MAISA SOARES GUI DEMASE

ESTUDO DE FATORES DE CRONICIDADE DAS DISFUNÇÕES TEMPOROMANDIBULARES

STUDY OF TEMPOROMANDIBULAR DISORDERS CHRONICITY FACTORS

PIRACICABA
2014

UNIVERSIDADE ESTADUAL DE CAMPINAS
FACULDADE DE ODONTOLOGIA DE PIRACICABA

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Tese apresentada à Faculdade de Odontologia de Piracicaba da Universidade Estadual de Campinas como parte dos requisitos exigidos para a obtenção do título de Doutora em Biologia Buco Dental, na Área de Anatomia.

Thesis presents to the Piracicaba Dental School of the University of Campinas in partial fulfillment of the requirements for the degree of Doctor in Dental Biology, in Anatomy area.

Orientadora: Profa. Dra. Célia Marisa Rizzatti Barbosa.

Este exemplar corresponde à versão final da tese defendida por Maisa Soares Gui Demase e orientada pela Profa. Dra. Célia Marisa Rizzatti Barbosa.

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RESUMO

A dor persistente relacionada às disfunções temporomandibulares (DTM) é reconhecida como a terceira condição de dor crônica mais prevalente em todo o mundo. Todavia, os fatores envolvidos na transição da fase aguda para a fase crônica ainda permanecem incertos. Além disso, há subgrupos de pacientes com DTM que são refratários ao tratamento. Um modelo heurístico de influências causais desta disfunção propôs que dois principais fenótipos intermediários: sofrimento psicológico e de amplificação da dor (hiperalgesia e alodinia), contribuiriam para o aparecimento e persistência das DTM. Além disso, no atendimento ao paciente crônico com DTM é difícil determinar especificamente o que pode ou não estar relacionado à dor para cada paciente individualmente. O conhecimento dos fatores persistentes e abordagens de tratamento que enfatizem a sua flexibilidade e que satisfaçam as necessidades individuais destes pacientes podem representar uma nova direção na pesquisa para o tratamento da dor crônica associada à DTM. Desse modo, o objetivo deste trabalho foi investigar fatores (de sofrimento psicológico e de amplificação da dor) relacionados ao processo de cronificação da dor facial nas DTM. Para tanto, após o levantamento bibliográfico elaborado no primeiro artigo, apresentamos também dois artigos desenvolvidos na Faculdade de Odontologia de Piracicaba e um artigo desenvolvido durante estágio no exterior na Universidade da Carolina do Norte (EUA), ambos com desenho de estudo transversal (caso-controle), os quais abordam fatores de sofrimento psicológico e qualidade do sono em pacientes com diferentes manifestações de dor relacionada à DTM. Nestes dois primeiros estudos de campo, comparamos subgrupos de DTM que foram classificados de acordo com a presença ou ausência de dor generalizada, a fim de avaliar, em primeiro lugar, os domínios de qualidade de vida e verificar quais os componentes que mais afetam a capacidade funcional dos pacientes com dor facial. Posteriormente investigamos também possíveis correlações entre a intensidade da dor facial com sintomas depressivos e de somatização. Para a obtenção dos

dados utilizamos, respectivamente, o questionário de qualidade de vida SF-36 e o eixo II do questionário RDC-TMD. Os resultados mostraram que pacientes com dor localizada na face e pacientes com dores generalizadas pelo corpo compartilham prejuízos nos aspectos emocionais. A capacidade funcional em subgrupos de DTM só foi afetada pela dor e pela presença de dor generalizada. Além disso, independentemente dos grupos avaliados, houve uma correlação positiva, não só entre a dor facial e depressão, mas também com a somatização. No último estudo, nosso objetivo foi investigar associações entre a qualidade do sono e sinais de hiperalgesia e alodinia, em pacientes com DTM e controle, avaliados respectivamente pelo Índice de qualidade do sono de Pittsburgh e pelo Teste Sensorial Qualitativo. Foi encontrado que a má qualidade do sono está associada com estímulos dolorosos térmicos e mecânicos (hiperalgesia), mas não com alodinia. Portanto, conclui-se que os aspectos emocionais, a somatização, os sintomas depressivos e a baixa qualidade do sono podem estar relacionados ao desenvolvimento da dor crônica associada às DTM e à generalização da dor para outras regiões do corpo, a qual está também associada à incapacidade funcional.

Descritores: Dor facial; Dor Crônica, Síndrome da Disfunção da Articulação Temporomandibular.

ABSTRACT

Persistent pain related to temporomandibular disorders (TMD) is recognized as the third most prevalent chronic condition of pain in the world. However, the factors involved in the transition from the acute to the chronic phase remain uncertain. Furthermore, there are subgroups of patients with TMD that are noresponders to treatment. A heuristic model of causal influences of this dysfunction has proposed two major intermediate phenotypes: psychological distress and pain amplification (hyperalgesia and allodynia), contribute to the TMD onset and persistence. Furthermore, for chronic care of patient with TMD is difficult to determine specifically what can or cannot work for every patient individually. Knowledge of persistent factors and treatment approaches that emphasize the flexibility and satisfy the individual necessities of these patients may represent a new direction in research for the treatment of chronic pain associated with TMD. Thus, the aim of this study was to investigate factors (psychological distress and pain amplification) related to the process of TMD chronic facial pain development. To do so, first the literature review was presented in this study, then we present two articles developed at the Piracicaba Dental School and also an article during an exchange program at the University of North Carolina, both with cross-sectional design (case-control studies), which address psychological distress factors and sleep quality in patients with different manifestations of TMD-related pain. First two studies compared TMD subgroups that were classified according to the presence or absence of widespread pain in order to evaluate quality of life domains and which components most affect the functional capacity of facial pain patients. Later, we also investigated possible correlations between the intensity of facial pain and depressive symptoms, and also, somatization. For data collection we used, respectively, the ShortForm-36v2® Health Surveys and RDC/TMD axis II history questionnaire. The results showed that patients with localized facial pain and patients with generalized body pain share impairments on emotional aspects. Functional capacity was only affected by the pain and the presence of widespread pain. Moreover, regardless of the group assessed, there was a positive correlation

not only between facial pain and depression, but also with somatization. In the latest study, our aim was to investigate associations between sleep quality and signs of hyperalgesia and allodynia in patients with TMD and controls, respectively evaluated by the Pittsburgh Sleep Quality Index and the Sensory Qualitative Test. Our findings showed that poor sleep quality is associated with noxious thermal and mechanical stimuli (hyperalgesia), but it is not associated with allodynia. Therefore, we could conclude that the emotional aspects, somatization, depressive symptoms and poor sleep quality could be related with the development of chronic pain associated with TMD and pain generalization to other body regions, which is also associated with disability.

Keywords: Facial Pain; Chronic Pain; Temporomandibular Joint Dysfunction Syndrome.

SUMÁRIO

Não há duas pessoas que irão descrever a dor na mesma forma ou ter exatamente a mesma experiência de dor. (Wittink et al., 2012)

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INTRODUÇÃO

A dor envolve tanto a sensação, quanto a emoção. Dores no corpo estão relacionadas com as respostas emocionais e as dores emocionais estão ligadas com as respostas corporais. A dor crônica envolve uma complexa interligação de múltiplos fatores e, portanto, é importante reconhecer que o dano tecidual não é a única fonte de dor, mas também que é impossível separar as funções da mente e do corpo quando tratamos a dor (Wittink et al., 2012).

A dor crônica é definida como a dor de longa duração. E o ponto mais conveniente de divisão entre dor aguda e crônica (não oncológica) é o período de três meses (Larner, 2013). A definição da *International Association for the Study of Pain* - IASP (2012) compreende a dor sem valor biológico aparente, que persiste além do tempo de cicatrização do tecido normal.

A dor persistente relacionada às disfunções temporomandibulares (DTM) é reconhecida como a terceira condição de dor crônica mais prevalente em todo o mundo, atrás somente das dores de cabeça tensional e lombalgias (Dworkin, 2011).

Esta disfunção abrange um grupo de condições musculoesqueléticas e neuromusculares que envolvem a articulação temporomandibular (ATM), os músculos mastigatórios e todos os tecidos associados (de Leeuw e Klasser, 2013). A dor associada à DTM pode ser clinicamente expressa como dor do músculo mastigatório ou dor da ATM (sinovite, capsulite, osteoartrite). A mastigação ou outra atividade mandibular em geral pode agravar a dor musculoesquelética. A dor na DTM pode ser (mas não necessariamente) associada à disfunção do sistema estomatognático (ruídos ou travamento da ATM e limitação do movimento mandibular (IASP, 2013).

Todavia, os fatores envolvidos na transição da fase aguda para a fase crônica na DTM permanecem incertos (Galli et al., 2009). Além disso, há um subgrupo de pacientes com DTM para o qual o tratamento não é efetivo, ou seja,

são refratários ao tratamento. Estes pacientes apresentaram escores menores de estratégias de enfrentamento, e pontuam mais em pessimismo e catastrofização do que os indivíduos do grupo controle (Litt e Porto, 2013).

Um modelo heurístico de influencias causais que contribuem para o aparecimento e persistência das DTM foi recentemente proposto. Este modelo apresenta dois principais fenótipos intermediários: sofrimento psicológico e de amplificação da dor. Interações entre fenótipos intermediários ocorrem na presença de contribuições ambientais que concorrem ainda mais para o início e a persistência da dor da DTM (Maixner et al., 2011).

Sofrimento psíquico é considerado como uma consequência do desconforto e frustrações apresentado pela doença (McCreary et al., 1991). Amplificação da dor refere-se às alterações nos processos do sistema nervoso periférico e central que têm o efeito de amplificar a resposta à estímulos nociceptivos perceptuais. Além disso, é conceituada como uma construção geral que engloba fenômenos mais específicos (por exemplo, sensibilização central – hiperalgesia e alodinia) (Maixner et al., 2011).

Dores desta natureza e preocupações com as mesmas, muitas vezes proporcionam um sofrimento significativo e incapacidade funcional e têm sido associadas com o uso inadequado de serviços médicos e de sinistros de seguros de alto custo (Asmundson et al., 1999). Além disso, no atendimento ao paciente com DTM crônica é difícil determinar especificamente o que pode funcionar ou não funcionar para cada paciente individualmente. O conhecimento dos fatores persistentes e abordagens de tratamento que enfatizam a flexibilidade e, que satisfaçam as necessidades individuais destes pacientes poderia representar a nova direção na pesquisa de tratamento para a dor crônica associada à DTM (Litt e Porto, 2013).

Desse modo, o objetivo deste estudo foi investigar fatores (de sofrimento psicológico e de amplificação da dor) relacionados ao processo de cronificação da dor facial nas disfunções temporomandibulares.

CAPÍTULOS

Esta tese foi elaborada de acordo com a Resolução CCPG/002/2013 que regulamenta o formato alternativo para teses de Doutorado permitindo a inserção de artigos científicos de autoria ou co-autoria do candidato. Esta tese está composta de quatro capítulos, assim intitulados:

- **Capítulo 1 :** CHRONICITY FACTORS OF TEMPOROMANDIBULAR DISORDERS: A REVIEW OF LITERATURE.
    - Aceito para publicação na Brazilian Oral Research.

- **Capítulo 2 :** QUALITY OF LIFE IN TEMPOROMANDIBULAR DISORDER PATIENTS WITH LOCALIZED AND WIDESPREAD PAIN.
    - Aceito para publicação na Brazilian Journal of Oral Sciences.

- **Capítulo 3 :** FACIAL PAIN IS CORRELATED WITH PSYCHOLOGICAL DISTRESS REGARDLESS OF PAIN MANIFESTATION.
    - Submetido para publicação na Journal of Oral and Facial Pain and Headache (#1419) conforme Anexo 1.

- **Capítulo 4** : SLEEP QUALITY AND EXPERIMENTAL PAIN SENSITIVITY: A CROSS-SECTIONAL STUDY.
    - Ainda não submetido para publicação.
    - Desenvolvido em período de estágio no exterior na Universidade da Carolina do Norte em Chapel Hill (EUA).

CHRONICITY FACTORS OF TEMPOROMANDIBULAR DISORDERS: A REVIEW OF LITERATURE.

MAISA SOARES GUI; CÉLIA MARISA RIZZATTI BARBOSA.

Abstract

Background: Commonly, the experience of facial pain persists long after any identifiable organic pathology has healed and it has been mostly noticed that there are subgroups of Temporomandibular Disorders (TMD) patients for whom no treatment is effective. Thus, the knowledge of current persistent pain factors in TMD could help to identify a personalized treatment approach. **Aim**: To conduct a literature review, performing an update on factors related with TMD development and persistence. **Methods:** A bibliographic search for the period January 2000 to December 2013 was performed. **Results:** The literature findings showed that chronic TMD is not only marked by psychological distress (Somatization and Depression, Affective Distress; Fear of Pain; Fear of Movement; Catastrophizing) and pain amplification characteristics (hyperalgesia and allodynia), but also those factors seem to interact among themselves in the TMD development. Our review demonstrate that upregulated serotonergic pathway, sleep problems and gene polymorphism also influence in chronicity TMD process. **Conclusion:** We concluded that chronic TMD process is marked by psychological distress and pain amplification and these factors appear to interact each other, working as contributing factors for chronic TMD, which certainly complicate pain management and emphasizes the importance of multidisciplinary assistance for chronic TMD patients.

Keywords: Craniomandibular Disorders, Chronic Pain, Facial pain.

Introduction

Temporomandibular Disorders (TMD) persistent pain is acknowledged to be one of the most prevalent chronic pain conditions, falling behind common tension headache and back pain as the third most prevalent chronic pain condition worldwide.(1)

Nevertheless, the factors involved in the transition from the acute phase of TMD into the chronic phase remains unclear. TMD chronic facial pain is most often caused by a myoarthropathy of the masticatory system in particular by a myogenous form. (2)

A recent study suggested that there is a subgroup of TMD patients for whom treatment is not effective, that is, a discrete set of treatment nonresponders who are not really like other patients. Nonresponders were likely to score higher on depression, had lower self-efficacy and coping scores, and scored higher on pessimism and catastrophizing than their peers.(3)

A heuristic model of causal influences contributing to onset and persistence of TMD and related conditions was proposed. This model displays two principal intermediate phenotypes (psychological distress and pain amplification) that contribute to onset and persistence of TMD. Interactions between intermediate phenotypes take place in the presence of environmental contributions that further contribute to onset and persistence of painful TMD. (4)

Psychological distress is regarded as a consequence of the discomfort and frustrations presented by the disorder. (5) Pain amplification refers to alterations in peripheral and central nervous system processes that have the net effect of amplifying the perceptual response to nociceptive stimuli. Pain amplification is conceptualized as a general construct that subsumes more specific phenomena (e.g. hyperalgesia, allodynia - central sensitization) (4) .

Pain of this nature, and preoccupation therewith, often leads to significant distress, suffering, and functional disability and has been associated with

inappropriate use of medical services and high cost insurance claims. (6) Furthermore, in chronic TMD patient care is difficult to determine specifically what can work or not work for each individual patient. The knowledge of TMD persistent factors and treatment approaches that emphasize flexibility and meeting the individual needs of patients could represent the new direction in treatment research for TMD-related chronic pain.(3)

The objective of our literature review is performing an update on factors related with TMD development and persistence.

Methods

A bibliographic search of electronic bibliographic databases (Medline, Pubmed, Lilacs and Scielo) for the period January 2000 to December 2013 was performed utilizing the keywords: “Temporomandibular Disorders” and “Chronic Orofacial Pain” combined with: “Catastrophizing”; “Coping behavior”; “Fear”; “Emotional stress”; “Somatization Disorder”; “Affective Disorders”; “Depression”; “Hyperalgesia”; “Pain sensitivity”; “Pain Threshold”; “Central Sensitization”; “Sleep disorders”.

First, two independently reviewers read the abstracts and those were selected by consensus to the following inclusion criteria: Patients with TMD diagnosis and chronic orofacial pain. Articles were then read and evaluated for inclusion into the literature review.

Additional inclusion criteria for research articles were as follows: Investigations of the relationship between psychological distress and TMD, and investigations about pain amplification in TMD. All the research articles included had a sample population aged 18 or older, both genders, and they had cross-sectional study designs.

Results

Psychological Distress

Psychological factors play an important role in the expression of pain around the world(1). In TMD, the importance of psychosocial factors derives from studies demonstrating an association between psychosocial measures and both the severity and persistence of TMD-related clinical symptoms, (7) underlining the significance of psychosocial factors for pain chronification.(8)

In addition, multiple psychological factors (global psychological symptoms, stress and negative affectivity, passive and active coping) have been implicated as potential risk factors for the development of painful TMD. (4) A summary of these literature review findings about the relationship of psychological distress and TMD is presented in Table 1.

Table 1. Summary findings of cross-sectional studies about psychological distress and temporomandibular disorders.

Author	Construct (Questionnaire)	Study Design	Main Findings
Manfredini et al. (2010)(9)	Depression and Somatization levels (Symptoms Checklist-90 [SCL-90])	Observational Study. N=1,149 TMD of different world sites.	Pain-related disability was found to be strongly related with depression and somatization levels as well as associated with pain duration.
Park et al. (2010)(34)	Depression, Somatization, and somatization without pain (RDC/TMD axis II)	Case-control study. N= 36 normal subjects and 39 TMD patients.	Every score of the psychological profiles was higher for TMD patients compared with normal subjects.
Kim et al. (2012)(33)	Depression and Somatization (RDC/TMD axis II)	Observational Study. N=317 TMD patients	Myofascial pain group showed more severe depressive and nonspecific physical symptoms than internal derangement group.
Fillingim et al. (2011)(7)	Somatic Awareness (Pennebaker Inventory of Limbic Languidness –PILL; SCL-90R-Somatization).	Case-control study. N= 3,263 controls and 185 TMD cases.	TMD cases reported higher levels (odds ratios exceeding 2.0) of increased somatic awareness compared to controls.
Monteiro et al. (2011) (13)	Trait-anxiety and State-anxiety (State-Trait Anxiety Inventory)	Case-control study. N= 101 controls and 49 TMD cases.	The correlation between trait-anxiety levels and chronic orofacial pain degrees was significant and positive.
Turner et al. (2001)(31)	Beliefs, coping, and catastrophizing (The Coping Strategies Questionnaire and The Survey of Pain Attitudes)	Observational Study. N=118 TMD patients.	Significant associations were found between pain beliefs and activity interference; depression, and non-masticatory jaw activity limitations; catastrophizing and activity interference; and also coping and activity interference.
McNeil et al. (2001)(16)	Fear of pain (Fear of Pain Questionnaire-II)	Cross-sectional study. N= 40 orofacial pain patients and 40 matched controls.	Orofacial pain patients reported significantly greater fear of severe pain.
Visscher et al. (2010)(17)	Fear of movement (Tampa Scale for Kinesiophobia for TMD.	Observational study. N= 301 TMD complain patients.	Fear of movement was related to pain, joint sounds, and jaw locking.

Global Measures of Psychological Function

Somatization and depression are examples of global psychological symptoms. A recent study(9) looked at data across widely separated clinical sites from different cultures and from different countries. The researchers found the prevalence of severe somatization symptoms in the overall TMD sample was 28.5%. The prevalence of severe depression increased with the rate of pain-related impairment, ranging from 16.7% in TMD patients with no disability, to 53.8% in TMD patients with high disability, severely limiting impairment.

However, it is unclear whether depression and somatization are derived from chronic pain or whether they are risk factors for the development of chronic pain.(10)

Affective Distress and Psychosocial Stress

Anxiety is a relatively permanent state of worry and nervousness characterized by physical symptoms usually accompanied by compulsive behavior or attacks of panic.(11) The level of anxiety could be correlated with facial pain and TMD patients who are more anxious seem to be at greater risk of developing chronic pain.(12)

In order to evaluate anxiety, The State-Trait Anxiety Inventory includes two 20-item questionnaires, the State Anxiety Inventory and the Trait Anxiety Inventory. For each item, participants are asked to indicate either how they ‘‘generally feel’’ (trait anxiety) or how they ‘‘feel right now’’ (state anxiety) using a 4-category scale (not at all, somewhat, moderately so, extremely so).(7,13)

Anxiety sensitivity was defined as the fear of anxiety symptoms (e.g., palpitations, dizziness, gastrointestinal upset) arising from the belief that they will have harmful social, somatic, and/or psychological consequences. (6) Elevated levels of anxiety about pain and fear of pain contribute to disability and interference with life activities and functioning.(14)

If pain (e.g. caused by an injury or strain) is interpreted as threatening (pain catastrophizing), pain-related fear evolves. This leads to avoidance/escape,

followed by disability, disuse and depression. The last will maintain the pain experiences, thereby fueling the vicious circle of increasing fear and avoidance. A more direct causal link between pain-related fear and pain is assumed to be mediated by hypervigilance. In patients who do not catastrophize, pain-related fear will probably not occur. These patients are likely to confront daily activities rapidly, leading to fast recovery.(15)

Once anxiety sensitivity directly exacerbates fear of pain and that anxiety sensitivity indirectly exacerbates pain-related avoidance via its effects on fear of pain, anxiety sensitivity plays a role in the fear and avoidance responses of patients with persistent pain.(6)

Fear of pain could be defined as a highly specific negative emotional reaction to pain, eliciting stimuli involving a high degree of mobilization for avoidance/escape behavior as well as visceral arousal and cognitive/affective distress, (16) and is a central construct in the cognitive-behavioral models.(6)

Fear of Movement

Among psychological determinants of TMD onset and persistence, evidence is growing for fear of movement to play an important role in the development of chronic pain. (17,18) Although musculoskeletal disorders like low back pain and fibromyalgia fear of movement is prevalent, in TMD patients, this construct has received attention just recently.(17)

A recent longitudinal cohort study of acute low back pain patients further supported the hypothesis that baseline fear of movement is predictive of future perceived disability.(19)

Analysis of the Tampa Scale for Kinesiophobia for Temporomandibular Disorders TSK-TMD subscales showed that the TMD functional problems were strongly associated with activity avoidance, but not with somatic focus.(17)

Coping and Catastrophizing

Coping strategies have been defined as constantly changing cognitive and

behavioral efforts to manage specific external and/or internal demands that are appraised as taxing or exceeding the resources of the person. (20,21) Catastrophizing has been assessed in numerous studies also using the Coping Strategies Questionnaire (CSQ) (22) and can be defined as expecting or worrying about major negative consequences from a situation, even one of minor importance. (20)

Findings from a study with 101 chronic TMD patients indicated that treatment nonresponders accounted for 16% of the sample and did not differ from treatment responders on temporomandibular joint pathology, but that they reported more psychiatric symptoms, poorer coping, and higher levels of catastrophizing.(3)

To examine coping strategies, the CSQ has also been used. This questionnaire consists of 27 items relating to how individuals cope with pain. Participants can indicate the frequency with which they engage in specific coping activities when experiencing pain, using a 7-category numerical scale ranging from 0 (never do that) to 6 (always do that). It yields 6 subscales reflecting the pain coping strategies that individuals could use: diverting attention, catastrophizing, praying and hoping, ignoring pain sensations, re-interpreting pain sensations, and coping self-statements.(7)

As showed in table 1, all these psychosocial factors differing between cases and controls raises the possibility that such psychosocial variables may represent predisposing risk factors for the development of chronic pain. However, it should be considered the nature of the studies (cross-sectional design) that prevent temporal conclusions from being drawn.

Pain Amplification

A summary of our literature review findings about pain amplification and TMD is presented in Table 2.

The multiple bodily pain conditions in TMD have been associated with generalized alterations in pain processing. (23) However, it is not fully understood which parts of the peripheral or central nervous systems could play a role when

hyperalgesia or allodynia have become maladaptive rather than protective. (24) And for reasons still unknown, TMD can manifest as localized pain or in conjunction with widespread pain.(25)

It was suggested that primary insomnia may either share a common substrate underlying central sensitivity and/or play a causal role in the development of hyperalgesia in TMD patients.(26)

In addition, the mechanisms contributing to pain amplification are believed to include both decreased function in pain inhibitory systems and enhancement in pain facilitatory pathways. Maixner et al. (2011) (4) explained that pain amplification represents both a trait-like characteristic potentially conferred by genetic endowment, but also a phenotype that can develop over time in response to emergent biological processes and/or environmental exposures. Pain amplification could manifest as heightened responsiveness to quantitative sensory testing as well as spontaneous clinical pain from deep tissues such as muscles, joints, and visceral organs.

In order to distinguish TMD as regional musculoskeletal pain syndrome from a widespread pain syndrome (fibromyalgia), Pfau et al. (2009) (27) found a sensitive subgroup resembling fibromyalgia patients and this group showed more expanded pain areas on superimposed pain drawings and generalized changes in pain perception over cheek, trapezius and hand dorsum in contrast to insensitive TMD patients with more localized changes without fulfilling fibromyalgia diagnostic criteria in most subjects.

Table 2. Summary findings of cross-sectional studies about pain amplification and temporomandibular disorders.

Author	Measurements	Study Design	Main Findings
Smith et al. (2009)(26)	Laboratory measures of pain sensitivity and polysomnogra-phic studies.	Observational Study. N = 53 myofascial TMD subjects.	It was suggested that the association of primary insomnia and hyperalgesia at a non-orofacial site could be linked with central sensitivity and could play an etiologic role in idiopathic pain disorders.
Pfau et al. (2009)(27)	Patients' tender point scores, pain drawings and quantitative sensory testing profiles.	Case-control study. N = 23 TMD patients and N = 18 patients with fibromyalgia.	The group of TMD patients was inhomogeneous with respect to their tender point count with an insensitive group (n = 12) resembling healthy controls and a sensitive TMD group (n = 9) resembling fibromyalgia patients. And sensitive TMD patients had a short pain duration arguing against a transition from TMD to fibromyalgia over time.
Park et al. (2010)(34)	Thermal pain sensitivity thresholds	Case-control study. N= 36 normal subjects and 39 TMD patients.	TMD patients were more sensitive to thermal pain, which resulted in a higher Cold Pain Thereshold, and lower Heat Pain Thereshold and Heat Pain Tolerance Threshold values compared with normal subjects.
Sipilä et al. (2011)(39)	Muscle and Joint standardized palpation force (respectively 10N and 5 N)	Observational Study. N= 6227 TMD subjects.	Masticatory muscle pain on palpation and TMD joint pain on palpation was associated with back, neck and shoulder pain and pain in joints. TMD findings were associated with pain in several locations.
Chen et al. (2012)(23)	Pressure pain thresholds and Heat pain threshold and tolerance.	Case-control study. N= 76 TMD subjects with widespread body palpation tenderness (WPT), N= 83 TMD subjects and N=181 non-TMD matched controls.	TMD subjects with WPT presented with reduced pressure pain thresholds in both cranial and extracranial regions compared to TMD subjects without WPT. TMD subjects and controls did not differ with regards to heat pain threshold and tolerance at the site outside of orofacial region. Heat pain tolerance in TMD subjects with WPT was slightly lower.

Serotonin and Gene Polymorphism

A recent study revealed a distinct role for a serotonergic pathway in pathophysiology of TMD, (28) and it was suggested that people with localized TMD might have an upregulated serotonergic pathway due to cases with localized TMD differed in allelic frequency of single nucleotide polymorphisms that mapped to a serotonergic receptor pathway, when compared to healthy controls.

In addition, amitriptyline proved to be an efficient alternative treatment for chronic pain in TMD patients probably due to your property to reduce the recapture of serotonin in the synaptic gap, increasing your actuation time.(29)

Localized facial pain could also be influenced by mechanisms operating through the stimulation of peripheral HT2 receptors that are modified by an individual's genetic landscape. (28) Moreover, the same authors highlighted that localized TMD subgroup had less depressive mood than the TMD subgroup with widespread pain, which is consistent with activation of a central serotonin receptor pathway.

Other study(30) recently proposed a model, in which negative affect (neuroticism) and genetics (5HTTLPR - Serotonin Transporter Polymorphism) are argued to lead to disrupted sleep via an increase in stress-reactivity, and further that the interaction of these variables leads to an increase in learned negative associations, which further increase the likelihood of poor sleep and the development of insomnia, common phenotypes in TMD.

Discussion

Chronic TMD is not only marked by psychological distress and pain amplification, but also these factors appear to interact with each other. This review of literature shows that upregulated serotonergic pathway, sleep problems and gene polymorphism has also influenced in chronic TMD process.

Psychological distress has been related with masticatory function, which could explain its influence on TMD chronicity. Recent findings show that catastrophizing measured as a trait has been linked to greater levels of depression, activity interference, and perceived jaw interference in TMD patients.(3)

However, no process variable (Catastrophizing and Coping) was associated significantly with the objective measure of jaw impairment in a previous study. Beliefs and catastrophizing explained significant portions of the variance in non-masticatory jaw activity (e.g. laughing and yawning) limitations, but none of the process variables were associated with masticatory jaw activity (e.g. eating an apple) limitations.(31)

There were also significant positive correlations between depression and jaw amplitude and stress and jaw velocity for standardized, but not free chewing. This study provided data suggesting that psychological factors, manifesting in depression and stress, play a role in influencing the association between pain and motor activity.(32)

It was suggested that patients with myalgia could be experiencing more stressful life circumstances and more negative illness impact, (5) and these patients showed more severe depressive and nonspecific physical symptoms than internal derangement group. (33) In another study, (34) the myogenous pain subgroup had significantly higher somatization scores than normal and arthrogenous pain subgroups, and higher depression scores than normal subjects.

Even though in TMD patient's pain is the major complaint, the presence of functional problems (independent of pain) is especially associated with higher levels of fear of movement. (17) Pain-related fear is more disabling than pain itself and pain-related fear is related to poor behavioral performance.(35)

On the other hand, patients with more positive affect, additional social support, an adequate treatment adherence and a feel-good spirituality, felt better with the disease conditions and consequently had a better quality of life. (36) Pain beliefs are important predictors for treatment outcome and need to be considered in the management of patients with chronic facial pain. (8)

A recent prospective study (OPPERA study) shows that two important risk factors for elevated TMD incidence are greater numbers of comorbid pain conditions and greater extent of nonspecific orofacial symptoms. Other important baseline risk factors were preexisting bodily pain, heightened somatic awareness,

and greater extent of pain in response to examiners' palpation of the head, neck, and body. (37) These findings support the heuristic model(4) by demonstrating a prominent contribution of psychological distress, particularly somatic symptoms. Pain amplification and autonomic function had smaller effects that also support the basic domains of the proposed heuristic model.

Other study of OPPERA group showed that measures of catastrophizing and active pain coping, well-established constructs associated with chronic pain, were not significant predictors of TMD first onset, (38) but they could play a role in the perpetuation of TMD symptoms.

Taken together, psychological distress, sleep problems, upregulated serotonergic pathway and gene polymorphism could act as chronicity factors for TMD and pain amplification, since they also acting as pain-perpetuating factors. These literature findings are in line with a multifactorial etiology of chronic facial pain, shifting the perspective away from a local towards a more central etiology with dysregulations in the stress and pain modulating system. (2)

To understand the way in which a person responds to persistent pain we must look not only at the physical parameters, but also beyond to consider factors such as cognitions, coping strategies, life events, and personality.(6)

Conclusion

Our literature review brings together current studies showing that several aspects work as contributing factors for chronic TMD, which certainly complicate pain management and highlight the importance of multidisciplinary assistance for TMD patients.

Chronic TMD process is marked by psychological distress and pain amplification and these factors appear to interact each other. We concluded that psychological distress factors (e.g. somatization, catastrophizing and depression), poor sleep and polymorphisms related to generalized alterations in pain processing are more associated with TMD development and persistence than mechanical factors (e.g. clenching) and, therefore, they have had a greater focus on current researchers.

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QUALITY OF LIFE IN TEMPOROMANDIBULAR DISORDER PATIENTS WITH LOCALIZED AND WIDESPREAD PAIN

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Abstract

Aim Here we compared TMD subgroups that were classified according to the presence or absence of widespread pain (WDP) in order to assess the quality of life domains and verify which components more affect the functional capacity of facial pain patients. **Methods** A cross-sectional study was conducted and the Short Form-36 Health Survey was applied in order to assess life quality. **Results** We evaluated 39 TMD with WDP patients, 37 localized TMD patients and 40 subjects free of complaint. Our results show that TMD with WDP patients differed significantly from healthy controls in all SF-36 components and localized TMD patients ranked between them. We also observed that patients with bodily pain and TMD with WDP have respectively, 4.16 and 49.42 times more likely to have low functional capacity. **Conclusions** Functional capacity in TMD subgroups was only affected by bodily pain and widespread pain presence. These patients features high chance of low functional capacity. Furthermore, localized TMD patients and TMD with widespread pain share impairments of role-emotional.

Keywords: Facial Pain; Temporomandibular joint dysfunction syndrome; Quality of Life.

Introduction

Temporomandibular disorders (TMD) are defined as a set of conditions affecting the masticatory muscles or joints and exhibiting pain as their primary characteristic.[1,2] It has been described that individuals with TMD could display diffuse hyperalgesia and allodynia [3,4] and it was suggested that they have a fundamental problem with pain or sensory processing rather than an abnormality confined to a specific region of the body where pain is perceived to originate. [5,6]

Recently, two TMD clinical subgroups were proposed based on findings showing a group of TMD patients that was split with respect to patients' tender point score (one of the diagnosed criteria for fibromyalgia) into an insensitive subgroup resembling healthy control subjects and into a sensitive subgroup resembling patients with fibromyalgia. [1] The distinction between localized and generalized pain in TMD patients was recognized as an important for both, patient diagnosis and for proper understanding of the etiology and pathophysiology of chronic pain. [4,7]

Numerous psychological and behavioral factors are well-established influences upon a wide range of pain conditions including TMD pain.[2] A facial pain prospective study identified that psychological and behavioral factors have become significant influences upon TMD pain.[8] Other study also supported the interpretation that psychosocial parameters may be independent predictors for the development of chronic pain conditions and their generalization. [1]

The Short-form-36v2 is a global health-related quality of life measurement [9] that could help identify the similarities and differences in those TMD patients. Indeed, the knowledge of how physical and mental components influence the quality of life and how the person realizes these events in your life have been increasing related to the etiology of chronic pain. Previous studies clearly demonstrated the psychological process, i.e. emotion could modulate pain, and vice-versa. [10,11]

The aim of this study is to compare TMD subgroups that were classified according to the presence or absence of widespread pain in order to assess the

quality of life domains and verify which components more affect the functional capacity of facial pain patients.

Material and methods

Study design

A cross-sectional study was conducted in free pain healthy subjects and two subgroups of TMD patients recruited from the clinic of the Piracicaba Dental School and the communities surrounding the school from January 2010 to November 2012.

Ethical Procedures

This study was approved by the Ethics Committee on Research Involving Human Subjects under protocol number 137/2009. After a verbal presentation of the project, the volunteers signed an informed consent form to participate in the study.

Participants

For TMD case, patients with myogenic facial pain diagnosed using the Research Diagnostic Criteria for TMD (RDC/TMD)[12] were invited to participate. The RDC/TMD clinical examination was performed by calibrated examiners on all subjects. The inclusion criteria were gender (female), due to the higher prevalence of TMD and longer duration of the condition[14] in women[13], and the presence of symptomatic TMD.

Exclusion criteria were the presence of systemic diseases, polyarthritis, exposure to macro facial trauma, dislocated joints, use of orthodontic braces, dental pain, and the presence of sinusitis, ear infections, cancer and hormonal disorders.

After that, subgroups of TMD patients were defined according to the presence or absence of widespread pain palpation tenderness (WDP). The patients without WDP were classified as “localized TMD” subgroup. A group of TMD with WDP was identified on the basis of their tender point count, which is an easy practicable screening tool for those patients. [1]

Briefly, WDP was presented when the palpation of 18 body sites elicited pain at diagonally opposite quadrants of the body (i.e., above and below the waist, on both the left and right sides) [1,7] . Three pounds of digital palpation pressure were applied bilaterally for 2 seconds to each site by calibrated examiners. At each location, a response of pain to palpation was recorded as tenderness.

Control subjects had neither TMD nor widespread pain classification. Then, a control group of female individuals without complaint, which were free of any body or facial pain condition was also recruited and invited to participate.

Variables and Data sources

Quality of life was assessed by generic multidimensional instrument: The ShortForm-36v2® Health Surveys (SF-36) [9] . Briefly, this questionnaire measures eight health domains: Physical Functioning, Role-Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional and Mental Health. [9] The score for each scale varies from 0 to 100, and the higher the score corresponds to better life and provides psychometrically-based physical component summary (PCS) and mental component summary (MCS) scores.

The Mental Health measure has been shown to be useful in screening for psychiatric disorders, as has the MCS Measures. [15] The MCS had a sensitivity of 74% and a specificity of 81% in detecting patients diagnosed with depressive disorder. [15] The SF-36 has been widely used in research with excellent metric properties (sensitivity, validity and reliability), [16] and it was translated and validated for the Portuguese language. [17]

Statistical Methods

The data were analyzed by Kruskal Wallis and Dunn considering the significance level of 5%, because the data do not meet the assumptions of parametric analysis. The values of life quality items and age were dichotomized by the median of the sample.

Following bivariate analysis was performed by associating each variable with functional capacity. Variables with $p \leq 0.20$ in bivariate analysis were tested in a multiple logistic regression model, remaining in the model those with $p \leq 0.05$.

Results

We aimed to investigate 120 subjects (40 per group). However we had missing data of one TMD with WDP participant and three localized TMD participants withdrew from this study. Therefore, here we investigated 40 free-TMD healthy controls (aged 50.93±12.34), 37 localized TMD patients (aged 24.92±5.0) and 39 TMD patients with widespread pain (aged 53.21±9.34).

There was statistical difference in age of localized TMD patients when compared to TMD patients with WDP and controls ($p<0.001$, Tukey-Kramer Multiple Comparisons Test), possibly due to localized facial pain appears earlier than facial pain with WDP.

The main result of our study is that TMD with WDP patients significantly differ from healthy controls in all components while localized TMD patients ranked in-between (Table 1). However, emotional factors did not differ between TMD subgroups and General Health, Mental Health, Physical Function and Role-Physical domains were not different between localized TMD and controls.

Table 1. Median, Minimum and Maximum values obtained of the eight components of the SF-36.

SF-36Scale (0-100)	Groups								
	Control (n=40)			Localized TMD (n=37)			TMD + WDP (n=39)		
	Median	Minimum	Maximum	Median	Minimum	Maximum	Median	Minimum	Maximum
Physical Functioning	97.5 **A**	65.0	100.0	90.0 **A**	60.0	100.0	35.0 **B**	10.0	95.0
Role-Physical	100. **A**	0.0	100.0	100.0 **A**	0.0	100.0	0.0 **B**	0.0	100.0
Bodily Pain	84.0 **A**	31.0	100.0	61.0 **B**	0.0	84.0	22.0 **C**	0.0	82.0
General Health	79.5 **A**	40.0	100.0	72.0 **A**	5.0	100.0	47.0 **B**	5.0	92.0
Vitality	80.0 **A**	45.0	100.0	45.0 **AB**	0.0	80.0	20.0 **B**	0.0	90.0
Social Functioning	100.0 **A**	37.5	112.5	75.0 **B**	0.0	100.0	25.0 **C**	0.0	100.0
Role-Emotional	100.0 **A**	0.0	100.0	66.7 **B**	0.0	100.0	0.0 **B**	0.0	100.0
Mental Health	76.0 **A**	32.0	96.0	60.0 **A**	1.0	92.0	44.0 **B**	4.0	100.0

Zero is the worst score and a hundred is the best score. Medians followed by different letters horizontally differ ($p \leq .05$).

Regardless of the other variables we could also observe that patients with more bodily pain and widespread pain have, respectively, 4.16 and 49.42 times more likely to have lower functional capacity than healthy controls (Table 2).

Table 2. Influence of the components of the SF-36, age and group in the component of functional capacity of research subjects.

Variable	Categories	Low Physical Functioning			Gross Analysis			Adjusted analysis (logistic regression)		
		N	N	%	Odds	IC 95%	p	Odds	IC 95%	p
Age	**Low**	58	18	31%	Ref					
	High	58	34	58.6 %	3.15	1.46-6.75	0.0028			
Group	**Controls**	40	4	10.0 %	Ref			Ref		
	Localized TMD	37	11	29.7 %	3.81	1.09-13.30	0.0580	2.67	0.68-10.40	0.1243
	TMD + WDP	39	37	94.9 %	37.00	10.45-130.97	<0.0001	49.42	7.49-325.92	<0.0001
Role-Physical	**Low**	51	41	80.4 %	20.13	7.80-51.92	<0.0001			
	High	65	11	16.9 %	Ref					
Bodily Pain	**Low**	57	42	73.7 %	13.72	5.58-33.75	<0.0001	4.16	1.22-14.14	0.0224
	High	59	10	17%	Ref			Ref		
General Health	**Low**	58	38	65.6 %	5.97	2.66-13.41	<0.0001			
	High	58	14	24.1 %	Ref					
Vitality	**Low**	58	42	72.4 %	12.60	5.16-30.74	<0.0001			
	High	58	10	17.2 %	Ref					
Social Functioning	**Low**	52	39	75%	11.77	4.91-28.22	<0.0001			
	High	64	13	20.3 %	Ref					
Role-Emotional	**Low**	49	32	65.3 %	4.42	2.01-9.72	<0.0001			
	High	67	20	29.8 %	Ref					
Mental Health	**Low**	52	35	67.3 %	5.69	2.55-12.70	<0.0001			
	High	64	17	26.5 %	Ref					

The values of the quality of life items and age were dichotomized by the median of the sample.

Discussion

The life quality components of localized TMD patients ranked in-between TMD with WDP patients and healthy controls. Furthermore, only presence of widespread pain and bodily pain affect the functional capacity of the individual.

Our results also show that role-emotional (problems with work or other daily activities as a result of emotional problems) is not significantly different between TMD subgroups and could represent a common point that differs both from the control group. However, there was a great difference between localized TMD and TMD with WDP (respectively, 66.7 and 0).

As limitations of the study, this was cross-sectional study and temporal conclusions cannot be drawn (e.g., we don't know if the emotional problems occurred before or after pain). In addition, there is a lack of control group matching with localized TMD group, in respect to age.

Potential psychosocial risk factors for chronic TMD were identified, revealing components constructs as stress and negative affectivity, global psychosocial symptoms, passive pain coping, and active pain coping [8] that provide evidences of associations between psychosocial factors and TMD.

Furthermore, strong support was provided that chronic widespread pain is one manifestation of the process of somatization, which was described as the expression of personal and social distress through physical symptoms[18] and elevated nocturnal masseter muscle activity was related to higher intensity of headache and higher somatization in TMD patients. [19]

However, it was previously described that TMD subgroups ("sensitive" with generalized increased evoked pain, and "insensitive" with localized pain complaint) did not differ with respect to psychological parameters and sensitive TMD had short pain duration than fibromyalgia patients. [1]

In general, painful stimuli elicit considerable cognitive and emotional activity in the brain.[20] The notion that widespread pain syndromes, as fibromyalgia, might represent generalized neurobiological amplification of sensory stimuli has some support from functional imaging studies suggesting that the insula is the most

consistently hyperactive neurocortical region of the pain matrix. This region has been noted to play a critical role in sensory integration, with the posterior insula serving a purer sensory role, and the anterior insula being associated with the emotional processing of sensations. [5]

Another recent study demonstrated that rejection and physical pain are similar not only in that they are both distressing, but also they share the same common somatosensory representation. [21]

Emotional modulation of muscle pain was also associated with polymorphisms in the serotonin transporter gene and indicated that polymorphisms that lead to a high expression of the serotonin transporter gene are highly associated with the ability to modulate deep types of pain in relation to the emotional state. Further, only studied participants with a high expression of the serotonin transporter experienced a significantly changed perception of jaw muscle pain depending on their emotional state.[22]

Taken together, all these factors appear to indicate that emotional characteristics could be predisposing factors of these chronic facial pain conditions.

Despite of the age difference, Physical Function and Role-Physical domains did not differ between localized TMD and controls. Low physical functioning was considerably more related to TMD with widespread pain and it means very limited in performing all physical activities, including bathing or dressing. [15]

It could be related with pain but, particularly, with helplessness and small practice of pain coping. This refers to a belief that nothing can be done to resolve a problem, characterized by emotional, motivational, and cognitive deficits. [23]

While positive emotions lead to pain reduction [10], pain catastrophizing may lead to hyperalgesia via processes independent of spinal nociception, perhaps related to the subjective evaluation of pain (e.g., memory, attention). [24]

Our findings also show that the distinction between localized and generalized pain in TMD is important both for patient diagnosis and for treatment target. Once psychosocial factors play a role in the pathogenesis of

musculoskeletal pain[25], the knowledge of TMD subgroups characteristics and their functional impairments could help to target treatment approach.

Therefore, we concluded that functional capacity in TMD subgroups was only affected by bodily pain and widespread pain presence. These patients features high chance of low functional capacity. Furthermore, localized TMD patients and TMD with widespread pain share impairments of role-emotional.

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FACIAL PAIN IS CORRELATED WITH PSYCHOLOGICAL DISTRESS REGARDLESS OF PAIN MANIFESTATION.

MAISA SOARES GUI; MARCELE JARDIM PIMENTEL; MARTA CRISTINA DA SILVA GAMA; MARCELO CORREA ALVES; CELIA MARISA RIZZATTI BARBOSA.

ABSTRACT

AIM Here we investigated possible correlations between facial pain intensity with depression and somatization in patients with different facial pain manifestations and controls **METHODS** This was a cross-sectional study that investigated a control group and a case with myogenous facial pain with and without widespread pain. Parameters of psychological profiles (depression and somatization) and characteristics pain intensity (CPI) for facial pain analyses were obtained from the RDC/TMD axis II history questionnaire. Data was analyzed through residual correlations in order to exclude the effect of the groups. **RESULTS** It was investigated 38 free-TMD healthy controls, 37 localized TMD patients and 39 TMD patients with widespread pain. We found positive correlations between CPI and psychological profiles. **CONCLUSION** Regardless of the group, there was a positive correlation not only between facial pain and depression, but also with somatization, suggesting that these psychological distress factors could be related with TMD chronification process.

Keywords: Facial Pain; Temporomandibular Joint Dysfunction Syndrome; Depression; Somatization Disorder.

INTRODUCTION

Pain involves both sensation and emotion. Physical pains are linked with emotional responses, and emotional pains are linked with physical responses. In addition, chronic pain involves a complex interconnection of multiple factors.[1]

A recent study demonstrated that rejection and physical pain are similar not only in that they are both distressing, but also they share the same common somatosensory representation.[2] Further, emotional state is involved on pain perception. Studied participants who had high expression of the serotonin transporter experienced a significantly changed perception of jaw muscle pain depending on their emotional state.[3]

Among chronic pain conditions, Temporomandibular Disorders (TMD) is one of the most prevalent.[4] TMD encompass a group of musculoskeletal and neuromuscular conditions that involve the temporomandibular joint, the masticatory muscles, and all associated tissues[5] and exhibiting pain as their primary characteristic.[6]

In addition, multiple physiological and psychological regulatory domains, not only may contribute to the pathophysiology of pain in TMD and other bodily pain conditions,[7] but also, depression and stress play a role in influencing the association between facial pain and motor activity.[8]

The factors responsible for the transition to chronic pain could be psychosocial, psychological, behavioral, genetics, prior trauma or disease, pain severity, injury, and duration, and failure to recognize and treat the acute injury.[9]

Measures of psychological functioning predicted first onset of TMD and somatic symptoms were most strongly associated with TMD onset.[10] TMD persistent pain could present multiple bodily pain conditions and widespread pain, i.e. central sensitization manifestation, as hyperalgesia and allodynia. [11,12,13]

Whether psychological distress aspects (as depression symptoms and somatization) were correlated with facial pain, regardless of the group with different manifestations of pain, and whether those measures are more related with generalized manifestations of pain, these findings could help to understand the

process of TMD pain chronification.

Therefore, our objective was to investigate possible correlations between facial pain intensity with depression and somatization in patients with different facial pain manifestations and controls.

METHODS

Study Design

This was a cross-sectional study that investigated possible correlations between facial pain and parameters of psychological profiles. To do so, we investigated a control group (without pain) and a case with myogenous facial pain with and without widespread pain.

Setting

The subjects were recruited from the clinic of the Piracicaba Dental School and the communities surrounding the school from January 2010 to November 2012. This study was approved by the Ethics Committee on Research Involving Human Subjects under protocol number 137/2009. After a verbal presentation of the project, the volunteers signed an informed consent form to participate in the study.

Participants

We aimed to investigate 120 subjects, into three groups: 1. TMD with localized pain; 2. TMD with widespread pain and 3. Control group.

The first two groups (TMD case) consisted of patients with myogenic facial pain diagnosed using the Research Diagnostic Criteria for TMD (RDC/TMD). Myogenous pain was defined as pain at facial, masticatory muscles, temporal, preauricular and inner ear areas at rest or during function; Pain during palpation at more than 3 sites among the 20 muscle sites (1 of 3 sites must be on the pain side).

TMD patients were defined and divided according to the presence or absence of widespread pain (WDP) palpation tenderness. The patients without WDP were classified as “localized TMD” group. A group of “TMD with WDP” was

identified on the basis of their tender point count, which is an easy practicable screening tool for those patients. [12]

The RDC/TMD clinical examination was performed by calibrated examiners on all subjects. The inclusion criteria were gender (female) and the presence of symptomatic TMD. Exclusion criteria were the presence of systemic diseases, polyarthritis, exposure to macro facial trauma, dislocated joints, use of orthodontic braces, dental pain, and the presence of sinusitis, ear infections, cancer and hormonal disorders.

Briefly, WDP was presented when the palpation of 18 body sites elicited pain at diagonally opposite quadrants of the body (i.e., above and below the waist, on both the left and right sides). Three pounds of digital palpation pressure were applied bilaterally for 2 seconds to each site by calibrated examiners. At each location, a response of pain to palpation was recorded as tenderness. [13]

Control subjects had neither TMD nor widespread pain classification. Then, a control group of female individuals without complaint, which were free of any body or facial pain condition was also recruited and invited to participate.

Psychological Profiles

Parameters of psychological profiles from the RDC/TMD axis II history questionnaire including depression and somatization were analyzed. The method of assessing depression and somatization was derived from the Symptom Checklist- 90-Revision (SCL-90-R), as previous described. [14,15]

Briefly, depression index was obtained from 20 items and the resultant raw mean score was regarded as the depression scale. The depression index was graded as normal (<0.535), Moderate (0.535-1.105) and Severe (>1.105).

The somatization scale was obtained by calculating the raw mean score from the responses to 12 items of non-specific physical symptoms. Somatization without pain scale was also calculated by adding the score from responses to 7 items of the nonspecific physical symptoms and dividing the sum by the number of answered questions. The 5 items excluded from the somatization scale are

exclusively concerned with the patient's pain experiences including headache, chest area pain, and muscle.

Chronic Facial Pain

The chronic facial pain is assessed on RDC/TMD axis II by chronic pain grade classification (GCP).[13] The GCP scale includes 6 items that rate the intensity of current pain, as well as intensity and pain interference with activities in the past 6 months. GCP scale score is zero (no TMD pain in prior 6 months), when there is negative answer on question #3 (Any TMD pain reported in the prior month?).

Here we used only Characteristics Pain Intensity (CPI) for facial pain measurement. The CPI was calculated based on questions #7, #8 and #9 of axis II of RDC/TMD. Briefly, How would you rate your facial pain on a 0 to 10 scale at the present time that is right now? In the past six months, how intense was your worst pain rated on a 0 to 10 scale? In the past six months, on the average, how intense was your pain rated on a 0 to 10 scale where 0 is "no pain" and 10 is "pain as bad as could be"? (That is, your usual pain at times you were experiencing pain).

For participants characteristics we analyzed Disability Points, which were calculated summed points for Disability Days (question #10 – loss of work days) with Points for Disability Score (questions #11, #12 and #13 from RDC-TMD).

Statistical Methods

Data was analyzed through residual correlations in order to exclude the effect of the groups. Normality was tested by Shapiro-Wilk test and Spearman Correlation Coefficient (rs) was calculated when non-normal variables were contrasted and the Pearson Correlation Coefficient (r) was selected only to Somatization With Pain analysis.

To all statistical tests, the level of significance of 5% was set . All analysis was calculated by the SAS System (SAS Institute Inc. The SAS System, release 9.3. SAS Institute Inc., Cary:NC. 2010).

RESULTS

Participants

Here we investigated 38 free-TMD healthy controls, 37 localized TMD patients and 39 TMD patients with widespread pain, flow diagram of study participants are presented in figure 1.

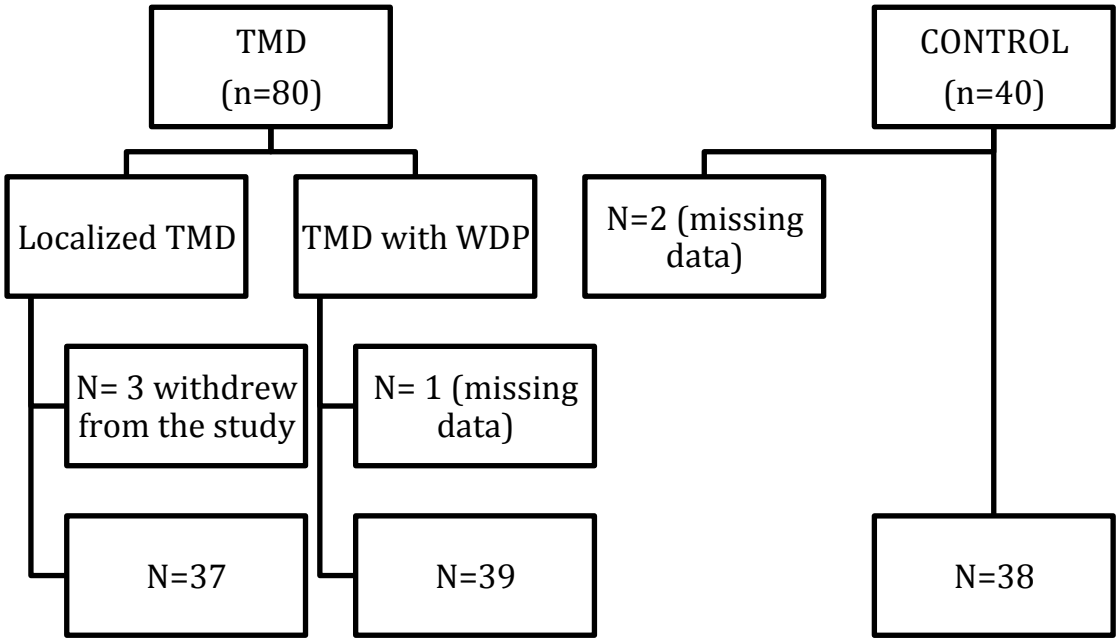

Figure 1. Flow diagram of study participants.

Descriptive data

Characteristics of study participants are presented on Table 1. The control group had no TMD pain in prior 6 months (CPI=0), whereas TMD patients could be considered with high intensity facial pain in general means.

Disability, Depression and Somatizations scores were higher in TMD with WDP group than Localized TMD group, and both groups showed higher scores than control group. In general means, the depression index was classified as “Normal” on controls, “Moderate” on Localized TMD and “Severe” on TMD with WDP.

Table 1. Characteristics of study participants (n=114).

Variable	Groups		
	Control Group (n=38)	Localized TMD (n=37)	TMD with WDP (n=39)
Age	51.95 (11.90)	24.95 (4.89)	53.03 (8.78)
Facial Pain (CPI) (0-100)	0 (0)	54.33 (19.77)	48.49 (28.99)
Disability (0-6)	0.03 (0.6)	0.58 (0.97)	1.08 (1.76)
Depression (0-4)	0.42 (0.34)	1.04 (0.81)	1.35 (0.79)
Somatization (0-4)	0.24 (0.37)	0.74 (0.76)	1.67 (0.96)
Somatization with pain (0-4)	0.31 (0.33)	0.91 (0.77)	1.77 (0.83)

Main Results

We tested the effects of the Characteristic Pain Intensity (CPI) for facial pain on Depression Symptoms (Fig. 2), Somatization with and without Pain (Fig. 3 and 4) with results showing that there is a positive correlation between CPI and psychological profiles. In another words, the greater the chronic facial pain characteristics, the higher the values reported for depression symptoms and somatization.

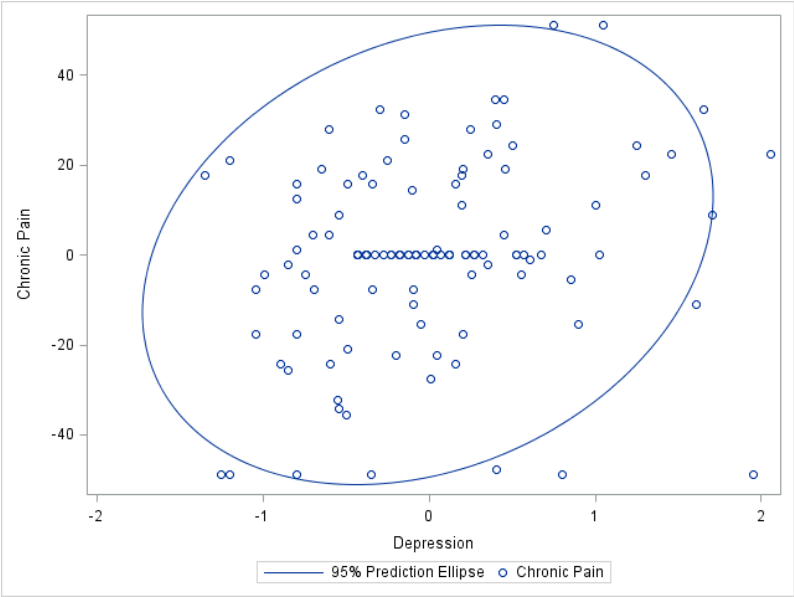

Figure 2. Positive Spearman Residual Correlation between Chronic Pain Intensity (CPI-RDC/TMD) and Depression (rs = 0.25915, p=0.0048) of 114 subjects from the study.

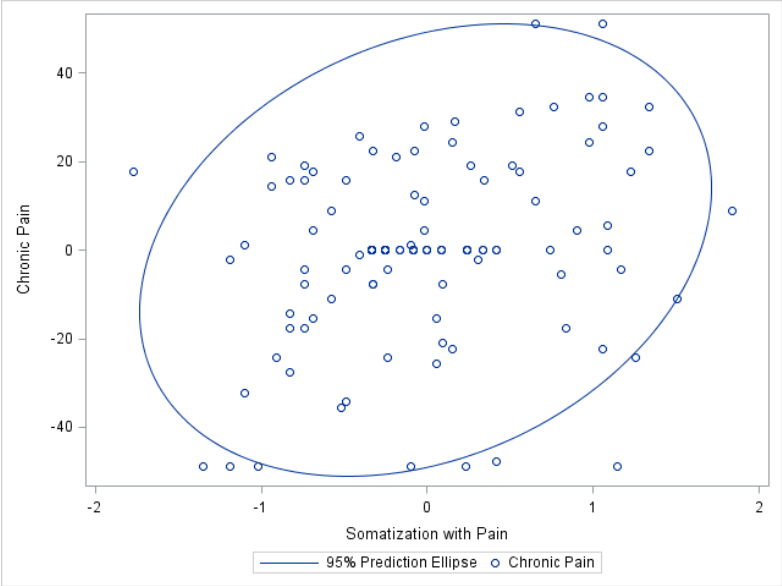

Figure 3. Positive Pearson Residual Correlation between Chronic Pain Intensity (CPI-RDC/TMD) and Somatization with Pain (r=0.27420 p=0.0028) of 114 subjects from the study.

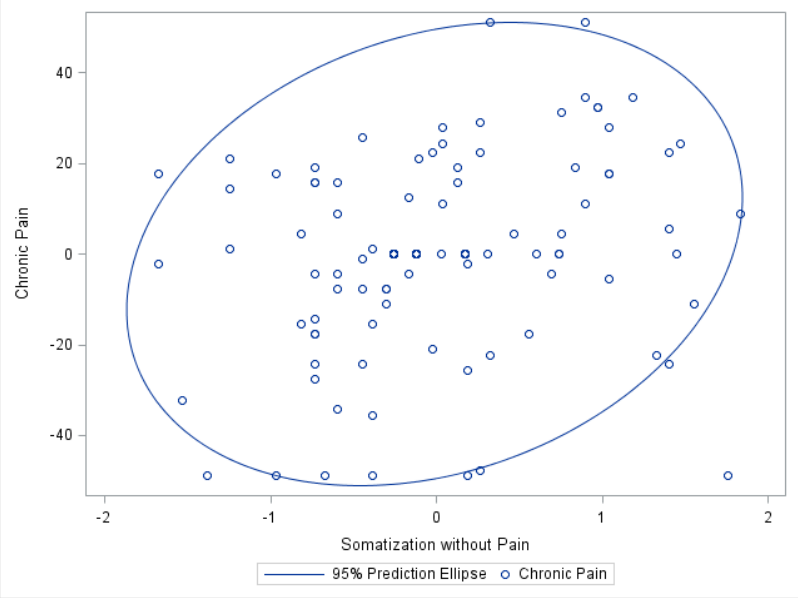

Figure 4. Positive Spearman Residual Correlation between Chronic Pain Intensity (CPI-RDC/TMD) and Somatization without Pain (rs = 0.29005 p= 0.0015) of 114 subjects from the study.

DISCUSSION

Our descriptive data showed that depression symptoms and somatization are more common in TMD patients with widespread pain manifestations. In addition, our main finding is that regardless of group, facial pain is correlated with those measures of psychological distress and vice-versa.

Among all possible factors related to chronic pain, the weak correlation found in the present study for depression and somatization should be taken for consideration due to the multifactorial nature of pain. As limitations of our study, there was a lack of control group matching with localized TMD group, in respect to age. In addition, this was a cross-sectional study and temporal conclusion cannot be draw.

A recent prospective study showed that, among 202 possible risk factors for elevated TMD incidence, the greater numbers of comorbid pain conditions and

greater extent of nonspecific facial symptoms were the most important risk factors. Other important baseline risk factors were preexisting bodily pain, heightened somatic awareness, and greater extent of pain in response to examiners' palpation of the head, neck, and body.[16]

Other studied showed that there were not significant differences in onset rates of back pain, abdominal pain or TMD pain by severity or chronicity of depressive symptoms.[17] It was also suggested that peripheral and/or central sensitization presented in chronic facial pain patients appears to take place regardless of the patient's psychological profiles. [14]

A possible explanation for those results is psychological distress and chronic pain could have development on separate pathways, but with common triggering factors.

The nature of cross-sectional studies usually raises hypotheses about chronic pain physiopathology related to reverberant circles. For example, pain-spasm-pain cycle[18] and bidirectional action on depression and pain[19] were frequently described.

However, another likely hypothesis is the existence of a common mechanism that could cause, influence or enhance the most of the abnormalities reported by chronic pain patients. In line of this, recent studies[20, 21] have described that chronic pain could be a result of ''gliopathy'', which was described as dysregulations of glial functions in the central and peripheral nervous system.

Glial mediators have been shown to powerfully modulate excitatory and inhibitory synaptic transmission at presynaptic, postsynaptic, and extra synaptic sites.[20] Glial pro inflammatory mediators within the dorsal horn of the spinal cord appear to contribute to self-perpetuating pain.[21]

Furthermore, the activation of astrocytes in the anterior cingulate cortex plays a crucial role in the development of negative emotions and long-term potentiation during pain hypersensitivity after peripheral inflammation.[22] Alterations in glial cells (astrocytes and microglia) in cortical and limbic brain regions might be the origin of such emotional and cognitive chronic pain-associated impairments.[23]

Other studies that investigated transition from acute to chronic pain concluded that brain structural differences, most likely existing before the back pain–inciting event and independent of the back pain, predispose subjects to pain chronification. [24]

In addition, TMD patients had diffuse abnormalities in the microstructure of white matter tracts related to sensory, motor, cognitive, and pain functions, with a highly significant focal abnormality in the corpus callosum.[25]

Taken together, our results and the literature findings could raise the hypothesis that impairments on glia cells function could be the key to understanding the coexistence of many factors (e.g. depression, anxiety, muscle hypertonia, sleep problems[26], somatization) associated with chronic pain, including facial pain.

However, what still needs to be determined is whether emotional state is not related with a specific pain condition, but with the process of pain chronification as result of dysregulations of glial functions.

CONCLUSION

Regardless of the group, there was a positive correlation not only between facial pain and depression, but also with somatization, suggesting that these psychological distress factors could participate of TMD chronification process.

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SLEEP QUALITY AND EXPERIMENTAL PAIN SENSITIVITY: A CROSS-SECTIONAL STUDY.

Maisa Soares Gui, Marta C da Silva Gama, Eric Bair, Célia M. Rizzatti Barbosa.

Abstract

Sleep disturbance may contribute to the development and maintenance of pain by contributing to generalized hyperalgesia, however, it is not fully understood which part or function of the peripheral or central nervous systems, associated with sleep problems, could play a role for changes in pain sensitivity. Here we aim to investigate associations with sleep quality and signs of hyperalgesia and allodynia. To access multiple aspects of experimental pain sensitivity we used quantitative sensory testing for comparison between "poor sleepers" (n=1,697) and "good sleepers" (n=2,603) classified according to Pittsburgh Sleep Quality Index. We found that patients with poor sleep quality presented lower pressure pain threshold in facial and bodily sites and lower heat pain tolerance, but no association with allodynia. Although we also observed a different response in mechanical and thermal nociceptive after sensations, no relationship was found between poor sleep quality and second pain (windup), or pain with response of the second order neurons (temporal summation). Therefore we conclude that poor sleep quality is mainly associated with noxious thermal and mechanical stimuli, i.e., hyperalgesia related to decrease in threshold and it has some influence on suprathreshold hyperalgesia.

Introduction

It is well known that increased pain perception and sensitivity may constitute a risk factor for the development of chronic pain [1,2] likewise poor sleep increases the likehood onset of chronic widespread pain (CWP). [3,4]

The possibility that sleep disturbance may contribute to the development and maintenance of pain by contributing to generalized hyperalgesia has also been described. [5,6] However, it is not fully understood which parts of the peripheral or central nervous systems could play a role when hyperalgesia or allodynia have become maladaptive rather than protective. [7]

It has been suggested that sleep continuity disturbance may impair endogenous pain-inhibitory function and increases spontaneous pain, supporting a possible pathophysiologic role of sleep disturbance in chronic pain. [8] Although, a bi-directional association between sleep and pain was also been described, [9,10] the relationship was somewhat stronger for the prospective association of sleep with pain on the following day when compared to prospective association of pain with later sleep. [11]

Not only a prospective study showed that subjects presented poor sleep, somatization and health-seeking behavior, were 12 times more likely to present CWP [3] but also a restorative sleep was independently associated with the resolution of CWP. [4] In addition, the poorer the sleep, the greater the number of tender points in patients with fibromyalgia. [10]

Moreover, sleep deprivation decreased thermal pain threshold [12] and primary insomnia was related to decreased pressure pain threshold at the masseter and decreased heat pain threshold in temporomandibular disorder (TMD) patients. [5] Disrupting slow wave sleep for several consecutive nights was associated with increased pain threshold and fatigue, the same features identified of fibromyalgia patients. [13]

Facial pain is comorbid with widespread bodily pain [14,15] and a heterogeneous multisystem dysregulations may exist in painful TMD. [16,17] As well as fibromyalgia, TMD is classified in the family of central sensitivity syndromes [18,19]

and fatigue, poor sleep, insomnia [5] and sensitivity to noxious and nonnoxious stimuli are features in common. [19,20]

After all, whether sleep problems could provide these hyperalgesic changes, which part of the somatosensory system could be affected by sleep disturbance needs further investigations. [21] Whether sleep problems were related with a specific aspect of pain sensitivity, we could better understand the role of sleep disturbs in chronic pain conditions, e.g. TMD and fibromyalgia.

Thereby, quantitative sensory testing (QST) is a set of valuable tool to access multiple aspects of experimental pain sensitivity. [22] An advantage of QST protocol over electrophysiological methods is its sensitivity to the sensory plus signs of hyperalgesia and allodynia. These QST parameters also characterize the function of the nociceptive system, which is not possible with standard methods of clinical neurophysiology. [23]

Therefore, our aim was to investigate associations with sleep quality and signs of hyperalgesia and allodynia.

Methods

Study design

A cross-sectional study was conducted and subjects, that were enrolled in OPPERA baseline case-control study, [24] were recruited between May 2006 and November 2008 from communities in and around academic health centers at four US study sites: Chapel Hill, NC; Baltimore, MD; Buffalo, NY and Gainesville, FL.

As described elsewhere, [22,25] the OPPERA baseline case-control study used advertisements, emails, flyers and word-of-mouth to recruit people who had chronic TMD and people who did not.

Among 4,300 OPPERA study participants, here we selecting subjects according to sleep quality. People who had poor sleep quality constitute “Cases” and people who had good sleep quality, “Controls”.

The OPPERA study was reviewed and approved by institutional review boards at each of the 4 study sites and at the data coordinator center, Battelle Memorial Institute.

Participants

The OPPERA baseline case-control data contains 1042 subjects with chronic TMD and 3258 TMD-free subjects. The study criteria for all study participants were: aged 18 to 44 years; fluent in English; negative responses to each of 10 question regarding significant medical conditions; no history of facial injury or surgery; not receiving orthodontic treatment; not pregnant or nursing.

In the current study, we used the Pittsburgh Sleep Quality Index (PSQI) for the classification of quality of sleep and as selection group criteria, which provides a score of severity and nature of sleep disorders during the preceding months. The highest score is 21 points, and scores above 5 indicate that sleep quality has been compromised. [5]

The PSQI is the most commonly administered self-report sleep measure. Internal consistency was found to be high, with Cronbach's alpha of .83, and test-retest reliability for Global PSQI scores was .85.7. [26]

All study participants verbally agreed to screening interview done by telephone, and they provided informed, signed consent for all OPPERA study procedures.

Measurements

Quantitative Sensory Testing was conduct in three sensory domains, in the following order: pressure pain, mechanical cutaneous pain, and heat pain. The OPPERA methodological procedure for QST was previously described. [22]

Hyperalgesia Measurement

Briefly, pressure pain threshold were assessed using a commercially available pressure algometer (Somedic; H€orby, Sweden). Five body sites were

tested, bilaterally, in the following order: 1) the center of the temporalis muscle; 2) the center of the masseter muscle; 3) overlying the temporomandibular joint; 4) the center of the trapezius muscle; and 5) overlying the lateral epicondyle. The protocol involved manual application of the algometer, with which the examiner would increase pressure at a steady rate (30 kPa/s), until the participant indicated first pain sensation by pressing a button.

Heat pain sensitivity was assessed using a commercially available thermal stimulator (Pathway; Medoc; Ramat Yishai, Israel). Stimuli were applied on the ventral forearm. Heat pain threshold was determined using a protocol similar to that for PPT. The ATS thermode (2.56 cm^2) was manually placed in contact with the skin at a temperature of 32°C. After a few seconds, the temperature increased at a rate of .5°C/second until the participant pushed a button indicating s/he just then felt a pain sensation.

The temperature of the thermode at the time of the button press was recorded as a threshold estimate. This was repeated 4 times, moving the thermode to a new site on the forearm each time. Following this, pain tolerance was estimated using the same protocol.

The sole difference was that the participant was instructed to press the button when s/he could no longer tolerate the pain. This was repeated 4 times, moving the thermode for each trial. For both threshold and tolerance testing, a ceiling temperature was set at 52°C, which was entered as the threshold or tolerance estimate if the participant failed to press the button on a given trial. For both the threshold and tolerance protocols, participants were first given practice runs on a site distant from subsequent testing, in order to verify the participant's understanding of the protocol.

Allodynia Measurement

Mechanical pain threshold (pricking pain sensitivity) was assessed using a set of weighted probes, manufactured locally, matching those used by the German Neuropathic Pain Network [23,24] . This set of probes had a flat contact area of .2-mm

diameter, and exerted forces between 8 and 512mN. Stimuli were applied to the dorsum of the digits 2 to 4. Measures included pain threshold, ratings of pain intensity in response to the 2 largest stimulus intensities, and temporal summation of pain.

Pain threshold was derived using an adaptive staircase method, calculated as the geometric mean of 5 series of ascending and descending stimulus intensities. If subjects gave 2 ‘‘no’’ responses in a row using the 512-mN probe, the staircase was halted and a value of 512 was used as the threshold value.

Suprathreshold Measurements

Mechanical aftersensation and temporal summation

Suprathreshold cutaneous mechanical pain sensitivity was assessed using a protocol similar to that of the German Neuropathic Pain Network.[23] Participants judged the pain intensity evoked by suprathreshold stimuli, verbally reporting a number between 0 and 100, without a visual reference.

Participants were instructed that ‘‘0’’ represented no pain, while ‘‘100’’ represented the most intense pain imaginable.

Participants reported pain intensity after a single stimulus (applied for approximately .5 sec), and then again after a series of 10 stimuli were applied at 1-second intervals. For the series of 10 stimuli, participants were asked to report an overall pain intensity for the series of stimuli. At 15 and 30 seconds after the series-of-10 stimuli was administered, participants were asked to rate the pain intensity of any residual sensation at the stimulated finger.

Participants were also asked if any residual nonpainful sensations were present at the 30-second time point. This testing series (a single stimulus followed by a series-of-10) was conducted 4 times with the 256-mN probe (probe 6), and then with the 512-mN probe (probe 7).

Temporal Summation of pricking pain (Mechanical Windup) was calculated as the difference between the rating of the series-of-10 stimuli and the rating of the single stimulus.

Heat aftersensation and temporal summation

Following heat pain tolerance testing, participants judged the pain intensity evoked by suprathreshold heat stimuli, verbally reporting a number between 0 and 100. As with pricking pain ratings, participants were instructed that ‘‘0’’ represented no pain, while ‘‘100’’ represented the most intense pain imaginable.

Participants were told that they would receive 10 thermal stimuli in a row, and would be verbally cued to report their peak pain intensity after each stimulus.

Statistical Methods

Participants with a PSQI global score of 5 or greater were classified as cases (poor sleepers) and those with a PSQI global score of less than 5 were classified as normal sleepers (controls). The mean value (and associated standard error) of each QST measure was calculated separately for cases and controls.

Weighted generalized estimated equations were used to test the null hypothesis of no association between sleep quality and each QST measure after controlling for potential confounders similar to the methodology described in Monsees et al. (2009). Generalized estimating equations were used rather than conventional regression models because OPPERA is a case-control study and TMD case status is associated with both sleep quality and pain sensitivity. Thus, TMD case status may confound the association between these variables without appropriate adjustment. Each model also included additional covariates to control for other potential confounding variables.

Three models were calculated for each QST variable. The first model contained covariates for TMD case status plus dummy variables for OPPERA study site. The second model included covariates for case status and study site as well as age, gender, and race.

For both of these models, the coefficient for sleep quality was calculated (which corresponds to the adjusted difference between cases and controls for each

measure) along with the p-value for testing the null hypothesis that this coefficient is equal to 0.

Results

Among 4,300 OPPERA study participants, 1,697 were classified as "poor sleepers" (PSQI>5) and constituted “case” and 2603 participants as "good sleepers" (PSQI<=5) and constituted control group. Sociodemographic characteristics were previously described. [25]

Patients with poor sleep quality presented lower pressure pain threshold in facial and bodily sites and lower heat pain tolerance. However no differences in mechanical pain threshold was found (Table 1).

Table 1. Variation between poor sleepers cases and good sleep controls in hyperalgesia and allodynia measurements.

	Controls		Cases		Adjusted for study site				Adjusted for study site, age, gender, and race			
Stimulus	**Mean**	**SE**	**Mean**	**SE**	**SOR**	**p-value**	**L 95% CI**	**U 95% CI**	**SOR**	**p-value**	**L 95% CI**	**U 95% CI**
Pressure pain threshold												
Temporalis muscle	217,34	1,52	151,07	1,80	0,86	0,0001	0,80	0,93	0,86	0,0001	0,79	0,92
Masseter muscle	201,00	1,39	129,92	1,58	0,88	0,0004	0,82	0,94	0,87	0,0006	0,81	0,94
TM Joint	182,06	1,20	122,23	1,49	0,87	0,0001	0,80	0,93	0,86	0,0002	0,80	0,93
Trapezius muscle	367,36	2,59	277,24	3,88	0,90	0,0030	0,84	0,96	0,90	0,0094	0,84	0,98
Lateral Epicondyle	384,87	2,59	300,55	4,11	0,88	0,0006	0,81	0,94	0,87	0,0007	0,80	0,94
Heat Pain Tolerance												
threshold	46,17	0,04	45,37	0,08	0,89	0,0012	0,83	0,96	0,91	0,0148	0,84	0,98
Mechanical pain threshold												
Threshold	251,95	3,02	157,79	4,20	0,98	0,5119	0,91	1,05	0,97	0,4242	0,90	1,04

We can observe an increase in suprathreshold response because all mechanical after sensations differs between cases and controls and three thermal after sensations had different response when compared with good sleep patients (Table 2).

However, Table 3 shows that no relationship was found between sleep quality and second pain (windup), or pain with response of the second order neurons (temporal summation).

Table 2. Variation between poor sleepers cases and good sleep controls in suprathreshold hyperalgesia measurements.

	Controls		Cases		Adjusted for study site				Adjusted for study site, age, gender, race			
Stimulus	**Mean**	**SE**	**Mean**	**SE**	**SOR**	**p-value**	**L 95% CI**	**U 95% CI**	**SOR**	**p-value**	**L 95% CI**	**U 95% CI**
Mechanical Suprathresold												
Mechanical Single Stimulus (Probe 6)	9,33	0,24	12,59	0,48	1,01	0,8284	0,94	1,08	1,03	0,3796	0,96	1,11
Mechanical Single Stimulus (Probe 7)	17,14	0,36	21,61	0,70	1,05	0,1477	0,98	1,13	1,06	0,1069	0,99	1,14
Mechanical Aftersensation (Probe 6, 15 sec.)	3,14	0,13	6,84	0,40	1,10	0,0154	1,02	1,18	1,10	0,0160	1,02	1,19
Mechanical Aftersensation (Probe 7, 15 sec.)	1,54	0,08	3,90	0,30	1,10	0,0186	1,02	1,19	1,09	0,0263	1,01	1,19
Mechanical Aftersensation (Probe 6, 30 sec.)	8,48	0,27	14,30	0,61	1,15	0,0002	1,07	1,23	1,14	0,0005	1,06	1,23
Mechanical Aftersensation (Probe 7, 30 sec.)	4,83	0,19	8,85	0,49	1,14	0,0006	1,06	1,22	1,12	0,0029	1,04	1,21
Heat Supratheresold												
Thermal Aftersensation (46 degree, 15 sec.)	8,62	0,26	13,27	0,55	1,12	0,0021	1,04	1,20	1,11	0,0051	1,03	1,20
Thermal Aftersensation (48 degree, 15 sec.)	13,22	0,32	19,12	0,65	1,06	0,1000	0,99	1,14	1,05	0,2009	0,97	1,13
Thermal Aftersensation (50 degree, 15 sec.)	15,60	0,35	22,97	0,71	1,11	0,0052	1,03	1,19	1,09	0,0159	1,02	1,18
Thermal Aftersensation (46 degree, 30 sec.)	4,74	0,19	7,60	0,40	1,07	0,0572	1,00	1,15	1,06	0,1295	0,98	1,14
Thermal Aftersensation (48 degree, 30 sec.)	8,31	0,25	12,14	0,52	1,06	0,0888	0,99	1,14	1,05	0,2089	0,97	1,13
Thermal Aftersensation (50 degree, 30 sec.)	9,23	0,27	14,08	0,57	1,10	0,0080	1,03	1,18	1,09	0,0219	1,01	1,17

Table 3. Variation between poor sleepers cases and good sleep controls in temporal summation analyses.

	Controls		Cases		Adjusted for study site				Adjusted for study site, age, gender, race			
Stimulus	**Mean**	**SE**	**Mean**	**SE**	**SOR**	**p-value**	**L 95% CI**	**U 95% CI**	**SOR**	**p-value**	**L 95% CI**	**U 95% CI**
Mechanical												
Mechanical Windup (Probe 6)	9,70	0,22	13,58	0,45	1,02	0,5338	0,95	1,10	1,03	0,4934	0,95	1,11
Mechanical Windup (Probe 7)	17,27	0,29	20,92	0,54	1,05	0,1529	0,98	1,13	1,05	0,2126	0,97	1,12
Heat												
Temporal Summation: First Pulse (46 degrees)	36,88	0,54	43,25	0,95	1,05	0,2120	0,97	1,12	1,02	0,5448	0,95	1,10
Temporal Summation: First Pulse (48 degrees)	45,85	0,57	52,60	0,97	1,04	0,2521	0,97	1,12	1,02	0,6667	0,94	1,09
Temporal Summation: First Pulse (50 degrees)	58,77	0,58	66,12	0,93	1,02	0,5124	0,95	1,10	0,99	0,8082	0,92	1,07
Temporal Summation: Delta (46 degrees)	18,11	0,44	15,61	0,75	1,01	0,7778	0,94	1,08	1,02	0,5984	0,95	1,09
Temporal Summation: Delta (48 degrees)	21,74	0,44	19,81	0,72	1,01	0,7949	0,94	1,08	1,01	0,7008	0,95	1,09
Temporal Summation: Delta (50 degrees)	19,24	0,44	16,98	0,68	1,02	0,5561	0,95	1,09	1,04	0,2464	0,97	1,12
Temporal Summation: AUC (46 degrees)	446,51	5,00	490,60	8,56	1,05	0,1672	0,98	1,13	1,03	0,3942	0,96	1,11
Temporal Summation: AUC (48 degrees)	554,28	4,88	601,75	7,93	1,05	0,1862	0,98	1,12	1,02	0,5370	0,95	1,10
Temporal Summation: AUC (50 degrees)	659,55	4,53	710,36	6,87	1,04	0,2741	0,97	1,11	1,01	0,6963	0,94	1,09
Temporal Summation: Slope (46 degrees)	5,53	0,13	5,20	0,22	1,01	0,7714	0,94	1,08	1,01	0,7320	0,95	1,08
Temporal Summation: Slope (48 degrees)	6,37	0,14	5,83	0,22	1,02	0,6076	0,95	1,09	1,01	0,7552	0,94	1,08
Temporal Summation: Slope (50 degrees)	6,05	0,15	5,45	0,22	1,04	0,3214	0,97	1,11	1,04	0,2428	0,97	1,11

Discussion

Hyperalgesia may include both a decrease in threshold and an increase in suprathreshold response[7] and it is possible that a large number of conditions may cause hyperalgesia and mechanical allodynia.

Regardless of the presence or absence of TMD, our main findings show that poor sleep could be mainly related with decrease in threshold (noxious thermal stimuli) and hyperalgesia of deep tissues (noxious mechanical stimuli), i.e., neurons with free nerve endings. [27] Because patients with poor sleep quality presented lower pressure pain threshold and lower heat pain tolerance.

There is a different response in mechanical and thermal nociceptive after sensations in poor sleep patients, which indicate that sleep problems could be related with increase in suprathreshold response. However, no relationship was found between poor sleep quality and second pain (windup) or pain with response of the second order neurons (temporal summation).

Once windup and temporal summation produces characteristics associated with centrally-mediated hyperalgesia, but is not identical to central sensitization or hyperalgesia, [28] our outcomes indicate that sleep problems could not be directly involved with all central neurologic processes.

In addition, whether mechanical pain threshold were considered allodynia (Ab-fiber function), poor sleep was not associated with pain in response to a nonnociceptive stimulus. Therefore, we can reinforce that poor sleep mainly impairs primary nociceptive neurons function and their nociceptive modulatory systems.

These results could be explained by the fact that sleep problems exerts a specific hyperalgesic effect, which cannot be related with changes in somatosensation in general. [12] For example, the presence of heat hyperalgesia gives evidence for peripheral sensitization, whereas the isolated presence of mechanical allodynia indicates central sensitization [29] and manipulation of the frequency of repetitive thermal stimulation and observation of after-sensations provide further tests of central sensitization. [30]

The mechanisms whereby sleep might interfere in pain processing are still unknown. However, it was confirmed that there is increased tenderness, diffuse myalgia and fatigue over 3 nights of noise-induced disruption of slow wave sleep

(SWS) in normal middle-aged women [31] and also, an analgesic effect related to SWS recovery was found. [32]

Although fibromyalgia patients show distinctive patterns of alpha intrusion in non-REM sleep that was associated with longer duration of pain symptoms and superficial sleep, [33] both REM sleep and SWS interruption (non-REM stage 3 and 4) could decrease pressure pain threshold. [32]

Research in animals and humans showed that serotonin metabolism in the central nervous system plays a role in the regulation of NREM sleep and pain sensitivity. [34] Recent findings show that people with localized TMD may have an upregulated serotonergic pathway, due to a risk index representing combined effects of 6 single nucleotide polymorphisms from the serotonergic pathway associated with greater odds of localized TMD. [35]

Furthermore, amitriptyline proved to be an efficient alternative treatment for chronic pain in TMD patients probably due to your property to reduce the recapture of serotonin in the synaptic gap, increasing your actuation time. [36]

Other studies have shown that partial sleep loss could alter endogenous pain inhibition and subsequent development of spontaneous pain. Disrupted sleep continuity could cause loss of diffuse noxious inhibitory process controls, which refers to the phenomenon whereby one noxious stimulus inhibits the pain produced a second noxious stimulus. [8]

Patients with chronic TMD pain, which had better sleep continuity, were related to better functioning of diffuse noxious inhibitory controls. [37] As well as, a significant negative relationship between inhibitory conditioned pain modulation efficacy and PSQI total score was detected in fibromyalgia patients. [38]

Patients with fibromyalgia also have an impaired mechanism for descending pain inhibition and that this deficiency is paired with a diminished activation of the rostral anterior cingulated cortex and the brainstem, two regions that play an important role in the central pain regulatory system. [39]

In healthy volunteers sleep deprivation produced a significant overnight decrease in heat pain thresholds. Cold pain thresholds tended to decrease also

during sleep deprivation, whereas pain complaints were not induced by sleep deprivation. [12]

All these findings raise the hypothesis that sleep problems could interfere on inhibitory systems and sleep disruption produces maladaptive effects on central pain-modulatory systems. [21,40]

Implications and Limitations

This was a cross-sectional study that prevented temporal conclusions from being drawn, once it remains unclear whether sleep problems occurred before or after hyperalgesia. In addition, only self-report information about sleep was performed, and polysomnography could be providing other valuable insights.

However, our study, with a large sample size, helps to consolidate that sleep disturbances are involved with hyperalgesia, in support of previously work that suggest that sleep disturbances may contribute to the development and maintenance of chronic pain by contributing to generalized hyperalgesia [5] and it does not seem to be directly related with all central processing of pain aspects.

Conclusion

Poor sleep quality is associated with noxious thermal and mechanical stimuli (hyperalgesia) and some influence on suprathreshold hyperalgesia, but it is not associated with allodynia. Neither second pain (windup) nor temporal summation seem to be directly associated with poor sleep quality.

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CONSIDERAÇÕES

A revisão da literatura levantou a complexa interação entre diferentes fenótipos presentes na DTM crônica. Já os demais estudos desenvolvidos mostraram que os aspectos emocionais, a somatização, os sintomas depressivos e a baixa qualidade do sono estão relacionados ao desenvolvimento da dor crônica associada às DTM e à generalização da dor para outras regiões do corpo, associada à incapacidade funcional.

Por definição, para dor crônica (dor que persiste ao longo do tempo) a duração dos sintomas é relevante. Tanto a cronicidade, como a transição tem componentes de tempo que são essenciais para a caracterização da transição da dor aguda para dor crônica. (Larner, 2013)

No entanto, para a ampla compreensão da dor crônica é relevante estudar todo o processo envolvido no desenvolvimento desta condição, o qual foi definido como uma mudança no estado de saúde sobre um período de tempo (Marineau, 2005) e que varia entre os indivíduos. Assim, a dor se torna a doença principal e a amplificação da dor será resultante de alterações no sistema nervoso periférico e central.

Mansour et al. (2013) mostraram que diferenças estruturais no cérebro (substância branca cerebral), provavelmente já existente antes do evento inicial de lombalgia e independente da dor nas costas, predispôs indivíduos a dor crônica. Neste estudo foi encontrada uma função anormal do sistema nervoso central, caracterizada pelo aumento da conectividade de áreas corticais, as quais levariam a cronificação da dor.

Este estudo é relevante na medida em que levanta um caminho fisiopatológico possível para a dor crônica e poderia explicar a grande interação de sintomas relacionados à dor encontrados em nosso estudo.

A dor é tratada como experiência subjetiva com fatores biológicos, psicológicos, e componentes comportamentais associados com dano tecidual real ou potencial. Desse modo, estes fatores podem se inter-relacionar como fatores

desencadeantes e perpetuantes da dor, mas também podem ser resultantes de processos alterados no sistema nervoso central (como a disfunção das células glias).

O aumento da conectividade de áreas corticais e a disfunção glial poderiam ser resultantes das características individuais de percepção das situações cotidianas, do enfrentamento e/ou catastrofização? Ou seja, as características emocionais e comportamentais do indivíduo poderiam levar a tais alterações, as quais resultariam em maior probabilidade para o desenvolvimento da dor crônica a partir de um fator desencadeante? Ou ainda, fatores genéticos e polimorfismos poderiam provocar tais alterações?

Atualmente o modelo biopsicossocial é o frequentemente aceito como modelo para transição da dor aguda para a crônica e enfatiza um complexo interação entre fatores biológicos, psicológicos, comportamentais e fatores sociais no desenvolvimento e perpetuação da dor. (Gatchel et al., 2007)

Além disso, compreender e interpretar os sintomas (crenças e cognições) modula a experiência da dor e previne o desuso e a incapacidade. Com base nas opiniões pessoais e apreciação processos, a pessoa pode optar por ignorar a dor e continuar a trabalhar ou deixar o trabalho, abster-se de todas as atividades, e assumir o papel de doente. (Larner, 2013)

As implicações clínicas deste estudo enquadram-se na prevenção secundária do paciente com dor. O profissional da saúde deve identificar as características do paciente que podem predispô-lo para o desenvolvimento da dor crônica e, desse modo, iniciar uma intervenção precoce, que se preconiza ter enfoque multiprofissional.

Assim, no paciente com dor facial, a identificação precoce destes fatores de risco poderiam evitar o aparecimento da dor generalizada, ou seja, em outros locais distantes do local de dor inicial.

CONCLUSÃO

A partir dos resultados observados neste estudo conclui-se que os aspectos emocionais do paciente, os sintomas físicos não específicos (somatização), os sintomas depressivos e a baixa qualidade do sono podem estar relacionados ao desenvolvimento da dor crônica associada às DTM e à generalização da dor para outras regiões do corpo, a qual está também associada à incapacidade funcional.

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ANEXO 1

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CERTIFICADO

O Comitê de Ética em Pesquisa da FOP-UNICAMP certifica que o projeto de pesquisa **"Análise de polimorfismo do gene receptor micro-opióide (OPRM1) e estudo sobre prevalência, diagnóstico e tratamento alternativo em pacientes portadores de distúrbios do sono, fibromialgia, e disfunção temporomandibular"**, protocolo nº 137/2009, dos pesquisadores Maisa Soares Gui, Célia Marisa Rizzatti Barbosa e Luana Maria Martins de Aquino, satisfaz as exigências do Conselho Nacional de Saúde - Ministério da Saúde para as pesquisas em seres humanos e foi aprovado por este comitê em 27/10/2009.

The Ethics Committee in Research of the Piracicaba Dental School - University of Campinas, certify that the project **"Analysis of polymorphism gene of micro-opioid receptor (OPRM1) and study on prevalence, diagnosis and alternative treatment in patients with sleep disorders, fibromyalgia, and tempormandibular dysfunction"**, register number 137/2009, of Maisa Soares Gui, Célia Marisa Rizzatti Barbosa and Luana Maria Martins de Aquino, comply with the recommendations of the National Health Council - Ministry of Health of Brazil for research in human subjects and therefore was approved by this committee on Oct 27, 2009.

Prof. Dr. Pablo Agustin Vargas
Secretário
CEP/FOP/UNICAMP

Prof. Dr. Jacks Jorge Junior
Coordenador
CEP/FOP/UNICAMP

Nota: O título do protocolo aparece como fornecido pelos pesquisadores, sem qualquer edição.
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