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A Narrative Review of the Dental Implications of Optogenetics Recognized by the 2026 Nobel Prize in Physiology or Medicine

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Abstract

The 2026 Nobel Prize in Physiology or Medicine recognizes discoveries concerning light-gated ion channels and optogenetics. For dentistry, the immediate value of this work is the ability to test how particular cells contribute to oral sensation and function. This narrative review examines foundational studies and representative primary research on dental nociception, trigeminal pain, salivation, mastication, taste, dental pulp stem cells, craniofacial muscle function, and bacterial behavior. A purposive selection was drawn from targeted searches of PubMed-indexed records, publisher websites, and official sources, with a verification update on October 8, 2026. Findings were synthesized descriptively, without quantitative pooling, and assessed separately from proposed clinical applications. In rodents, optogenetic experiments have linked intradental neurons to protective jaw-opening responses, altered injury-associated facial hypersensitivity, and identified circuits involved in salivation and oral movement. Cultured human dental pulp cells have shown preliminary changes in neural differentiation markers. These findings support research use, but they do not establish effectiveness in dental patients. Direct optical interventions require reliable genetic delivery and tissue access, evaluation of construct persistence, assessment of immune responses and heating, and preservation of protective sensory and motor function. This review proposes using optogenetically identified targets to guide drug or conventional neuromodulation research while direct optical interventions undergo further evaluation. Both routes require replicated findings in relevant disease models and outcomes that reflect patient benefit.

Categories: Neurology, Oral Medicine, Dentistry
Keywords: dental pain, dental pulp regeneration, mastication, optogenetics, orofacial function, salivary secretion, translational research, trigeminal neuropathic pain

Introduction And Background

Tooth pain, salivary secretion, and chewing depend on interactions among sensory cells, autonomic pathways, and motor networks. Clinical examination can identify a disturbed function but often cannot isolate the cellular contribution. Optogenetics allows investigators to perturb a defined population at a chosen time and test whether its activity changes an oral response.

On October 5, 2026, the Nobel Prize in Physiology or Medicine was awarded to Peter Hegemann, Georg Nagel, and Karl Deisseroth for discoveries concerning light-gated ion channels and optogenetics [1]. The underlying work developed over decades. Studies of algal channelrhodopsins established light-sensitive membrane conductance, followed by genetically targeted optical control of mammalian neurons [2-4]. This progression made it possible to investigate cellular contributions to behavior with a degree of timing and targeting unavailable to many conventional perturbations.

The oral and craniofacial applications of optogenetics have already been reviewed [5]. The present review revisits this literature in light of the Nobel recognition and selected developments in 2025 and 2026. Its purpose is to distinguish established experimental findings from dental applications that remain hypotheses, and to identify the evidence needed to connect the two.

This distinction matters particularly in pain research. Dental nociceptive pain, injury-related trigeminal neuropathic pain, and classical trigeminal neuralgia are clinically different entities. The International Classification of Orofacial Pain provides a framework for separating such presentations [6]. A finding in an animal model should therefore be interpreted in relation to the process modeled, rather than extended to every painful condition within the trigeminal territory.

Methods

Literature Identification and Scope

Literature discovery on October 6, 2026, used targeted web retrieval of PubMed-indexed records, publisher

articles, and official institutional sources. Search terms combined optogenetics or optogenetic with dental, trigeminal, salivary, mastication, orofacial, taste, dental pulp stem cells, facial nerve, bacterial virulence, immunogenicity, and thermal constraints. Exact title and DOI searches checked individual records, and references of retrieved publications identified relevant earlier experiments. No lower publication-date limit was applied.

A verification update on October 8, 2026, repeated exact-record checks and searches restricted to pubmed.ncbi.nlm.nih.gov, including "(optogenetics OR optogenetic) (dental OR trigeminal OR orofacial)" and "optogenetic (salivation OR mastication OR taste)". These were web-engine queries directed at indexed records, not a comprehensive native PubMed/MEDLINE search. Scopus and Web of Science were not searched. The search sources, dates, terms, and verification procedures are summarized in Table *1*.

Search stage	Source or search restriction	Date	Search terms or procedure
Initial literature identification	Targeted web retrieval of PubMed-indexed records, publisher articles, and official institutional sources	October 6, 2026	Reported term groups: optogenetics or optogenetic combined with dental, trigeminal, salivary, mastication, orofacial, taste, dental pulp stem cells, facial nerve, bacterial virulence, immunogenicity, and thermal constraints
Dental and trigeminal literature update	Web search restricted to pubmed.ncbi.nlm.nih.gov	October 8, 2026	(optogenetics OR optogenetic) (dental OR trigeminal OR orofacial)
Salivary, oral motor, and taste literature update	Web search restricted to pubmed.ncbi.nlm.nih.gov	October 8, 2026	optogenetic (salivation OR mastication OR taste)
Dental pulp stem-cell literature update	Web search restricted to pubmed.ncbi.nlm.nih.gov	October 8, 2026	optogenetic "dental pulp stem cells"
Thermal-safety source verification	Web search restricted to sciencedirect.com	October 8, 2026	"Pulp response to externally applied heat" "5.5"
Bibliographic and source verification	Indexed records, publisher websites, and official institutional sources	October 6 and 8, 2026	Exact title and DOI searches; comparison of bibliographic metadata and source content
Identification of earlier experiments	Reference lists of retrieved publications	October 6, 2026	Reference checking to identify relevant foundational and earlier experimental studies

TABLE 1: Literature identification and verification strategy.

The table documents the purposive literature-identification and verification procedures used for this narrative review. The initial search entry summarizes reported term groups rather than a retained verbatim query; the four domain-restricted update queries are reproduced exactly as recorded. Searches used web engines to retrieve indexed and publisher records rather than comprehensive native database screening. No lower publication-date limit was applied. Scopus and Web of Science were not searched. Full-text interpretation was restricted by source availability. The eligibility criteria, the extraction items, and the reporting standard are described in the text.

Study Selection and Narrative Synthesis

Selection was purposive, with primary studies of dental nociception, trigeminal pain, salivation, mastication, taste, dental pulp cells, and craniofacial muscle function forming the application sections. Foundational experiments explained the tools, while studies outside the oral and craniofacial region addressed methodological questions, safety, or human feasibility. The review concerns genetically encoded control by light; conventional laser therapy, photobiomodulation, and photodynamic therapy are outside its scope. Selected nonoptogenetic studies provide physiological context rather than evidence of an optogenetic treatment effect.

Full text was examined when accessible; otherwise, interpretation was limited to the indexed abstract and bibliographic record. Institutional sources supported the prize announcement and regulatory discussion.

The existing oral and craniofacial review established the field's prior scope rather than replacing primary experiments.

Literature discovery and draft selection were assisted by AI (ChatGPT, OpenAI, Inc., San Francisco, CA, USA). A second pass within the same workflow checked bibliographic details and the interpretation of the selected studies; there was no independent screening by two human reviewers. This was a purposive narrative review without exhaustive screening or a formal study-level risk-of-bias assessment.

For each study, the review considered the model, manipulated target, measured outcome, and limits of dental inference. Findings were grouped by oral function and discussed in relation to the model studied. Direct oral and trigeminal experiments were distinguished from studies providing methodological or translational context. No meta-analysis, meta-regression, or review-level hypothesis testing was performed; no pooled effect sizes, p-values, or CIs were calculated. The diverse models and outcomes do not support a common treatment-effect estimate.

Review

What optogenetic experiments can establish

Optogenetics requires a light-responsive molecular construct in the cells to be manipulated. Nagel et al. characterized channelrhodopsin-1 as a light-gated proton channel and channelrhodopsin-2 (ChR2) as a directly light-gated cation channel [2,3]. Boyden et al. combined ChR2 expression with optical stimulation to control mammalian neuronal firing on a millisecond timescale [4]. These studies established a method for perturbing electrical activity, not evidence of efficacy against a dental disease.

Excitation and inhibition require different tools. Development of the light-driven chloride pump halorhodopsin enabled suppression of neuronal firing and complementary use with ChR2 [7]. Later work on soma-targeted anion-conducting channelrhodopsins improved inhibitory performance while addressing unwanted axonal excitation [8]. Consequently, a description of light-mediated inhibition must specify the construct and cellular compartment; the color of the light alone does not establish the direction of the physiological effect.

Activation that produces a response supports sufficiency under the experimental conditions. Inhibition that prevents a response can support necessity, provided that off-target effects and general impairment have been excluded. Neither result establishes that a target is safe to manipulate indefinitely or that the same intervention benefits a patient. Rescue experiments, complementary perturbations, and physiological measurements strengthen causal interpretation.

Optogenetic actuation differs from measurements and perturbations often used alongside it. Calcium imaging provides an intracellular calcium signal from which neuronal activity can be inferred [9]. Receptor-based chemogenetics uses engineered receptors activated by a selected ligand to modify cellular signaling [10]. A combined study should therefore attribute each observation to the method that produced it, rather than describe every experimental result as optogenetic.

Dental nociception and protective reflexes

Ronan et al. identified intradental high-threshold mechanonociceptors in mice that responded as tooth structure became compromised. Their experiments combined imaging with optogenetic and chemogenetic manipulation. Chemogenetic activation produced pain-associated behavior, whereas transient optogenetic activation triggered a rapid jaw-opening reflex involving the digastric muscle [11]. The study connects dental sensory activity to an observable protective action.

For analgesia, the practical question is whether abnormal sensitivity can be reduced while preserving the responses that limit mechanical damage. Future studies should assess discomfort-related outcomes alongside protective oral behavior. A higher withdrawal threshold alone would not answer that question.

Bernal et al. implicated odontoblast transient receptor potential canonical 5 channels in dental cold sensing [12]. This provides a complementary example of target identification outside an optogenetic intervention. For tooth sensitivity, the useful next question is which cellular signals drive inflammatory hypersensitivity and which preserve protective sensation.

Peripheral and central trigeminal pain

Peripheral pain experiments established that optogenetic manipulation can change nociceptive behavior outside the brain. Iyer et al. delivered excitatory or inhibitory opsins to peripheral sensory pathways in nontransgenic mice. Transdermal light could evoke nocifensive behavior or reduce injury-associated hypersensitivity, depending on the construct [13]. The model involved the sciatic system, so its relevance to dentistry is methodological rather than direct.

Kc et al. delivered adeno-associated viral constructs encoding ChR2 and enhanced halorhodopsin (eNpHR3.0) under a human synapsin promoter to the trigeminal ganglion of rats with infraorbital nerve constriction. The authors described this preparation as a trigeminal neuralgia model. Activating eNpHR3.0 with yellow light reduced abnormal thalamic firing and hypersensitivity-related behavior; ChR2 activation with blue light produced a different pattern, including persistent hypersensitivity [14]. The manipulation altered injury-associated trigeminal signaling, and its direction depended on the expressed tool and stimulation protocol.

Central pathways provide additional targets. Moon et al. reported that optogenetic inactivation of the anterior cingulate cortex altered pain-associated behavior and thalamic activity in a rat model of infraorbital nerve injury [15]. These experiments are useful for mapping circuits that sustain pain beyond the peripheral site of injury. They do not establish a clinical indication for intracranial intervention in dental patients.

Nerve constriction studies may use the label trigeminal neuralgia, but their experimentally induced injury and hypersensitivity should be distinguished from the clinical categories in the International Classification of Orofacial Pain [6,14,15]. Translation requires a defined patient phenotype and outcomes that capture spontaneous pain, oral function, and treatment burden in addition to evoked responses.

Glial signaling and the emotional dimensions of pain

In a separate study, Kc et al. used a glial fibrillary acidic protein-directed halorhodopsin construct in the trigeminal nucleus caudalis of rats with infraorbital nerve constriction. Light-driven manipulation of the targeted astrocytes altered hypersensitivity-related behavior and thalamic discharge [16]. The findings motivate further investigation of glial involvement, with independent verification of cell targeting and construct physiology before assigning the behavioral change to a particular astrocytic mechanism.

Lu et al. used human functional MRI to identify the parafascicular nucleus as a candidate region, then investigated distinct neuronal ensembles in a mouse model of trigeminal injury. Manipulating different mouse pathways altered facial hypersensitivity or anxiety-like behavior separately [17]. Thus, the human component localized an association, while the mouse experiments provided the causal circuit evidence.

For dental pain research, these findings argue for measuring distress and function alongside pain intensity. Rodent anxiety-like behavior is not equivalent to a patient's dental phobia. The separable pathways nevertheless provide a basis for testing whether relief of pain and relief of its associated distress respond differently to an intervention.

Salivary control and oral motor function

Park and Lee identified a brainstem salivatory circuit in mice and showed that activating cholinergic neurons in the inferior salivatory nucleus could evoke saliva secretion. Their work also distinguished local sensory input from cortical input involved in anticipatory salivation [18]. These findings provide access to a physiological process that is clinically important but difficult to dissect using salivary output alone.

Testing this approach in salivary hypofunction requires a disease model with characterized glandular reserve. Increased neural drive may have little value if the gland cannot respond. Preclinical studies should measure salivary flow, gland structure, and durability of the response. Any subsequent clinical study should prespecify both measured secretion and patient-reported dryness as outcomes.

Oral movements have been examined at several levels. Mercer Lindsay et al. used selective optogenetic activation to demonstrate parallel corticobulbar pathways coordinating orofacial actions [19]. Sungeelee et al. identified Phox2b-expressing supratrigeminal neurons involved in the oral phase of feeding; broad activation or inhibition interrupted voluntary feeding sequences in mice [20]. These findings show the importance of coordinated circuit activity, rather than indicating that increasing or decreasing one node necessarily improves function.

Falardeau et al. stimulated the cortical masticatory area optogenetically in awake, head-fixed mice, evoking rhythmic jaw movements and mapping brainstem c-Fos expression. Their sensory-input experiments instead used electrical stimulation of the trigeminal tract in vitro with calcium imaging; the activation patterns differed partly between these preparations [21]. The work suggests candidate sites for studying sensory-motor integration. Testing bruxism, temporomandibular disorders, or adaptation to a prosthesis would require a model of the specific condition.

Taste and oral sensory function

Vandenbeuch et al. selectively activated type III taste cells in mice and recorded chorda tympani responses. Concurrent optical activation reduced neural responses to several tastants, supporting modulation within the taste bud before sensory information reaches the brain [22]. The measured outcome was a change in nerve activity, not recovery from a taste disorder.

At the cortical level, Peng et al. used optogenetic manipulation to investigate taste-associated behavior in mice [23]. Together with the peripheral experiments, this work offers a way to test where a sensory disturbance arises. Applying it to dysgeusia would require a defined deficit and evidence that changing the targeted pathway improves taste-related function.

A study of dysgeusia would need to link the cellular or circuit effect to taste recognition and food-related behavior. Subsequent clinical assessment would also need to address quality of life. A changed response to a tastant alone does not show that eating has become safer or more satisfactory.

Dental pulp cells and craniofacial motor models

Dental pulp stem-cell research predates optogenetics. Gronthos et al. isolated human dental pulp cells that formed a dentin/pulp-like complex after transplantation into immunocompromised mice [24]. This nonoptogenetic experiment established a biological foundation for tissue research.

Niyazi et al. introduced ChR2 into human dental pulp stem cells and applied pulsed blue light. They reported neuron-like morphological changes and increased expression of Nestin, doublecortin, and microtubule-associated protein 2 [25]. These endpoints provide preliminary evidence relevant to neural differentiation. They do not establish mature electrical function, synaptic integration, or successful pulp reinnervation. The reported marker changes also leave the causal signaling sequence unresolved; a calcium-dependent differentiation mechanism would require direct testing.

The next step for regenerative endodontics is to test electrical function and cell survival within a vascularized tissue environment. Functional integration and an appropriate response to injury would be more informative than neural markers alone; persistent pain would be an adverse outcome. The reported differentiation endpoints provide no basis for predicting dentin repair or whole-tooth regeneration.

Vajtay et al. stimulated denervated whisker-pad muscles after facial nerve transection in mice and characterized their functional and transcriptional properties [26]. Evoked movement revealed the state of the muscle despite loss of nerve input. A rehabilitation claim would additionally require evidence of useful voluntary function; direct contraction alone does not show facial nerve repair.

Bacterial behavior as a controllable research variable

Optogenetic tools can regulate microbial processes as well as mammalian cells. Xia et al. introduced a photoactivated adenylate cyclase into *Pseudomonas aeruginosa*, enabling light-dependent control of intracellular cyclic adenosine monophosphate, twitching motility, and infection behavior. In their mouse infection model, illumination increased lesion severity [27]. The experiment demonstrates controllability of virulence, not antimicrobial benefit.

For oral research, this approach could help construct models that separate bacterial behavior from other components of an infection. Testing a comparable system in clinically relevant oral organisms or polymicrobial biofilms would be necessary before making a dental claim. Engineered *Pseudomonas* results should not be generalized to naturally occurring cariogenic or periodontal biofilms, and they do not justify exposing an infection to light as treatment.

Representative experiments, their measured outcomes, and the limits of dental interpretation are summarized in Table *2*.

Domain	Model and manipulation	Observed finding	Limit of interpretation
Tooth protection	Mouse intradental neurons; optogenetic activation [11]	Rapid jaw opening via digastric contraction	Reflex activation is not evidence of clinical analgesia
Peripheral facial pain	Rat infraorbital nerve constriction; trigeminal ganglion manipulation [14]	Inhibition altered hypersensitivity and thalamic firing	Nerve-injury model; no dental anesthesia trial
Glial contribution	Rat nerve-injury model; GFAP-directed construct in brainstem astrocytes [16]	Behavioral and thalamic responses changed	Targeting and construct physiology require validation
Pain and affect	Mouse circuit manipulation combined with human MRI observations [17]	Sensory and anxiety-related pathways were distinguishable	Human findings were associative; manipulation was in mice
Salivary secretion†	Mouse salivatory nucleus; activation of cholinergic neurons [18]	Saliva secretion was evoked	Effectiveness in diseased glands was not established
Pontine feeding control	Mouse Phox2b-expressing supratrigeminal neurons; activation or inhibition [20]	Voluntary feeding sequences were interrupted	Normal ingestion circuit; functional restoration was not tested
Cortical mastication control	Mouse cortical masticatory area; optogenetic stimulation [21]	Rhythmic jaw movement and brainstem c-Fos expression	No treatment study of bruxism or temporomandibular disorders
Taste processing	Mouse type III taste cells; selective activation [22]	Reduced nerve responses to several tastants	Modulation is not recovery from dysgeusia
Pulp cells†	Human dental pulp stem cells in vitro; ChR2 and light [25]	Neural markers increased; neuron-like morphology appeared	Functional neurons and pulp reinnervation were not demonstrated
Facial muscle function†	Denervated mouse whisker-pad muscle; direct activation [26]	Evoked movement permitted muscle characterization	Evoked contraction is not nerve regeneration
Bacterial behavior†	Engineered *Pseudomonas aeruginosa*; light-controlled cAMP [27]	Motility and infection severity increased	Research model; no antimicrobial efficacy

TABLE 2: Representative experiments and the limits of dental translation.

Selected primary experiments are grouped by domain, with the model, observed outcome, and boundary of dental interpretation shown for each study. Each row summarizes one selected publication. The table is a qualitative summary, not a meta-analysis: nothing was pooled, no effect estimates were extracted, and these outcomes do not share a scale on which they could be compared. † This application is illustrated by one primary publication in this review. The symbol does not indicate the total literature in the field or establish independent replication.

cAMP, cyclic adenosine monophosphate; ChR2, channelrhodopsin-2; GFAP, glial fibrillary acidic protein

Requirements for translation

Technical precision does not remove the need for appropriate controls. Owen et al. showed that illumination can heat brain tissue and influence neuronal activity even without the intended opsin effect [28]. Dental experiments should therefore include matched light-only and construct-only controls and evaluate temperature at the target tissue. An observed behavioral effect may otherwise reflect the illumination protocol rather than selective cellular manipulation.

Dental thermal safety requires evidence from the tissue to be illuminated. Baldissara et al. evaluated healthy human teeth exposed to temperature increases of 8.9-14.7 °C and reported low short-term susceptibility to injury under their experimental conditions [29]. This preliminary result does not define a safe exposure for optogenetic stimulation, diseased pulp, or repeated illumination. A dental protocol should measure temperature at the target and examine exposure duration, tissue viability, and structural injury rather than import a numerical limit from brain experiments.

The physiological consequences of inhibitory tools also depend on where and how they are used. Mahn et al. found that manipulating presynaptic terminals could produce effects different from those expected from simple neuronal silencing, including altered spontaneous release [30]. Their later work improved somatic targeting of anion-conducting channelrhodopsins [8]. These findings argue for direct validation of the chosen construct in the relevant oral or trigeminal preparation, rather than adopting a brain protocol unchanged.

Immune responses are a separate concern. Maimon et al. reported loss of optogenetic expression and adverse neural and muscular consequences associated with ChR2 expression in a rat peripheral motor preparation [31]. This finding should not be generalized to every construct or tissue, but it makes durability and immune assessment essential components of a translational program. Immediate behavioral benefit would not establish long-term safety.

Light delivery presents another practical boundary. External illumination may reach a superficial experimental target, whereas a deep ganglion or brainstem target may require an implanted optical path. The stimulation step can be noninvasive even when gene delivery or device placement is invasive [13,14]. In teeth, feasibility would have to be demonstrated for the actual target location and optical path, with attention to tissue heating and structural consequences.

The single ophthalmology study included here serves only as a human feasibility example. Sahel et al. reported partial visual recovery in one blind patient after retinal gene delivery combined with an external light-delivery device [32]. This demonstrates a possible human implementation, while leaving dental efficacy untested. Differences in tissue access, disease biology, and acceptable treatment burden prevent direct transfer of that result to routine dental procedures.

Switching off illumination can stop a particular stimulation protocol, but it does not remove an introduced genetic construct. Accordingly, assessment must consider the duration and biological consequences of expression as well as the reversibility of the immediate response. U.S. FDA guidance on human gene therapy describes risk-based decisions about long-term follow-up; it does not prescribe the same surveillance period for every product [33].

Two routes to dental benefit should be considered. One uses optogenetics to identify a causal target that can later be addressed with a drug or a conventional neuromodulation method. The other develops a direct optogenetic intervention requiring validated delivery, light access, and longitudinal safety. The first route may be more practical for some dental conditions because it does not require gene delivery to the eventual patient. This is a proposed translational framework, not a demonstrated comparison of clinical effectiveness. The proposed routes are summarized in Figure *1*.

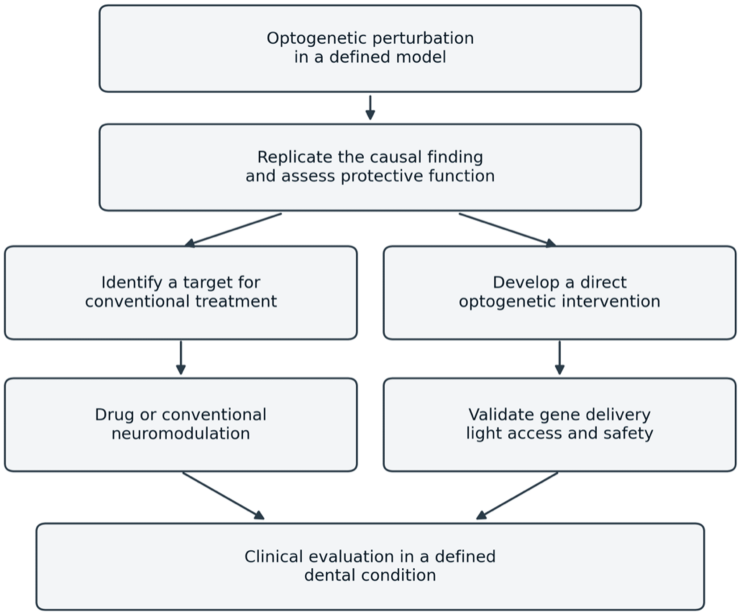

FIGURE 1: Proposed routes from optogenetic experiments to dental benefit.

This schematic illustrates two proposed routes from optogenetic experiments to dental benefit. One uses experimentally identified causal targets to guide drug or conventional neuromodulation research; the other involves developing direct optogenetic interventions, requiring further validation of gene delivery, light access, and safety. Arrows represent proposed development steps rather than established clinical effectiveness. The schematic was created by the author in Apple Keynote (Apple Inc., Cupertino, CA, USA). ChatGPT (OpenAI, Inc., San Francisco, CA, USA) assisted only with locating and organizing the source information. No patient images or quantitative experimental data are presented.

Discussion

Clinical Implications and Priorities for Research

The immediate dental contribution of these experiments is to clarify disease mechanisms and identify candidate targets. They provide no clinical basis for replacing established care with an optical gene-based intervention. Pain is a useful starting point because its sensory, protective, and affective components can be studied separately.

For pain studies, clinically meaningful success would include improved spontaneous pain and oral function, alongside preservation of necessary sensation and avoidance of motor impairment. For salivary studies, success would require sustained secretion in a defined disease phenotype and a benefit that patients experience. Regenerative investigations would need functional tissue integration, not a change in marker expression alone.

The next study should address the gap between the observed mechanism and the proposed dental application. Replication in a relevant model comes first. Direct optical intervention would also require a clinically realistic delivery method and an acceptable balance of benefit and treatment burden. A drug or conventional intervention that acts on an optogenetically identified target could offer dental benefit without optical gene delivery to the patient.

Table *3* sets out proposed study priorities and outcomes that would help determine whether a mechanistic finding warrants further dental translation.

Research priority	Next study needed	Meaningful outcome
Dental and trigeminal pain	Replicate a target in a defined disease model; control for sensory and motor impairment	Less spontaneous pain with preserved protective oral behavior
Salivary hypofunction	Characterize glandular reserve before testing sustained neural stimulation	Sustained flow, gland integrity, and improvement in experienced dry mouth
Oral motor dysfunction	Test a specific impairment rather than normal circuit activation alone	Improved chewing or feeding without disrupted coordination
Taste dysfunction	Link peripheral or central modulation to a defined sensory deficit	Better taste recognition and food-related function
Regenerative pulp research	Assess electrical function, vascular support, integration, and response to injury	Viable integrated tissue with appropriate sensory function
Direct optogenetic intervention	Validate construct, targeting, optical access, immune effects, and follow-up	Durable benefit with an acceptable treatment burden and safety profile

TABLE 3: Proposed research steps and outcomes needed for dental translation.

Each row pairs a proposed next study with outcomes relevant to dental translation. These priorities derive from the review synthesis and are not outcomes already demonstrated in patients. Their feasibility requires evaluation in the relevant condition. This table sets out proposed designs and outcome domains. It holds no measured data and no effect estimates.

Limitations of the Evidence and This Review

The studies discussed differ in species, cell targeting, construct, anatomical site, illumination protocol, and outcome. Rodent withdrawal thresholds, electrophysiological responses, cell markers, and feeding behavior are not interchangeable measures of patient benefit. The selection therefore supports a qualitative appraisal and should not be interpreted as a ranking of treatment effect sizes.

Within this selection, salivary secretion, neural differentiation of pulp cells, facial muscle function, and engineered bacterial behavior are each illustrated by one primary publication (Table *2*). This reflects the scope of the review rather than the total number of studies in those fields. Such examples identify candidate mechanisms but do not establish independent replication, disease relevance, or performance during chronic stimulation. Intracranial experiments also offer limited direct information about treatment feasibility in a dental setting.

This review used purposive retrieval of indexed records and publisher material rather than an exhaustive database search. It is consequently vulnerable to selection and publication bias. The initial search is

documented as term groups rather than a complete query, which limits exact reproducibility. Access to full text was variable, and no formal assessment of the complete methodological reporting of every paper was undertaken. The discussion is restricted accordingly to verifiable experimental findings and clearly identified research proposals.

A subsequent focused synthesis should assess animal intervention studies using domain-level judgments from the Systematic Review Centre for Laboratory Animal Experimentation (SYRCLE) risk-of-bias tool [34] and examine reporting against Animal Research: Reporting of In Vivo Experiments (ARRIVE) 2.0 [35]. These address different questions: potential bias and reporting completeness. Neither was formally applied here. The absence of those assessments limits confidence in the evidence and is not remedied by proposing future study criteria.

The Nobel recognition creates a timely opportunity to communicate the field, but it does not strengthen the clinical evidence of an individual dental application. Further work should test the specific target, intervention, disease model, and outcome that a proposed clinical claim requires.

Conclusions

Optogenetics provides dentistry with a method for testing causal relationships in oral sensation and function. Representative studies support its research value in dental protective reflexes, injury-associated trigeminal pain, salivary control, mastication, and taste. Dental pulp cell and craniofacial muscle experiments offer additional, earlier-stage opportunities.

The evidence reviewed does not establish clinical effectiveness in dental patients. Progress depends on preserving useful sensory and motor function, reproducing the mechanisms in relevant disease models, and resolving delivery and safety requirements. Dental benefit may arise first through drugs or conventional neuromodulation directed at targets identified optogenetically. For dentistry, the Nobel recognition highlights a research method whose clinical value will depend on how well these remaining questions are answered.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Volodymyr Kachmar

Acquisition, analysis, or interpretation of data: Volodymyr Kachmar

Drafting of the manuscript: Volodymyr Kachmar

Critical review of the manuscript for important intellectual content: Volodymyr Kachmar

Supervision: Volodymyr Kachmar

Disclosures

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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