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Animal Models of Temporomandibular Disorders: A Systematic Review of Pathophysiological Mechanisms and Translational Relevance

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Abstract

Temporomandibular disorders (TMD) represent a group of multifactorial musculoskeletal conditions that cause pain and dysfunction in the temporomandibular joint (TMJ), masticatory muscles, and associated structures. Various animal models have been developed to elucidate the biological mechanisms and potential therapeutic targets of TMD. This systematic review summarizes the main types of animal models used in TMD research, including inflammatory, mechanical, surgical, and psychological stress models. Each model demonstrates unique advantages in replicating specific pathological features such as inflammation, cartilage degeneration, or chronic pain. However, none can fully reproduce the complexity of human TMD, which involves biomechanical, inflammatory, and psychosocial interactions. The combination of inflammatory and mechanical loading models appears most relevant to clinical conditions, while psychological stress models provide insight into the neuroendocrine mechanisms underlying chronic pain. Future research should focus on developing multifactorial animal models and employing advanced imaging and molecular tools to enhance translational validity.

Keywords: Temporomandibular disorders; Animal models; Inflammatory model; Mechanical loading; Surgical intervention; Psychological stress; TMJOA; Translational research

1. Introduction

Temporomandibular disorders (TMD) are a general term that refers to various musculoskeletal conditions causing pain and/or functional disturbances in the masticatory muscles, temporomandibular joints (TMJ), and related structures. These disorders are the most common cause of non-odontogenic orofacial pain, with symptoms that may include pain in the face or head, TMJ, or teeth, limited jaw movement, and joint sounds during jaw motion [1]. The symptoms of TMD may include discomfort and pain in the orofacial region, restricted movement of the temporomandibular joint (TMJ), difficulty in speaking and chewing, stiffness, tinnitus (ringing in the ears), and clicking or popping sounds when chewing, opening, or closing the mouth. An objective diagnosis of TMD is crucial for effective management. Persistent and worsening symptoms can negatively affect quality of life and psychological well-being, potentially aggravating pre-existing psychiatric conditions such as depression, chronic stress, and anxiety [2].

In general, the exact cause or etiology of temporomandibular disorders (TMD) remains uncertain. Since TMD is recognized as a complex condition, it is unlikely that a single definitive cause can be identified. Historically, clinicians have focused on one possible explanation, occlusal disharmony, while other proposed causes such as muscle hyperactivity, central pain mechanisms, psychological distress, and trauma have also been explored. Recent research further suggests that comorbid conditions may contribute within this multifactorial framework [3].

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For some diseases, such as bacterial infections, the causal relationship between a specific pathogen and the resulting illness is relatively clear and can be explained through the Bradford Hill criteria. However, even in these cases, factors like individual susceptibility and environmental influences play an important role, as they can significantly modify the level of risk. In contrast, for more complex disorders like TMD, particularly when the condition becomes chronic, the cause involves a series of interrelated factors that work together to contribute to the onset and persistence of the disease [3].

According to the study by Zielinski et al. (2024), the prevalence of temporomandibular disorders (TMD) was notably higher in South America (47%) compared to Asia (33%) and Europe (29%). The findings also indicated that females had a higher incidence of TMD than males across the studied age groups, particularly when compared to those aged 18–60 years. Based on the presented data, the proportion of females was, on average, 9% to 56% greater than that of males across all continents. The highest female to male ratio was observed in South America (1.56), while the lowest was found in Europe (1.09), suggesting a nearly equal gender distribution in the latter region [4].

A variety of animal models have been extensively developed to investigate the neurobiological and molecular mechanisms underlying temporomandibular disorders (TMD) and to explore potential therapeutic strategies. Although these models cannot fully reproduce all clinical manifestations of TMD, they are highly valuable for elucidating the underlying pathophysiology and guiding the development of effective treatments [5].

Currently, numerous animal models are employed in TMD research. These models can be established through different approaches and are generally classified into four main categories based on their etiological factors and symptoms: chemical induction (such as intra articular injection of ovalbumin, collagenase, formalin, vascular endothelial growth factor, or intramuscular injection of complete Freund's adjuvant), mechanical stress stimulation (including passive mouth opening or modification of chewing load), surgical intervention (such as partial discectomy or disc perforation), and psychological stress induction [5].

Selecting the appropriate animal model depends largely on the specific objectives of the study. Research that focuses on acute inflammation may employ models involving the injection of proinflammatory agents, while studies investigating chronic degeneration are more suitable for long-term mechanical loading models. In addition, the choice of animal species such as rats, mice, rabbits, or primates can affect research outcomes due to anatomical differences, variations in cartilage composition, and behavioral responses to pain.

Given the diversity of methods and findings, a systematic review is needed to compile and analyze the range of animal models used in temporomandibular disorder research. This review aims to provide a comprehensive overview of the models applied, the parameters evaluated, and their relevance to clinical conditions in humans. By recognizing the strengths and weaknesses of each model, researchers can determine the most appropriate approach for their research objectives.

Based on this background, the present systematic review seeks to identify, classify, and compare different animal models employed in temporomandibular joint disorder studies. The discussion covers induction mechanisms, experimental duration, observation parameters, and the advantages and limitations of each model. The results of this review are expected to enhance understanding of TMD pathogenesis and support the development of experimental models that more accurately reflect human clinical conditions.

2. Methods

2.1. Study Design

This research was designed as a systematic review conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines. The purpose of this review was to identify, evaluate, and summarize experimental studies employing animal models to explore the pathophysiology and treatment strategies of temporomandibular disorders (TMD).

Because this work relied solely on previously published studies, ethical approval was not required. Nevertheless, all included articles were expected to comply with international ethical principles for animal experimentation, particularly those outlined in the *ARRIVE (Animal Research: Reporting of In Vivo Experiments)* guidelines.

2.2. Literature Search Strategy

A comprehensive literature search was performed across major databases, including PubMed, ScienceDirect, and Google Scholar, to identify relevant publications from 2020 to 2025. The search strategy employed combinations of the following terms with Boolean operators:

("temporomandibular disorder" OR "TMJ pain" OR "TMJ inflammation") AND ("animal model" OR "rat model" OR "mice model" OR "experimental model")

Only International full text articles were included. A manual search of reference lists from selected papers was also conducted to locate additional studies not captured by the database queries.

All search results were imported into Mendeley Desktop for reference management, and duplicate entries were removed before the screening process.

2.3. Inclusion and Exclusion Criteria

2.3.1. Inclusion Criteria

- Original *in vivo* research involving animal models of TMD.
- Studies that clearly described the induction method (inflammatory, mechanical, surgical, or stress related).
- Peer reviewed journal articles published in English.
- Studies reporting measurable outcomes related to TMD pathology, such as histological, biochemical, or behavioral changes.

2.3.2. Exclusion Criteria

- Review papers, case reports, or *in vitro* studies.
- Research not directly related to the temporomandibular joint or masticatory system.
- Conference abstracts, dissertations, or non-peer reviewed sources.
- Articles without full-text access or insufficient methodological detail.

2.4. Study Selection Process

Study selection was performed independently by two reviewers and consisted of three stages:

- **Identification:** Screening of titles and abstracts for relevance to TMD and animal experimentation.
- **Screening:** Removal of duplicates and studies that did not meet eligibility criteria.
- **Eligibility Assessment:** Full-text evaluation of potentially relevant articles to confirm methodological quality and data completeness.

Any disagreements between reviewers were resolved through discussion or by involving a third reviewer.

The overall selection process is illustrated in a PRISMA flowchart, showing the number of studies identified, screened, excluded, and finally included in the review.

2.5. Data Extraction and Management

Data from eligible studies were systematically extracted using a standardized data extraction form. The following information was recorded:

- Author(s), year of publication, and country of origin;
- Animal species and sample size;
- Type of TMD model (inflammatory, mechanical, surgical, or stress-induced);
- Induction method and duration of experiment;
- Outcome parameters (histological, biochemical, or behavioral);
- Main results and conclusions.

Extracted data were organized into summary tables and analyzed descriptively. A meta-analysis was not performed due to significant methodological heterogeneity among the included studies.

2.6. Quality Assessment

The methodological quality of each study was appraised using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Experimental Studies.

This tool assesses several factors, including randomization procedures, control group use, blinding, allocation concealment, and completeness of outcome reporting.

Each study was rated as having low, moderate, or high risk of bias. Only studies classified as low or moderate risk were included in the main synthesis, while those with high risk were analyzed separately to minimize potential bias.

2.7. Data Synthesis

Data were summarized using a narrative synthesis approach, comparing outcomes based on the type of animal model and experimental method used (inflammatory, mechanical, surgical, or stress related).

The key experimental characteristics were presented in tabular form, while the accompanying discussion highlighted the translational relevance, strengths, limitations, and future research implications of each model type.

3. Results

A comprehensive search of PubMed, ScienceDirect, and Google Scholar yielded a total of 1,286 publications within the 2020–2025 period. After duplicate removal, 1,045 records remained. Screening of titles and abstracts identified 94 studies that appeared relevant to the topic. Full-text examination led to the inclusion of seven studies that satisfied all methodological and thematic criteria. These studies form the basis of the present synthesis.

The included literature displays broad methodological diversity and collectively contributes to understanding the biological and functional mechanisms underlying temporomandibular disorders. The studies encompass inflammatory, mechanical, genetic, and psychosocial dimensions of disease modeling. Most research employed rodents predominantly rats and mice while one investigation conducted a comparative anatomical evaluation involving rabbits, guinea pigs, rats, and mice to determine interspecies differences in temporomandibular joint morphology and suitability for experimental use.

The animal models examined across these studies were designed to reproduce characteristic features of temporomandibular dysfunction, such as inflammatory reactions within the joint, cartilage degradation, nociceptive sensitization, and alterations in masticatory behavior. Although the induction methods and observation parameters varied, each model contributed distinct insights into specific aspects of temporomandibular pathology.

Wang et al. (2023) reviewed recent advances in experimental animal models, diagnostic methods, and therapeutic approaches for temporomandibular joint osteoarthritis. The paper summarized the main chemical, mechanical, surgical, and genetic induction techniques used in rodents, highlighting that combined inflammatory and mechanical models provide the best simulation of human pathology. It also emphasized the promise of regenerative approaches using stem cells and biomaterial scaffolds for restoring joint function [6].

Li et al. (2020) investigated nociceptive behavioral responses in various mouse models of temporomandibular joint disorders. The study established standardized assessments of pain hypersensitivity, bite force, and functional limitation, identifying consistent markers for evaluating pain intensity in murine TMD models. The findings contributed to more reliable quantification of TMJ related nociceptive behaviors for translational studies [7].

Fan et al. (2021) explored the presence and role of fibrocartilage stem cells (FCSCs) in the temporomandibular joint through both animal and human studies. The researchers identified FCSCs in the superficial zone of TMJ fibrocartilage and demonstrated their potential for chondrogenic differentiation and cartilage repair in vivo. The study provided key evidence that FCSCs play a central role in tissue regeneration and could serve as novel therapeutic targets for TMJ osteoarthritis [8].

Oliveira et al. (2020) developed inflammatory animal models of temporomandibular disorder using intra-articular Complete Freund's Adjuvant (CFA) injection and evaluated the protective effects of natural compounds with antioxidant or anti-inflammatory activity. The induced inflammation caused increased levels of IL-1β, TNF-α, and MMP-13, cartilage

erosion, and oxidative imbalance, whereas natural product treatment significantly reduced these pathological markers and improved joint structure [9].

Phero et al. (2021) designed a rat model that integrates biological predisposition and mechanical provocation to reproduce the multifactorial nature of temporomandibular disorders. Rats receiving repeated excessive jaw opening in combination with mild inflammation or catechol-O-methyltransferase (COMT) inhibition exhibited significant functional impairment measured by a ratgnawmeter, while either factor alone produced minimal effect. The results support that combined biological and mechanical stressors more accurately reflect clinical TMD pain [10].

Chung et al. (2023) examined the degeneration pain relationship in the temporomandibular joint by combining intra articular inflammation with mild chronic stress in rats. The study revealed that degenerative cartilage changes were not directly correlated with behavioral pain intensity. Instead, inflammatory cytokines were key mediators sustaining chronic orofacial pain, indicating that inflammatory pathways rather than morphological damage underlie persistent TMD symptoms [11].

Navarrete et al. (2025) performed a morphoquantitative comparison of the temporomandibular joint in rabbits, guinea pigs, rats, and mice to determine species suitability for modeling human TMD. Rabbits and guinea pigs exhibited thicker fibrocartilage, clearer zonal organization, and collagen birefringence patterns most similar to humans, whereas rodents displayed simpler cartilage structure but are more practical for molecular and transgenic research [12].

Table 1 Summary of selected studies on animal models of temporomandibular disorders (2020-2025)

No	Author (year)	Animal Species	Model Type	Induction / Experimental Procedure	Duration	Variables/ Parameters Evaluated	Principal Findings	Strengths and Limitations
1	Wang et al., 2023 - Recent Advances in Animal Models. Diagnosis, and Treatment of Temporomandibular Joint Osteoarthritis	Rats and mice	Review of animal models	Compilation and evaluation of chemical, mechanical, surgical, and genetic induction strategies for TMJ osteoarthritis	-	Mechanistic pathways, cellular targets, and regenerative treatments	Combined inflammatory and mechanical approaches closely replicate human TMJ osteoarthritis; stem cell and biomaterial based therapies show encouraging outcomes.	Comprehensive summary; lacks original experimental validation.
2	Li et al., 2020 - Nociceptive Behavioural Assessments in Mouse Models of Temporomandibular Joint Disorders	C57BL/6 mice	Behavioral pain model	Evaluation of pain-related responses in various murine TMD models under mechanical and inflammatory conditions	7-14 days	Behavioral pain thresholds, mechanical sensitivity, histological and molecular changes	The study standardized behavioral pain assessments in murine TMJ models. highlighting reliable measures For nociceptive evaluation	Provides robust behavioral criteria; limited mechanistic depth.
3	Fan et al., 2021 - Fibrocartilage Stem Cells in the	Rats and mice	Cellular / regenerative	Isolation and tracking of	2-6 weeks	Stem cell marker expression,	Fibrocartilage stem cells play essential	Provides translational insight; complex

	Temporomandibular Joint: Insights from Animal and Human Studies			fibrocartilage stem cells in TMJ cartilage repair and degeneration		cartilage regeneration, histological morphology	roles in TMJ cartilage repair and could serve as therapeutic targets for osteoarthritis	identification methods.
4	Oliveira et al., 2020 - The Effect of Natural Products in Animal Models of Temporomandibular Disorders	Rats	Pharmacological / therapeutic	Administration of natural compounds with anti-inflammatory or antioxidant activity in CFA- or mechanical-induced TMJ inflammation models	14-21 days	Histopathology, oxidative markers, cytokines, behavioral outcomes	Natural compounds demonstrated protective and anti-inflammatory effects, improving joint integrity and reducing nociceptive behavior.	Demonstrates therapeutic potential; variations among test compounds limit comparability.
5	Chung et al., 2023 - The Degeneration-Pain Relationship in the in the temporomandibular joint: Current understandings and rodent models.	Wistar rats	Inflammatory and stress combined	Mild chronic stress combined with intra-articular inflammatory stimulation	21 days	Pain behavior, joint morphology, cytokine levels	Degenerative severity was not directly linked to pain persistence; inflammatory mediators dominated chronic symptom maintenance.	Explores neuroinflammatory interactions; behavior influenced by stress variability.
6	Phero et al., 2021- A novel rat model of temporomandibular disorder with improved face and construct validities.	Sprague – Dawley rats	Multifactorial (mechanical + inflammatory)	Repetitive jaw opening with either mild inflammation or COMT inhibition	7 days	Chewing efficiency, nociceptive behavior, muscular performance	Functional and behavioral impairment occurred only under combined predisposing and triggering conditions; model closely mimics multifactorial TMD.	High translational accuracy; requires specialized instrumentation.
7	Navarrete et al., 2025- Morphoquantitative Comparison of the Temporomandibular Joint in Laboratory Species: Rabbit, Guinea Pig, Rat and Mouse.	Rabbit, guinea pig, rat, mouse	Comparative morphometric	Histological and morphometric evaluation using toluidine blue and Picrosirius red staining	-	Cartilage thickness, fibrocartilage zonation, cell density, collagen arrangement	Rabbits and guinea pigs displayed fibrocartilage structures closest to humans; rodents remain advantageous for molecular studies due	Established anatomical reference for model choice; lacks behavioral validation

							to reproducibility.	

The collective evidence from these studies reflects the wide range of animal models available for investigating temporomandibular disorders. Commonly assessed outcomes included behavioral indicators of pain, histological and morphometric alterations in joint tissues, cytokine and oxidative stress profiles, and neural activation patterns associated with chronic nociception. Although no individual model fully reproduces the complexity of human TMD, rodent models combining inflammatory and mechanical or psychological components demonstrate the highest translational relevance and provide reliable experimental platforms for elucidating disease mechanisms and evaluating potential therapeutic interventions.

Table 1 summarizes the main characteristics of animal models used in temporomandibular disorder (TMD) research. It presents each model type including inflammatory, mechanical, surgical, and psychological stress models, along with their induction methods, common animal species, main pathological features, and key advantages or limitations. This overview highlights how each model contributes to understanding TMD pathogenesis and supports the selection of appropriate models for specific research aims.

4. Discussion

This systematic review aims to summarize the various types of animal models used in studies on temporomandibular disorders (TMD) and to evaluate their relevance to clinical conditions in humans. Based on the literature analysis, the animal models employed in TMD research can be classified into four main categories: inflammatory, mechanical, surgical, and psychological stress models. Each model is designed to replicate specific aspects of TMD pathogenesis, including pain, inflammation, and structural changes within the joint.

4.1. Inflammatory Model

The inflammatory model is one of the most commonly used animal models in temporomandibular disorder (TMD) research, as it can replicate acute inflammatory responses similar to those observed in human conditions. This model is generally established through intra-articular injection of proinflammatory substances such as Complete Freund's Adjuvant (CFA), carrageenan, or formalin, which induce synovitis and inflammatory pain in the temporomandibular joint. Histopathological observations in CFA-induced models reveal inflammatory cell infiltration, thickening of the synovial membrane, cartilage degradation, and increased expression of inflammatory mediators such as TNF-α, IL-1β, and COX-2 [5].

Further research has shown that administration of CFA combined with type II collagen induces both local and systemic inflammatory responses, characterized by pannus formation, synovial thickening, and cartilage erosion. These effects are also associated with elevated levels of TNF-α, IL-1β, and IL-6, along with reduced IL-10 expression, indicating an imbalance between proinflammatory and anti-inflammatory cytokines. This model reproduces inflammatory and degenerative alterations resembling those observed in human TMD, validating its application in studies of temporomandibular joint pathology [13].

Although inflammatory models are relatively simple to perform and effective in mimicking acute inflammation and pain, they primarily represent short term or subchronic conditions, and therefore may not fully reflect the chronic degenerative nature of TMD in humans. Nevertheless, these models remain valuable tools for investigating the mechanisms of orofacial inflammatory pain and for evaluating the efficacy of anti-inflammatory and analgesic treatments [5].

4.2. Mechanical Model

The mechanical model of TMJOA, as a degenerative form of TMD, demonstrates that mechanical loading plays an important role in maintaining joint homeostasis. However, when the applied stress exceeds the tissue's repair capacity, it can trigger joint damage and even progress to osteoarthritis. The close relationship between the biomechanical function of the TMJ and occlusal condition supports those occlusal disturbances, such as severe malocclusion or jaw asymmetry, can be used to simulate the pathological process of TMJOA in experimental animals. Various induction methods such as orthodontic tooth movement, unilateral anterior crossbite, or bite raise have successfully replicated degenerative changes in the condyle and joint tissues resembling those seen in human TMJOA [14].

In addition, other mechanical factors such as indirect forces on the mandible or imbalanced muscle activity, either excessive as in forced jaw opening or reduced as in soft diet conditions, have been shown to cause metabolic changes in the condyle leading to osteoarthritic lesions. This indicates that imbalanced mechanical loading, whether due to abnormal occlusion or unbalanced masticatory activity, plays a significant role in the development of joint degeneration in osteoarthritic type TMD.

Although rat models are widely used because of their technical convenience and tolerance to mechanical device installation, anatomical differences in the TMJ between rats and humans cause the resulting model not to fully reflect the condition of human TMJOA. Therefore, the use of animals with TMJ structures more similar to humans, such as pigs or sheep, is recommended for future research. This mechanical model is considered representative because it directly mimics the disease process of TMJOA caused by occlusal disorders, making it an important tool for understanding the mechanisms of pathological changes and underlying degenerative processes in TMD [14].

4.3. Surgical Model

Animal models induced by surgical interventions are among the most ideal tools to imitate human pathological conditions, particularly in temporomandibular disorders (TMD). This review aims to define the similarities and differences among various surgical animal models. Surgical methods, including anterior disc displacement, disc perforation, and discectomy, can better match actual human pathological conditions and address research problems. All surgical interventions can cause TMJOA as a degenerative form of TMD, but the extent of the resulting pathology varies from one another [15].

4.4. Psychological Stress Model

Psychological stress has been shown to play a crucial role in the onset and progression of TMD, which can occur when an individual perceives an inability to cope with a “challenge” or fails to respond appropriately to emotional or physical threats. Psychological stress conditions such as anxiety and depression are associated with TMJ disorders or dysfunction and can negatively affect quality of life. In addition, psychological stress may lead to spasms and imbalance in the masticatory muscle groups. Since psychological factors are recognized as risk factors for TMD, several experimental animal models have been developed to simulate TMD based on psychological influences. Animals exposed to strong emotional stress exhibit masticatory muscle dysfunction, and abnormal TMJ movement combined with impaired muscle activity is a key factor that alters load bearing capacity and causes uneven stress distribution in the joint. Prolonged exposure to such adverse stress states induces ultrastructural and degenerative changes in the TMJ, consistent with pathological characteristics observed in TMD [5].

Psychological stress can influence the hypothalamus through neural pathways, triggering the release of corticotropin releasing hormone (CRH), which subsequently stimulates the secretion of adrenocorticotropic hormone (ACTH) from the pituitary gland. ACTH then acts on the adrenal cortex to facilitate the synthesis and release of glucocorticoids. Overall, psychological stress models highlight the role of emotional and psychological factors in the pathogenesis of TMD. Consequently, psychological interventions such as stress management training, biofeedback, and habit reversal therapy have proven effective in alleviating pain symptoms in TMD patients [5].

4.5. Limitations and Future Research Directions

Although these models provide a broad understanding of the biological mechanisms underlying TMD, there are several limitations in their application. Anatomical and physiological differences between species, such as cartilage thickness and condylar morphology, may influence research outcomes and limit the translational validity to humans. In addition, many studies lack standardized methods for induction, experimental duration, and observation parameters, thereby restricting the ability to compare results across studies. Future research should focus on developing multifactorial animal models that integrate mechanical, inflammatory, and psychological aspects to better reflect the clinical conditions of TMD patients. The use of transgenic animals and advanced imaging and molecular technologies also holds great potential to enhance the understanding of pathogenesis and to support the evaluation of regenerative therapies.

4.6. Translational Implications

In general, the combination of inflammatory and mechanical models is considered the most relevant for mimicking human TMD conditions, as it reflects the interaction between biomechanical loading and the tissue immune response. These models also provide opportunities to evaluate various therapeutic approaches, such as anti-inflammatory agents, stem cell based regenerative therapies, and neuromodulatory interventions. The findings from these animal models are

expected to strengthen the scientific foundation for developing more effective therapeutic strategies, while also offering a deeper understanding of the complex interactions among biological, mechanical, and psychological factors in TMD.

5. Conclusion

Animal models of temporomandibular disorders (TMD) have provided valuable insights into the biological and biomechanical mechanisms underlying joint degeneration and dysfunction. Each model, whether inflammatory, mechanical, surgical, or psychological, contributes to simulating specific pathological features of human TMD. Inflammatory models help elucidate cytokine mediated joint inflammation, while mechanical loading models demonstrate the role of occlusal disturbances and stress imbalance in cartilage degeneration. Surgical interventions reproduce structural damage such as disc perforation or discectomy, and psychological stress models reveal the influence of neuroendocrine and emotional factors in chronic pain associated with TMD.

Despite these advancements, current animal models still face several limitations in replicating the complex interactions between mechanical, inflammatory, and psychosocial factors present in human TMD. Future research should focus on developing multifactorial and standardized models that integrate these elements to enhance clinical relevance. The application of transgenic animal technologies and advanced imaging or molecular tools is expected to improve understanding of TMD pathogenesis and accelerate the discovery of effective regenerative and therapeutic strategies.

Compliance with ethical standards

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References

[1] Kapos FP, Exposto FG, Oyarzo JF, et al. Temporomandibular disorders: a review of current concepts in aetiology, diagnosis and management. Oral Surgery WILEY 2020; 321–334.

[2] Warzocha J, Gadomska-Krasny J, Mrowiec J. Etiologic Factors of Temporomandibular Disorders: A Systematic Review of Literature Containing Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) and Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) from 2018 to 2022. Healthcare (Switzerland); 12. Epub ahead of print 1 March 2024. DOI: 10.3390/healthcare12050575.

[3] Ohrbach R, Sharma S. Temporomandibular disorders: Definition and Etiology. 2023.

[4] Zieliński G, Pająk-Zielińska B, Ginszt M. A Meta-Analysis of the Global Prevalence of Temporomandibular Disorders. Journal of Clinical Medicine; 13. Epub ahead of print 1 March 2024. DOI: 10.3390/jcm13051365.

[5] Xiang T, Tao ZY, Liao LF, et al. Animal models of temporomandibular disorder. Journal of Pain Research 2021; 14: 1415–1430.

[6] Wang D, Qi Y, Wang Z, et al. Recent Advances in Animal Models, Diagnosis, and Treatment of Temporomandibular Joint Osteoarthritis. Tissue Engineering - Part B: Reviews 2023; 29: 62–77.

[7] Li J, Ma K, Yi D, et al. Nociceptive behavioural assessments in mouse models of temporomandibular joint disorders. Int J Oral Sci; 12. Epub ahead of print 1 December 2020. DOI: 10.1038/s41368-020-00095-0.

[8] Fan Y, Cui C, Li P, et al. Fibrocartilage Stem Cells in the Temporomandibular Joint: Insights From Animal and Human Studies. Frontiers in Cell and Developmental Biology; 9. Epub ahead of print 27 April 2021. DOI: 10.3389/fcell.2021.665995.

[9] Oliveira JP, Nampo FK, Souza MTS, et al. The effect of natural products in animal models of temporomandibular disorders. Journal of Applied Oral Science 2020; 28: 1–10.

[10] Phero A, Ferrari LF, Taylor NE, et al. A novel rat model of temporomandibular disorder with improved face and construct validities. Life Sci 2021; 1–26.

[11] Chung MK, Wang S, Alshanqiti I, et al. The degeneration-pain relationship in the temporomandibular joint: Current understandings and rodent models. Frontiers in Pain Research; 4. Epub ahead of print 2023. DOI: 10.3389/fpain.2023.1038808.

[12] Navarrete J, Mendoza F, Iturriaga V, et al. Morphoquantitative Comparison of the Temporomandibular Joint in Laboratory Species: Rabbit, Guinea Pig, Rat and Mouse. 2025.

[13] Ananias FEF, dos Santos VAB, Groppo FC, et al. Inflammatory and degenerative effects of induced osteoarthritis/rheumatoid arthritis models on temporomandibular joint of rats. Arch Oral Biol; 150. Epub ahead of print 1 June 2023. DOI: 10.1016/j.archoralbio.2023.105693.

[14] Zhao Y, An Y, Zhou L, et al. Animal Models of Temporomandibular Joint Osteoarthritis: Classification and Selection. Frontiers in Physiology; 13. Epub ahead of print 28 April 2022. DOI: 10.3389/fphys.2022.859517.

[15] Zhou J, Ren R, Li Z, et al. Temporomandibular joint osteoarthritis: A review of animal models induced by surgical interventions. Oral Diseases 2023; 29: 2521–2528.