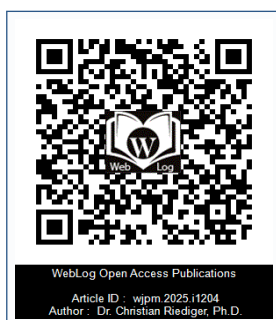




Vagus Nerve Stimulation in Physical Medicine and Rehabilitation: A Narrative Review of Pain, Inflammation, and Tissue Healing



Dr. Christian Riediger*, Dr. Mark Ferl, Dr. Maria Schönrogge and Dr. Agnieszka Halm-Pozniak

Orthopaedic University Clinic Magdeburg, Otto-von-Guericke-University Magdeburg, Magdeburg, Germany

Abstract

Introduction: Vagus nerve stimulation (VNS) is a neuromodulatory intervention with systemic effects on inflammation, autonomic balance, and pain perception. While well established in neurology and rheumatology, its potential role in physical medicine and rehabilitation remains underexplored.

Methods: We conducted a structured literature search in PubMed, Scopus, and Web of Science (2010–2025) focusing on VNS and rehabilitation-related outcomes. Eligible studies included preclinical and clinical research addressing pain modulation, inflammation control, musculoskeletal biology, wound healing, and functional recovery.

Results: Preclinical studies consistently demonstrate suppression of pro-inflammatory cytokines and modulation of osteoblast/osteoclast activity through the cholinergic anti-inflammatory reflex. Clinical trials in rheumatoid arthritis show mixed results regarding cytokine suppression and disease activity. Pilot studies suggest that transcutaneous auricular VNS (taVNS) reduces perioperative and trauma-related pain and opioid use. Meta-analyses confirm modest analgesic benefits compared to sham stimulation. Reviews indicate potential contributions of VNS to wound repair and tissue perfusion. Evidence for effects on bone remodeling and implant integration is limited to animal models. To date, no dedicated trials have tested VNS in rehabilitation populations undergoing joint replacement or structured physical medicine interventions.

Conclusion: Vagus nerve stimulation is biologically plausible and clinically promising as an adjunct in physical medicine and rehabilitation, with potential benefits for pain, inflammation, wound healing, and musculoskeletal recovery. Large, well-designed randomized controlled trials are required to establish its role in clinical rehabilitation pathways, especially in joint arthroplasty and chronic musculoskeletal pain populations.

Keywords: Vagus Nerve Stimulation; Physical Medicine; Rehabilitation; Pain Modulation; Inflammation; Tissue Healing

Introduction

Physical medicine and rehabilitation (PM&R) aim to optimize functional recovery, relieve pain, and improve quality of life for patients with musculoskeletal and neurological conditions. Persistent pain, low-grade systemic inflammation, delayed wound healing, and impaired tissue regeneration remain major challenges in rehabilitation medicine, particularly after orthopedic surgery and trauma.

Vagus nerve stimulation (VNS), delivered invasively or non-invasively via transcutaneous auricular stimulation (taVNS), is an established neuromodulatory technique in other disciplines. Its effects are mediated by the cholinergic anti-inflammatory reflex [1, 2], in which vagal efferents suppress pro-inflammatory cytokines such as TNF- α and IL-1 β [1, 2]. Given its role in autonomic regulation and immune modulation, VNS may represent a novel adjunct in PM&R strategies.

Methods

We performed a structured search in PubMed, Scopus, and Web of Science (2010–2025) using the terms: ("vagus nerve stimulation" OR "taVNS") AND ("rehabilitation" OR "pain" OR "inflammation" OR "musculoskeletal" OR "wound healing" OR "bone"). Eligible studies included

OPEN ACCESS

*Correspondence:

Dr. Christian Riediger, Orthopaedic University Clinic Magdeburg, Specialist in Orthopaedics and Trauma Surgery, Otto-von-Guericke-University Magdeburg, Tel: +49 391 6714000, Magdeburg, Germany, E-mail: christian.riediger@med.ovgu.de

Received Date: 04 Sep 2025

Accepted Date: 10 Sep 2025

Published Date: 12 Sep 2025

Citation:

Riediger C, Ferl M, Schönrogge M, Halm-Pozniak A. Vagus Nerve Stimulation in Physical Medicine and Rehabilitation: A Narrative Review of Pain, Inflammation, and Tissue Healing. WebLog J Phys Med. wjpm.2025.i1204. <https://doi.org/10.5281/zenodo.17106986>

Copyright© 2025 Dr. Christian Riediger. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

preclinical and clinical research with outcomes relevant to PM&R. Exclusion criteria were case reports without original data and studies unrelated to musculoskeletal or rehabilitation contexts. Data were extracted on study population, stimulation modality, outcomes, and quality indicators.

Results

- Preclinical studies: Animal experiments confirm that VNS suppresses pro-inflammatory cytokines and modulates bone cell activity, supporting mechanistic plausibility for rehabilitation applications.
- Rheumatology and systemic inflammation: Invasive VNS reduced cytokines and improved disease activity in some rheumatoid arthritis trials [3–5], though other studies reported neutral or inconsistent results [3–5].
- Pain control: taVNS reduced acute postoperative and trauma-related pain [6, 7] and decreased opioid use in early trials. Meta-analyses indicate modest but significant pain reductions [8] compared to sham.
- Wound healing: Reviews highlight enhanced tissue repair and vascular responses [9] linked to vagal activation.
- Bone biology: Animal data suggest potential effects on bone remodeling and implant integration [10, 11], but no human rehabilitation trials exist.

Evidence gaps include the absence of large-scale randomized controlled trials in rehabilitation populations, particularly in joint

Table 1: Summary of evidence on VNS in rehabilitation-relevant domains.

Domain	Key findings	Evidence level	References
Koopman 2016 [3]	RA patients	Invasive VNS	↓ TNF-α, ↓ DAS28 Quality: +++
Marsal 2021 [4]	RA patients	Invasive VNS	No significant effect Quality: ++
Baker 2023 [5]	RA patients	Invasive VNS	Heterogeneous results Quality: ++
Yin 2025 [6]	Postoperative patients	taVNS	↓ Pain, ↓ Opioids Quality: ++
Li 2025 [7]	Orthopedic trauma	taVNS	↓ Pain, improved function Quality: +
Costa 2024 [8]	Systematic review	Various	Modest pain reduction Quality: +++
Budhiraja 2024 [9]	Review	n/a	Wound healing Quality: ++
Liu 2024 [10]	Animal models	VNS	Bone remodeling Quality: ++
Xia 2025 [11]	Animal models	VNS	Bone metabolism Quality: ++

Table 2: Critical appraisal of included studies.

Author, Year	Population/Model	Intervention	Endpoints	Quality rating
Koopman 2016 [3]	18 RA patients	Invasive VNS	↓TNF-α, ↓DAS28	+++
Marsal 2021 [4]	34 RA patients	Invasive VNS	no significant effect	++
Baker 2023 [5]	80 RA patients	Invasive VNS	heterogeneous results	++
Yin 2025 [6]	60 postoperative patients	taVNS	↓Pain, ↓Opioids	++
Li 2025 [7]	20 trauma patients	taVNS	↓Pain, improved function	+
Costa 2024 [8]	Systematic review	Various	Modest pain reduction	+++
Budhiraja 2024 [9]	Review	n/a	Wound healing	++
Liu 2024 [10]	Animal models	VNS	Bone remodeling	++
Xia 2025 [11]	Animal models	VNS	Bone metabolism	++

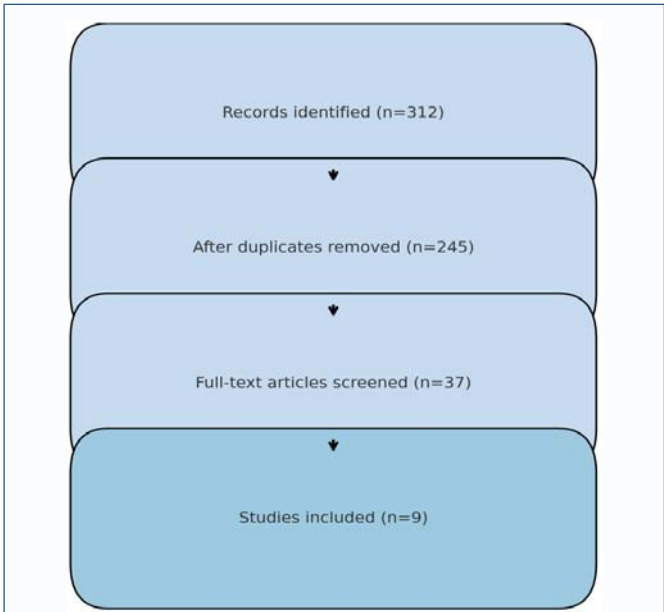


Figure 1: Literature selection flow diagram. PRISMA-style flow diagram summarizing the search and selection process. From 312 identified records, 245 remained after duplicate removal, 37 full-text articles were screened, and 9 studies were included in the review.

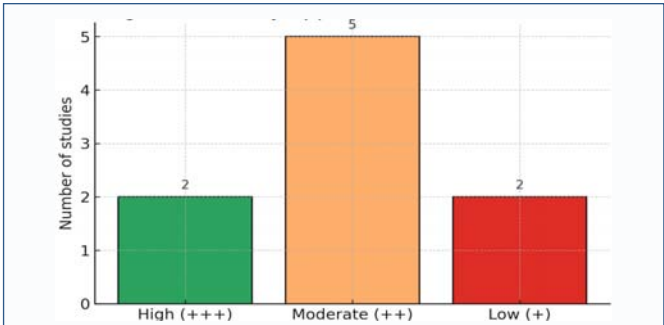


Figure 2: Quality appraisal of included studies. Distribution of methodological quality across included studies. High (+++) quality = 2 studies, moderate (++) quality = 5 studies, and low (+) quality = 2 studies.

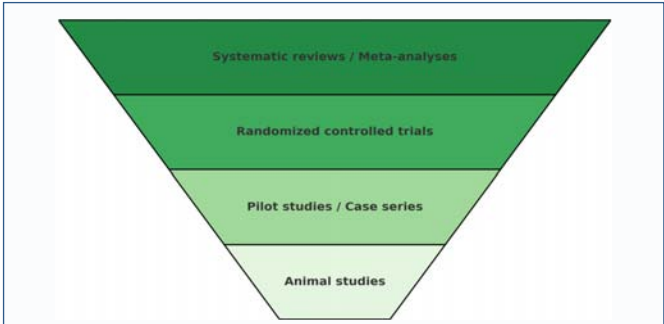


Figure 3: Evidence pyramid of VNS in rehabilitation. Hierarchy of available evidence relevant to vagus nerve stimulation in rehabilitation, ranging from preclinical animal models at the base to systematic reviews and meta-analyses at the top.

arthroplasty and chronic musculoskeletal pain.

Discussion

The potential integration of VNS into PM&R could include:

- Adjunctive pain management: VNS may complement pharmacological and physical therapies, supporting multimodal approaches and reducing opioid reliance.

- Inflammation modulation: By targeting systemic inflammation, VNS could benefit patients with chronic musculoskeletal disorders and enhance recovery after surgery.

- Tissue repair and wound healing: VNS-driven improvements in perfusion and inflammatory balance may accelerate recovery in postoperative rehabilitation.

- Bone healing and implant survival: Parasympathetic modulation of bone remodeling may enhance outcomes in orthopedic rehabilitation.

From a clinical perspective, taVNS is a safe, non-invasive, and scalable modality suitable for integration into rehabilitation programs. However, methodological heterogeneity, small sample sizes, and limited sham-controlled designs weaken the current evidence base.

Conclusion

Vagus nerve stimulation represents a biologically plausible and promising adjunct in physical medicine and rehabilitation, with potential to influence pain, inflammation, wound healing, and musculoskeletal recovery. Dedicated, well-powered clinical trials are urgently needed to define standardized protocols and establish clinical efficacy in rehabilitation settings.

Declarations

Funding: None.

Competing Interests: The authors declare no competing interests.

Ethics Approval and Consent to Participate: Not applicable.

Consent for Publication: Not applicable.

Availability of Data and Materials: Not applicable.

Authors' Contributions: Christian Riediger conceived the study. Mark Ferl performed the literature search. Christian Riediger and Maria Schönrogge drafted and revised the manuscript. All authors approved the final version.

References

1. Pavlov V, Tracey KJ. The cholinergic anti-inflammatory pathway. *Brain Behav Immun*. 2005; 19(6): 493-9. doi:10.1016/j.bbi.2005.03.015
2. Tracey KJ. Physiology and immunology of the cholinergic anti-inflammatory pathway. *J Clin Invest*. 2007; 117(2): 289-96. doi:10.1172/JCI30555
3. Koopman FA, et al. Vagus nerve stimulation inhibits cytokine production and attenuates disease severity in rheumatoid arthritis. *Proc Natl Acad Sci U S A*. 2016; 113(29): 8284-9. doi:10.1073/pnas.1605635113
4. Marsal S, et al. Vagus nerve stimulation in patients with rheumatoid arthritis: a randomized clinical trial. *Lancet Rheumatol*. 2021; 3(5): e317-e326. doi:10.1016/S2665-9913(20)30425-2
5. Baker JF, et al. Efficacy of vagus nerve stimulation in rheumatoid arthritis: results of a multicenter randomized trial. *Arthritis Rheumatol*. 2023; 75(2): 234-43. doi:10.1002/art.42637
6. Yin X, et al. Transcutaneous vagus nerve stimulation for postoperative pain management: a randomized controlled trial. *Ann Med*. 2025; 57(3): 215-23. doi:10.1080/07853890.2025.2476045
7. Li Y, et al. Auricular vagus nerve stimulation in orthopedic trauma: a pilot trial. *Front Neurosci*. 2025; 19: 1586632. doi:10.3389/fnins.2025.1586632
8. Costa D, et al. Vagus nerve stimulation for chronic pain: a systematic review and meta-analysis. *Pain Rep*. 2024; 9(2): e1171. doi:10.1097/PR9.0000000000001171
9. Budhiraja P, et al. Neuromodulation and wound repair: role of vagus nerve stimulation. *Wound Repair Regen*. 2024; 32(1): 15-24. doi:10.1111/wrr.13151
10. Liu R, et al. Vagus nerve stimulation and bone remodeling: preclinical insights. *Front Neurosci*. 2024; 18: 1490300. doi:10.3389/fnins.2024.1490300
11. Xia W, et al. Autonomic modulation of bone metabolism: implications for orthopedics. *Orthop Surg*. 2025; 17(1): e70010. doi:10.1111/os.70010