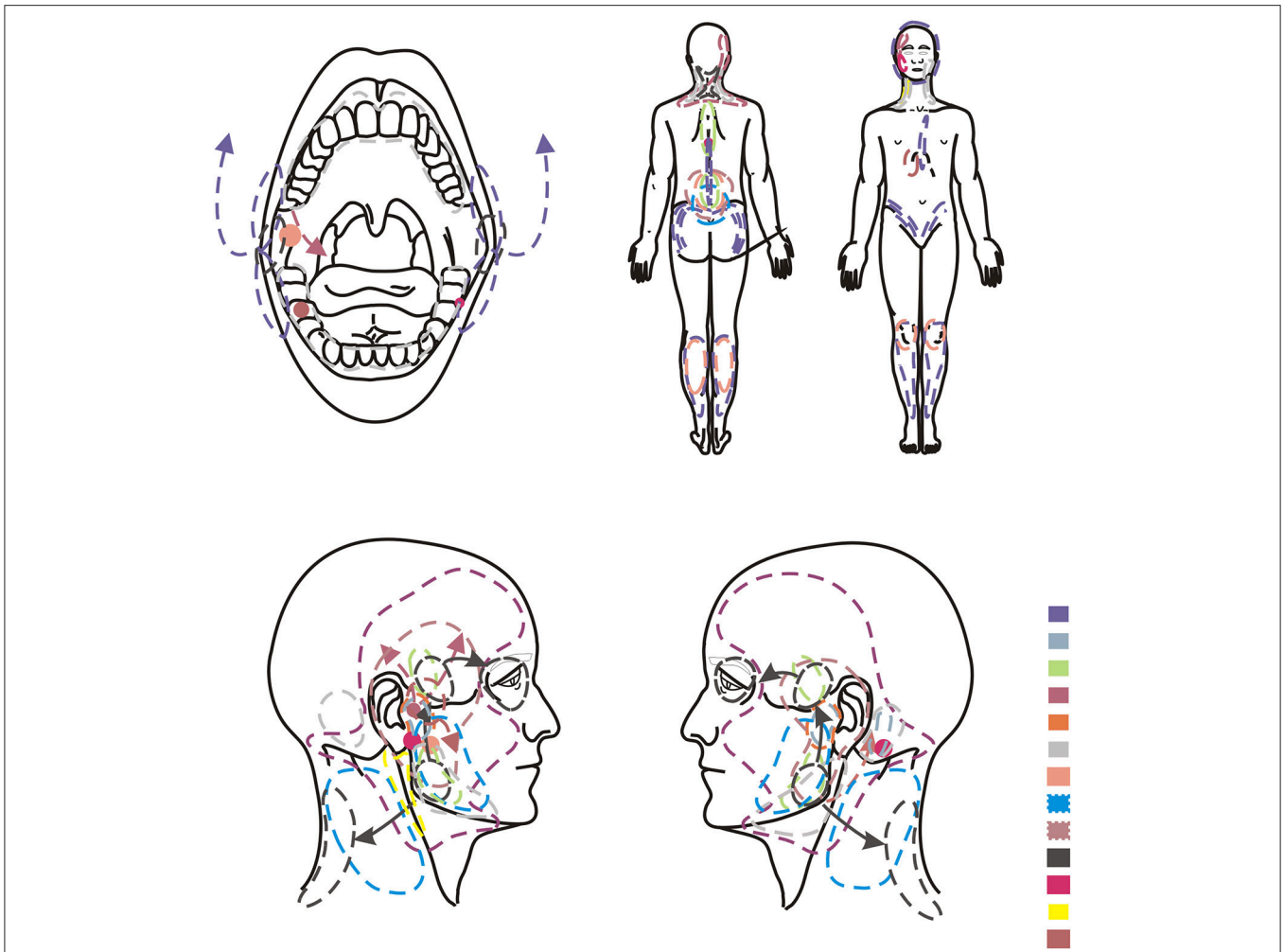

FIGURE 2 | Orofacial and general pain location in group of men ($n = 13$).

TABLE 1 | TMD-Pain Screener results (Axis I of DC/TMD) in the whole study group ($n = 50$), group of women ($n = 37$), and men ($n = 13$).

TMD Pain screener	Reference value	Whole study group $n = 50$	Group of women $n = 37$	Group of men $n = 13$
Dubious presence of TMD	0–3	15 (30.00%)	11 (29.73%)	4 (30.77%)
The potential presence of TMD	4–6	35 (70.00%)	26 (70.27%)	9 (69.23%)

The number of people (n) and percentages (%) are given.

to detect the specified effect was on the medium level (Fisher's Exact Unilateral Test: $p = 0.03943$, 1-ß = 0.5351020) (**Table 3**). 92.31% of men and 62.16% of women suffered from pain in this area (**Table 3**). A similar tendency was found with regard to the right TMJ ($\chi^2 = 6.628870$, $p = 0.01003$). In this case, the test's power was slightly higher (Fisher's Exact Unilateral Test: $p = 0.01048$, 1-ß = 0.7871910). 84.62% of men and 43.24% of women suffered from pain of the right temporomandibular joint (**Table 3**). With regards to other areas of the body, the test's power to detect the specified effect was low (1-β < 0.5) (**Table 3**).

The study group indicated 40 different areas of the body affected by pain (**Figure 3**). Up to three isolated pain locations were declared by a total of six subjects. One person identified 17 affected areas (**Figure 3**). Forty four people reported pain in at least four regions of the body.

DISCUSSION

The incidence of specific types of temporomandibular joint disorders with respect to the DC/TMD classification, depending on the studied population, is variable. John et al. stated that in a

TABLE 2 | Graded Chronic Pain Scale v.2.

GCPS v.2.	Description	Whole study group $n = 50$	Group of women $n = 37$	Group of men $n = 13$
Grade 0	No TMJ pain in the last 6 months	3 (6%)	2 (5%)	1 (8%)
Grade I	Low intensity of pain Low disability	30 (60%)	24 (65%)	6 (46%)
Grade II	High intensity of pain Low disability	6 (12%)	4 (11%)	2 (15%)
Grade III	High Disability Moderately Limiting	6 (12%)	2 (5%)	4 (31%)
Grade IV	High Disability Severely Limiting	5 (10%)	5 (14%)	0 (0%)

(GCPS v.2.) results in the whole study group (n = 50), group of women (n = 37) and men (n = 13). The number of people (n) and percentages (%) are given.

group of 416 women, 27.4% were cases of myofascial pain, 21.4% subjects had myofascial pain associated with mobility restriction of the mandible, 44.2% were patients with dislocation of the disc with the possibility of reduction, and 6.3% cases were the displacement of the disc without reduction (15). Arthralgia was found in 33.2% of cases, osteoarthritis in 3.6%, and osteoarthritis in 3.4%. Many patients had more than one diagnosis (15). On the other hand, a study carried out among Swedish dentistry students without overt dysfunctions revealed the occurrence of disorders in 30% of the subjects. According to the DC/TMD criteria, the most frequent pathologies were disorders from the myalgia group (16).

In the presented study it was found that the potential presence of functional disorders of temporomandibular joints can affect up to 70% of patients, including 26 women and 9 men (**Table 1**). The remaining 15 people displayed dubious results. The study revealed a broad spectrum of disorders of the II axis of the DC/TMD protocol in relation to the bodychart (pain drawing) (**Figures 1**, **2**). The importance of the biopsychosocial component in the assessment of temporomandibular joint disorders, including myofascial dysfunction, was suggested.

The results of this study obtained on the basis of the bodychart reflect the characteristic profile of myofascial disorders associated with referred pain (**Table 3**, **Figures 1**, **2**). Attention was paid to the multifaceted nature of the ailments indicated by the respondents, as well as a typical pattern of transfer from trigger points (**Figures 1**, **2**). Suvinen et al. reported that extensive pain is related to a higher risk of depression and somatization, reduced levels of overall health status, increased propensity to sleep disorders, decreased pain control capacity, and increased healthcare needs compared to patients with localized pain (17). In the group of 135 people examined by the above-mentioned author, 21% patients suffered from local myalgia and 20% declared pain limited to the examined body area within the head and neck (1). Fifty nine percent of the respondents reported generalized pain covering many zones of the body: 28.2% declared severe and 30.8% moderate disability determined by their complaints (17).

In our study, the patients were a homogeneous group of people with myofascial pain with pain referral. With regard to the bodychart, only two people indicated ailments limited to two places of occurrence (**Figure 3**). Forty eight subjects declared the presence of pain in three or more zones, which suggests serious pathologies and raises the risk of developing systemic disorders based on central sensitization of pain, which promotes the possibility of chronic pain (12, 18). In these cases, the need for general treatment should be considered with respect to the DC/TMD recommendations (12).

Particular attention should be paid to pain in the cervical, thoracic and lumbar spine observed in ± 50% of the subjects (**Table 3**) (**Figures 1**, **2**). The obtained results may indicate co-occurring postural abnormalities, bad habits, poor ergonomics in everyday activities, and the resultant need for postural reeducation. The direct binding factor for the masticatory dysfunction is undoubtedly upper cervical spine disorders. This is dictated by both the anatomophysiological aspects of the C0-C2 complex (Occiput-Axis), including a neurological component (C2 nerve root), and often also traumatic etiology of whiplash related to this segment. An injury contributes to the temporomandibular joint disorder directly or through a delayed response, most often controlled by means of central sensitization of pain (19). This promotes the transition of the acute phase into a chronic one, thereby initiating the occurrence of chronic pain (19).

Bogduk et al. emphasize the role of convergence between cervical and trigeminal afferents in the trigeminocervical nucleus. This author indicates that nociceptive afferents from C1, C2, and C3 spinal nerves converge with the first division of the trigeminal nerve, which mediates referred pain from the neck to the head (to occipital, auricular, parietal and orbital regions) (20).

Pain from the cervical zygapophysial joints, which has constant segment patterns, must also be mentioned. Pain within zygapophysial joints at the C2-C3 level is referred toward the front of the head. Pain from C3-C4 and C4-C5 remains within the posterior part of the neck. A typical location of spreading pain from C5-C6 is supraspinous fossa of the scapula. C6-C7 generates spreading pain caudally over the scapula (21).

Pedroni et al. noted that most frequently the pain area indicated by TMD patients was the cervical spine (92.85%) and scapular region (50%). The third most commonly observed

TABLE 3 | Orofacial and general pain distribution with respect to the bodychart (pain drawing) in the whole study group ($n = 50$), group of women ($n = 37$), and men ($n = 13$).

Area of the body	The number of people (n) and percentages (%) with respect to the whole study group ($n = 50$)	The number of people (n) and percentages (%) with respect to the group of women ($n = 37$)	The number of people (n) and percentages (%) with respect to the group of men ($n = 13$)	*Chi*^{2} Pearsons			Fisher's Exact Unilateral Test	with respect to Fisher's Exact Unilateral Test
				Chi^2	df	$p =$	$p =$	Power (1-ß)
Cervical spine Cx	28 (56.00%)	23 (62.16%)	5 (38.46%)	2.193077	1	$P = 0.13863$	$P = 0.12404$	0.3096000
Thoracic spine Tx	24 (48.00%)	16 (43.24%)	8 (61.54%)	1.290047	1	$P = 0.25604$	$p = 0.20828$	0.1962761
Lumbar spine Lx	24 (48.00%)	18 (48.65%)	6 (46.15%)	0.0239885	1	p = 0.87691	$p = 0.56717$	0.0336837
Sacrum Sc	9 (18.00%)	6 (16.22%)	3 (23.08%)	0.3067796	1	$p = 0.57966$	$p = 0.42950$	0.0781242
Pelvis	5 (10.00%)	5 (13.51%)	0 (00%)	1.951952	1	$p = 0.16238$	$p = 0.20573$	0.0539917
Temporal muscle on the right side	26 (52.00%)	20 (54.05%)	6 (46.15%)	0.2405512	1	$p = 0.62381$	$p = 0.43283$	0.0670719
Temporal muscle on the left side	24 (48.00%)	20 (54.05%)	4 (30.77%)	2.089664	1	$p = 0.14830$	$p = 0.13055$	0.2965980
Masseter muscle on the right side	35 (70.00%)	23 (62.16%)	12 (92.31%)	4.162954	1	$p = 0.04132$*	$p = 0.03943$ *	0.5351020
Masseter muscle on the left side	34 (68.00%)	26 (70.27%)	8 (61.54%)	0.3370735	1	$p = 0.56152$	$p = 0.39997$	0.0841976
Musculus sternocleidomastoideus on the right side	6 (12.00%)	3 (8.11%)	3 (23.08%)	2,041202	1	$p = 0.15309$	$p = 0.17292$	0.2675022
Musculus sternocleidomastoideus on the left side	7 (14.00%)	3 (8.11%)	4 (30.77%)	4.103094	1	$p = 0.04280$*	$p = 0.06485$	0.4687233
TMJ on the left side	34 (68.00%)	27 (72.97%)	7 (53.85%)	1.617341	1	$p = 0.20346$	$p = 0.17649$	0.2405843
TMJ on the right side	27 (54.00%)	16 (43.24%)	11 (84.62%)	6.628870	1	$p = 0.01003$*	$p = 0.01048$*	0.7871910
Area of the lower angle of the left scapula	4 (8.00%)	4 (10,81%)	0 (0.00%)	1.527615	1	$p = 0.21647$	$p = 0.28678$	0.0150241
Area of the lower angle of the right scapula	4 (8.00%)	4 (10.81%)	0 (0.00%)	1.527615	1	$p = 0.21647$	$p = 0.28678$	0.0150241
Right shoulder	16 (32.00%)	13 (35.14%)	3 (23.08%)	0.6428091	1	$p = 0.42270$	$p = 0.33102$	0.1141421
Left shoulder	16 (32.00%)	14 (37.84%)	2 (15.38%)	2.228812	1	$p = 0.13546$	$p = 0.12409$	0.3233793
Thoracic outlet	3 (6.00%)	3 (8.11%)	0 (0.00%)	1,121334	1	$p = 0.28963$	$p = 0.39643$	0.0023215
Right hip band	2 (4.00%)	2 (5.41%)	0 (0.00%)	0.7319820	1	$p = 0.39224$	$p = 0.54367$	0.0001234
Left hip band	1 (2.00%)	1 (2.70%)	0 (0.00%)	0.3585218	1	$p = 0.54933$	$p = 0.74000$	0.0000000
Sternum	3 (6.00%)	2 (5.41%)	1 (7.69%)	0.0892054	1	$p = 0.76519$	$p = 0.60357$	0.0334427
Right knee	6 (12.00%)	4 (10.81%)	2 (15.38%)	0.1905752	1	$p = 0.66244$	$p = 0.49710$	0.0614422
Left knee	6 (12.00%)	4 (10.81%)	2 (15.38%)	0.1905752	1	$p = 0.66244$	$p = 0.49710$	0.0614422
Right shinbone	4 (8.00%)	2 (5.41%)	2 (15.38%)	1.301636	1	$p = 0.25391$	$p = 0.27462$	0.1743806
Left shinbone	3 (6.00%)	1 (2.70%)	2 (15.38%)	2.743251	1	$p = 0.09767$	$p = 0.16793$	0.2638459
Teeth 18-14	6 (12.00%)	5 (13.51%)	1 (7.69%)	0.3087003	1	$p = 0.57848$	$p = 0.50290$	0.0191525
Teeth 13-11	2 (4.00%)	1 (2.70%)	1 (7.69%)	0.6237006	1	$p = 0.42968$	$p = 0.45633$	0.0562780
Teeth 21-23	2 (4.00%)	1 (2.70%)	1 (7.69%)	0.6237006	1	$p = 0.42968$	$p = 0.45633$	0.0562780
Teeth 24-28	6 (12.00%)	5 (13.51%)	1 (7.69%)	0.3087003	1	$p = 0.57848$	$p = 0.50290$	0.0191525
Teeth 34-38	6 (12.00%)	4 (10.81%)	2 (15.38%)	0.1905752	1	$p = 0.66244$	$p = 0.49710$	0.0614422
Teeth 31-33	3 (6.00%)	2 (5.41%)	1 (7.69%)	0.0892054	1	$p = 0.76519$	$p = 0.60357$	0.0334427

(Continued)

TABLE 3 | Continued

Area of the body	The number of people (*n*) and percentages (%) with respect to the whole study group (*n* = 50)	The number of people (*n*) and percentages (%) with respect to the group of women (*n* = 37)	The number of people (*n*) and percentages (%) with respect to the group of men (*n* = 13)	*Chi*^{2} Pearsons			Fisher's Exact Unilateral Test	Fisher's Exact Unilateral Test with respect to Fisher's Exact Unilateral Test
				Chi^2	df	*p* =	*p* =	Power (1-ß)
Teeth 41-43	4 (8.00%)	3 (8.11%)	1 (7.69%)	0.0022598	1	$p = 0.96209$	$p = 0.72538$	0.0008206
Teeth 44-48	7 (14.00%)	5 (13.51%)	2 (15.38%)	0.0279733	1	$p = 0.86717$	$p = 0.59435$	0.0350405
Palate	1 (2.00%)	1 (2.70%)	0 (0.00%)	0.3585218	1	$p = 0.54933$	$p = 0.74000$	0.0000000
Right hand	1 (2.00%)	1 (2.70%)	0 (0.00%)	0.3585218	1	$p = 0.54933$	$p = 0.74000$	0.0000000
Left hand	2 (4.00%)	2 (5.41%)	0 (0.00%)	0.7319820	1	$p = 0.39224$	$p = 0.54367$	0.0001234
Right pterygomandibular ligament	8 (16.00%)	6 (16.22%)	2 (15.38%)	0.0049500	1	$p = 0.94391$	$p = 0.65896$	0.0156287
Left pterygomandibular ligament	11 (22.00%)	10 (27.03%)	1 (7.69%)	2.095721	1	$p = 0.14771$	$p = 0.14412$	0.2889457
Right eye	1 (2.00%)	0 (0.00%)	1 (7.69%)	0.3585218	1	$p = 0.54933$	$p = 0.74000$	0.0726438
Left eye	1 (2.00%)	0 (0.00%)	1 (7.69%)	0.3585218	1	$p = 0.54933$	$p = 0.74000$	0.0726438

The number of people (n) and percentages (%) are given. $^*p < 0.05$ *statistical significance.*

location was TMJ (42.85%), followed by masseter muscle (35.71%), temporal muscle (21.42%), and frontal region (28.57%) (22).

Wright et al. indicated the significance of postural re-education in reducing pain in temporomandibular joints, as well as in attempts to improve the extent of mouth opening (23). Komiyama et al. also emphasize the importance of postural correction in the treatment of patients with myofascial pain with reduced mobility of the mandible (24). Other reports support the positive effect of postural exercises as well as active and passive exercises directed to the lower jaw and the cervical spine (25).

Based on the presented results, the bodychart appears to be an extremely useful diagnostic screening tool. It constitutes a part of the comprehensive biopsychosocial assessment as well as the way of programming therapy in patients with temporomandibular joint disorder (17).

According to the chronic pain scale GCPS v 2.0, grade I of complaints was observed in 60% of the subjects (**Table 2**). In the case of grades II and III of disorders, 12% results were recorded in each group. A severe functional limitation was found in 10% of patients. Manfredini et al. emphasize the fact that current research on chronic pain in patients with masticatory dysfunction indicates that the mean incidence in grades I and II of disorders in relation to the GCPS v 2.0 scale is 35–40%, for grade III, 15–18%, and in grade IV it reaches 3–6% (26). This author indicates that the first research on the second axis of the DC/TMD protocol noted a strong relationship between GCPS and somatization as well as weak links with levels of depression (27). On the other hand, multicenter data from more representative samples indicate an important relationship between somatization, depression and GCPS, thus supporting the early view that the three main elements of the second axis of the protocol are closely related (28).

It is also interesting to note that in the case of patients with musculoskeletal pain and temporomandibular joint disorders, chronic pain is the cause of limited activity in everyday life, as well as psychosocial dysfunction (29–32). At the moment, in the case of chronic pain assessment, the interval time of existing ailments is binding. The main criterion is the presence of symptoms lasting for over 3 or 6 months (25). Manfredini et al. additionally point to the essence of qualitative features of chronic pain, i.e., durability, intensity or fluctuations, and the significance of conditions related to emotional anxiety or being the cause of a lack of instruction (26, 33).

The results obtained with regard to GCPS v 2.0 differed from those listed in the literature and are most likely determined by the homogeneity of the study group, only including cases of myofascial pain with referral. According to Reiter et al., study results are often conditioned by the social context, ethnic origin, culture, personality traits, as well as the level of intelligence (34).

In turn, in the studies by Olivo et al. carried out in a group of 45 women aged 18–50 years old with temporomandibular joints dysfunction with myogenic etiology, grade I of chronic pain intensity was found in 19 people with respect to the GCPS scale, grades II and IV only in one case, respectively, and grade III in 24 subjects (35). On the other hand, in a mixed group including both myofascial disorders of the craniofacial region

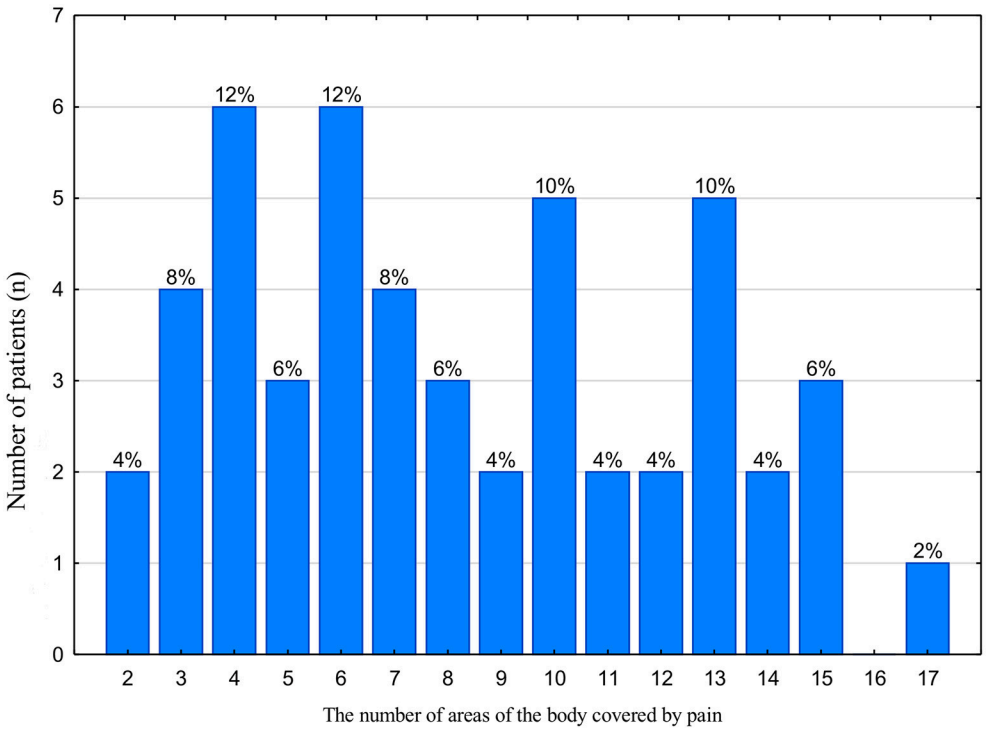

FIGURE 3 | Location of the pain areas in the whole study group ($n = 50$). The number of patients and the corresponding percentage in the study group are given.

and temporomandibular joint disorders, there were 12 cases in grade I of chronic pain severity, three people in grade II, 22 patients in grade III and seven in grade IV out of 44 people affected by the dysfunction (35).

Our study was designed to induce reflection of clinicians treating patients with temporomandibular joint disorders. Pain locations indicated the multifaceted nature of complaints in people who potentially declared good health. The bodychart revealed the size of the patients' problems. Many areas of complaints may suggest processing disorders and central sensitization. Pain drawings emphasized the essence of the biopsychological component in this group of patients and the need to cooperate in an interdisciplinary team.

Strengths and Limitations of the Study

Standardized procedures (DC/TMD protocol) allow the study to be repeated in similar research projects with the observation of comparable findings. Clear documentation of "Pain Drawing" allows other researchers using the DC/TMD protocol to assess the validity of the study results. The use of the Pain Drawing (DC/TMD protocol) emphasizes the need for holistic treatment in patients with craniofacial disorders. The bodychart reflects the specific profile of myofascial pain with referral. It is possible to estimate the cost and benefits of clinical prosthetic and physiotherapeutic procedures. In each case it is possible to determine the possible pattern of descending or ascending hereto or unilateral disorders corresponding to the craniomandibular dysfunction.

Self-reported information obtained from the bodychart may be inaccurate or incomplete. The clinical protocol for examining patients in accordance with the guidelines of DC/TMD requires precision and is time-consuming. Due to extensive DC/TMD instruments, it is not possible to present all data in one study, which may result in the omission of information that is key for the subject's case. Some information is difficult to receive through DC/TMD protocol, particularly on sensitive topics such as role of dura mater in TMJ disorders. The DC/TMD protocol does not include a clinical examination of many muscles affecting the mobility of the mandible. Interdisciplinary cooperation with physiotherapists is necessary. Research methods are inflexible, and the protocol is imposed in advance. The expanded DC/TMD questionnaire (Axes I and II) may alienate respondents. The bodychart results may mask or ignore underlying structural causes or sources of pain. Due to the small research group, further studies in this area are needed.

CONCLUSION

The bodychart is an effective research and clinical tool which allows one to reflect unconscious pain. The patients with myofascial pain with referral suffer from general ailments in different regions of the body. Only the frequency of pain of the right masseter muscle and right temporomandibular joint differed with respect to gender. The suggestion that the prevalence of pain in other areas of the body varies between men and women has

not been confirmed. Due to the small sample size, such differences cannot be excluded. Further studies in this area are needed.

ETHICS STATEMENT

The project was carried out after obtaining the consent of the Bioethical Commission of the Medical University of Białystok No R-I-002/322/2016. The research was performed in accordance with the Helsinki Declaration of the World Association of Physicians and the principles of Correct Clinical Trial Guidance (Guidelines for Good Clinical Practice). Participation in the project was voluntary. Patients had obtained comprehensive information about the nature, scope of clinical activities and the course of the proceedings. At each stage, the respondents had the right to refuse to participate in the study, without any corresponding consequences. Participation in the study was preceded by a patient's written consent.

AUTHOR CONTRIBUTIONS

JK conceived and planned the study. JK and KS carried out the experiment. JK and KS contributed to sample preparation. TS contributed to the interpretation of the results. JK and KS took the lead in writing the manuscript. TS supervised the project. All authors discussed the results and contributed to manuscript revision, read and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2019.00546/full#supplementary-material

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