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ABSTRACT

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PERSPECTIVES ON THE USE OF TRACTOGRAPHY IN PATIENTS WITH TEMPOROMANDIBULAR DISORDERS: A LITERATURE REVIEW

Aim: To analyze current literature on the application of diffusion tensor imaging (DTI) and fiber tractography in patients with temporomandibular joint disorders (TMD), focusing on both central and peripheral neural pathways involved in pain modulation, nociceptive transmission and sensorimotor integration.

Materials and Methods: A systematic literature search was conducted using scientific databases (e.g., PubMed, Scopus, Google Scholar) with keywords such as "diffusion tensor imaging," "DTI," "tractography," "temporomandibular disorders (TMD)," and "orofacial pain". The review encompasses studies reporting quantitative DTI parameters – fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD) – and correlates these measures with clinical outcomes in TMD patients. Both central structures (cerebral hemispheres, brainstem-pain modulatory hubs) and peripheral structures (trigeminal nerve, masseter and lateral pterygoid muscles) are evaluated.

Results: Early investigations primarily focused on microstructural alterations in the trigeminal nerve, revealing changes in white matter integrity that correlate with nociceptive signal transmission and disease. Recent studies have extended these analyses to central pathways, with advanced DTI techniques mapping brainstem fibers such as the rostral ventromedial medulla (RVM) and periaqueductal gray (PAG), which play a pivotal role in descending pain modulation. DTI also demonstrates tract-specific abnormalities in temporomandibular disorder: bilaterally reduced FA in the trigeminal nerves, elevated MD/RD in pain-related white matter (e.g., posterior limb of the internal capsule), and disrupted connectivity in limbic–sensorimotor circuits (including the uncinate fasciculus). Quantitative DTI parameters have demonstrated significant differences between TMD patients and healthy controls, indicating increased ADC

and altered FA values in both peripheral and central pathways. Peripheral analyses further highlight increased ADC and subgroup-specific FA reduction in the lateral pterygoid and masseter muscles, particularly in anterior disc displacement without reduction (ADDWoR). Integration of DTI data with functional MRI further elucidates neuroplastic changes following therapeutic interventions, such as occlusal splint therapy, and correlates these changes with improvements in pain perception and sensorimotor function.

Discussion: The evidence suggests that DTI is a promising tool for identifying early neural alterations associated with TMD and for monitoring the efficacy of treatment modalities. Unlike non-specific chronic pain syndromes, TMD exhibits distinctive DTI signatures involving trigemino-thalamo-cortical projections, brainstem modulatory circuits (PAG–RVM), and peripheral muscle fibers. These tract-specific changes support the concept of TMD as both a peripheral and central pain disorder. However, challenges remain in optimizing data processing and standardizing acquisition protocols to enhance the reproducibility and clinical utility of DTI metrics. Future studies should also integrate multimodal imaging and advanced models (e.g., diffusion spectrum imaging, NODDI) to improve specificity and support biomarker development.

Conclusions: Diffusion tensor imaging and fiber tractography provide valuable quantitative insights into the neural alterations underlying TMD. These techniques have significant potential for improving diagnostic accuracy, tailoring individualized treatment strategies, and monitoring neuroplastic changes related to pain modulation and rehabilitation. DTI metrics, such as reduced FA and increased MD in trigeminal and brainstem tracts, combined with peripheral muscle abnormalities, may serve as candidate biomarkers for TMD. Further research is needed to refine image processing algorithms and integrate multimodal imaging data for advancing clinical applications in TMD management.

Keywords: Diffusion tensor imaging; Fiber tractography; Medical imaging; Temporomandibular disorders; Orofacial pain; Neuroplasticity; Pain modulation.

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РЕЗЮМЕ

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ПЕРСПЕКТИВИ ЗАСТОСУВАННЯ ТРАКТОГРАФІЇ У ПАЦІЄНТІВ ІЗ РОЗЛАДАМИ СКРОНЕВО-НИЖНЬОЩЕЛЕПНИХ СУГЛОБІВ: ОГЛЯД ЛІТЕРАТУРИ

Мета. Проаналізувати сучасну літературу щодо застосування дифузійно-тензорної візуалізації (DTI) та волоконної трактографії у пацієнтів із розладами скронево-нижньощелепного суглоба (РСНЩС), з фокусом на центральні й периферичні нервові шляхи, що залучені до модуляції болю, ноцицептивної передачі та сенсомоторної інтеграції.

Матеріали та методи. Виконано систематичний пошук у наукових базах даних (зокрема PubMed, Scopus, Google Scholar) за ключовими словами: «diffusion tensor imaging», «DTI», «tractography», «temporomandibular disorders (TMD)», «orofacial pain». В огляд включено дослідження з кількісними DTI-показниками –

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фракційна анізотропія (FA), середня дифузійність (MD), аксіальна дифузивність (AD) та радіальна дифузивність (RD) – і їхніми кореляціями з клінічними наслідками у пацієнтів із РСНЩС. Оцінювали як центральні структури (півкулі головного мозку, модулювальні центри стовбура мозку), так і периферичні (трійчастий нерв, жувальний та латеральний крилоподібний м’язи).

Результати. Ранні роботи зосереджувалися на мікроструктурних змінах у трійчастому нерві, демонструючи порушення цілісності білої речовини, що корелюють із ноцицептивною передачею та тривалістю захворювання. Останні дослідження розширили аналіз на центральні шляхи: за допомогою передових DTI-підходів картують волокна стовбура мозку, зокрема ростральну вентромедіальну медулярну зону (RVM) і періакведуктальну сіру речовину (PAG), які відіграють ключову роль у низхідній модуляції болю. DTI також виявляє тракт-специфічні аномалії при РСНЩС: двобічне зниження FA у трійчастих нервах, підвищення MD/RD у ділянках білої речовини, пов’язаних із болем (наприклад, задня ніжка внутрішньої капсули), та порушення зв’язності в лімбіко-сенсомоторних контурах (зокрема у гачкоподібному пучку). Кількісні DTI-параметри достовірно відрізняються між пацієнтами з РСНЩС і здоровими контролями, що вказує на підвищення ADC та зміну FA як у периферичних, так і в центральних шляхах. Периферичний аналіз додатково підкреслює зростання ADC і підгрупно-специфічне зниження FA у латеральному крилоподібному та жувальному м’язах, особливо при передньому зміщенні диска без репозиції (ADDWoR). Інтеграція DTI-даних із функціональною МРТ прояснює нейропластичні зміни після терапевтичних втручань (наприклад, оклюзійні шини) та пов’язує їх із покращенням сприйняття болю і сенсомоторної функції.

Обговорення. Наявні дані свідчать, що DTI є перспективним інструментом для раннього виявлення нейронних змін, пов’язаних із РСНЩС, і моніторингу ефективності лікування. На відміну від неспецифічних хронічних больових синдромів, РСНЩС демонструє характерні DTI-«підписи», що охоплюють тригеміно-таламо-кортикальні проєкції, мозковостовбурові модулювальні контури (PAG–RVM) і периферичні м’язові волокна. Такі тракт-специфічні зміни підтримують уявлення про РСНЩС як про розлад із поєднаними периферичними та центральними компонентами болю. Водночас залишаються виклики, пов’язані з оптимізацією обробки даних і стандартизацією протоколів отримання зображень для підвищення відтворюваності та клінічної корисності DTI-метрик. Подальші дослідження мають інтегрувати мультимодальні підходи й розширені дифузійні моделі (наприклад, diffusion spectrum imaging, NODDI), щоб підвищити специфічність і сприяти розвитку біомаркерів.

Висновки. Дифузійно-тензорна візуалізація та трактографія надають цінні кількісні відомості про нейронні зміни, що лежать в основі РСНЩС. Ці методики мають значний потенціал для підвищення діагностичної точності, персоналізації лікувальних стратегій і моніторингу нейропластичних змін, пов’язаних із модуляцією болю та реабілітацією. DTI-метрики, зокрема зниження FA та підвищення MD у трійчастих і мозковостовбурових трактах у поєднанні з периферичними м’язовими аномаліями, можуть слугувати кандидатними біомаркерами РСНЩС. Потрібні подальші

роботи для вдосконалення алгоритмів обробки зображень і інтеграції мультимодальних даних з метою просування клінічних застосувань DTI у веденні пацієнтів із РСНЩС.

Ключові слова: дифузійно-тензорна візуалізація; волоконна трактографія; медична візуалізація; розлади скронево-нижньощелепного суглоба; орофаціальний біль; нейропластичність; модуляція болю.

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INTRODUCTION

Diffusion tensor imaging (DTI) is a magnetic resonance imaging technique that enables non-invasive assessment of the microstructure of brain white matter by quantifying the anisotropy of water diffusion. The main quantitative parameters of DTI include fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD). In clinical practice, FA and MD are most frequently applied [1–3], as they support the reconstruction of nerve fiber tracts using tractography algorithms. This approach provides valuable insights into the integrity and organization of neural pathways, which are essential for investigating neuropathological processes related to pain modulation [4]. DTI can also complement other brain mapping modalities. For example, anatomical information derived from DTI can be integrated with functional MRI (fMRI) data to achieve three-dimensional visualization of subcortical brain structures linked to specific cortical regions [5, 6]. Thus, DTI offers a promising avenue for more detailed examination of pain mechanisms [2, 7, 8]. Initially, DTI studies focused mainly on the cerebral hemispheres. Today, however, DTI extends to brainstem regions, where major tracts associated with trigeminal nerve activity are located. Additionally, several investigations have explored the correlation between masticatory muscle condition and nociceptive system involvement in chronic pain syndromes related to the temporomandibular joint. Nonetheless, challenges remain in improving data processing algorithms and refining methodological approaches [1, 2, 4]. Temporomandibular joint disorders (TMD) encompass a wide range of conditions that impair joint function, causing pain, restricted mobility, and other dysfunctions [9].

Traditional diagnostic methods, such as clinical examination and standard radiological techniques, are insufficient to elucidate the neuronal mechanisms underlying these disorders. In this context, DTI serves as a powerful tool to investigate alterations in neural networks related to pain processing and sensorimotor integration in patients with TMD. The aim of this article is to analyze contemporary literature DTI and fiber tractography in TMD, clarifying their diagnostic and monitoring value.

MATERIALS AND METHODS

A literature search from 2009 onward was conducted using Scopus, PubMed, Wiley Online Library, and Google Scholar. The following keywords were used: **“**diffusion tensor imaging,” “DTI,” “tractography,” and “temporomandibular disorders (TMD**)**”. The search yielded 18 records in PubMed, 37 in Google Scholar, and 3 in Scopus. After screening and eligibility assessment, 21 studies were included. A brief synopsis of these sources is provided in Table 1.

RESULTS

Early DTI research primarily examined pathological changes in trigeminal-system pathways among patients with chronic pain. DTI-based modeling has detected abnormalities in the trigeminal nerve and associated white matter, establishing neuroanatomical correlations with clinical symptoms [10]. Additionally, DTI helps identify both established and emerging pathophysiological mechanisms of chronic pain. Overall, the literature can be broadly divided into two domains: central pathway DTI and peripheral structure DTI (Fig. 1) [11].

DTI has also confirmed abnormalities in the trigeminal nerve and brainstem: patients with TMD show bilaterally reduced fractional anisotropy (FA) in the trigeminal nerves compared with healthy controls, and this reduction negatively correlates with pain duration (the longer the TMD history, the lower the FA) **[**10, 11]; brainstem DTI further implicates nociceptive pathways relevant to TMD [4].

Table 1 – Comparison of the main studies on related topics

№	Author	Study Title	Year	Type of research	Research objectives	Key results
1.	Byrd et al.	fMRI Study of Brain Activity Elicited by Oral Parafunctional Movements	2009	OA	Investigate brain activity associated with parafunctional movements of the oral cavity.	In parafunctional movements, there is less activation in the motor cortex, the accessory motor area (SMA), the sensorimotor cortex (SMC), the insular cortex (INS), the caudate nucleus (CAU) and the striatal system (PUT).
2.	Greven M. et al.	The amount TMJ Displacement Correlates with Brain Activity	2011	OA	Analyze the correlation between TMJ dislocations and brain activity.	Significant changes in the activation of the amygdala (amygdala) were observed during jaw compression at different degrees of TMJ displacement. At a 0.5 mm shift, activation was stronger than at a 0.7 mm shift, suggesting emotional responses to a change in jaw position, also unlike other studies, there was no activation of the anterior cingulate cortex (ACC) during jaw compression Patients with TMD have an increase in activity in the right primary motor cortex. TMD in the primary motor and sensorimotor cortex The authors suggest that this is due to different mechanical stimuli from different teeth
3.	Otsuka K. et al.	Influence of the TMJ position on limbic system activation	2011	OA	Analyze the change in the activity of the cerebral cortex and limbic system	Changes in the position of the lower jaw caused changes in the anterior cingulate cortex (ACC), insula and amygdala in all subjects. The results indicate an interdependence between occlusion, the position of the TMJ, and the "emotional circle" (limbic system) of the human brain.
4.	Sood м. et al.	Orthodontic tooth movement is associated with orofacial mechanical and thermal hypersensitivities and face sensorimotor cortex neuroplasticity	2013	DISS	Investigate neuroplastic changes in the motor cortex of the face during orthodontic movement of teeth in rats.	Functional connectivity between sensorimotor areas (S1 and M1) shows significant changes during orthodontic treatment, which may indicate neuroplastic processes in the brain during orthodonic tooth movement.
5.	Lin et al.	Brain signature of chronic orofacial pain: a systematic review and meta-analysis on neuroimaging research of trigeminal neuropathic pain and temporomandibular joint disorders	2014	MA	To analyze functional and structural changes in the brain in patients with neuropathic trigeminal pain and TMD	Tractography revealed significant changes in the thalamocortical pathways, especially in the primary somatosensory cortex (S1), showed changes in the connections between the prefrontal cortex and the basal ganglia, suggesting a role for cognitive modification and reward processing in chronic pain. These changes are important for understanding the effects of cognitive factors on pain perception in patients with neuropathic trigeminal pain and TMD
6.	Barroso J et al.	Brain mechanisms of chronic pain: critical role of translational approach	2014	MA	Analyze neuroimaging data for chronic orofacial pain and determine the brain mechanisms involved.	The main brain areas involved in pain processing include the insular cortex, thalamus, cingulate gyrus, and somatosensory cortex. There is a violation in the interaction between the insular cortex, thalamus and other areas associated with pain in chronic orofacial pain
7.	Lai et al.	fMRI Study on Human Subjects with Sudden Occlusal Vertical Dimension Increase	2015	OA	Investigate brain activity caused by an increase in interalver height	The fMRI study showed significant changes in the medial frontal gyrus, precentral and postcentral gyrus, within 2 weeks.
8.	Ariji, Y., Koyama, S., Sakuma, S., Nakayama, M., & Ariji, E.	Regional brain activity during jaw clenching with natural teeth and with occlusal splints: a preliminary functional MRI study.	2016	OA	Investigate changes in brain activity during bruxing and compare with two types of splint	BOLD signals, increased in BA44, 45 and the cerebellum. Signals dependent on the level of blood oxygenation were amplified in these areas and in BA17, 18 during compression with a soft splint. The use of a hard bus increased the BOLD signals in BA6 and BA20, 37 to the previously mentioned areas. Blood oxygenation-dependent signals in the left BA6, left BA20, 37, and right BA44, 45 were significantly higher when compressed with a rigid splint than with natural teeth.
9.	Zhang et al..	Spontaneous brain activity and connectivity in female patients with temporomandibular joint synovitis pain:	2018	OA	To study spontaneous brain activity and connectivity in patients with TMJ synovitis pain	In patients with TMJ, there was a weaker positive functional connectivity between the anterior part of the insular cortex (rAI) and the middle part of the cingulate cortex (MCC) and a weaker negative functional connectivity between rAI and the right pretsuneus. These changes indicate disturbances in the

№	Author	Study Title	Year	Type of research	Research objectives	Key results
		a pilot functional magnetic resonance imaging study				interaction between the structures responsible for pain and sensory integration.
10.	Lin et al.	Meta-analysis of brain mechanisms of chewing and clenching movements	2018	MA	Investigate the sequence of brain activation during chewing and squeezing movements in different studies, based on literature sources	Tractography revealed reliable activation of the bilateral primary motor cortex (M1), secondary motor cortex (SMA), primary somatosensory cortex (S1), and secondary somatosensory cortex (S2) during chewing and clenching of teeth, activation bilaterally of the thalamus and left posterior part of the cerebellum.
11.	Ernst et al.	Effects of centric mandibular splint therapy on orofacial pain and cerebral activation patterns	2019	OA	To study how mandibular splint therapy affects pain perception and brain activation patterns.	One of the important findings of the study was a decrease in activity in the primary sensorimotor cortex (S1) and the anterior insular cortex after therapy, between the primary motor cortex (M1) and the anterior insular cortex and a decrease in activity in the cerebellum, which was associated with a decrease in activity in the insular cortex, a decrease in activity in the cerebellum was also found
12.	Slynko I, Nekhlopochyn O, Robak K.	Using spinal cord tractography as a predictor regression of neurological disorders in patients with severe vertebral spinal cord injury of the cervical spine	2019	OA	Overview of DTI Techniques for Neurosurgical Applications	Provides practical analysis of DTI applications in neurosurgery, with a focus on structural changes in white fibers of the brain.
13.	Moayedi, M., & Hodaie, M.	Trigeminal nerve and white matter brain abnormalities in chronic orofacial pain disorders	2019	OA	Investigate trigeminal nerve abnormalities in chronic pain	Detects specific changes in the white matter of the trigeminal nerve associated with chronic pain, providing the basis for diagnostic approaches.
14.	Dammann et al.	Association of decrease in insula fMRI activation with changes in trait anxiety in patients with craniomandibular disorder (CMD)	2020	OA	Investigate the effect of splint therapy on activation and reduction of anxiety in patients with CMD.	Patients with dysfunction of craniomandibular (CMD) disorders show altered activation of the anterior insular cortex (rAI) a decrease in anxiety correlated with a change in rAI activation, which indicates a possible mechanism of treatment influence on the psycho-emotional state of patients. There has been a decrease in functional connectivity between the anterior insular cortex and the MCC.
15.	Yin, Y., He, S., Xu, J., et al.	The neuro-pathophysiology of temporomandibular disorders-related pain: a systematic review of structural and functional MRI studies	2020	LR	Systematically review the results of MRI examinations for pain associated with TMD	Summarizes the significance of structural and functional changes detected by MRI for the prediction of TMJ pain syndromes.
16.	Mills et al.	Altered Brainstem Pain Modulating Circuitry Functional Connectivity in Chronic Painful Temporomandibular Disorder	2021	OA	Assess changes in brainstem pain chains in TMD patients	It was found that in patients with painful TMJ disorders (temporomandibular disorders, TMD), there was a decrease in functional connectivity between the right anterior insular cortex (rAI) and the middle cingulate gyrus (MCC). This indicates a violation of the brain's ability to modulate pain in these patients, reducing the negative functional connectivity between rAI and the right lobe of the precuneus.
17.	Zeng et al.	Recent advances in Magnetic Resonance Neuroimaging for Trigeminal Neuralgia	2021	LR	Provide an overview of recent advances in neuroimaging techniques for trigeminal neuralgia.	A decrease in anxiety was noted to be associated with a decrease in activation of the anterior insular cortex (AI). Activation in the posterior insular cortex was also correlated with changes in anxiety levels, but the effect was less pronounced than in the anterior insular cortex
18.	Lin et al.	Dental Neuroimaging: The Role of the Brain in Oral Functions	2022	BOOK	Generalization of available research methods on neuroimaging in dentistry.	Modern methods of neuroimaging in dentistry have been analyzed

№	Author	Study Title	Year	Type of research	Research objectives	Key results
19.	Zhang, Y., & Furst, A. J.	Brainstem Diffusion Tensor Tractography and Clinical Applications in Pain	2022	OA	Investigate the application of brainstem tractography in pain studies	Highlights the importance of tractography in assessing brainstem pain, demonstrating specific neural connections that influence pain perception.
20.	Sugano, T., Yoda, N., Ogawa, T., et al.	Application of Diffusion Tensor Imaging Fiber Tractography for Human Masseter Muscle	2022	OA	Explore the application of DTI to study the human masticatory muscle	Demonstrates successful visualization of masticatory muscle fibers by DTI, detecting structural changes under prolonged stress.
21.	Liu S, Wan C, Li H, Chen W, Pan C.	Diffusion tensor imaging of the lateral pterygoid muscle in patients with temporomandibular joint disorders and healthy volunteers	2022	OA	Perform functional evaluation of the lateral pterygoid muscle using diffusion tensor imaging (DTI) in patients with rTMJ.	Patients with TMD in general and the ADWR and ADWOR subgroups had significantly higher ADC scores in both SHLPM and IHLPM than in volunteers. At the same time, significant differences in FA in SHLPM and IHLPM. Among the three TMD subgroups, FA in the ADWR subgroup, the ADWR and ADWOR subgroups had significantly higher ADCs, lower FAs than those in the ND group. No significant difference in diffusion variables was found between ADWR and ADWOR. In the ADWOR group, the osteoarthritis group had significantly lower FA values in the IHLPM than in the non-osteoarthritis group

Article type:
OA – Original Research, DISS – Dissertation, MA – Meta-Analysis, LR – Review Publication, EX – Experimental

1. DTI of the central pathways

Trigeminal nerve and white matter of the brain

The first studies in this area aimed to describe structural changes in the trigeminal nerve and associated white matter in patients with chronic orofacial pain, thereby identifying abnormalities in white-matter microstructure involved in the pathological transmission of nociceptive signals. For example, an approximately 10% reduction in fractional anisotropy (FA) and increased diffusivity in the trigeminal nerve were documented in the TMD group [12]. These changes appear specific to orofacial pain and are not observed in non-orofacial chronic pain syndromes affecting other body regions [10].

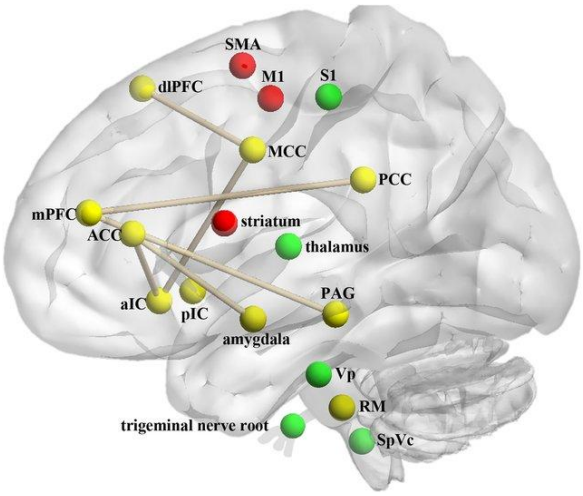

Figure 1 – Scheme of the main areas were is a change in the functional activity of brain structures according to the the DTI study in patients with chronic pathology of the TMJ Yin and colleagues (2020)

These findings laid the groundwork for a deeper understanding of the pathogenesis of orofacial pain in the context of TMD. Subsequently, with the advancement of magnetic resonance neuroimaging, an overview of modern approaches to neuroimaging of the trigeminal nerve in trigeminal neuralgia was presented [7]. Although that work focused on trigeminal neuralgia, it emphasized the importance of DTI for detecting microstructural changes in the peripheral branches of the trigeminal nerve, which share pathophysiological features with TMD. Further research shifted toward central elements, particularly brainstem structures involved in pain regulation. Zhang and Furst (2022) demonstrated that changes in the structural organization of regions such as the rostral ventromedial medulla (RVM) and periaqueductal gray (PAG) correlate with increased nociception [4]. These results suggest that dysfunction of central tracts may contribute to the maintenance of chronic pain in TMD patients and may co-occur with depressive disorders. In addition to structural analysis, contemporary researchers have focused on the functional organization of central pathways. Mills et al. (2021) analyzed both static and dynamic functional connectivity (FC) in the brainstem and reported increased static connectivity between the RVM and the spinal trigeminal nucleus, along with greater variability (dynamic FC) of these connections in patients with painful TMD. Together, these findings point to an imbalance between pain-inhibitory and pain-facilitatory systems, a hallmark of chronic pain pathophysiology [13]. Consistent with these observations, white-matter integrity within trigeminal pathways shows reduced FA and elevated diffusivity metrics in chronic TMD, in line with sustained nociceptive input and central sensitization [10, 11].

The brainstem and pain modulation pathways

Over time, researchers increasingly focused on the central pathways that regulate pain. They showed that structural changes in regions such as the RVM may be associated with increased transmission of nociceptive signals, potentially contributing to chronic pain in TMD [14].

Brain changes were found in pathways responsible for abnormal pain perception, including the classic trigemino-thalamo-cortical system and the lateral and medial pain systems. Dysfunction and maladaptive changes were also identified in the default mode network, the top-down antinociceptive periaqueductal gray-raphe magnus pathway, as well as the motor system. TMD patients displayed altered brain activations in response to both innocuous and painful stimuli compared with healthy controls. Additionally, evidence indicates that splint therapy can alleviate TMD-related symptoms by inducing functional brain changes. In summary, MRI research provides important novel insights into the altered neural manifestations underlying chronic pain in TMD. Such kind of findings indicate dysfunction of the descending pain-modulatory pathways, specifically the periaqueductal gray (PAG)–rostral ventromedial medulla (RVM) axis in TMD [11].

One study employed the single modality of DTI to investigate changes of fractional anisotropy (FA) and mean diffusivity (MD) in patients with TMD [12].

Primary sensorimotor cortex and projection pathways

TMD does not always lead to remapping of the somatosensory cortex, unlike some other chronic pain conditions. However, diffusion changes are detected in the white-matter bundles that link sensorimotor areas. In patients with TMD, researchers have reported lower fractional anisotropy (FA – an index of how coherently water diffuses along nerve fibers) and higher radial diffusivity (RD – diffusion across, rather than along, fibers) in the posterior limb of the internal capsule

(PLIC, which carries motor fibers). This pattern points to disorganization of projection pathways involved in motor control of the masticatory muscles. In another study, FA within the primary somatosensory cortex (S1) did not differ from healthy controls [15].

Limbic and temporal structures

Patients with TMD also show diffusion abnormalities in tracts connecting the temporal lobe with frontal regions. Notably, the uncinate fasciculus (UNC), a bundle linking the anterior temporal lobe to the orbitofrontal cortex, appears affected in TMD: the right UNC shows reduced FA alongside increased mean diffusivity (MD) and RD. These findings reflect alterations within affective–cognitive pain networks (the limbic system), consistent with the impact of chronic TMD pain on mood and memory [15].

Lin C. S. described regional changes in brain function during chewing and clenching movements [16] and in the context of chronic orofacial pain [17]. Earlier, Otsuka et al. (2011) reported that changes in mandibular position alter activity in the anterior cingulate cortex (ACC), insula, and amygdala in all participants, supporting an interdependence between occlusion, TMJ position, and limbic-system responses [18]. Subsequently, Zhang J. et al. (2018) emphasized the value of DTI for assessing brainstem pain pathways, demonstrating specific neural connections that shape pain perception [19]. Additionally, Sood (2013) observed functional connectivity changes between sensorimotor regions (S1 and M1) during orthodontic treatment, suggesting neuroplastic processes associated with tooth movement [20].

2. DTI of peripheral structures

Special attention has been paid to peripheral muscle structures, such as the masseter, since dysfunction of this muscle is **a** characteristic feature of TMD. Sugano et al. (2022) applied DTI to optimize acquisition and analysis parameters in the masseter muscle.

In the lateral pterygoid muscle, diffusion metrics demonstrate higher apparent diffusion coefficient (ADC) and principal eigenvalues with subgroup-specific reductions in FA among patients with anterior disc displacement, particularly those without reduction, relative to healthy volunteers [8]. Complementarily, DTI fiber-tractography of the masseter enables reliable reconstruction of muscle architecture and captures loading-related alterations relevant to TMD pathophysiology [2].

Their study accurately determined the orientation and length of muscle fibers, contributing to the development of individualized approaches to TMD diagnosis and treatment by correlating muscle architecture with clinical symptoms [2]. According to Liu et al. (2021), DTI evaluation of the lateral pterygoid muscle (LPM) enabled quantitative measurement of diffusion parameters, such as the apparent diffusion coefficient (ADC) and fractional anisotropy (FA), in patients with TMD and healthy volunteers [8]. The results showed that patients with TMD have significantly increased ADC values and principal eigenvalues compared to volunteers, indicating muscle hypertonicity and microstructural change. Differences in FA, reflecting the degree of diffusion anisotropy, were pronounced in the subgroup with anterior disc displacement without reduction (ADDWoR), which may indicate reduced fiber coherence [1].

Use of DTI to assess the condition of key masticatory muscles involved in TMD enables objective quantification of hypertonicity and dysfunction, stratification of disease stages, planning of individualized therapy, and monitoring of treatment efficacy [21].

Across recent studies, TMD is characterized by tract-specific alterations in both central and peripheral compartments. Centrally, reduced FA and increased diffusivity within trigeminal pathways and brainstem nociceptive hubs (e.g., PAG) align with impaired pain-modulatory control [10,11]. Peripherally, lateral pterygoid and masseter muscles exhibit abnormal diffusion profiles (ADC↑/eigenvalues↑; subgroup-specific FA↓) consistent with muscle dysfunction in disc displacement phenotypes [2, 8]. Together, these DTI signatures support a dual-mechanism model – central sensitization and peripheral myogenic changes, potentially useful for stratifying TMD patients and monitoring therapy [2, 4, 8, 12].

Clinical significance of DTI metrics

Although DTI parameters in TMD show promise for reflecting symptom severity, the evidence remains heterogeneous. Several studies report that lower fractional anisotropy (FA), a diffusion-based index of white-matter fiber organization, within specific tracts is associated with higher pain intensity [15, 24]. Psychological factors that are common in TMD: depression, somatization, and pain catastrophizing, may also modulate diffusion metrics [25, 26]. For example, higher helplessness scores have been linked to increased FA in the cingulum bundle and in connections between somatosensory and premotor regions, alongside reduced FA in motor pathways such as the posterior limb of the internal capsule (PLIC). This pattern can be interpreted as a neuroplastic response, in which marked psychological distress relates to atypical plasticity within affective–cognitive circuits and motor projections controlling the masticatory musculature. Other reports similarly note close associations between TMD pain and heightened anxiety, depressive symptoms, and somatic sensitivity; however, direct correlations

between these measures and DTI metrics have not yet been replicated consistently across cohorts [15].

DISCUSSION

Current research shows that DTI provides detailed information about white-matter microstructure at both peripheral and central levels [7,10]. Importantly, while some diffusion abnormalities, such as reduced FA or increased MD, are shared across various chronic pain syndromes, recent studies have identified diffusion signatures that appear more specific to TMD. For instance, alterations within trigemino-thalamo-cortical projections and the uncinate fasciculus have been observed in TMD-related orofacial pain but are less consistently reported in non-orofacial pain cohorts [10, 11]. Similarly, diffusion changes in the lateral pterygoid and masseter muscles demonstrate a pattern of increased ADC and subgroup-specific FA reduction in disc displacement without reduction (ADDWoR), providing a structural correlate unique to TMD pathophysiology [2, 8]. These observations suggest that DTI can differentiate TMD from other chronic pain conditions by capturing both trigeminal-system involvement and peripheral myogenic alterations. Consequently, DTI metrics may serve not only as general markers of central sensitization but also as potential biomarkers specific to TMD diagnosis and monitoring. Among the most reproducible findings are reduced fractional anisotropy (FA) and increased mean and radial diffusivity (MD/RD) within white-matter tracts involved in trigeminal nociception and affective–motor processing of pain**,** including the posterior limb of the internal capsule**,** cingulum pathways**,** and the uncinate fasciculus [15]**.** Elevated diffusivity in the masticatory muscles is also observed in the setting of joint dysfunction [8]. Unlike non-specific chronic pain**,** patients with TMD show clear involvement of the trigeminal system from the peripheral nerve to the brainstem captured by DTI metrics**.** This pattern supports differential diagnosis and a clearer view of pathogenesis: TMD should be considered not only a local joint disorder but also a central pain condition with features of CNS plasticity [11].

Owing to its high spatial resolution, DTI detects subtle alterations in the organization of neural tracts responsible for pain transmission, enabling early identification of neuropathological changes in the trigeminal nerve, brainstem, and other structures involved in pain modulation, including the rostral ventromedial medulla (RVM**)** and periaqueductal gray (PAG) [4]. One key prospect for tractography is quantifying treatment-related changes in the structural and functional organization of these tracts. Combining DTI with functional connectivity analysis makes it possible to track neuroplastic dynamics following therapeutic interventions, such as occlusal splints or other pain-modulating strategies, thereby clarifying pathogenetic mechanisms and providing objective criteria for treatment monitoring and adjustment [4, 12]. Notably, converging DTI evidence now links brainstem pain-modulatory circuitry (PAG/RVM) and trigeminal pathways to the chronic TMD phenotype, while muscle-level diffusion abnormalities in the lateral pterygoid and masseter reflect peripheral contributors, together reinforcing a central-peripheral framework for TMD pathophysiology [2, 4, 8, 12].

Evaluating therapy-induced neuroplasticity in tract structure and organization may help determine the effectiveness of pain redistribution and adaptation within central pain networks, which is critical for managing patients with TMD [12, 22, 23].

Taken together, these findings indicate that DTI not only reflects general features of chronic pain but also reveals structural and functional patterns specific to temporomandibular disorders, supporting its role as a promising modality for differential diagnosis and individualized treatment monitoring.

CONCLUSIONS

1. Using DTI to measure fractional anisotropy (FA) and mean diffusivity (MD) offers a promising approach for early detection of pathological changes in patients with TMD, supporting timely treatment. Moreover, DTI enables assessment of neuroplastic changes after therapeutic interventions (e.g., oral splints, orthodontic appliances, prosthodontic treatment), helping clinicians evaluate treatment effectiveness and tailor therapy to individual patient characteristics.

2. Despite significant progress, several methodological limitations persist. In particular, data-processing pipelines, acquisition parameter optimization, and standardization of ROI segmentation require further refinement to improve accuracy and reproducibility. This is especially important for subtle peripheral structures and complex central pathways, where small artifacts can meaningfully bias interpretation

3. Recommendations for future research. Future work should prioritize advanced analytical algorithms, improvements in acquisition hardware and protocols, and large-scale clinical studies to validate current findings. Integrating multimodal approaches (DTI, fMRI, arterial spin labeling [ASL]) will support a more comprehensive understanding of TMD pathophysiology and accelerate development of new therapeutic strategies.

4. DTI is a valuable and promising tool in the research and treatment of temporomandibular joint disorders. It advances a deep understanding of the neural mechanisms and neuroplasticity opening opportunities for diagnosis, monitoring, and prediction

of treatment effectiveness. Continued research may enable new therapies aimed at restoring neural network function and improving quality of life in TMD. Overall, DTI shows high potential for characterizing structural brain changes in these patients.

PROSPECTS FOR FUTURE RESEARCH

The accumulated evidence demonstrates that DTI is a powerful tool for studying central and peripheral substrates implicated in TMD pathogenesis. The progression from early trigeminal-nerve assessments [10] to contemporary brainstem mapping [4] and peripheral muscle-fiber analyses [1, 2] highlights a steady expansion of neuroimaging capabilities. Collectively, these studies deepen our understanding of chronic-pain pathophysiology and open new avenues for diagnostic and therapeutic advances in TMD.

Modern DTI enables a comprehensive assessment of central and peripheral components of pain transmission and modulation and holds strong potential for clinical application in TMD [1, 7, 10, 17]. Continuing advances in high-resolution imaging and the development of standardized brainstem atlases should improve accuracy and reproducibility. Integrating DTI with other modalities, such as fMRI, offers a unified view of structural and functional changes and supports the development of diagnostic biomarkers [2, 4]. A pragmatic research pathway is a treatment-monitoring paradigm: a TMD patient begins with a baseline DTI to characterize white-matter status, including trigeminal fibers and brainstem structures governing pain transmission and modulation. Following a therapeutic intervention (e.g., a splint), a repeat scan after 2–4 weeks assesses neuroplastic changes in central pathways. Reduced dysfunction in regions such as the RVM and PAG may appear as increased FA or decreased MD, indicating improved microstructural integrity. Combining DTI with fMRI then allows tracking of both structural and functional dynamics, linking symptom reduction to normalization of connectivity in modulatory systems [4, 12].

Future research directions include strengthening clinico-imaging correlations for DTI metrics. Larger cohorts are needed to determine whether specific measures, such as fractional anisotropy (FA) within defined tracts, can serve as biomarkers of pain intensity, disease duration, or psychosocial context [15].

Prospective pre-/post-treatment DTI studies in TMD would enable objective evaluation of therapeutic efficacy and may help track recovery across both central and peripheral pathways. From a technological standpoint, adopting advanced diffusion methodologies is timely. Diffusion spectrum imaging (DSI) has already shown greater sensitivity to complex muscle-fiber architecture than conventional DTI [27]. Using DSI or high-angular-resolution diffusion approaches (e.g., HARDI) can provide more detailed information about microstructural changes in muscles and nerves in TMD. In addition, applying artificial intelligence (machine learning) to multimodal neuroimaging datasets opens the door to new diagnostic strategies and objective markers of therapeutic success.

AUTHOR CONTRIBUTIONS

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1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work.
2. Drafting the work or revising it critically for important intellectual content.
3. Final approval of the version to be published.
4. Agreement to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

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