Journal of Dental Sciences

Volume 21 | Issue 2 Article 2

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Bahrami,, Rashin; Pourhajibagher, Maryam; Gharibpour, Fateme; Rezazadeh, Amirmorteza; and Bahador, Abbas () "The effect of photobiomodulation therapy on neurosensory recovery of infra-alveolar nerve following iatrogenic trauma: A literature review," *Journal of Dental Sciences*: Vol. 21: Iss. 2, Article 2.
Available at: https://jds.ads.org.tw/journal/vol21/iss2/2

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Review article

The effect of photobiomodulation therapy on neurosensory recovery of infra-alveolar nerve following iatrogenic trauma: A literature review

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Received 26 October 2025; Final revision received 11 November 2025
Available online 1 April 2026

KEYWORDS
Photobiomodulation therapy;
Trauma;
Inferior alveolar nerve;
Iatrogenic trauma

Abstract In recent years, Photobiomodulation therapy (PBMT), or so-called low-level laser therapy, has gained dental researchers' attention as a promising non-invasive treatment method, which can be implemented for neurosensory recovery of the inferior alveolar nerve (IAN) following iatrogenic trauma caused by dental procedures, such as orthognathic surgery, implant placement, and molar extractions. This study reviews the findings from clinical studies within the past 10 years evaluating the efficacy of PBMT in these settings. Through assessing varying results, we understood that generally they accelerate nerve healing and improve patient-reported outcomes, such as oral health-related quality of life. The known mechanism

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https://doi.org/10.1016/j.jds.2025.11.010
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of action for low-intensity light sources, typically lasers or LEDs, that are used in PBMT is to enhance cellular metabolism, reduce inflammation, and promote nerve regeneration. The most commonly applied parameters of PBMT in the dental practice are wavelengths between 630 and 1064 nm, energy densities between 3 and 12 J/cm^2, and treatment time between 15 and 90 s per point per session. Although its clinical potential is great, the extensive application of PBMT is restricted due to variability in treatment protocols and lack of standardization. This review emphasizes the need for further studies that include longer follow-ups and more consistent protocols, which can optimize the application of PBMT, making it incorporable into routine clinical practice for neurosensory recovery following dental procedures.

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Introduction

Neurosensory dysfunction in the oral and maxillofacial region represents a significant complication associated with a variety of dental procedures, including orthognathic surgery, third molar extraction, implant placement, anesthesia injection, and rigid internal fixation.[1,2] Among peripheral nerves, the trigeminal nerve is particularly susceptible to complex injuries, with the inferior alveolar and lingual branches being the most frequently affected.[3] Consequently, iatrogenic nerve injuries can substantially impair patients' quality of life (QoL) by inducing sensory deficits, psychological distress, and notable social and functional limitations.[3] To address these challenges, treatment strategies are generally categorized into three main approaches: surgical intervention, pharmacological therapy, and physiological management.[4]

According to Seddon's classification, nerve injuries are divided into neurapraxia, axonotmesis, and neurotmesis. Except for neurotmesis, which generally necessitates microsurgical intervention, the other two forms occur more frequently and are typically treated using conservative methods.[1] Recently, photobiomodulation therapy (PBMT), or low-level laser therapy (LLLT), has been recognized as an innovative approach for nerve repair, offering a safe, effective, and non-invasive treatment option with fewer side effects compared to conventional methods.[1,5,6] Evidences suggest that PBMT can reduce inflammation, accelerate wound healing, and alleviate pain and discomfort.[7,8] Several mechanisms have been proposed to account for these effects. The most widely accepted hypothesis indicates that photons in the red and near-infrared spectral regions are absorbed by cytochrome *c* oxidase (CCO), resulting in the dissociation of inhibitory nitric oxide and triggering a cascade that enhances electron transport, increases mitochondrial membrane potential, and promotes ATP synthesis.[6] Furthermore, PBMT has been shown to facilitate axonal growth and support nerve regeneration through activation of photosensitive membrane channels and extracellular latent growth factors, such as transforming growth factor beta 1 (TGF-β1), in both spinal cord and peripheral nerve injuries.[6] In addition, the photochemical and photobiological effects of PBMT at the cellular level mitigate inflammatory processes, thereby further enhancing the efficiency of nerve regeneration.[7]

Importantly, the clinical efficacy of PBMT in treating inferior alveolar nerve (IAN) injuries is highly dependent on the accurate selection of device parameters, including wavelength, power density, energy density, and irradiation time, as cortical bone at the injury site can significantly affect light penetration.[7] Taken together, these findings underscore the necessity of optimizing PBMT protocols to achieve maximal therapeutic outcomes. Nevertheless, evidence on the application of low-intensity laser therapy for IAN injuries remains scarce, especially in the form of clinical trials. In addition, only a few systematic reviews have focused on implant-associated adverse effects, despite their increasing frequency in dental practice.

Therefore, this review aimed to evaluate the efficacy of PBMT in promoting neurosensory recovery of the IAN following iatrogenic trauma. The accumulated evidence supports PBMT as a safe and effective intervention, highlighting its potential to improve functional outcomes and QoL in affected patients.

Mechanisms of photobiomodulation therapy for neurosensory recovery

PBMT enhances neurosensory recovery through three main biological pathways based on previous studies (Fig. 1) including mitochondrial stimulation, nerve regeneration, and anti-inflammatory effects:[6,9–13]

1. Mitochondrial stimulation: CCO, a light-sensitive molecule located in the mitochondrial respiratory chain, acts as the primary chromophore responsible for photon absorption. When exposed to light with red and infrared wavelengths, CCO absorbs specific wavelengths, leading to the displacement of nitric oxide and activation of the electron transport chain, which ultimately increases mitochondrial membrane potential and enhances ATP synthesis.
2. Nerve regeneration: PBMT facilitates axonal growth and neurite outgrowth by modulating ion channel activity and promoting the release of growth factors essential for neural repair, like TGF-β1.

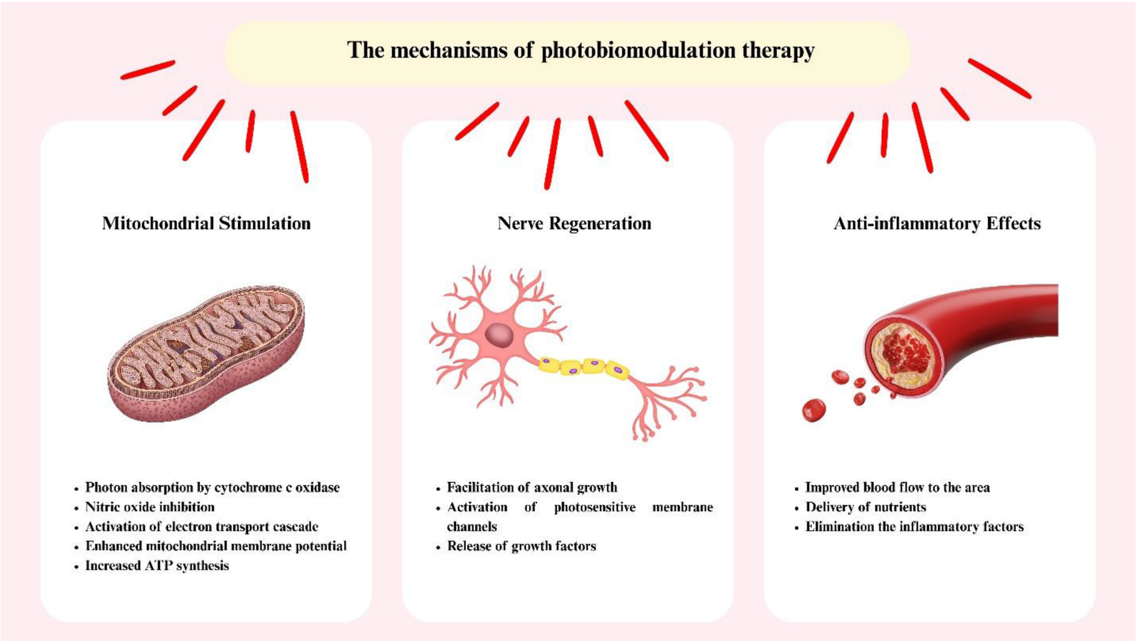

Figure 1 Mechanisms of photobiomodulation for neurosensory recovery (ATP, Adenosine triphosphate).

3. Anti-inflammatory effect: PBMT improves local blood circulation, enhances the delivery of oxygen and nutrients to injured sites, reduces inflammatory mediators, and creates a more favorable environment for tissue regeneration.

Clinical evidence on photobiomodulation therapy for infra-alveolar nerve injuries

Several clinical trials have studied the clinical application of PBMT for neurosensory recovery of the IAN following iatrogenic injuries caused by dental treatments (Table 1). Since oral health-related quality of life (OHRQoL) and daily activities of patients are affected by the injuries, the timely and efficient acceleration of nerve recovery through options like PBMT is particularly significant. Unfortunately, a delayed or incomplete recovery can lead to long-term functional limitations, discomfort, and emotional distress, underlining the importance of treatment. Variable protocols are described for PBMT, such as laser wavelengths, energy densities, and session durations, that have hindered its widespread clinical application. However, the growing body of research consistently supports PBMT's efficacy, especially in enhancing nerve regeneration and improving sensory recovery. In this section, the findings from key recent studies are integrated, making it possible to establish a more comprehensive understanding of PBMT's potential in treating IAN injuries.[14—23]

The relationship between wavelength, energy density, and treatment outcomes has been a subject of interest in multiple studies. Baydan et al. For example, studied the effectiveness of GRR laser (904/650 nm) and Epic10 laser (940 nm) in lower lip paresthesia that may happen after a sagittal split ramus osteotomy (BSSO). Their study indicated that both therapies can make a better impact in improving neurosensory recovery than the vitamin B control group, with GRR laser showing a slightly superior clinical outcome, maybe due to its deeper tissue penetration. These findings, on the one hand, prove that laser therapy is superior to conventional treatments like vitamin B therapy.[14] Also, in the other made the laser penetration depth a crucial factor for effective nerve regeneration, and emphasizes that it is important to optimize the laser parameters to achieve the best possible results. Building on this, Yazdani et al. evaluated the effects of LLLT using an Nd:YAG laser (1064 nm, 12 J/cm^2) on IAN paresthesia and dysesthesia in patients following oral surgeries. They demonstrated LLLT's significant role in improving the sensory recovery, particularly in injuries that were less than six months old, and substantial improvements in two-point discrimination and pain intensity (VAS). As the nerve's regenerative capacity is intact for some time after the injury or surgery, these findings suggest that PBMT can be most effective when administered as soon as possible.[15] D'avila et al. used a 940-nm laser in patients undergoing orthognathic surgery. They recorded a significantly reduced pain and trismus, and a faster improvement in the mouth opening in the laser-treated group.[16] Both studies underline PBMT's ability to address immediate postoperative symptoms.[15,16] The faster recovery of paresthesia in D'Avila's study was not statistically significant, which highlights the complexity of nerve regeneration and the possible need for a more targeted therapeutic strategy or additional treatment sessions for optimal results.[16]

Santos et al. assessed LLLT in two different postoperative periods following BSSO and reached the same result as Yazdani et al. and D'avila et al.[15—17] Briefly, they divided patients into two groups, giving LLLT in the early postoperative period (within 30 days) to one group, and studying the other group for persistent sensory

Table 1 Main characteristics of clinical studies evaluating the effect of photobiomodulation therapy on infra-alveolar nerve injury following iatrogenic trauma.

Population			Cause of nerve injury	Photobiomodulation therapy				Follow-up period	Assessment methods	Main outcomes	Refs
Groups (n = sample size)	Gender (male/female)	Age (mean ± SD)		Laser source	Wavelength	Energy density	Treatment frequency/duration				
GRR laser group (n = 10)	8/22	18-40 (mean = 23.43)	BSSO	GaAlAs laser + LED	904 and 650 nm	9 J	10 min each session (5 min for transmucosal and 5 min for transcutaneous laser application)/10 sessions (twice a week)	5 weeks (treatment duration)	Brush test (direction determination) Two-point discrimination test Pinprick test VAS for pain and sensitivity.	Both laser treatments (GRR and Epic10) were more effective than vitamin B in promoting nerve regeneration, with GRR laser showing slightly better outcomes.	14
Epic10 laser group (n = 10)				GaAlAs laser	940 nm	5 J					
Vitamin group (n = 10)				-	-	-					
PBMT group (n = 25) Placebo group (n = 25)	10/15 10/15	N/A	Dental implant Third molar extraction Orthognathic surgery	Nd:YAG laser	1064 nm	12 J/cm^2	15 s at each point/10 sessions (twice a week with a 3-day interval)	N/A	Two-point discrimination test for neurosensory assessment VAS for pain	Significant improvement in paresthesia and dysesthesia based on VAS index and two-point tests. Improvement seen after 6–9 sessions of laser therapy, especially for injuries under 6 months in duration.	15
PBMT group (n = 10) Control group (n = 10)	3/7 5/5	N/A	Orthognathic surgery	InGaAsP semi-conductor diode laser (Epic X™, Biolase®)	940 nm	21.12 J/cm^2	5 s at each point (totaling 37.5 s per point, and 300 s per hemiface)/Twice a week until 30 days (Immediately after surgery, 24- and 48-h post-surgery, total of 11 sessions).	30 days post-surgery	VAS for pain Modified method for facial edema measurement Digital caliper for trismus (mouth opening). Fine paintbrush for neurosensory assessment	PBMT had these advantage: Postoperative pain reduction. Significant improvement in trismus (mouth opening). Decrease in facial edema. Recovery of neurosensory function (paresthesia).	16
Short postoperative period group (within 30 days/n = 10) Late postoperative period group (6 months–1 year/n = 10)	7/13	35.6 ± 11.6	BSSO	MM optics twin flex evolution	780 nm	157.5 J/cm^2	90 s at each point/5 sessions (with 3–4-week intervals between each session)	5 sessions, with intervals of 3–4 weeks between sessions	Semmes-Weinstein monofilament test to evaluate sensory response before and after each treatment session.	Sensorineural recovery in the mandibular region (mental foramen, chin, lower lip) and significant improvement in recovery on the experimental side (PBMT) compared to control side, especially in the short postoperative group.	17
PBMT group (n = 33) Placebo group (n = 9)	13/23 2/7	25.8 29.8	BSSO	GaAlAs diode laser	810 ± 20 nm	31.8 J/cm^2	270 s per session (27 J per site)/Laser sessions on days 1, 2, 3, 5, 10, 14, 21, and 28 after surgery	2 years (follow-up evaluations at 28 days, 60 days, 6 months, 1 year, and 2 years after surgery)	VAS for pain and sensitivity Sensitivity threshold test Two-point discrimination test Pain discrimination test Thermal discrimination test (for both warm and cold stimuli)	Significant neurosensory recovery in the laser group compared to the Sham group. At 2 years post-surgery, 93.94 % of participants in the laser group reported normal pain perception, and 69.7 % recovered normal two-point discrimination. In the Sham group, these figures were lower, showing the effectiveness of photobiomodulation in enhancing nerve recovery after BSSO.	18

PBMT group (n = 20) Placebo group (n = 20)	9/11 9/11	25.7 ± 4.06 27.35 ± 3.35	SSRO	Diode laser	810 nm	8.4 J/cm^2 per site	60 s per point (4 min total per side, 8 min per session)/10 sessions (immediately after surgery and repeated on days 1, 2, 3, and then every other day for the next two weeks.)	12 months (immediately after surgery, 3 months, 6 months, and 1 year)	Two-point discrimination test Thermal test for heat and cold sensitivity Contact direction test (ability to detect fine brush strokes) Pinprick test (ability to detect sharp sensations) Patient satisfaction (subjective scoring between 0 and 10)	The PBMT group showed significant improvement in mechanoreceptor recovery, as evidenced by the two-point discrimination, contact direction test, and pinprick test. Also, the PBMT group reported higher satisfaction in sensory recovery compared to the control group.	19
PBMT group (n = 10) Placebo group (n = 10)	5/5 3/7	24.1 ± 4.6 22.8 ± 3.6	SSO	Low level laser + LED	810 (laser) and 632 (LED) nm	5 (laser) and 2 (LED) J/cm^2	90 s per region (12 min in total for each session)/10 sessions (on days 1, 2, 3, 7, 14, and 28 after surgery)	6 months (with assessments at 1 week, 2 weeks, 2 months, and 6 months)	VAS for pain and sensation Brush stroke test (directional discrimination) Two-point discrimination Contact detection (Semmes-Weinstein monofilaments) Pinprick test Thermal discrimination (ethyl chloride spray)	Significant improvement in VAS scores, two-point discrimination, and brush stroke test in the intervention group compared to the control group. The laser therapy group showed better recovery of neurosensory function, particularly in the VAS and two-point discrimination tests, within 2 weeks post-surgery.	20
16 patients, with one side receiving laser therapy and the other side serving as a control.	5/11	23.1 ± 4.4	BSSO	Low level laser (Thor dd2 control unit)	660 (intraoral laser) and 810 (extraoral laser) nm.	1.5 (660 nm) and 7 (810 nm) J/cm^2 per point	10 s per point (for each wavelength)/applied at 24-, 48-, and 72-h post-surgery, followed by extraoral irradiation twice a week for 3 weeks	60 days after surgery (evaluations on postoperative days 15, 30, 45, and 60)	Two-point discrimination test Patient evaluation (done by a blinded examiner before surgery and at various postoperative intervals)	Significant improvement in two-point discrimination** on the laser-treated side compared to the control side, especially on postoperative days 45 and 60.	21
12 patients	6/6	18-54 (mean = 30)	BSSO	GaAlAs laser	808 nm	100 J/cm2	28 s per point/Two sessions per week, with a minimum of 10 sessions	Evaluations at the first, fourth, seventh, and tenth sessions	Mechanoreceptor tests (brushing) Nociceptor tests (thermal tests with hot gutta-percha and Endo-frost) VAS for pain Evaluation of sensitivity return in different areas of the mandible.	Significant improvement in the subjective response of patients on the treated side. Recovery of neurosensory function was accelerated, and greater comfort was observed in the treated area compared to the control side.	22
PBMT group (n = 15) Electroacupuncture group (n = 15) Placebo group (n = 30)	11/9	20–37	Orthognathic surgery and genioplasty	Low level laser (MM optics)	780 nm	10 J/cm2	6 s per point/Twice per week for 4 months	4 months following the surgery	Mechanical brushing test Two-point discrimination test Electric pulp test VAS for tactile sensitivity	Significant recovery of tactile sensitivity was observed in the electroacupuncture group, particularly in the chin and lower lip regions. The PBMT group did not show significant differences compared to the control group.	23

Abbreviations: BSSO, Bilateral sagittal split ramus osteotomy; GaAlAs, Gallium–aluminum–arsenide; GRR laser, a new-generation diode laser; InGaAsP, Indium gallium arsenide phosphide; J/cm^2, Joules per square centimeter; J, Joule; SD, Standard deviation; SSO, sagittal split osteotomy; SSRO, Sagittal split ramus osteotomy; Nd:yag, Neodymium-doped yttrium aluminium garnet; Nm, Nanometer; N/A, Not applicable; Refs, References; Led, Light-emitting diode; PBMT, Photobiomodulation therapy; VAS, Visual analog scale.

abnormalities by giving LLLT 6 months to 1-year post-surgery. As expected, significant improvements in sensory function were observed in the first group, particularly after the fifth session. The findings supporting early treatment further strengthen the argument for prompt administration of PBMT after surgical trauma.

A two-year follow-up study was conducted by Guarini et al. to examine the long-term effects of PBMT on neurosensory recovery following BSSO. At the end of the study, the parameters were evaluated. 93.94 % of the patients in the laser group reported normal pain perception, and 69.7 % recovered normal two-point discrimination, showing a sustained recovery. However, the recovery rates related to the control group patients were significantly lower, suggesting that not only does PBMT accelerate initial recovery but also contributes to long-term functional improvements.[18] The longitudinal nature of this study makes it a valuable addition to the existing research by emphasizing the lasting effects of PBMT on nerve regeneration, complementing the earlier findings. Similarly, Esmaeelinejad et al. evaluated LLLT's effects on neurosensory recovery following SSRO and found that LLLT significantly improved mechanoreceptor recovery, because of superior performance in the two-point discrimination test and other sensory assessments.[19] It was valuable that patients in the LLLT group also experienced higher satisfaction with their sensory recovery. These results resonate with the findings of Guarini et al.[18] They also enjoyed seeing the greater patient satisfaction and long-term recovery following the use of PBMT.[19] Furthermore, the consistent improvements in both sensory function and patient satisfaction reinforce the therapeutic value of PBMT across different surgical settings.

Another precious research was performed by Mohajerani et al., where they used a combination of LLLT with LED therapy post-surgery. As expected, the targeted groups exhibited significant improvements in sensory function, particularly in the early weeks following surgery.[20] If the overall treatment effect is enhanced by this approach, one hope is that PBMT can be further optimized by incorporating multiple non-invasive therapies. The effectiveness of LLLT in accelerating neurosensory recovery following BSSO is also reflected in the studies performed by Eshghpour et al. and Buysse Temprano et al. These results are so consistent across various studies that they underscore the robustness of PBMT as a treatment for IAN injuries and strengthen the evidence for its clinical application.[21,22]

Common protocol of photobiomodulation therapy

Although it seems that variable treatment protocols are employed across studies, in fact, there is a common range of parameters used for PBMT in dental settings, including wavelengths ranging from 630 nm to 1064 nm, energy densities from 3 J/cm^2 to 12 J/cm^2, and treatment durations between 15 s and 90 s per point. Also, the treatment frequency is slightly different in the studies and typically ranges from twice a week to three times a week, with most studies reporting a treatment course of 5—10 sessions. The logic behind the selection of treatment parameters is the specific injury site and the severity of the nerve damage. For example, for deeper nerve tissues to achieve therapeutic outcomes, longer irradiation times and higher energy densities are required.

Limitations and challenges for clinical use

Although one expects the widespread clinical use of PBMT, there are several challenges that hinder this usage. One challenge is the variability of evaluated parameters such as wavelength, power density, energy density, and irradiation time, which makes it difficult to compare results and establish universal guidelines and standardized treatment protocols. Then there are patient-related factors including the severity and location of the nerve injury, and individual variations in healing responses that often influence the effectiveness of PBMT. Furthermore, in many clinical trials, the sample sizes are small and follow-up periods are short, so the findings and the long-term assessment of treatment efficacy cannot be generalized. The other challenge is diffusion of light energy across cortical bone; that can affect the effectiveness of the treatment, particularly in the case of deep nerve injury. Careful attention to treatment parameters is thus necessary for the procedure. It is true as well that the special equipment required for the therapy may not be accessible in all healthcare facilities. Finally, there is the lack of knowledge on the part of healthcare workers on the safety of the PBMT. With this appreciation of challenges, it is clear that there remains research need to refine PBMT protocols and complete the gaps in evidence to make it a trusted procedure in clinical practice.

Conclusion

In conclusion, PBMT has positive effects on accelerating nerve regeneration, reducing inflammation, and improving patient-reported outcomes such as pain relief and QoL. Various laser and LED protocols have been employed across studies, and the most effective ones on sensory recovery used wavelengths ranging from 630 nm to 1064 nm, energy densities from 3 to 12 J/cm^2, and treatment durations between 15 and 90 s per point. PBMT has yielded promising results, but since there are several issues that hind its clinical use such as treatment protocol inconsistencies, lack of standardization, and the influence of patient-related factors (including the severity of nerve damage and the location of the injury). Small sample sizes and short follow-up duration limit most studies and make it difficult to draw definitive conclusions regarding the long-term efficacy of PBMT. Unfortunately, light energy penetrates through cortical bone and not only complicates the treatment of deep nerve injuries but also necessitates the researcher to carefully select the treatment parameters. Long-term future research with large sample size will need to optimize the clinical use of PBMT, by standardizing treatment protocols and considering patient-related factors influencing treatment outcomes. Overall, PBMT has emerged as a safe, efficacious, and minimally invasive approach to facilitating neurosensory recovery in the case of IAN injury patients. PBMT may be incorporated into routine practice of dental and maxillofacial surgery. However, further studies are warranted to validate treatment regimens and bring this modality into its rightful place in standard treatment of nerve injury due to dental treatment.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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