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REVIEW

Latest Advancements in Transcutaneous Electrical Nerve Stimulation (TENS) and Electronic Muscle Stimulation (EMS): Revisiting an Established Therapy with New Possibilities

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Abstract: Transcutaneous Electrical Nerve Stimulation (TENS) and Electronic Muscle Stimulation (EMS) are non-invasive therapies widely used for pain relief and neuromuscular adaptation. However, the clinical research supporting the efficacy of TENS in chronic pain management is limited by significant methodological flaws, including small sample sizes and inconsistent reporting of stimulation parameters. TENS modulates pain perception through various techniques, targeting specific nerve fibers and pain pathways. High-frequency TENS is effective for segmental pain control, while low-frequency TENS, reliant on endogenous opioid pathways, may be less effective in opioid-tolerant patients. Additionally, TENS may influence autonomic functions, such as micro-perfusion and sympathetic tone, further broadening its therapeutic potential. EMS, on the other hand, enhances muscle strength and neuromuscular function, particularly in rehabilitation settings, by recruiting additional muscle fibers and improving neuromuscular efficiency. To address the limitations in existing clinical applications, future advancements in TENS and EMS technologies should focus on real-time optimization of stimulation parameters, consistent therapy delivery, and improved accessibility. Integrating automated and personalized adjustments can help streamline treatment, enhance patient compliance, and overcome traditional barriers to the effective implementation of these modalities. Additionally, developing systems that enable remote monitoring and customization of therapy protocols will expand the usability of TENS and EMS in diverse care settings. Future research must focus on rigorous study designs, standardized protocols, and meaningful patient-centered outcomes to fully realize the therapeutic potential of these modalities. Innovations like NXTSTIM EcoAI™ represent a significant advancement in delivering tailored, effective, and patient-friendly pain management and rehabilitation strategies.

Keywords: chronic pain, TENS, EMS, neurotransmitters, gate control theory, central sensitization

Introduction

Transcutaneous Electrical Nerve Stimulation (TENS) and Electronic Muscle Stimulation (EMS) are non-invasive therapeutic techniques that utilize adjustable electrical currents to deliver targeted analgesic efficiency and promote neuromuscular adaptation. These devices are typically portable, battery-operated, and can be utilized either independently by patients or under the guidance of a healthcare provider. Although both modalities involve the application of electrical currents, they serve distinct therapeutic purposes. TENS units are primarily employed for analgesia, targeting pain modulation, while EMS devices are designed to elicit muscle contractions, facilitating neuromuscular training and rehabilitation.[1] TENS has been widely applied in managing chronic pain conditions such as neuropathic pain,

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osteoarthritis, and fibromyalgia, as well as acute pain scenarios like post-surgical recovery and labor pain. EMS, on the other hand, is commonly used in rehabilitation for conditions such as stroke-related motor impairment, muscle atrophy due to prolonged immobilization, and sports-related injuries requiring neuromuscular re-education. Both methods are also explored in managing peripheral vascular diseases by enhancing local circulation.

The application of electrical stimulation for therapeutic purposes dates back to the first century, with historical evidence suggesting that contact with electric fish was utilized as a method for analgesia.[2] The scientific understanding of electrical energy and electrophysiology has advanced considerably over time. A pivotal moment in this evolution occurred in 1965 when Ronald Melzack and Patrick Wall[3] introduced the Gate Control Theory of Pain in their seminal work, "Pain Mechanisms: A New Theory." This theory elucidated the mechanisms by which synaptic transmission in sensory nerve fibers is modulated, providing a foundational framework for the development and application of electrotherapy for pain management.[4] In the 1970s, neurosurgeon Clyde Norman Shealy further advanced the field by developing a device that utilized low-voltage electrical currents delivered through transcutaneous electrodes. This innovation laid the groundwork for the modern TENS unit as it is used today.[5]

TENS Therapy Clinical Pathways

TENS is a device currently used for pain management through electrical stimulation. It delivers low-voltage electrical currents to the skin via electrodes, which are placed at or near the site of pain. The primary mechanism of action of TENS involved modulating the nervous system to alter perception of pain (Figure 1).

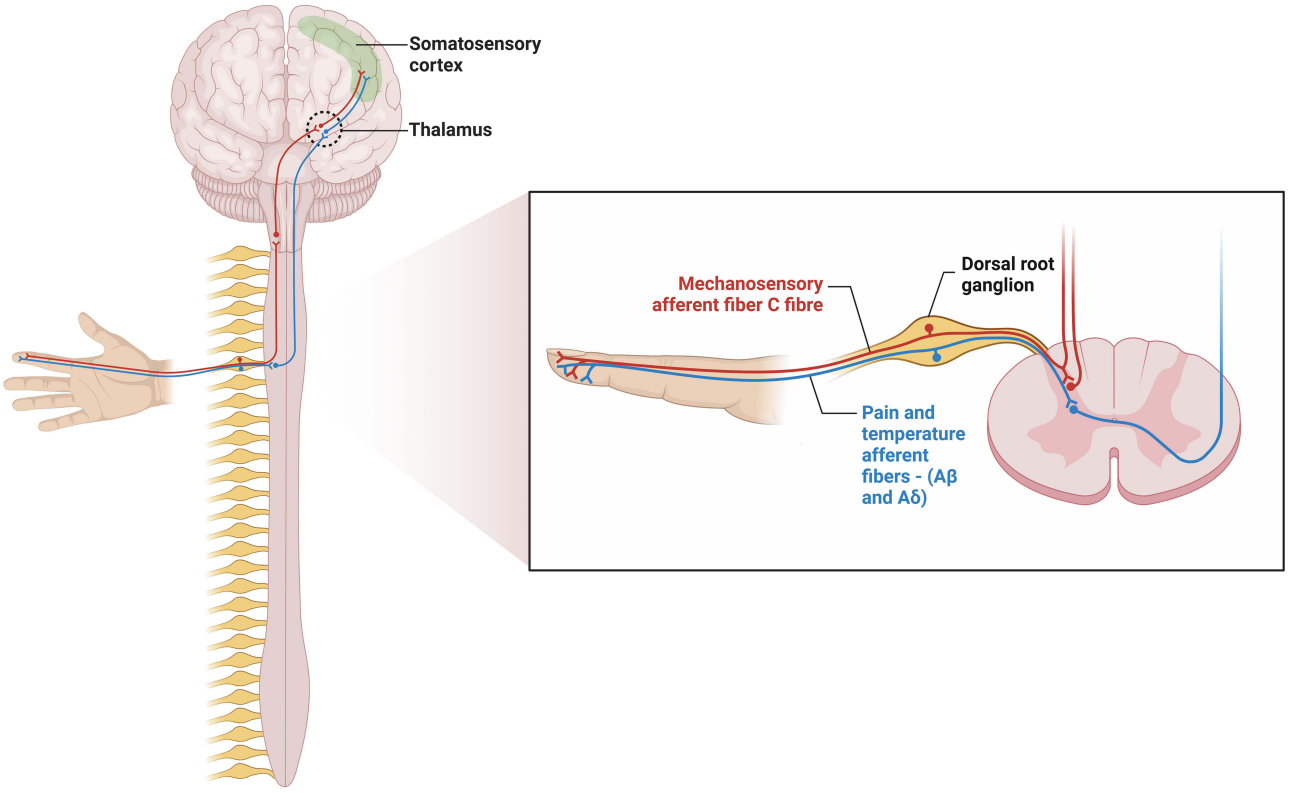

Figure 1 Somatosensory excitatory and inhibitory afferent pathways from the periphery to central circuit:[6] This schematic illustrates the somatosensory excitatory and inhibitory afferent pathways from the periphery to central circuits, emphasizing the role of TENS in modulating pain perception. Nociceptive signals originate from peripheral nociceptors and are transmitted via Aδ and C fibers to the dorsal root ganglion. These signals then travel through the spinothalamic and trigeminothalamic tracts to the thalamus, where they are relayed to the somatosensory cortex for pain perception. Additionally, TENS activates descending inhibitory pathways originating from the brainstem, including serotonergic and noradrenergic tracts, which suppresses nociceptive signaling at the spinal level (Created in BioRender. Green, (**M**) (2024) https://BioRender.com/o00z001).

TENS therapy is a versatile modality that adjusts pulse amplitude (mA), frequency (pulses per second), and pulse width (μs) to generate various current patterns tailored to specific therapeutic needs.[7] The primary techniques of TENS therapy include:

- Conventional TENS: Utilizes high-frequency stimulation (50–100 hz) with a narrow pulse width (50–200 μs) and low intensity. This technique primarily targets Aβ fibers; large-diameter, non-noxious sensory fibers. By creating non-painful paresthesia, conventional TENS inhibits the nociceptive transmission to the central nervous system.[8,9]
- Acupuncture-like TENS: Employs low-frequency stimulation (2–4 hz) with a longer pulse width (100–400 μs) and higher intensity. This technique stimulates Aδ fibers; smaller-diameter sensory fibers, leading to activation of descending inhibitory pain pathways. Acupuncture-like TENS is generally used less frequently compared to conventional TENS.[10]
- Burst mode TENS: Combines elements of both conventional and acupuncture-like TENS. It delivers pulses in bursts, typically at low frequency but with high intensity, often resulting in muscle contractions. Burst mode is thought to offer a more profound analgesic effect by merging the immediate pain relief provided by conventional TENS with the prolonged benefits of acupuncture-like TENS.[11,12]

Over the years, our understanding of the mechanisms underlying TENS and EMS therapies, along with their clinical indications, has advanced significantly. This review seeks to evaluate the current evidence and identify potential avenues for future research and application of these therapeutic modalities.

Physiology of TENS

Several mechanisms have been proposed to elucidate the physiological effects of TENS. Central to understanding TENS is the Gate Control Theory of Pain, which posits that TENS activates large-diameter myelinated Aβ fibers. This activation stimulates inhibitory interneurons in the substantia gelatinosa of the dorsal horn, thereby modulating nociceptive signal transmission and altering pain perception.[13] While the Gate Control Theory initially suggested that pain modulation occurs at the spinal cord level through segmental mechanisms, recent research has refined this view. High-frequency TENS, once thought to exert analgesic effects by exhausting small-diameter Aδ fibers, is now understood to primarily activate large-diameter Aβ fibers. This activation inhibits the transmission of nociceptive signals from smaller Aδ and C fibers via spinal cord inhibitory interneurons, consistent with segmental modulation.[14]

Moreover, TENS engages descending inhibitory pathways originating from the brainstem, which modulate pain perception through both spinal and supraspinal mechanisms. These descending pathways involve neurotransmitters such as serotonin (5-HT) and norepinephrine (NE), which are crucial for regulating spinal cord excitability and pain transmission.[15,16] Thus, the analgesic effects of TENS result from a complex interplay of segmental inhibition and descending modulation.

Endogenous Opioid Release and Receptor Activation

The activation of descending inhibitory pathways also leads to the release of endogenous opioids in the spinal cord. Specifically, high-frequency TENS has been associated with increased levels of endorphins in the lumbar cerebrospinal fluid (CSF), including methionine enkephalin and dynorphin A.[13] Methionine enkephalin predominantly binds to δ-opioid receptors, while dynorphin A interacts with κ-opioid receptors. These interactions are crucial for modulating pain at multiple levels.

Ligation of methionine enkephalin to δ-opioid receptors activates downstream signaling pathways that influences the excitability of spinal neurons and inhibit nociceptive signal transmission. Similarly, dynorphin A's interaction with κ-opioid receptors results in the modulation of pain through mechanisms such as reduced neurotransmitter release and altered neuronal firing patterns.[17]

Interactions with μ-Opioid Receptors

Interestingly, the effects of TENS can vary with the frequency of stimulation. Low-frequency TENS, which tends to activate μ-opioid receptors more selectively, is often associated with significant endogenous opioid release. Activation of μ-opioid receptors on neurons in the RVM and PAG can lead to a pronounced inhibition of the spinothalamic tract, which

conveys pain signals from the spinal cord to the thalamus. This pathway interruption is integral to the analgesic effects of low-frequency TENS.[18,19]

However, chronic pain conditions are frequently associated with μ-opioid receptor tolerance, which can diminish the efficacy of low-frequency TENS. This tolerance results in reduced responsiveness of μ-opioid receptors to endogenous opioids, potentially limiting the therapeutic benefit of low-frequency TENS in such patients. Conversely, high-frequency TENS might preferentially engage δ-opioid receptors, which may not be as prone to tolerance development, thereby offering a more consistent analgesic effect in individuals with μ-opioid receptor tolerance (Figure 2).[20] In patients with chronic pain, prolonged opioid use may lead to receptor desensitization or downregulation, thereby reducing the analgesic effects of therapies that depend on these pathways. As a result, alternative TENS modalities, such as high-frequency TENS, which may engage non-opioid mechanisms, could be more beneficial for this patient population.[13]

Novel Findings

Recent studies suggest that TENS-induced analgesia may also be influenced by autonomic nervous system activity. Specifically, at certain intensities of electrical stimulation, activation of large-diameter Aδ fibers may lead to transient increases in microperfusion, a phenomenon that can be quantitatively assessed using laser Doppler imaging. This increase in blood flow is particularly relevant in regions affected by ischemia or claudication, where enhanced perfusion could alleviate localized hypoxia and reduce metabolic byproducts that contribute to pain.[24]

Mechanistically, the increase in microperfusion may facilitate the removal of pro-inflammatory mediators and promote tissue oxygenation, thereby mitigating pain at the site of injury.[25] Furthermore, the autonomic response elicited

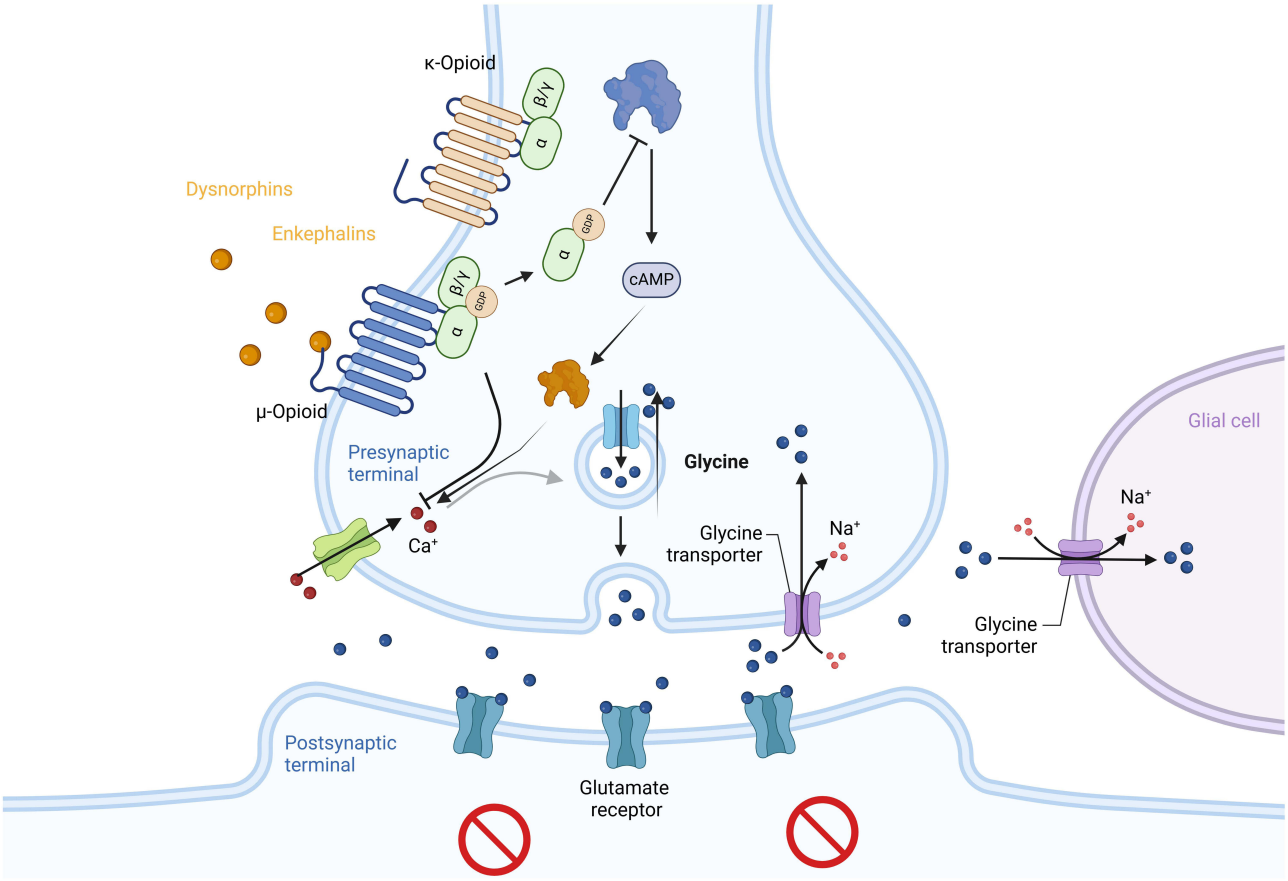

Figure 2 Opioid receptor activation interrupts spinothalamic tract pain transmission:[21–23] The analgesic effects of TENS involve modulation of the activity of descending inhibitory pathways leading to increased release of endogenous opioids, such as endorphins, enkephalins, and dynorphins. These activate opioid receptors, triggering the release of inhibitory neurotransmitters, including glycine, which further attenuate nociceptive signaling the spinal and supraspinal levels (Created in BioRender. Green, (**M**) (2024) https://BioRender.com/d918047).

by TENS may involve a reduction in sympathetic tone, leading to decreased heart rate and blood pressure.[20] These cardiovascular effects could indirectly contribute to pain relief by reducing overall physiological stress and enhancing parasympathetic activity, which is associated with a more relaxed state. Thus, TENS not only modulates pain through direct neural mechanisms but may also exert systemic effects via autonomic pathways, contributing to its analgesic efficacy in certain clinical contexts. These findings highlight the complex interplay between neural and vascular responses in TENS therapy and suggest potential avenues for optimizing stimulation parameters to maximize therapeutic outcomes, particularly in patients with compromised vascular function.[13] Furthermore, the effects of TENS therapy on allodynia to cold stimuli was attenuated by the administration of phentolamine, an agent known to block alpha-adrenergic receptors, suggesting that modulation of autonomic activity may be contributory to TENS therapy.[26]

Overall, multiple mechanisms have been proposed to explain the physiological basis of TENS analgesia. These include the Gate Control Theory, activation of descending inhibitory pathways, release of endogenous opioids and modulation of autonomic pathways. Nociceptive input is modulated at various levels, including the peripheral, spinal, and descending inhibitory systems.

Clinical Use and Evidence of EMS

The advent of EMS and voluntary isometric training (VOL) has markedly advanced the field of strength training. Recent research has delved into the comparative efficacy of these techniques, offering new insights into their impact on muscle activation and strength development in both athletic and rehabilitative contexts.

Traditionally, it was believed that VOL training was superior for enhancing isometric strength due to its direct engagement of voluntary muscle contractions. However, recent studies challenge this paradigm by demonstrating that EMS, when applied effectively, can elicit comparable or even superior strength gains across various muscle contraction patterns. Notably, research by[27] revealed significant improvements in muscle strength with both EMS and VOL training, suggesting that EMS can match VOL in inducing strength adaptations across different contraction modalities. The finding that EMS enhanced isometric torque more effectively than VOL was particularly noteworthy, implying that EMS may also be beneficial for enhancing dynamic strength.[27,28]

The molecular mechanisms underlying these effects are increasingly understood. EMS activates motor neurons through electrical impulses delivered to the muscle via electrodes. This stimulation not only recruits a higher proportion of muscle fibers but also promotes muscle hypertrophy and strength gains by increasing the release of anabolic signaling molecules and enhancing neuromuscular junction efficiency. The increased isometric torque observed with EMS is likely due to improved synchronization and recruitment of motor units, which contrasts with the more gradual strength gains typically associated with VOL training.[29,30]

In clinical applications, neuromuscular electrical stimulation (NMES) has shown promise in rehabilitating patients with motor impairments. For instance,[31] demonstrated that NMES could significantly improve motor function and gait in individuals with hemiplegia. By targeting specific muscle groups and stimulating muscle contractions, NMES facilitates motor recovery and enhances mobility, making it a valuable tool in post-stroke rehabilitation.

Further supporting the utility of electrical stimulation in rehabilitation[32] investigated its role in post-operative recovery following arthroscopic partial meniscectomy. This study assessed the effectiveness of both electrical stimulation and electromyographic (EMG) biofeedback in augmenting muscle strength and functional recovery after surgery. The results underscored the potential of these modalities in enhancing post-surgical rehabilitation outcomes, highlighting their role in accelerating muscle function recovery and improving overall rehabilitation protocols.

The collective evidence from these studies underscores the versatility and effectiveness of EMS and NMES in diverse contexts, ranging from sports performance enhancement to clinical rehabilitation. Both EMS and NMES have demonstrated substantial benefits in activating muscle groups, improving strength, and facilitating motor recovery in various populations, including athletes, post-surgical patients, and individuals with neurological impairments.

To maximize the therapeutic benefits of EMS and NMES, further research is necessary to elucidate the detailed molecular mechanisms that underpin the observed improvements in muscle activation and strength. Additionally, long-term studies are needed to evaluate the durability of these effects across different patient populations and training regimens. Understanding these mechanisms and the long-term implications of EMS and NMES will enhance their

application in performance enhancement and rehabilitation settings, offering valuable insights into optimizing muscle function and recovery.

Clinical Application and Evidence

The effectiveness of TENS in pain reduction has been the subject of numerous clinical studies and meta-analyses. A comprehensive meta-analysis by Johnson et al pooled pain intensity scores from a variety of conditions, providing moderate-strength evidence that TENS significantly reduces immediate pain compared to placebo.[33] This analysis underscores the potential of TENS as a versatile analgesic tool across different pain etiologies. Despite these promising findings, the literature reveals significant gaps, particularly in the form of limited meta-analyses with sufficient data to draw robust conclusions. A recent review by Paley et al identified only three meta-analyses that provided a statistically sound evaluation of TENS efficacy.[34] These analyses supported the use of TENS for chronic musculoskeletal pain and labor pain, suggesting that clinicians should consider TENS as a viable option in therapeutic pain management. However, the scarcity of high-quality meta-analyses emphasizes the need for more rigorous studies to solidify the evidence base for TENS.

Applications of TENS in Acute Pain

TENS has shown promise in the management of acute pain, offering immediate, non-pharmacological analgesic and anxiolytic effects. Although the clinical data are limited by small sample sizes and methodological challenges such as inadequate blinding, initial studies suggest that TENS may reduce pain scores in acute settings. For instance, procedural pain associated with sigmoidoscopies, colonoscopies, hysteroscopies, post-cardiothoracic surgical pain, hemophilia-related pain, and acute low back pain has been shown to respond favorably to TENS.[35]

In prehospital care, TENS has demonstrated efficacy in reducing pain severity and anxiety without significant adverse side effects, highlighting its potential as a safe and effective intervention in acute settings.[36]

TENS and Opioid Sparing Effects

The opioid crisis has heightened the need for alternative pain management strategies that reduce opioid consumption and associated risks, such as respiratory depression, sedation, constipation, and tolerance. TENS may offer an opioid-sparing effect, particularly in post-surgical pain management. A study comparing TENS to intravenous opioids after gynecological surgery found that, while TENS did not significantly reduce pain scores as measured by the Visual Analog Scale (VAS), it did result in reduced opioid consumption and shortened recovery time in the Post-Anesthesia Care Unit (PACU).[37] This suggests that TENS may contribute to analgesia through mechanisms not fully captured by traditional pain scales, potentially enhancing recovery by minimizing opioid use.

Supporting this, a meta-analysis by Bjordal et al reported a dose-dependent reduction in post-operative analgesic consumption with TENS, consistent with previous systematic reviews. The findings emphasize that appropriate frequency and intensity of TENS are crucial for achieving significant opioid-sparing effects. By reducing the need for opioid analgesia, TENS may mitigate the extensive side effect profile associated with opioids, offering a safer alternative for post-operative pain management.[38]

TENS in Management of Labor Pain

The application of TENS during labor has produced mixed results, reflecting the variability in study designs and patient populations. A Cochrane review in 2009 provided only limited evidence supporting TENS for labor pain relief, though it did note that TENS may enhance a sense of autonomy in laboring patients, which could justify its use as an option for those seeking non-pharmacological pain management.[39] This psychological benefit, although subtle, could justify offering TENS as an option for women seeking non-pharmacological pain management strategies during labor.

More recent evidence from a systematic review conducted in 2020 indicates a slight but statistically significant reduction in pain scores during labor with the use of TENS, compared to placebo or standard care.[40] This suggests that TENS may provide modest analgesic benefits, although its effectiveness appears to be influenced by factors such as electrode placement, frequency and intensity of stimulation, and the timing of application relative to labor progression.

In conclusion, there is a need for further prospective studies to investigate TENS efficacy in labor pain management.

TENS for Management of Chronic Musculoskeletal Pain

TENS has been increasingly explored as a therapeutic option for patients with chronic musculoskeletal pain, particularly in cases where pain is localized to multiple joints and anatomical regions. A comprehensive meta-analysis evaluated the efficacy of TENS across various joint sites, including the neck, low back, shoulder, knee, and hands. The analysis revealed significant pain reduction at rest for a range of chronic musculoskeletal conditions, underscoring the potential of TENS as a component of a multimodal pain management strategy.[41] These findings are particularly relevant given the frequent presentation of patients with diffuse musculoskeletal pain involving multiple sites, supporting the utility of TENS in such complex clinical scenarios.

The efficacy of TENS in chronic musculoskeletal pain was further substantiated by a randomized controlled trial conducted by Vance et al, which investigated the effects of high-frequency and low-frequency TENS in patients with knee osteoarthritis. The study demonstrated a significant increase in the pressure pain threshold, indicating that TENS may be particularly effective in mitigating deeper pressure-related pain associated with this condition. However, the trial did not observe significant changes in cutaneous mechanical or heat pain thresholds, suggesting that TENS may have a more targeted effect on deeper somatic pain rather than superficial or thermal pain modalities.[42] These results highlight the need for further investigation to better understand the specific mechanisms by which TENS modulates pain in different musculoskeletal conditions and anatomical regions.

The literature on the use of TENS for chronic low back pain presents a more mixed picture. A Cochrane review in 2008, which was limited by a lack of adequately controlled trials, concluded that the evidence was insufficient to make a definitive recommendation for TENS in this patient population.[43] However, a more recent meta-analysis conducted in 2016 provided evidence of significant pain reduction as measured by the Visual Analog Scale (VAS) in patients with chronic low back pain treated with TENS.[44] These findings suggest that while TENS may offer pain relief for some patients with chronic low back pain, further high-quality, randomized controlled trials are needed to clarify its role and optimize treatment protocols in this context.

While the evidence supports the use of TENS as part of a multimodal approach for managing chronic musculoskeletal pain, especially in cases involving multiple joints, its efficacy appears to vary depending on the specific type of pain and anatomical location. Continued research is essential to refine the application of TENS and fully elucidate the mechanisms underlying its analgesic effects across different musculoskeletal conditions.

TENS for Management of Neuropathic Pain

The evidence surrounding the use of TENS for neuropathic pain remains inconclusive, largely due to the limitations in the available data. The 2017 Cochrane review on this topic highlighted the scarcity of high-quality studies with sufficient sample sizes and rigorous controls, making it difficult to draw definitive conclusions about the efficacy of TENS in treating neuropathic pain conditions such as postherpetic neuralgia, postoperative neuropathic pain, post-stroke pain, phantom limb pain, and trigeminal neuralgia.[45]

Neuropathic pain is characterized by abnormal sensory processing in the nervous system, often resulting from nerve injury or dysfunction. Pathophysiology involves a complex interplay of peripheral and central mechanisms, including ectopic discharges, altered sodium and calcium channel expression, and sensitization of dorsal horn neurons. These mechanisms contribute to the heightened pain sensitivity and spontaneous pain experienced by patients. Given this intricate pathophysiology, interventions targeting multiple levels of the nervous system, such as TENS, are appealing.

The review reported that TENS was associated with a low incidence of adverse effects, with the most common being local skin irritation, which underscores its favorable safety profile compared to pharmacologic therapies that carry risks of systemic side effects. However, the lack of robust evidence supporting its efficacy in neuropathic pain conditions underscores the need for well-designed, adequately powered randomized controlled trials (RCTs) to evaluate TENS's role in this context.

Further emphasizing the need for more research, a recent systematic review pointed to the potential of self-initiated therapies, including TENS, as adjunctive treatments for peripheral neuropathy. The review suggested that TENS, along with meditation and exercise, could offer symptomatic relief and improve the quality of life for patients suffering from

neuropathic pain. This potential is particularly notable given the chronic nature of neuropathic pain and the challenges associated with long-term pharmacologic management, including issues of tolerance, dependence, and side effects. The ability for patients to self-administer TENS also offers a degree of autonomy and convenience, which may enhance adherence and overall treatment satisfaction. Nonetheless, the limited number of high-quality studies in this area highlights the ongoing need for rigorous clinical research to fully delineate the therapeutic potential and optimize the clinical application of TENS in neuropathic pain management.[46]

TENS and Fibromyalgia

Fibromyalgia is a complex, chronic condition marked by widespread musculoskeletal pain, fatigue, and tenderness, underpinned by central sensitization. This phenomenon, where the central nervous system (CNS) becomes hyperresponsive to sensory stimuli, plays a critical role in the pathophysiology of fibromyalgia. Mechanistically, central sensitization involves altered neurotransmitter activity, including increased levels of serotonin and substance P, which potentiate nociceptive signaling. Additionally, dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis and autonomic dysfunction contribute to the disorder's multifaceted clinical presentation, exacerbating symptoms and complicating management.

Emerging evidence has identified TENS as a potential therapeutic option for fibromyalgia. A recently published randomized controlled trial conducted provided compelling data supporting the efficacy of TENS in this population. The study demonstrated that TENS significantly reduced movement-evoked pain, resting pain, and fatigue in patients with fibromyalgia, compared to both placebo TENS and no treatment.[47] These findings are particularly noteworthy given the chronic and often debilitating nature of fibromyalgia, where effective management strategies are limited.

While TENS has been extensively studied for its analgesic effects in various acute and chronic pain conditions, the trial by Dailey et al suggests that its benefits may extend beyond mere pain relief. The significant reduction in fatigue observed in fibromyalgia patients indicates that TENS could play a broader role in improving quality of life, addressing both pain and the pervasive fatigue that characterizes this condition. This expanded therapeutic potential warrants further investigation into the mechanisms by which TENS may influence not only nociceptive pathways but also other aspects of fibromyalgia's complex pathophysiology. As such, TENS represents a promising adjunct in the multimodal management of fibromyalgia, offering a non-pharmacological option that may enhance patient outcomes in this challenging condition.

TENS in Peripheral Arterial Disease

Peripheral Arterial Disease (PAD) is characterized by the progressive narrowing and occlusion of peripheral arteries, predominantly due to atherosclerosis. This pathological process is initiated by the formation of atherosclerotic plaques within the arterial walls, leading to a reduction in blood flow and a subsequent decrease in the delivery of oxygen and nutrients to the affected tissues. As PAD progresses, patients may experience intermittent claudication, characterized by pain and cramping in the legs during physical activity, which is relieved by rest. In advanced stages, PAD can lead to rest pain, ischemic ulcers, and gangrene, significantly increasing the risk of limb amputation and mortality.[48]

The pathophysiology of PAD involves several key mechanisms, including endothelial dysfunction, chronic inflammation, and thrombosis. Endothelial dysfunction, a hallmark of atherosclerosis, impairs the normal vasodilatory response and contributes to the development of atheromatous plaques. Chronic inflammation further exacerbates plaque formation and destabilization, while thrombosis can lead to acute ischemic events by occluding the already narrowed arteries.[49,50] Addressing these underlying mechanisms is essential for the effective management of PAD, as traditional interventions primarily focus on symptom relief and revascularization.

Recent investigations have explored the potential of TENS as an adjunctive therapy in the management of PAD, particularly in patients with intermittent claudication. Emerging evidence suggests that TENS may improve walking distance and exercise tolerance in this patient population.[51] These findings propose that TENS may confer therapeutic benefits beyond conventional pain relief, through both low-frequency and high-frequency stimulation modalities. Low-

frequency TENS (eg, 1–4 hz) may enhance local blood flow by stimulating neurovascular pathways, thereby improving endothelial function and reducing the impact of compromised arterial blood flow. In contrast, high-frequency TENS (eg, 50–100 hz) may predominantly influence pain modulation by activating large-diameter sensory fibers, which could lead to a reduction in pain perception and an increase in exercise tolerance.

These observations suggest that TENS may offer additional therapeutic benefits by influencing both vascular and neuronal mechanisms underlying PAD. However, the full extent of its clinical applications remains to be fully elucidated. Further research is warranted to delineate the molecular pathways involved and to optimize TENS protocols for the management of PAD, potentially offering a novel, non-pharmacological approach to improve outcomes in this challenging condition.

Complications and Contraindications of TENS and EMS

The majority of studies investigating the safety profile of TENS and EMS have not systematically assessed adverse event rates. Nevertheless, when adverse events are reported, the most common issue observed is local dermatologic reactions at the site of electrode application, a finding consistent across both active treatment and sham control groups.[52] Additionally, some studies have documented vasovagal symptoms, such as nausea and dizziness, among TENS users, though these occurrences are relatively rare.[20] The inconsistent reporting of adverse events across various reviews has made it difficult to conduct pooled analyses. For instance, in a 2019 Cochrane overview, three out of eight reviews reported no adverse events in the studies they examined, while the remaining reviews either documented only minor adverse events or did not address adverse events at all.[52] Despite the need for more rigorous and consistent reporting, current evidence suggests that TENS therapy is generally safe, with no serious adverse events reported.[53]

The contraindications to TENS and EMS are relatively few but important. Medico-legal recommendations from device manufacturers advise against the use of TENS over the eyes, areas of broken skin, or in patients with conditions such as epilepsy, pregnancy, or those with implanted electrical devices, including pacemakers, implantable cardioverter-defibrillators, or spinal cord stimulators. Additionally, the application of TENS directly over malignant sites is contraindicated due to the unknown effects of electrical stimulation on malignant cells and potential metastasis.[53] However, with proper clinical guidance, TENS and EMS therapies can often be safely administered at sites distant from implants or areas of concern, allowing for the careful application in a broader range of patients.

Discussion

Despite decades of research, the clinical efficacy of TENS remains uncertain. A 2019 overview of Cochrane reviews concluded that there is insufficient evidence to confidently determine whether TENS is beneficial or harmful for managing chronic pain. Specifically, the review was unable to draw definitive conclusions regarding TENS's impact on pain control, disability, health-related quality of life, use of pain-relieving medications, or overall patient impression of change.[52] Systematic reviews demonstrated have high risk of bias, lack of blinding, low sample size, and limited data on TENS parameters used in existing studies. Several factors influence the effectiveness of TENS therapy and the assessment of its efficacy, including stimulation intensity, treatment frequency, outcome measures, timing of outcome assessments, and the characteristics of the study population. It is essential for the design and evaluation of TENS research to account for these variables to ensure accurate and meaningful results.

TENS Parameters

Intensity (amplitude) of TENS stimulation is an important factor for analgesic effect from therapy. Studies have shown that stronger intensities produce greater analgesic effect[54,55] and therefore it is recommended that amplitude is increased as tolerated to a "strong, but comfortable" sensation.[56] The frequency of stimulation and of the therapy sessions also play a role in analgesic effect. While research supports a cumulative analgesic effect with repeated TENS therapy, repeated application of the same TENS stimulation may lead to analgesic tolerance.[56,57] Further, there is also evidence that low-frequency TENS stimulation, which acts via mu opioid receptors has decreased effect in patients that have tolerance to

opioid medications.[58] Without consistent reporting of stimulation parameters, frequency of sessions, and duration of therapy across clinical trials, assessing efficacy of the therapy is challenging. In 2011, Bennett and colleagues reviewed outcomes from 38 studies included in prior Cochrane reviews and found suboptimal dosing of TENS, among other factors, was a prevalent weakness.[59] In addition, use of TENS in reality may not be accurately reflected in clinical trials. Users who adopt the therapy long term may be learning and adjusting their optimal settings by trial and error. A recent review of factors affecting TENS outcomes has challenged the focus on specific stimulation parameters, arguing that the sensation of TENS stimulation itself plays a more critical role in achieving analgesic effects. It suggests that patients should be encouraged to adjust TENS settings to ensure they experience strong, non-painful stimulation, which may enhance therapeutic efficacy.[20]

Outcome Measurement

TENS therapy trials have explored a variety of outcomes, including pain intensity, functional improvement, range of motion, pain interference, affective responses to pain, pressure sensitivity measured by algometry, and analgesic consumption. Most studies prioritize pain intensity as the primary outcome, typically assessed using visual analogue scales (VAS) or numerical rating scales (NRS). The efficacy of TENS is thought to involve several molecular mechanisms, such as the modulation of pain pathways through the activation of large-diameter Aβ fibers, which can inhibit pain signal transmission via the gate control theory. Additionally, TENS may influence central mechanisms by promoting the release of endogenous opioids and modulating neurochemical pathways related to pain perception. Understanding these molecular interactions is crucial for evaluating how different TENS parameters impact various outcomes beyond just pain intensity, including functional improvements and changes in analgesic use. However, rating pain intensity as it relates to TENS therapy is not straightforward. Pain scores may be recorded during TENS therapy, immediately following a session, or at intervals between sessions. Patients may be providing ratings based on the sensation of paresthesia during therapy, the level of "distraction" from pain, or overall satisfaction with the therapy.[20] Immediate symptomatic relief should be differentiated from cumulative effects after repeat treatments. While TENS is used for symptomatic relief and may only provide temporary relief, that short term relief can lead to improved physical activity and participation in physical therapy which may ultimately lead to mitigating painful sensations. Therefore when TENS therapy is discontinued, long term outcome data is needed to discern if it was discontinued due to resolution of pain or lack of improvement with therapy.[20] TENS therapy has proven particularly effective in alleviating evoked pain, such as pain associated with movement and hyperalgesia. For instance, in patients with fibromyalgia, TENS has been shown to reduce pain experienced during walking but does not significantly affect resting pain.[60] In healthy individuals, TENS has been demonstrated to increase pain thresholds.[57] These findings suggest that TENS may be especially beneficial for managing pain triggered by physical activity while having a more limited impact on baseline pain levels. In healthy individuals, TENS has been shown to increase pain thresholds. Future studies should consider specifying the type of pain being assessed to better understand its impact on various outcomes.

Further, outcomes measured in studies may not reflect patient perceived benefits. A 2020 study comparing perceived benefits from experienced TENS users for chronic pain against previously used patient reported outcome measures, found a low level of match, suggesting traditional patient-reported outcome measures may be underestimating the benefit of TENS therapy.[61] Functional patient-reported outcomes including sleep, mood, return to work, and activity level may better capture the full extent of benefit.

Lastly, outcomes may be altered by concomitant use of analgesics as part of a multi-modal treatment plan. Study participants in both TENS therapy and placebo groups may be able to titrate analgesic medications, possibly obscuring a difference in treatment effect.

Sample Size and Study Population

A critical limitation in the current body of evidence regarding TENS is the inadequate sample sizes in many studies. Moore et al identified a high risk of bias in randomized controlled trials with fewer than 200 participants and meta-analyses with fewer than 500 participants.[62] As of 2021, the Cochrane database review noted that only two meta-analyses

had sufficiently large sample sizes, both concluding that TENS was more effective than placebo.[20,38,41] A 2023 meta-analysis addressed this issue by including a robust number of studies, with 381 trials comprising 2426 participants receiving TENS and 2415 receiving placebo, and 1594 participants receiving TENS versus 1561 receiving standard care. This analysis demonstrated a favorable effect of TENS compared to both placebo and standard care.[33] Notably, subgroup analyses by pain type or standard of care intervention, primarily pharmacologic or physiotherapy, did not alter the overall efficacy of TENS.

Additionally, combining data across different pain syndromes remains challenging due to clinical heterogeneity. The 2019 Cochrane review overview, which included eight reviews and fifty-one individual studies, either focused on specific pain syndromes or refrained from pooled analysis due to significant variability in study populations and interventions.[52] Johnson et al argue that the complex nature of pain, influenced by biological, psychological, and societal factors, further complicates the homogeneity of study populations. Furthermore, the mechanism of TENS is not pathology-specific, complicating the integration of diverse pain syndrome data.[20]

Challenges in Study Design

Designing studies to evaluate the efficacy of TENS presents significant methodological challenges. One major issue is the creation of a credible placebo treatment. Many trials compare TENS against placebo, standard clinical care, pharmacologic interventions, or no treatment at all. However, developing a true placebo for TENS is problematic due to the inherent electrical sensation associated with the therapy.

Patients undergoing TENS are likely to experience some degree of electrical stimulation, which can influence their perception and expectations. Attempts to address this challenge include using devices that deliver brief, non-therapeutic pulses initially, or limiting pre-treatment explanations about the sensations patients should expect. Despite these efforts, achieving a true placebo that completely mimics the non-treatment aspects of TENS while controlling for patient expectations remains elusive. This difficulty in blinding and placebo control can affect the validity of trial outcomes and complicate the interpretation of efficacy data. Future research should focus on refining methodological approaches to improve the reliability of placebo controls and enhance the robustness of TENS efficacy evaluations.

Synergistic Effects of TENS/ EMS

The integration of TENS and EMS presents an innovative approach to managing complex pain and neuromuscular conditions. Individually, TENS provides effective non-pharmacological pain relief by modulating nociceptive pathways, while EMS enhances neuromuscular function by eliciting muscle contractions that facilitate strength, endurance, and rehabilitation. Emerging evidence suggests that the synergistic application of TENS and EMS could amplify therapeutic outcomes by concurrently addressing pain and functional impairments. Combination therapy leveraging TENS and EMS has shown promise in conditions such as chronic low back pain, osteoarthritis, and post-stroke rehabilitation. For example, in chronic pain conditions, EMS-induced muscle activation can reduce stiffness and improve mobility, while TENS simultaneously alleviates pain, enabling more effective physical therapy sessions. In post-stroke rehabilitation, EMS facilitates motor recovery by strengthening atrophied muscles, while TENS modulates neuropathic pain and enhances patient compliance during therapy. This synergistic effect underscores the potential of combining these modalities for holistic patient care.

However, the clinical implementation of such combined approaches is often hindered by the complexity of customizing stimulation parameters for individual patient needs. To address this challenge, the NXTSTIM EcoAI™ system offers an advanced solution. By integrating artificial intelligence with dual-mode TENS and EMS functionality, EcoAI™ automatically adjusts stimulation parameters in real time based on patient feedback and therapeutic goals. This system eliminates the need for separate devices and streamlines therapy delivery, enhancing both efficacy and patient convenience. Furthermore, EcoAI™ enables remote monitoring and therapy adjustments, making it a practical tool for managing chronic conditions in diverse care settings.

Recommendations for Future Research

Given the limitations of existing studies on TENS and EMS, the following recommendations are proposed to enhance the robustness and applicability of future research:

1. Utilize comprehensive outcome measures: Future studies should incorporate meaningful and standardized outcome measures, including patient-reported outcomes assessing functional improvement, quality of life, and analgesic consumption. By capturing broader and more patient-centered metrics, this approach will provide a holistic understanding of therapy impact.
2. Extended duration of treatment and follow-ups: Long-term studies are essential to evaluate the sustained efficacy of TENS in chronic pain management. Current research often limits follow-ups to less than six weeks, which may not reveal the full therapeutic potential. Extended treatment periods should be implemented to capture the longevity of benefits and limitations.
3. Standardize TENS and EMS parameters: Detailed reporting of TENS and EMS parameters, such as stimulation duration, intensity, frequency, and electrode placement, is critical for reproducibility and comparability across studies. Table 1 provides a comprehensive summary of current device capabilities, emphasizing the need for parameter standardization.
4. Integration of real-world settings: Evaluating TENS and EMS therapies in practical, real-world applications, such as at-home use, will offer insights into their everyday effectiveness. The NXTSTIM EcoAI™ system, as described in Table 1, provides a significant opportunity to bridge this gap. By leveraging AI-driven, remote-compatible technology, EcoAI™ enables seamless monitoring and customization of therapy protocols, facilitating research in uncontrolled settings.
5. Ensure statistically validated sample sizes: To strengthen the evidence base, future research must aim for large-scale, multi-center randomized controlled trials. Collaborations with device manufacturers, such as those producing NXTSTIM EcoAI™, can offer access to real-world data and ensure statistically validated sample sizes.
6. Consistent reporting of adverse events: Consistent definitions and transparent reporting of adverse events are essential to establish the safety profile of TENS and EMS. This will allow researchers to reliably evaluate the risks and benefits of these therapies.
7. Training and skill development: Providing comprehensive training programs to optimize the use of TENS and EMS devices is vital. This includes ensuring proper electrode placement and effective customization of stimulation settings. Solutions like NXTSTIM EcoAI™ can further enhance these efforts by automating and personalizing therapy adjustments in real time.

Conclusions

Current evidence underscores the clinical utility of EMS and TENS in both rehabilitation and pain management. EMS has demonstrated efficacy in enhancing muscle function across a variety of clinical scenarios, including post-surgical recovery, stroke rehabilitation, and sports medicine, by directly stimulating muscle fibers and addressing atrophy and weakness. Similarly, TENS offers a non-pharmacological approach to managing pain in conditions ranging from chronic pain and fibromyalgia to peripheral arterial disease, modulating pain perception through peripheral nerve stimulation. Both therapies are generally safe, with minimal adverse events reported. Their ability to improve quality of life and reduce reliance on medications highlights their role as integral components of modern pain management and rehabilitation strategies.

Future directions Building on these findings, research must prioritize the refinement of therapeutic protocols and parameters, focusing on patient-centered outcomes and integrating real-world data. Innovations such as the NXTSTIM EcoAI™ system are poised to revolutionize the field by combining TENS and EMS into a unified platform with intelligent, remote-controlled features. This technology, detailed in Table 1, provides an avenue for optimizing therapy across diverse patient populations while ensuring accessibility and adherence. By addressing these gaps, future research can unlock the full clinical and molecular potential of TENS and EMS.

Table 1 Key Characteristics and Capabilities of EcoAI, TENS and EMS Devices

	ECOAI™	**TENS**	**EMS**
Pulse frequency (HZ)	Integrates both TENS and EMS, Utilising AI-software dependent neuromodulation to personalize therapy programs for various pain conditions, with frequencies up to 1200 hz.	Low-frequency TENS: 1–10 hz (commonly used for endorphin release and chronic pain relief). High-frequency TENS: 50–100 hz or more (commonly used for acute pain relief via gate control mechanisms).	Low frequency (1–10 hz): Used for endurance training and to stimulate slow-twitch muscle fibers. Medium to high frequency (20–100 hz): Used to stimulate fast-twitch muscle fibers for strength training or muscle recovery. Frequencies above 50 hz are commonly used for strength gains and explosive power.
Electrodes	2	Up to 4 simultaneously	2 or 4
Pulse duration (μs)	Typically ranges between 4–400microseconds. Wider spectrum of pulse width and frequency allows deeper and accurate stimulation on nerve, tissue and muscle groups to achieve various goals including pain relief, strengthening, relax, and releasing anti-inflammatory and pain suppressing agents	Typically ranges between 50–250 microseconds. Longer pulse durations may be more effective for deeper tissue stimulation.	Typically ranges between 200–400 microseconds. Longer pulse durations are used to activate larger muscle groups.
Amplitude (mA)	Adjustable based on comfort, pain and muscle response. 0–120mA.	Adjustable based on patient comfort. Typically ranges from 0–100 mA.	Adjusted according to the user's comfort level and muscle response. Ranges from 0–120 mA in most devices.
Treatment duration	Session last between 30–60 minutes. The frequency of use may range from several sessions daily to occasional treatments, depending on the severity and type of pain.	Sessions generally last 20–60 minutes. Frequency of use can vary from multiple sessions per day to periodic treatments depending on pain severity and type.	Commonly used ratios include 10 seconds "on" cycle, followed by 50 seconds "off" cycle for strength training. For endurance or recovery, shorter off times (eg, 10 seconds on, 10–20 seconds off) may be used.
Waveform	Biphasic symmetric or asymmetric waveform	Typically uses a biphasic symmetric or asymmetric waveform to minimize tissue irritation.	Biphasic symmetrical or asymmetrical waveforms are most commonly used to stimulate motor neurons while minimizing skin irritation.

(*Continued*)

Table 1 (Continued).

	ECOAI™	**TENS**	**EMS**
Modes of operation	Continuous mode: Provides steady, uninterrupted stimulation. Burst mode: Delivers groups of pulses at regular intervals. Intelligent mode: intelligently applying the right waveforms at the right time for the right purposes in a way to achieve optimal efficacy. Modulated mode: Amplitude, frequency, or pulse duration varies to prevent adaptation Strength mode: Utilizes high intensity with short on/off cycles to activate fast-twitch muscle fibers. Recovery mode: Features lower intensity and longer on/off cycles to target slow-twitch fibers and enhance circulation. Warm-up mode: Employs low frequency and amplitude to prepare muscles for activity.	Continuous mode: Steady stimulation. Burst mode: Groups of pulses delivered periodically. Modulated mode: Amplitude, frequency, or pulse duration varies to prevent adaptation	Strength mode: High intensity, short on/off cycles to stimulate fast-twitch fibers. Recovery mode: Lower intensity, longer on/off cycles to stimulate slow-twitch fibers and promote circulation. Warm-up mode: Low frequency and amplitude for preparing muscles for exercise
Remote therapy / patient platform compatible	Yes. Fully integrated with remote monitoring and therapy management tools, leveraging AI for real-time adjustments and feedback.	Limited, typically requiring manual adjustments and in-person sessions for optimization.	Limited, often requiring physical presence for programming and monitoring.

Notes: This table provides a detailed comparison of EcoAI, TENS, and EMS devices, highlighting their pulse frequency ranges, electrode configurations, pulse duration, amplitude, treatment duration, waveform types, modes of operation and compatibility with remote therapy platforms. The EcoAI system uniquely integrates both TENS and EMS functionalities, utilizing AI-dependent neuromodulation to personalize therapy programs for pain management and rehabilitation. It also supports remote monitoring and therapy adjustments, offering enhanced convenience and clinical applicability. In contrast, traditional TENS and EMS devices demonstrate limited remote capabilities and require manual parameter adjustments. The table underscores the importance of advanced systems like EcoAI for optimizing therapeutic outcomes across diverse patient populations.

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Disclosure

Maja Green and Krishnan Chakravarthy are employees of NXTSTIM Inc. Dr Melissa Murphy is a consultant, speaking, research, and a member of advisory board for Medtronic Inc, member of advisory board of Pacira Biosciences and Nervonik, consultant in Relievant, outside the submitted work. Dr Alaa a Abd-Elsayed is a Consultant of Curonix.The authors report no other conflicts of interest in this work.

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