The use of noninvasive neuromodulation in the treatment of chronic pain in individuals with temporomandibular dysfunction

O uso da neuromodulação não invasiva no tratamento da dor crônica em indivíduos com disfunção temporomandibular

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ABSTRACT

BACKGROUND AND OBJECTIVES: Faced with mechanisms of maladaptive neuroplasticity that can generate a memorialization of pain sensation in individuals with temporomandibular dysfunction, the transcranial direct current stimulation emerges as a possible treatment strategy for chronic pain. However, further studies are needed to demonstrate the efficacy of this therapeutic modality and its long-term effect. Thus, the present study aims to discuss the use of transcranial direct current stimulation in the treatment of temporomandibular dysfunction in individuals with chronic pain.

CONTENTS: The present review encompasses 40 articles, published between the years 2000 and 2016. The temporomandibular dysfunction is a disease characterized by a set of signs and symptoms that may include joint noise, pain in the muscles of mastication, limitation of mandibular movements, facial pain, joint pain and/or dental wear. Pain appears as a very present and striking symptom, with a tendency to chronicity, a condition that is difficult to treat and often associated with psychological factors such as anxiety and depression. Studies using transcranial direct current stimulation in patients with chronic pain symptomatology have been showing good results through neuromodulation of neuronal excitability. It is worth noting that it corresponds to a non-invasive technique, low cost, easy and quick to apply, besides having minimal adverse effects.

CONCLUSION: The transcranial direct current stimulation has shown promising results in the treatment of temporomandibular dysfunction pain, with the possibility of becoming a complementary technique to the existing treatments, and thus, providing a professional assistance of better quality and resolution to the patient with this disorder.

Keywords: Analgesia, Facial pain, Rehabilitation, Temporomandibular joint disorders, Transcranial direct current stimulation.

INTRODUCTION

Temporomandibular disorder (TMD) is a pathological condition that encompasses clinical problems related to masticatory musculature, temporomandibular joint (TMJ), or both structures¹. In many cases, individuals with this disease present pain as the most striking symptom, which may be
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Contents

This is a bibliographic survey carried out between January and September of 2016 in Pubmed and Virtual Health Library (BIREME), chosen due the fact of aggregating different databases, both international and national. Some books and several articles were selected, published between the years 2000 and 2016, which approached the theme of the present study. Descriptors such as “Analgesia”, “Orofacial pain”, “Transcranial direct current stimulation”, “Rehabilitation”, “Temporomandibular joint disorders” were used. 40 articles were selected to compose the literature review, since they fit the objective of this study.

TMD is a subgroup of craniofacial pain, constituting the main cause of orofacial pain of non-dental origin that may involve masticatory muscles, TMJ and/or associated structures. It has been defined as a pathological condition characterized by a set of signs and symptoms that may include joint noises, pain in the mastication muscles, limitation of mandibular movements, facial pain, headache, joint and/or dental wear. It is observed that the symptoms manifest themselves in a varied form, being related to the anatomical components that collapse by the disorder, depending on the physiological tolerance of each structure of the stomatognathic system.

It is estimated that approximately 40 to 60% of the population presents some detectable clinical signs of TMD, being more frequent in people between 20 and 40 years old. A very prevalent disease whose etiology is considered complex and multifactorial, being the result of an interrelationship between some main etiological factors: occlusal condition, trauma, psychological alterations, sources of deep pain stimulus and parafunctional activities. Studies in the behavioral area observed that TMD was often related to psychopathologies, which may present as a initiating, precipitating and even perpetuating factor.

TEMPOROMANDIBULAR AND EMOTIONAL DISORDERS

Pain appears in a very marked and present way in the TMD and may affect the development of daily activities, physical and psychosocial functioning, as well as the quality of life (IASP-International Association for the Study of Pain). Especially when chronic, pain is related to emotional factors, such as anxiety and depression, possibly due to a sharing and proximity of neural pathways of processing. Studies performed with patients with chronic TMD corroborate this relationship when they observe a positive correlation between the severity of this disease and the levels of anxiety and depression presented by the patients. In addition, women showed a greater propensity to present emotional stress and concomitant psychiatric disorders.

PAINFUL SYMPTOMS

According to IASP, pain is defined as an unpleasant sensory and emotional experience, being associated with or related to actual or potential tissue damage. Approximately 10% of the world population presents facial pain due TDM (IASP), and this painful symptom may be characterized as acute or chronic. Acute pain has a physiological and protective character, is self-limiting and responds to conventional therapies. It usually ceases after treatment of the causative factor. Chronic pain, however, does not have a biological character and persists after removing the cause, with a tendency not to respond...
to conventional therapies, requiring a multidisciplinary treatment to control pain.\textsuperscript{1,30}

Even eliminating the nociceptive stimulus, pain will not subside, because learning-related neuroplasticity mechanisms can lead to a memorization of the pain sensation\textsuperscript{1,13}, making it chronic, especially if it is a constant pain condition, without periods of complete remission\textsuperscript{1}. This memory for pain is due to functional and structural changes in the synapses underlying the painful experience, due to a repetitive pain stimulus that reinforces this circuit, and culminates in the establishment of brain memory traces that maintain the sensation of pain\textsuperscript{1,31,32}.

The painful experience is a complex phenomenon, which can be physiologically initiated by a somatic factor, but its permanence results from important structural and functional cortical modifications such as cortical atrophy and neuronal hyperactivity in different regions of the central nervous system (CNS)\textsuperscript{31,32}. It involves brain areas responsible for emotion, perception, motor planning, behavior and memory, such as the anterior insula, anterior cingulate cortex, somatosensory, motor area, limbic system and thalamus\textsuperscript{31-33}.

Studies observed that neuronal circuits responsible for the pain and emotion processing are associated, one overlapping the other, suggesting a mutual influence relationship\textsuperscript{3,4,28,29}. Based on these data, the principle that painful sensation does not depend only on the nature and intensity of the stimulus is reinforced. It is a multidimensional experience composed of emotional, sensory, and cognitive aspects\textsuperscript{3,4,9}. Thus, the chronic pain understanding should address the concept of learning, emotional and motivational state, as well as memory mechanism\textsuperscript{1,31}.

In view of the complexity and multidimensionality of painful experience, the diagnosis of TMD should be judicious, including the patient’s history, clinical examination and complementary tests, and the information collected mainly during anamnesis\textsuperscript{1}. It requires a research for psychological, physical and social factors, and a multidisciplinary team is usually required\textsuperscript{6,10,30,34}.

THERAPEUTIC ALTERNATIVES

In view of the above, when it comes to chronic pain, the mechanistic model of treatment is insufficient, and the dental surgeon must understand the man as a biopsychosocial being in order to implement and/or refer the patient to the most indicated alternative therapy. Some aim to treat the musculature, others act on dental occlusion or joint structures and there are those whose main focus is the psychoemotional factor\textsuperscript{6,10,30,34}.

In dental area, there are several treatment modalities for TMD, since this disease has a variety of symptoms. These include patient education in relation to self-care, behavior modification (including relaxation techniques), drugs, physical therapy, acupuncture, stabilizing occlusal plates, occlusal therapy (orthodontics, oral rehabilitation) and surgery. The need to give preference to reversible and non-invasive procedures is emphasized. Thus, invasive procedures such as surgical, orthodontic and occlusal adjustment are not first-choice treatments and their efficacy is still questionable\textsuperscript{1,35,36}. Among the therapies promoted by professionals from other areas are biofeedback, iontophoresis, ultrasound, transcutaneous electrical nerve stimulation (TENS), cognitive-behavioral therapy and meditation\textsuperscript{1,35,36}.

Despite the wide variety of strategies used to treat patients with TMD, some patients have a temporary and/or unsatisfactory relief response, generating hypotheses that emotional components often underlie treatment refractoriness and development of a memory for pain\textsuperscript{1-5,10,12,31}.

Given that chronic pain generates structural and physiological changes in the cerebral cortex, and these, in turn, are not irreversable\textsuperscript{11}. Thus, it is evident the need for a therapy that acts directly on the CNS. This action can occur through drugs, however, many individuals are refractory or present adverse effects, such as dependence and/or tolerance\textsuperscript{1,35,36}. Therefore, the importance of new treatments involving neuromodulation and neuroplasticity mechanisms is detached, such as TDCS, which can be a complementary alternative to the different types of treatment already in use\textsuperscript{12,13}.

Transcranial direct current stimulation

Neuromodulation techniques include TDCS, which is based on the use of a continuous electric current with the objective of modifying the neuronal membrane potential and consequently changing the pattern of cortical activity, besides restoring the normal activation of the centers processing the pain\textsuperscript{13,15,16,26}.

TDCS apparatus has two electrodes: an anode (positive pole) and a cathode (negative pole) that generate a low intensity DC current. Depending on the assembly, the flow will be either anodic, cathodic or both, where anodic stimulation results in increased neuronal excitability, while cathodic stimulation results in the opposite effect\textsuperscript{12,13}. In addition to interfering with the neuronal activity of areas located just below the electrodes, this technique also affects the interconnected cortical and subcortical regions\textsuperscript{16,17}.

TDCS effects can be divided essentially into neuromodulatory and neuroplastic. The first corresponds to the change generated in the resting potential of the membrane, without significant effects on the synaptic plasticity. On the other hand, secondary effects occur due to modifications of the synaptic force after the stimulation period, being dependent on the modulation of GABAergic and glutamatergic synapses. Thus, TDCS efficacy is influenced by the current density applied, which involves the stimulation duration, current amplitude, location and electrode size. In general, the stimulation parameters used are: duration between 5 to 30 minutes, intensity of 0.5 to 2.0 mA, size of the electrodes between 20 and 35cm²\textsuperscript{37}.

It is a simple, low-cost, safe, non-invasive, well-tolerated, and painless technique that can modulate brain activity locally, presenting therapeutic effects\textsuperscript{13,15,17,38}. These favorable characteristics stimulated the development of several clinical studies.
involving neurological and psychiatric disorders such as major depressive disorder, acute and chronic pain, motor rehabilitation, drug dependence, among other diseases \(^8\).

The application of active stimulation protocols has shown promise in some studies, with good results regarding the reduction of painful symptoms in patients with chronic pain, when compared to placebo stimulation \(^1^5^-^1^8,^2^2\). TDCS studies obtained a significant analgesic effect through anodic stimulation in the primary motor cortex (M1) \(^1^5,^1^7,^1^8\), possibly due to the secondary activation of the ipsilateral thalamus and other regions related to the pain processing and modulation, such as the cingulate cortex, prefrontal cortex and estriatum \(^1^2,^1^9\). Evidence also indicates that M1 cortex stimulation inhibits the activity of the ipsilateral primary somatosensory cortex (S1) \(^4^0\). For this purpose, the anode is positioned on the contralateral M1 cortex in the affected side in case of unilateral pain or on the M1 of the dominant hemisphere in case of bilateral pain, and the cathode on the supraorbital region contralateral to the anode \(^1^5,^1^7^-^1^8,^4^1\). This therapeutic effect on pain after stimulation of the M1 region was reproduced in different groups of patients with chronic pain resulting from diseases such as trigeminal neuralgia, TMD, post-stroke pain and fibromyalgia \(^1^3,^1^7,^1^8\). However, there is another option of assembly, applying the anode in the dorsolateral region of the left prefrontal cortex (DLPFC), which has also been demonstrating therapeutic effect \(^1^5,^1^6,^1^9,^4^1\), since this region shows a significant analgesic effect through anodic stimulation in the primary motor cortex \(^1^5\), possibly due to the second- ary activation of the ipsilateral thalamus and other regions related to the pain processing and modulation, such as the cingulate cortex, prefrontal cortex and estriatum \(^1^2,^3^9\). Evidence also indicates that M1 cortex stimulation inhibits the activity of the ipsilateral primary somatosensory cortex (S1) \(^4^0\). For this purpose, the anode is positioned on the contralateral M1 cortex in the affected side in case of unilateral pain or on the M1 of the dominant hemisphere in case of bilateral pain, and the cathode on the supraorbital region contralateral to the anode \(^1^5,^1^7^-^1^8,^4^1\). This therapeutic effect on pain after stimulation of the M1 region was reproduced in different groups of patients with chronic pain resulting from diseases such as trigeminal neuralgia, TMD, post-stroke pain and fibromyalgia \(^1^3,^1^7,^1^8\). However, there is another option of assembly, applying the anode in the dorsolateral region of the left prefrontal cortex (DLPFC), which has also been demonstrating therapeutic effect \(^1^5,^1^6,^1^9,^4^1\), since this region shows to be hypoactive in individuals with chronic pain \(^1^7^-^1^9\).

Although less explored, stimulation in DLPFC region may be a useful strategy to modulate affective-emotional cognitive networks associated with pain processing in patients with chronic pain, changing their perception through cortico-subcortical and cortico-cortical pathways, since this area seems to play an important role in the cortical processing of the pain emotional aspects \(^1^9,^4^1,^4^2\). Thus, it could be a good alternative in cases of chronic pain, in which the emotional components are often underlying the treatment refractiveness, possibly due to an anatomical relationship of quite proximity between the circuits of pain and emotions \(^3^1,^3^4,^3^8\).

Although TDCS seems to be an easy-to-use instrument, there is a minimal risk of serious adverse effects \(^4^3\). Through a systematic review, the most common side effects of active TDCS were pruritus (39.3%), tingling (22.2%), headache (14.8%), discomfort (10.4%), and burning sensation (8.7%) \(^4^3\). Thus, researches should follow protocols for TDCS application, which include parameters such as duration, intensity, standardization of adverse effects assessment and reports, among others \(^4^4\). Although the aforementioned technique has potential for pain management, the limited number of available randomized clinical trials and their heterogeneous results evidences the need for further scientific investigations regarding the technique efficacy, in order to identify the optimal stimulation parameters (intensity, repetition rate, time, electrode positions and stimulation polarity) since the stimulation protocols optimization in relation to specific populations of patients is an important aspect in the efficacy of said therapeutic technique, as well as to monitor its analgesic effects and probable psychological repercussion in the short, medium and long term \(^1^6,^1^9^-^2^2\).

**CONCLUSION**

TDCS has shown promising results in the treatment of chronic TMD pain, whose technique's differential involves a direct action in the CNS, through the neuromodulation of the painful stimulus' processing centers. Thus, it presents itself as a possible therapeutic strategy, aiming to complementing the range of existing treatment alternatives.

**REFERENCES**


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