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Diagnosis and treatment methods of central sensitization in temporomandibular disorders

Metody diagnostyki i leczenia centralnej sensytyzacji w dysfunkcjach skroniowo-żuchwowych

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Summary

Central sensitization (CS) occurs in many cases of chronic pain disorders. CS takes place within the central nervous system and manifests itself as intensified nociceptive signaling. The increased membrane excitability and synaptic efficacy present in this neuroplastic mechanism influence the development and intensification of pain associated with temporomandibular disorders.

In the following article, potential benefits of various diagnostic and therapeutic methods are presented. Traditional approaches in managing this disorder have been analysed as well as new alternative and innovative therapies that are still gaining importance in the medical fields.

Diagnostic methods such as comprehensive clinical assessment, detailed history taking and analysis of psychosocial aspects of the patient are essential components of accurate identification of the problem. To alleviate symptoms related to central sensitization effectively, a multifaceted approach is recommended, incorporating various

Streszczenie

Centralna sensytyzacja (CS) występuje w przypadku wielu przewlekłych schorzeń bólowych, których podłożem są zmiany w centralnym układzie nerwowym, manifestujące się wzmożonym sygnałem nocyceptywnym. Występująca w tym mechanizmie neuroplastycznym wyższa pobudliwość błon i skuteczność synaptyczna, wpływa na rozwój i nasilenie bólu związanego z zaburzeniami skroniowo-żuchwowymi.

W poniższej pracy zostały przedstawione potencjalne korzyści wielu metod zarówno diagnostycznych jak i terapeutycznych. Przeanalizowano tradycyjne podejście w leczeniu tego schorzenia, a także terapie nowe, alternatywne i innowacyjne, które dopiero zyskują na znaczeniu w dziedzinach medycyny. Metody diagnostyczne, takie jak kompleksowa ocena kliniczna, szczegółowy wywiad, czy analiza aspektów psychospołecznych pacjenta, stanowią nieodzowny element diagnostyki i postawienia prawidłowego rozpoznania. W celu skutecznego

aspects of CS. Based on numerous scientific publications, possible therapeutic approaches have been developed that may aid the dentists in alleviating symptoms associated with central sensitization.

A multidisciplinary and integrated combination of psychological, physical and pharmacological interventions appears to be the key to optimal management and reduction of symptoms associated with the presence of central sensitization in patients.

łagodzenia objawów związanych z CS, zaleca się podejście wielopłaszczyznowe, w którym terapia uwzględnia różnorodne aspekty tego zjawiska. Na podstawie wielu publikacji naukowych opracowano możliwe podejścia terapeutyczne, które mogą być pomocne lekarzom dentystom w minimalizowaniu objawów związanych z centralną sensytyzacją.

Wielodyscyplinarne i zintegrowane połączenie działań psychologicznych, fizycznych i farmakologicznych wydaje się być kluczem do optymalnego postępowania i niwelowania objawów związanych z obecnością centralnej sensytyzacji u pacjentów.

Introduction

Central sensitization (CS), occurring in various chronic pain conditions, is a neuroplastic mechanism that takes place within the central nervous system, associated with increased sensitivity and response to pain.[1,2] Enhanced neuronal function in nociceptive pathways is caused by higher membrane excitability and synaptic efficacy. This mechanism indicates the neuroplastic capabilities of the human nervous system in response to external stimuli inducing inflammation.[3,4] Central sensitization is responsible for altering patients' sensitivity when encountering pain.[3] The hypersensitivity associated with CS is triggered by a difference in sensory response caused by neutral stimuli that should not elicit any negative sensations.[3,4] Consequently, even mild stimuli can evoke an exaggerated pain response, significantly impacting the quality of patients' life.

Central sensitization also occurs in the context of temporomandibular disorders (TMD). Dysfunction in processing pain signals originating in this area, leads to an increased pain response. Often, central sensitization can be the primary factor causing chronic pain in TMD disorders.[5]

Acute pain, lasting less than three months, is a protective mechanism informing the human body of tissue damage, and can be controlled effectively.[6] Chronic pain persisting for more than three months is more challenging to diagnose and manage due to its complex etiology and pathogenesis.[7] Central sensitization is a component of chronic pain characterized by allodynia, hyperalgesia and radiation to areas distant from the primary damage.[8,9] Chronic pain in the orofacial region is often caused by nerve damage, tissue inflammation in this area and temporomandibular joint dysfunction. Additionally, it is often associated with various comorbid conditions such as depression, anxiety, stress, or sleeping disorders.[10] Both central and peripheral sensitization are believed to contribute to the aforementioned features of chronic pain.[9]

During the initiation process of the disease, two processes are particularly important in chronic muscle pain and TMD disorders, primarily affecting areas innervated by the trigeminal nerve. One of them is sensitization initiated by the activation of N-methyl-D-aspartate (NMDA) receptors, while the other is the weakening of inhibitory mechanisms associated with gamma-aminobutyric acid (GABA) and glycine receptors.[3,11-13]

Additionally, activation of NMDA receptors associated with abnormalities in the peripheral and central nervous systems leads to neuronal stimulation and the onset of chronic pain.[7,14,15] On the basis of researches by *Kimura* et al. and *Zhang* et al., it can be stated that regulation and activation of NMDA receptors within the course of the trigeminal nerve initiate intracellular cascades through calcium ion influx and protein kinase activation. This, in turn, regulates membrane excitability and increases nociceptive flow, resulting in the development of chronic inflammatory and neuropathic pain.[7,16,17]

This intensified, prolonged and repetitive reactivity of nociceptive receptors can lead to the phenomenon known as "wind-up".[18,19] There are many studies in which the terms "wind-up" and "central sensitization" are treated as synonyms.[18] However, according to *Woolf*, they are distinct phenomena and should not be confused. "Wind-up" mainly refers to the induced response resulting from repetitive synchronous stimulation of C fibers, usually occurring in experimental conditions.Central sensitization, on the other hand, arises from the asynchronous activation of primary afferent fibers, often induced by tissue or nerve damage. Nevertheless, it can be assumed that the "wind-up" phenomenon is one of several factors involved in initiating the process of central sensitization.[18,19]

Nociceptors in the temporomandibular joint can sensitize neurons in the central nervous system, especially within the trigeminal nerve nuclei.[13,20] Neurons in this area have more receptors associated with pain neurotransmitters.[13] Based on animal models, it has been observed that glutamate administration to the temporomandibular joint sensitizes nociceptors, thus increasing the area of facial skin where pain reactions occur, indicating the presence of central sensitization.[13,21] Additionally, patients with temporomandibular joint arthralgia exhibit increased sensitivity to pressure within the temporomandibular joint and stimulation of surrounding structures such as muscles or skin. This indicates a more generalized change in pain processing in the central nervous system resulting from persistent nociceptive stimuli from the painful temporomandibular joint area.[13,22]

Effective diagnosis and treatment of central sensitization in temporomandibular joint disorders are very demanding tasks for dentists. Many patients struggling with this problem experience recurrent pain despite therapy, and are not satisfied with the treatment outcomes. Dentists should approach each patient individually, using comprehensive and targeted therapeutic methods. This article will present basic diagnostic techniques that may be effective in diagnosing central sensitization and therapies that could potentially be applied to its treatment.

Diagnosis of central sensitization

Traditional diagnostic methods used in diagnosing central sensitization

The primary method in diagnosing central sensitization should involve a thorough patient interview during which the physician assesses the possibility of neuropathic pain, and differentiates its origin towards nociceptive pain or central sensitization.[23]

Neuropathic pain is characterized by sensations of burning, numbness, tingling, stabbing, and throbbing. It is accompanied by sensory disturbances, which can be categorized into positive symptoms, suggesting nervous system hyperreactivity, and negative symptoms, indicating loss of its function. Additionally, autonomic nervous system symptoms such as redness and sweating may occur.[23] Neuropathic pain is initially localized in the area innervated by the damaged nerve but can

gradually spread to other areas of the body.[23,24] Nociceptive pain is initially localized to the site of injury or tissue dysfunction, and typically subsides upon the removal of the causative factor. The absence of symptoms indicating nociceptive or neuropathic pain suggests a diagnosis of central sensitization.[23,25] In this case, pain often localizes in areas unrelated to the primary source and location of the cause. It is characterized by continuity, persistence and difficulty in description of symptoms by the patient. Often, there is no evidence of its occurrence in any diagnostic test results, and the pain associated with central sensitization can be described as "neuroanatomically illogical".[23]

In their review, *Kosińska* et al. mentioned three criteria that, during an interview, enable the physician to diagnose or exclude central sensitization.[23] When the first two criteria are met, the presence of central sensitization is very likely to be acknowledged. If only the first criterion is met, the interview should be continued, and the third criterion should be applied.[23,25]

The first criterion suggests that pain in central sensitization is disproportionate to the nature and extent of the pathology the patient is dealing with. The discomfort experienced by the patient is not proportional to the primary cause of pain and may not be directly related to the area of damage or pathology.[23,25,26]

The second criterion relates to specific characteristics of pain associated with central sensitization. Patients describe the pain as of a diffuse nature.[23,25] Additionally, there is hypersensitivity to stimuli that are normally non-painful, known as allodynia, and also an increased sensitivity to painful stimuli, known as hyperalgesia.[23,25,26] Simple techniques such as a light touch in the painful area can be used in physical examination to confirm allodynia, and light pricking or testing reactions to cold or warm stimuli in the case of hyperalgesia.[23,25]

The third criterion applies to the characteristic hypersensitivity in central sensitization, which is not limited to just the musculoskeletal system.[23,25,26] It may manifest itself not only as an increased pain response but also in reactions induced by chemical substances, temperature changes, electrical stimuli, stress or emotions. The interview with the patient should include questions about hypersensitivity to the aforementioned stimuli and their potential occurrence before the onset of painful symptoms.[23]

To conduct an assessment of the third criterion, a special questionnaire, the "Central Sensitization Inventory" – Part A (CSI), developed by *Mayer* et al., can be used. The questionnaire evaluates the severity of 25 symptoms associated with central sensitization. Each symptom is assessed on a scale from 0 (never) to 4 (always), resulting in a total score ranging from 0 to 100. If the questionnaire score is at least 40 points, and the patient simultaneously meets the first criterion – the presence of disproportionate pain, it can be assumed that the patient is experiencing pain resulting from central sensitization due to chronic pain syndrome.[23,26]

Imaging techniques of central sensitization

A review of available literature indicates a limited number of studies confirming the effectiveness of imaging tests in diagnosing central sensitization.

Magnetic resonance imaging (MRI) is a non-invasive diagnostic method that allows the imaging of various areas of the human body without the use of ionizing radiation.[27] According to studies conducted by *Cagnie* et al., based on MRI results, the presence of central sensitization may be associated with reduced gray matter volume in specific areas of the brain. These findings mainly concern brain areas related to pain and stress processing, such as the cingulate gyrus, insula, prefrontal

cortex, and parahippocampal gyrus.[28] Based on research by *Cifre* et al., *Cagnie* emphasizes that the anterior part of the cingulate gyrus and the insula are the main areas associated with transforming the affective components of pain.[28,29] The affective factors include anxiety or depression, which may alter pain perception.[30] Also, changes in pain processing are associated with chronic pain disorders, such as in the case of central sensitization.[31]

Based on the aforementioned studies, it can be assumed that MRI may be a helpful method in observing changes associated with central sensitization. Nevertheless, further research is needed to confirm the effectiveness of imaging tests in diagnosing central sensitization.

Treatment methods for central sensitization coexisting with temporomandibular dysfunction

The use of occlusal splints

Occlusal splints, also known as bite splints, are commonly used to relax masticatory muscles, prevent overload injuries to the temporomandibular joint (TMJ), protect teeth, and also manage and control headaches.[32] Patients treated with occlusal splints experience a change in the direction of occlusal forces, resulting in reduced strain on the TMJ structures and the surrounding structures.

Quoting the findings of a review by *Kapos* et al., peripheral sensitization of nociceptive neurons is not a sufficient mechanism to explain prolonged nociceptive reactions of masticatory muscles, suggesting that central sensitization mechanisms are also involved.[33] According to studies by *Xie* et al. performed on animal models, experimentally induced occlusal changes can contribute to the development of disorders and damage to the TMJ, masticatory muscles, and the nervous system.[34]

Changes in occlusion can induce diverse patterns of brain activity.[35] Based on the review by *Kapos* et al., it was found that the use of occlusal splints by patients, mainly during a night rest, leads to a short-term relief of pain associated with central sensitization of the TMJ.[33] Studies by *Kordas* et al. and *Ohkubo* et al. demonstrated that the use of splints may also decrease the activity of the brain and the masticatory muscles.[35-37] Based on the analysis of the above-mentioned studies, it can be concluded that the use of occlusal splints, by reducing muscle tension, may limit the activity of nociceptors responsible for the development of central sensitization in the temporomandibular region.

The use of splints enables achieving proper, symmetrical jaw movements, preventing unilateral strains. Simultaneously, cerebellar activation occurs, initially in the right hemisphere, and over time, as jaw movements become more balanced and symmetrical, in the left hemisphere.[35,38,39] Additionally, reduced activity of the insula leads to a reduction in pain symptoms.[35,40]

Patients with temporomandibular joint disorders exhibit abnormal responses of the cerebral cortex, as well as decreased motor function and cognitive capacity. This suggests an association between disorders in the stomatognathic system and the nervous system.[35,41] Patients with diagnosed temporomandibular dysfunction demonstrate increased anxiety, which is processed in the anterior part of the insula.[35,38] The use of occlusal splints may help reduce psychological tension and alleviate pain associated with anxiety by decreasing insular activity.[35]

In their publication, *Lickteig* et al. demonstrated that the use of occlusal splints was associated with a reduction in pain perception, which was more noticeable during jaw movements and to a smaller extent at rest. Pain reduction in this situation was associated with changes in blood oxygenation levels in the brain.[35,39]

Pharmacological treatment

Pharmacological treatment is an important element of therapy for temporomandibular disorders, including central sensitization, which aims to alleviate pain and reduce inflammation.

Non-steroidal anti-inflammatory drugs (NSAIDs) are the most commonly used group of drugs in the treatment of headaches, also in the temporomandibular region. These medications act by inhibiting cyclooxygenase, preventing the formation of pro-inflammatory prostaglandins.[5] In a study conducted by *Ta* et al., it was shown that naproxen significantly reduced clinical symptoms associated with TMJ problems.[42] *De Carli* et al. demonstrated that piroxicam, a cyclooxygenase-2 (COX-2) inhibitor, most effectively reduced TMJ pain during a month-long study.[43] However, according to studies conducted by *Woolf*, drugs that are not effective in treating central sensitization include NK1 receptor antagonists and COX-2 inhibitors. It should be noted, however, that COX-2 inhibitors are effective if central sensitization is induced by peripheral inflammation.[11] Apart from using NSAIDs in the form of oral medications, topical NSAIDs such as diclofenac may also be helpful in relieving pain associated with central sensitization of the TMJ. In studies by *Businco* et al., topically used diclofenac was proven to be very effective in treating symptoms of TMJ dysfunction, and there were no adverse effects associated with oral administration of the drug.[44]

Antiepileptic drugs, such as gabapentin and pregabalin, reduce neuronal excitability. Both have broad applications in the treatment of chronic pain in the maxillofacial area.[5] Due to their structural similarity to the inhibitory neurotransmitter GABA, they represent a therapeutic option in the treatment of neuropathic pain associated with TMJ disorders.[45] Studies by *Kimos* et al. showed that gabapentin had a significant beneficial effect on reducing pain in the TMJ area and the surrounding masticatory muscles.[46]

Rehabilitation

Temporomandibular disorders include a range of conditions affecting both the joint itself and its surrounding structures. They lead to pain, muscle tension and functional disturbances. Rehabilitation in the form of physiotherapy and physical therapy plays an important role in alleviating symptoms and improving the function of the masticatory apparatus.

Based on research conducted by *Kapos* et al., it can be inferred that physiotherapeutic treatments performed during the occurrence of pain in the muscles surrounding the temporomandibular joint significantly improve patients' quality of life and eliminate unpleasant symptoms. In the cited study, manual therapies showed greater effectiveness than the use of occlusal splints or transcranial direct current stimulation (tDCS).[33]

A variety of physiotherapeutic activities can significantly facilitate the control of temporomandibular disorders by improving jaw mobility, strengthening masticatory muscles and correcting postural abnormalities. According to studies by *Mienna* et al., patients experiencing pain in the TMJ area, whether local or generic, reported improvement after regularly performing supervised exercises of the neck muscles and of the musculoskeletal system of the masticatory apparatus.[47]

Transcranial Ultrasound Stimulation (TUS) is a non-invasive procedure used in the treatment of musculoskeletal disorders, including acute injuries of soft tissues, overuse syndromes, as well as chronic rheumatic diseases.[48] This therapy could be a potential treatment method for chronic pain associated with central sensitization of the TMJ. Further research is needed to confirm the effectiveness and optimal parameters of TUS in managing pain associated with central sensitization of

the musculoskeletal system of the masticatory apparatus.

Transcutaneous Electrical Nerve Stimulation (TENS) is used to reduce muscle activity, including that of the masticatory apparatus.[49] Mechanism of TENS is based on the theory of pain transmission and blockade through the stimulation of nerve fibers.[50]

Microcurrent Electrical Nerve Stimulation (MENS) is another therapeutic method using electrotherapeutic current which, when applied to the site of injury, evens out the flow, thus helping in the repair of damaged tissue. In their studies, *Saranya* et al. found that TENS and MENS could be used as a first-line therapeutic option for patients with acute and chronic pain in the muscles of the masticatory apparatus.[50] TENS and MENS, as therapeutic methods, could bring many benefits in managing pain associated with central sensitization of the TMJ. The effectiveness of these therapies may vary among patients, and optimal stimulation parameters, similarly as in the case of TUS, should be established and set in future researches.

Combining different physical therapies and integrating them into a comprehensive treatment plan may yield better results for patients struggling with central sensitization of the TMJ. The described treatment methods, by alleviating pain and muscle tension, could significantly improve patients' quality of life. However, further research is necessary to confirm their effectiveness and long-term effects.

Behavioral, psychological, and cognitive-based therapies

Traditional pharmacological and physical approaches provide symptomatic relief in temporomandibular disorders but often are insufficient in addressing the underlying mechanisms of central sensitization. Behavioral and psychological therapies become an equally important method by promoting relaxation, improving pain coping strategies, and by modifying patients' cognitive and emotional processes.

Cognitive-behavioral therapy (CBT) is one of the best known forms of psychotherapy. In this psychological-therapeutic approach, it is assumed that all learnt behaviours can be unlearnt and then relearnt.[51] Its goal is to modify patterns of thoughts and actions that negatively impact human well-being.[54] In the context of TMJ disorders, CBT could help patients identify and modify thoughts and behaviours associated with pain. According to research conducted by *Minakuchi* et al., the impact of CBT on managing chronic pain was assessed as minor due to the limited availability of well-designed studies.[52] Therefore, further research is needed to determine whether CBT could positively influence pain perception and overall standards of living in patients with central sensitization of the TMJ.

Biological feedback, also known as biofeedback, is a therapeutic technique that enables patients to increase awareness and control over certain physiological functions, such as muscle tension.[52,53] By learning to manage and regulate these functions, patients can influence their experience of pain and reduce its intensity.[52] Electromyographic (EMG) biofeedback is used to provide direct responses from the muscles. It is based on continuous feedback of EMG signals recorded in a specific muscle, whose function is supposed to be modified.[54]

Studies by *Florjanski* et al. showed that biofeedback therapy was useful in reducing masticatory muscle activity.[53] Additionally, in studies by *Criado* et al., we can find information regarding the effectiveness of EMG-biofeedback therapy in treating patients with occlusion-related pathologies, such as teeth clenching, soreness, tenderness, and stiffness of the masticatory muscles, as well as other

temporomandibular disorders.[54] By providing real-time feedback, biofeedback allows patients to learn to regulate their physiological responses, enabling them to improve their pain-coping mechanisms.[53,54] Biofeedback has shown promising results in managing pain associated with temporomandibular joint disorders and may also have benefits in coping with central sensitization.[52]

Cognitive-based interventions, such as neurobiological pain education and cognitive restructuring, aim to educate patients about the origins of pain. By promoting a better understanding of pain mechanisms, these interventions can help patients change their perspective on their pain experiences and reduce fear and pain-related anxiety.[55]

Mindfulness-based stress reduction (MBSR) is a method, which combines meditation, yoga and body awareness techniques to cultivate consciousness and acceptance of the present moment. MBSR has proven its effectiveness in reducing pain and improving psychological well-being in various chronic pain conditions.[56] As part of a comprehensive treatment plan for central sensitization of the TMJ, MBSR could help patients cope with pain and regulation of emotions.

In cases of diagnosed central sensitization of the TMJ, personalized treatment plans are crucial for optimal healing outcomes. Dentists should take into account individual patient characteristics, pain severity, psychosocial factors and treatment preferences when adjusting the therapeutic plan. Collaboration with psychotherapists and psychologists is advisable. A combination of multiple approaches into a congeneric treatment plan can address the multifaceted nature of central sensitization. Behavioral and psychological therapies, by modifying negative cognitive processes and by improving pain coping mechanisms, complement traditional pharmacological approaches and physical therapies. Such approaches should be considered in cases where conventional treatment methods do not yield satisfactory results in terms of improvement of patients' health. Conducting well-designed scientific studies in the future can help determine precisely the effectiveness of these interventions in the treatment of central sensitization of the TMJ.

Innovative treatment methods

Neuromodulatory techniques

Conventional treatment methods show varying degrees of success in treating central sensitization of the TMJ. Newer therapeutic methods are more often being implemented, as described below.

Transcranial Direct Current Stimulation (tDCS) is a non-invasive neuromodulatory technique that involves delivering low electrical current and modifying the level of cortical excitability.[57] By altering neuronal activity in the brain, tDCS aims to normalize abnormal pain responses associated with central sensitization. Studies on mice suggest that tDCS reduces allodynia induced by orofacial pain. Additionally, the research demonstrated the effectiveness of tDCS in controlling and reducing inflammatory pain in the orofacial area.[58] By targeting brain areas involved in pain processing, tDCS may counteract abnormal changes in neurons that contribute to the development of central sensitization.

Transcranial Magnetic Stimulation (TMS) is a technique that involves delivery of repetitive, short and highly focused magnetic pulses used to stimulate brain cells. This method uses magnetic fields to excite specific areas of the brain.[59] TMS can help normalize neuronal excitability and reduce pain intensity. Studies indicate that TMS may be a therapeutic option in treatment of neuropathic pain, as well as psychological symptoms associated with central sensitization. The cited study was conducted on

a patient struggling with knee osteoarthritis; however, this method could be a promising therapeutic approach for individuals suffering from pain associated with central sensitization of the temporomandibular joint.[60]

Another described technique is Spinal Cord Stimulation (SCS). It has been applied and approved for clinical use in various pathological conditions, including peripheral neuropathic pain.[61] It involves delivering electrical impulses to the spinal cord to disrupt pain signals before they reach the brain.[62] By interrupting the transmission of pain signals at the spinal cord level, SCS alleviates pain and restores normal pain processing mechanisms.[61,62] Results of studies conducted on mice show that in the case of central sensitization, SCS may alleviate its development in appropriately selected cases.[62]

Although further research is needed to fully clarify the clinical applications and mechanisms of these therapies, undeniably these innovative treatment approaches have the potential to enrich treatment plans for central sensitization of the temporomandibular joint area.

Alternative therapies

Various alternative therapies have gained attention in the recent years as potential approaches to treating pain, including that originating from the temporomandibular joint. Unfortunately, their effectiveness and mechanisms are not fully understood, but they potentially offer a targeted therapeutic approach to pain management of the central sensitization of the TMJ.

Cranial-sacral therapy, also known as craniosacral therapy, is a therapeutic method, which is based on the theory of the existence of movement restrictions within cranial sutures that negatively affect the harmonious flow of cerebrospinal fluid. All anatomical structures that are in direct contact with this fluid are part of the craniosacral system and theoretically can be affected by it. This therapy – when performed by a qualified specialist who is placing hands in specific areas on the human body – helps in the improvement of the patient's health.[63] It is important for the therapist to use gentle pressure to minimize interference with the circulation of cerebrospinal fluid. The aim of this therapy is to eliminate any tensions present in this system.[64] Although precisely focused studies on its effectiveness in treating central sensitization of the TMJ are limited, the craniosacral therapy has been shown to yield positive results in terms of pain reduction and relaxation, especially in chronic pain.[65] Through its impact on the nervous system, this therapy might potentially provide relief to patients with central sensitization of the TMJ.

The use of herbal remedies and dietary supplements constitutes another alternative pathway in managing TMJ pain, particularly due to their potential anti-inflammatory and analgesic properties.[66,67] Omega-3 fatty acids are associated with reducing inflammation and managing overall joint health. Studies have shown that Omega-3 fatty acids effectively reduce TMJ damage caused by rheumatoid arthritis in rats.[67] Although there are no specific studies on this phenomenon, Omega-3 fatty acids could be a complementary therapy element in the treatment of central sensitization of the TMJ. They could also be used as adjunctive therapy in reducing inflammatory processes associated with the TMJ structures.

Homeopathy is an alternative treatment method that provides individualized therapy for each patient. It uses medical substances in small doses, and as a result of the therapeutic process, the patient, not the disease, is treated. In other words, it involves the use of highly diluted substances that would cause similar symptoms to those the patient is experiencing at the time, to stimulate the body's innate ability to self-heal.[68] There is evidence that several patients with TMJ disorders experienced relief through the use of homeopathic techniques.[69] However,

currently there is a lack of scientific evidence concerning the effectiveness of homeopathy in managing central sensitization of the TMJ.

The therapies described above represent potential treatment methods for TMJ pain associated with central sensitization. As alternative medicine continues to evolve, further research is necessary to gain a more thorough understanding of the mechanisms and potential benefits in the treatment of central sensitization of the TMJ.

Based on research conducted by *Tran* et al., there is evidence supporting both the traditional and gradual approaches in managing TMJ disorders. During the initial treatment, all non-invasive techniques such as simple patient self-care, analgesic medications, or regular physiotherapy are important. New, innovative and alternative therapies still require further research. *Tran* et al. demonstrated limited evidence supporting the effectiveness of therapy using occlusal splints. Intra-articular use of corticosteroids, hyaluronic acid, as well as intramuscular application of botulinum toxin may provide relief to patients, especially those dealing with chronic TMJ disorders, as is often the case with central sensitization. Surgical interventions such as arthroscopy or TMJ surgeries still require further research to determine the actual benefits for patients.[70]

Conclusion

Central sensitization of the temporomandibular region is an undeniable cause of chronic pain, leading to many therapeutic challenges. It results in abnormal pain responses, increased sensitivity to pain signals and prolonged pain experiences. It plays a significant role in the pathophysiology of TMJ disorders, affecting pain perception, emotional well-being, and overall quality of life of patients struggling with this problem.

Accurate diagnosis and treatment of central sensitization are essential factors for developing comprehensive and targeted therapeutic approaches that go beyond traditional peripheral symptom relief. Dentists need to understand the complex mechanisms of central sensitization to implement evidence-based therapeutic methods that improve treatment results.

Due to the complicated nature of central sensitization of the temporomandibular region, research and collaboration among medical doctors of different specialties, psychotherapists, and physiotherapists should continue. This kind of multidisciplinary collaboration can lead to more effective care for patients struggling with central sensitization of the TMJ. Future research should focus on comparing the effectiveness of conventional and alternative treatment methods. Additionally, long-term studies should be conducted to assess treatment outcomes over extended periods of time. Continuing studies on this topic will play an important role in creating future treatment methods for central sensitization of the temporomandibular region, enabling patients to eliminate any pain associated with this condition.

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