



REVIEW

Programmable Neuromodulation after Myocardial Infarction: Toward Precision Control of the Neurocardiac Axis

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ABSTRACT: Myocardial infarction (MI) disrupts autonomic control across the neurocardiac axis, contributing to ventricular arrhythmias, adverse remodeling, and heart failure. Conventional neuromodulation can modify this response, but most approaches remain constrained by fixed targets and stimulation parameters that poorly reflect the evolving post-infarction state. Recent developments in responsive biomaterials, nanotransducers, ultrasound, sonogenetics, and self-powered bioelectronics offer new ways to control when, where, and how autonomic pathways are modulated. Rather than representing a single therapeutic modality, these technologies introduce different levels of spatial, temporal, and biological selectivity. These platforms differ in the type of control they provide, ranging from microenvironment-responsive regulation and externally triggered stimulation to cell-selective and sustained bioelectronic modulation. However, most of the available evidence remains preclinical. This Review discusses their application after MI, compares the control achieved by each platform, and examines the challenges that limit translation. Particular attention is given to the transition from externally programmed intervention toward sensing-guided and adaptive neurocardiac modulation.

KEYWORDS: Myocardial infarction; programmable neuromodulation; neurocardiac axis; autonomic remodeling; smart biomaterials; bioelectronics

1 Introduction

Myocardial infarction (MI) affects far more than the injured myocardium. Autonomic imbalance develops early after infarction, with heightened sympathetic drive, impaired parasympathetic regulation, and progressive remodeling of cardiac innervation [1,2]. Sympathetic fibers are disrupted within and around the infarcted region and subsequently regrow in a heterogeneous manner, particularly at the border zone, where uneven reinnervation can increase electrophysiological dispersion and arrhythmic vulnerability [3–6]. Neural remodeling is not confined to the myocardium. Structural and functional changes have been observed in the intrinsic cardiac nervous system after MI, while stellate ganglion neurons also undergo marked morphological and functional remodeling [7–9]. Central autonomic structures are involved as well, with post-MI alterations reported in heart–brain signaling and hypothalamic sympathetic regulation [10–14]. Together, these findings support the view that post-infarction autonomic remodeling extends across a broader neurocardiac network [15–18].

Autonomic pathways have therefore become attractive therapeutic targets after MI. Vagus nerve stimulation (VNS) has shown antiarrhythmic and cardioprotective effects [19–21], while stellate ganglion

blockade [22,23], cardiac sympathetic denervation [24,25], and spinal cord stimulation [26] provide complementary ways to suppress excessive sympathetic activity. Recent reviews and clinical series further support VNS across cardiovascular disease settings [27–30], while complementary evidence has accumulated for cardiac sympathetic denervation (CSD) [31–33], transcutaneous VNS [34], stellate-ganglion interventions, and non-invasive autonomic modulation [35–39]. Yet the post-infarction neural substrate is not static. Sympathetic overactivity and electrical instability are most pronounced early after MI, whereas neuroinflammation, nerve sprouting, and more persistent heart-brain remodeling become increasingly important during the following days and weeks. Most conventional approaches, however, still act on predefined anatomical targets with stimulation or inhibition parameters selected in advance [40–43]. This mismatch between an evolving disease process and a relatively fixed intervention remains a major limitation of current neuromodulation.

Recent bioengineering advances offer a way to address this limitation by increasing control over the intervention itself. Biomaterials, nanotransducers, ultrasound-based techniques, genetic engineering, and bioelectronic systems can now influence not only which neural pathway is targeted, but also when, where, and under what conditions modulation occurs [44–48]. This shift underlies the concept of programmable neuromodulation, in which key features of treatment—including the target, timing, intensity, and activation conditions—can be preset or adjusted. Responsive systems operate through predefined responses to biological or external triggers, whereas adaptive systems further incorporate physiological feedback to modify therapeutic output during treatment [49–52]. In this Review, we focus on disease-responsive platforms, remotely triggered and cell-selective strategies, and wireless or self-powered systems developed for post-MI neuromodulation. We further compare the type of control achieved by these approaches and discuss what will be required to move from externally programmed intervention toward sensing-guided and adaptive neurocardiac therapy (Fig. 1).

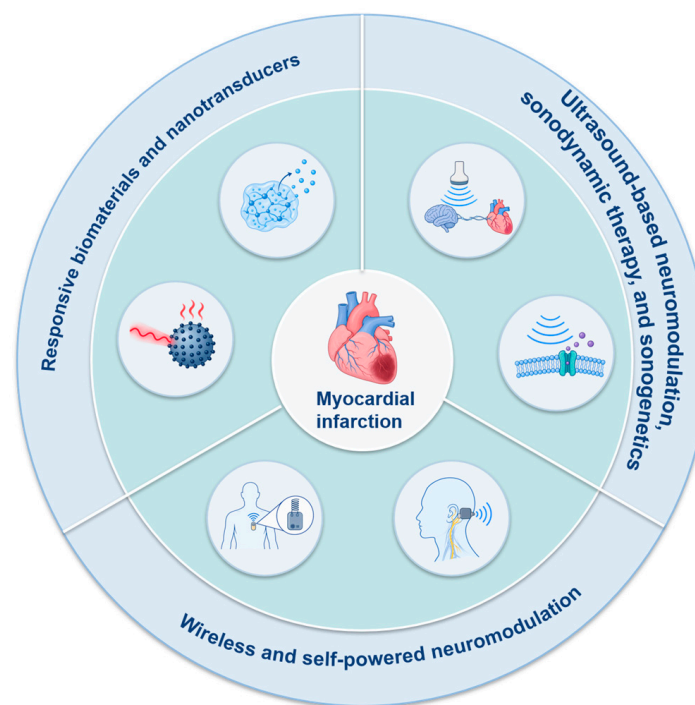


Figure 1: Overview of programmable neuromodulation strategies after myocardial infarction.

2 From Conventional Neuromodulation to Programmable Control

Neuromodulation has become an increasingly important strategy for reducing post-infarction arrhythmias and limiting adverse cardiac remodeling [19,21,26,53]. However, the level of evidence differs substantially among these approaches. Post-MI VNS has been supported mainly by experimental studies, whereas clinical VNS experience has largely come from broader cardiovascular populations. Stellate ganglion block and cardiac sympathetic denervation have entered clinical practice primarily as rescue or adjunctive strategies for refractory ventricular arrhythmias, while evidence for spinal cord stimulation after MI remains predominantly preclinical (Fig. 2a,b) [22,25,26,38,54]. The main limitation is therefore no longer whether autonomic activity can be altered, but how precisely this modulation can be delivered. Most conventional strategies rely on predefined anatomical targets and relatively fixed treatment parameters, which may lead to broad neural recruitment, limited target selectivity, and poor adaptation to the changing biological state of the infarcted heart (Table 1) [40,43,46,51,55].

Table 1: Comparison of conventional neuromodulation strategies relevant to post-MI autonomic regulation.

Approach	Target/Mechanism	Evidence/Clinical Status	Strength	Limitation
VNS	Parasympathetic activation; sympathetic suppression	Post-MI mainly preclinical [19–21]; broader cardiovascular clinical experience [27–30]	Reversible; adjustable	Often implant-based; variable parameters and efficacy
SGB	Temporary sympathetic blockade	Clinical use for refractory ventricular [22,23,35,54] arrhythmias/electrical storm	Rapid effect	Temporary; mainly rescue/bridging therapy
CSD	Surgical sympathetic denervation	Clinical use in selected refractory ventricular arrhythmias [24,25,31–33]	Sustained effect	Invasive; partly irreversible
SCS	Spinal/autonomic pathway modulation	Post-MI evidence mainly preclinical [26]	Adjustable	Implant required; limited post-MI clinical evidence

This limitation is particularly relevant after MI because autonomic remodeling evolves together with myocardial injury and repair [2,9,13]. Accordingly, the therapeutic need also changes over time. Rapid suppression of sympathetic overactivity may be beneficial during an arrhythmogenic phase, but the same intervention may become less appropriate once neural repair and chronic remodeling predominate. Programmable neuromodulation has emerged in response to this mismatch between a dynamic disease process and relatively static treatment. By allowing greater control over the timing, location, intensity, or activation conditions of therapy, these approaches may better match intervention to the evolving post-MI state [40,43,52,55]. Pathological signals may trigger local treatment, externally applied physical energy can provide reversible activation, molecular or genetic engineering can improve biological selectivity, and energy-harvesting technologies can support prolonged intervention. In this way, autonomic therapy is being extended from fixed stimulation toward more responsive, selective, reversible, and ultimately state-dependent control. The following section summarizes the smart technologies currently enabling this transition after MI [52,56].

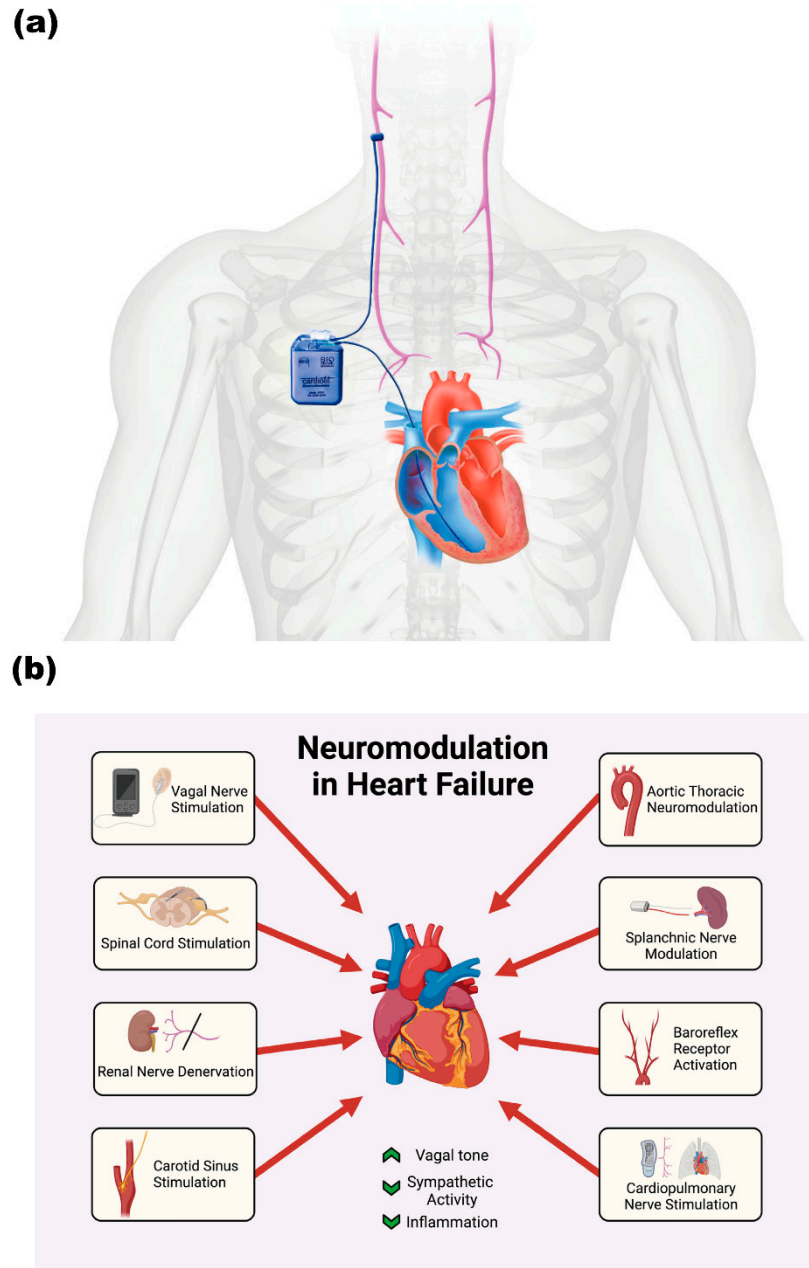


Figure 2: Conventional autonomic neuromodulation approaches relevant to cardiovascular disease. (a) Implantable vagus nerve stimulation system with cervical vagal stimulation delivered by an implanted pulse generator. (b) Major anatomical targets and device-based strategies used for cardiovascular autonomic modulation. (a) Reproduced from Anand et al. [57] under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives License. (b) Reproduced from Pahuja et al. [56] under the terms of the Creative Commons Attribution 4.0 International License (CC BY 4.0).

3 Smart Technologies for Programmable Neuromodulation after MI

Recent work has begun to move post-MI neuromodulation beyond fixed intervention toward systems in which treatment delivery can be controlled at several levels. Local pathological signals may regulate therapeutic release, externally applied physical energy can determine when modulation is activated,

engineered neural responses can improve biological selectivity, and wireless or energy-harvesting devices can support prolonged operation. These approaches differ substantially in mechanism and maturity, but they address the same problem: how to match autonomic intervention more closely to the spatial and temporal complexity of post-MI neural remodeling.

3.1 Responsive Biomaterials and Nanotransducers

The infarcted myocardium provides a biochemical environment that can itself be used to regulate treatment. Elevated reactive oxygen species (ROS), local acidosis, inflammatory signaling, and matrix remodeling are characteristic of myocardial injury and can serve as endogenous triggers for controlled therapeutic release [58–60]. Yang et al. developed an injectable hydrogel responsive to both pH and ROS, incorporating C-type natriuretic peptide (CNP) and semaphorin 3A (Fig. 3a) [61–63]. In experimental MI, the system reduced local inflammation and sympathetic nerve sprouting, improved electrical conduction, and attenuated adverse ventricular remodeling (Fig. 3b) [61]. Its importance lies less in sustained drug release itself than in the fact that therapeutic output is linked to the pathological microenvironment. In this sense, the material acts indirectly on post-infarction neuromodulation by modifying the conditions that drive neural remodeling rather than by acutely changing neuronal excitability.

This type of responsiveness is best suited to processes that develop over hours to days, including inflammation and abnormal reinnervation [58,61,64,65]. It is less appropriate for rapid fluctuations in neural activity. A hydrogel can respond to persistent changes in ROS or pH, but it cannot readily adjust therapy to a transient sympathetic surge or an impending ventricular arrhythmia. Disease-responsive materials may therefore be most useful for reshaping the local environment in which neural remodeling occurs, rather than for second-to-second autonomic control. The timescale of the biological trigger is, in effect, also the timescale of the therapeutic response.

By contrast, externally activated nanotransducers can influence neural activity more directly while providing a different form of programmability. Wang et al. reported a NIR-II-responsive Pt nanoshell with a photothermal conversion efficiency of 73.7% at 1064 nm and used it for temperature-dependent autonomic modulation in a canine model (Fig. 3c) [66]. Neural activation occurred at approximately 41.0–42.9°C, whereas inhibition was achieved at 45.0–46.9°C, consistent with differential engagement of thermosensitive channels such as TRPV1 and TREK1. *In vivo* modulation was maintained for approximately 5 min at the target temperature range, allowing rapid but reversible autonomic regulation. By controlling local temperature, the same platform could shift between parasympathetic activation and sympathetic inhibition and reduce ventricular arrhythmias in myocardial ischemia/reperfusion and MI models (Fig. 3d).

This approach differs fundamentally from conventional photothermal therapy. Here, heat is used as a controllable neural input rather than simply as a cytotoxic or tissue-modifying stimulus. Importantly, neural function returned close to baseline within several hours after irradiation, supporting the reversibility of this level of photothermal modulation. Because the external input can be adjusted rapidly, the neural response can change on a much shorter timescale than with microenvironment-responsive release. The two strategies therefore address different therapeutic needs: responsive biomaterials are better suited to sustained remodeling processes, whereas photothermal nanotransduction is more compatible with rapid modulation of neural activity. Optical penetration remains a major limitation, however [67]. Even within the NIR-II window, deeper autonomic structures are harder to reach than superficial peripheral targets, providing a strong rationale for the increasing use of acoustic energy in remote neuromodulation.

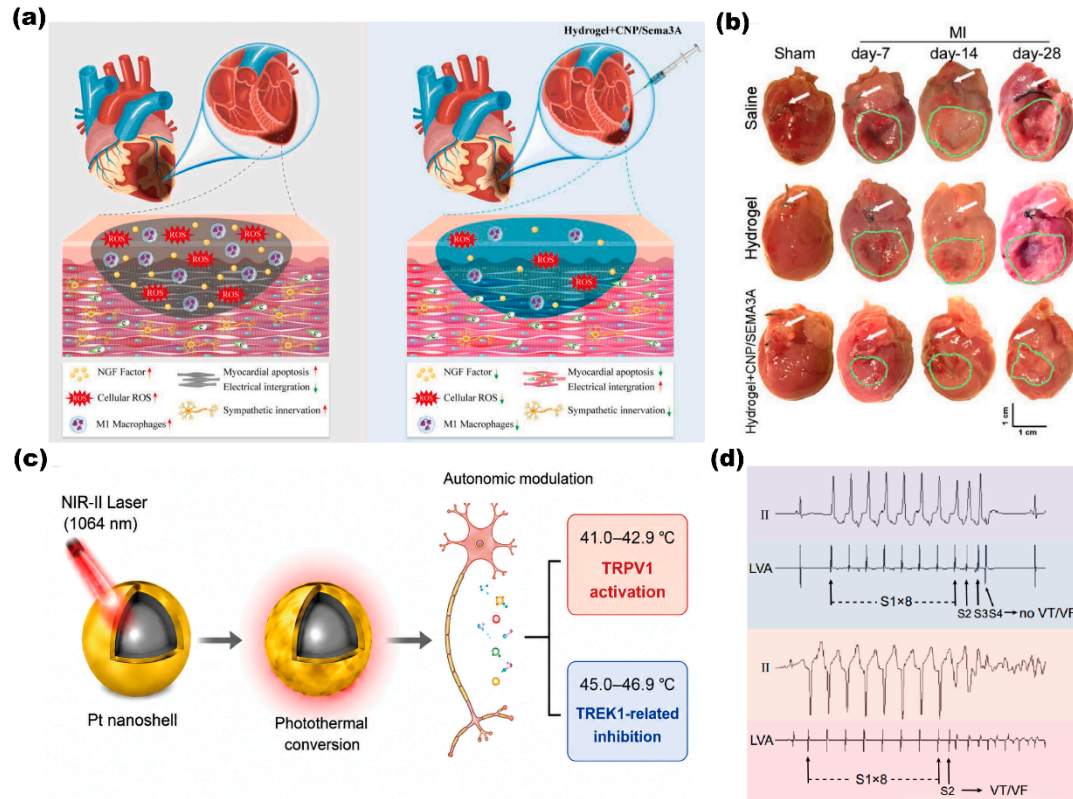


Figure 3: Responsive materials and externally activated nanotransducers for post-MI neurocardiac modulation. (a) Microenvironment-responsive hydrogel designed to influence inflammation and sympathetic remodeling after MI. (b) Representative cardiac morphology following hydrogel treatment. (c) NIR-II-responsive Pt nanoshell platform for temperature-dependent neural modulation. (d) Representative electrophysiological recordings illustrating the effect of photothermal neuromodulation on ventricular arrhythmia. Panels (a,b) reproduced from Yang et al. [61] with permission. Panels (c,d) reproduced and rearranged from Wang et al. [66] under the terms of the Creative Commons Attribution 4.0 International License (CC BY 4.0).

3.2 Ultrasound-Based Neuromodulation, Sonodynamic Therapy, and Sonogenetics

3.2.1 Direct Ultrasound Neuromodulation

Ultrasound is particularly attractive for neurocardiac modulation because it can reach relatively deep targets while preserving spatial focusing and external temporal control [68–70]. Early studies focused on peripheral autonomic structures. In a canine MI model, low-intensity focused ultrasound (LIFU) applied to the left stellate ganglion (LSG) reduced ganglion activity, prolonged ventricular effective refractory periods, and decreased ventricular arrhythmias without detectable histological injury. LIFU was delivered to the LSG for 10 min at 1.0–2.0 W, with significant modulation observed at 1.5 and 2.0 W. The local temperature increase remained below 1°C, arguing against simple thermal ablation as the main mechanism [71].

Subsequent work extended ultrasound modulation to central autonomic circuits. The hypothalamic paraventricular nucleus (PVN) is a major regulator of sympathetic outflow and becomes neuroinflammatory after MI. Xiang et al. showed that LIFU directed to the PVN reduced post-MI ventricular arrhythmias, suppressed LSG activity, and attenuated microglial activation and inflammatory signaling [72]. Because both acute and chronic MI models were included, the findings also suggested that PVN modulation may influence more than the immediate arrhythmic phase. Longer-term transcranial ultrasound studies have

since reported reductions in neuroinflammation, arrhythmia susceptibility, and adverse cardiac remodeling after MI using PVN-targeted stimulation for 15 min per day over 4 consecutive weeks [73]. Even so, focused ultrasound remains primarily an anatomically defined intervention, since multiple responsive cell types within the acoustic field may be affected.

3.2.2 Sonodynamic Therapy

Sonodynamic nanomedicine adds a molecular layer to this form of control. Hu et al. developed a long-wavelength-emissive organic nanosonosensitizer, BBTD-TPA, encapsulated in nanoparticles and delivered into the PVN (Fig. 4a) [74]. After local delivery of the nanosonosensitizer, LIFU was applied at 1.0 MHz and 2.0 W cm^{-2} for 10 min. Following low-intensity ultrasound exposure, the system promoted microglial autophagy through the ROS-AMPK-mTOR pathway, attenuated PVN neuroinflammation and sympathetic hyperactivity, and was associated with reduced myocardial injury and lower ventricular arrhythmia susceptibility (Fig. 4b–d). NIR-II imaging further showed that the nanoparticles remained detectable in the PVN for up to 12 h, providing a measure of local retention and clearance.

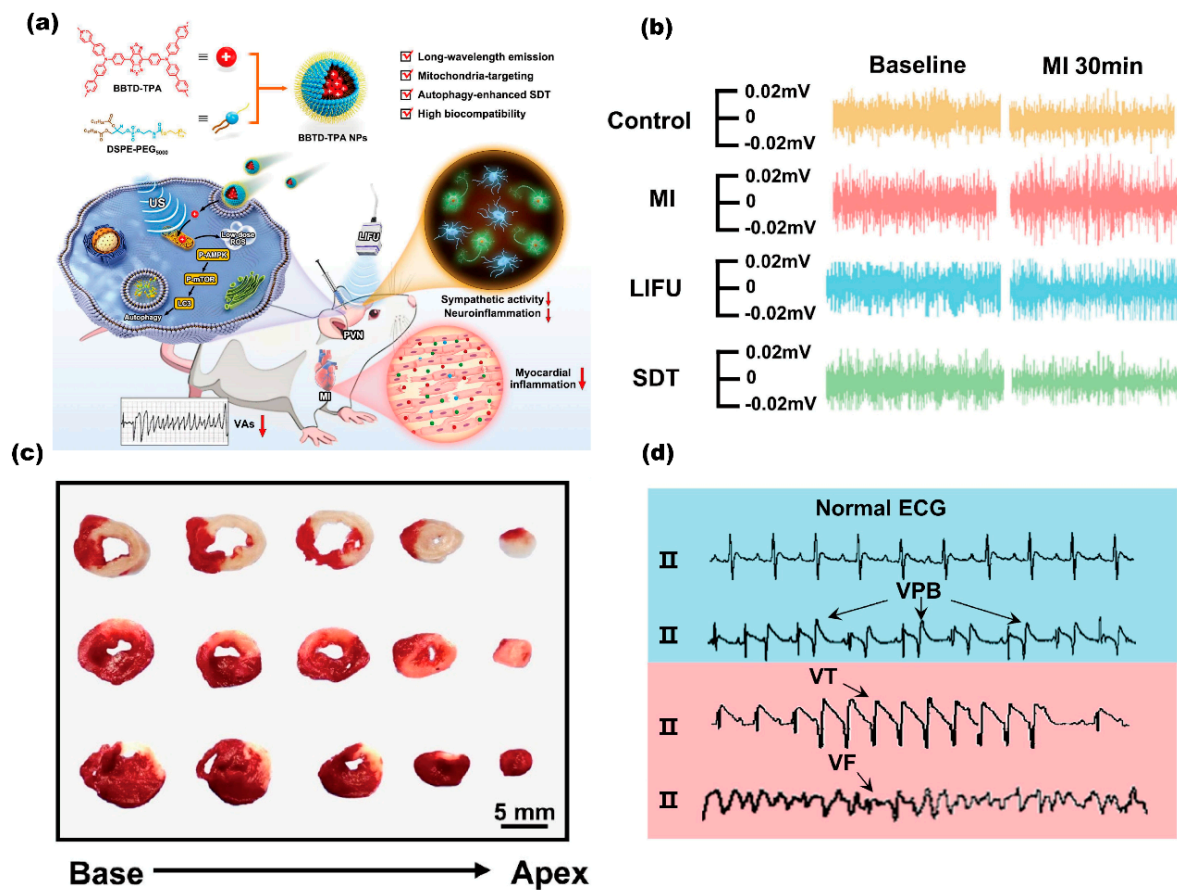


Figure 4: Ultrasound-triggered neuromodulation and sonodynamic intervention after myocardial infarction. (a) Nanosonosensitizer-based strategy targeting the post-MI neuroinflammatory environment. (b) Representative sympathetic nerve activity under control, MI, LIFU, and SDT conditions. (c) TTC-stained myocardial sections illustrating differences in infarct injury among groups. (d) Representative ECG patterns of normal rhythm and ventricular arrhythmias after MI. Panels (a–d) reproduced and rearranged from Hu et al. [74] under the terms of the Creative Commons Attribution 4.0 International License (CC BY 4.0).

The advantage of sonodynamic therapy is therefore not simply stronger ultrasound action. Rather, the nanosonosensitizer introduces biochemical amplification between the acoustic input and the downstream biological response. Unlike direct ultrasound neuromodulation, the principal effect here is mediated through modulation of the neuroinflammatory microenvironment rather than direct regulation of neuronal excitability. This may be useful when the therapeutic target is the inflammatory environment sustaining sympathetic activation rather than neuronal excitability alone. The trade-off is greater dependence on nanoparticle distribution, local dose, pharmacokinetics, and activation efficiency.

3.2.3 Sonogenetics

Sonogenetics adds another level of selectivity by making defined neural populations responsive to ultrasound. In 2025, Hu et al. expressed the mechanosensitive potassium channel TRAAK in PVN neurons using rAAV2/9 [75]. Transcranial ultrasound at 1.0 MHz and 2.0 W cm^{-2} was used to activate TRAAK-expressing neurons. Transcranial ultrasound activated TRAAK, promoted neuronal hyperpolarization, and reduced sympathetic output through the PVN–LSG–heart circuit. This intervention reduced malignant ventricular arrhythmias during acute MI and, with longer-term treatment, improved cardiac function, ventricular remodeling, and electrophysiological stability.

Viewed together, these approaches differ mainly in where selectivity is introduced. Focused ultrasound provides predominantly anatomical control, sonodynamic nanomedicine adds molecular amplification, and sonogenetics restricts acoustic responsiveness to engineered cells. Increasing selectivity, however, also increases translational complexity. Viral delivery to central autonomic nuclei, persistence of transgene expression, immune responses, and uncertainty regarding long-term reversibility remain important concerns [76–80]. The requirement for viral gene delivery therefore represents an additional translational barrier compared with ultrasound neuromodulation alone. For cardiovascular disease, where treatment may be required only during a defined stage of recovery, transient or non-viral sensitization could ultimately be more practical than permanent genetic modification. Acoustic dosing is another unresolved issue: frequency, intensity, duty cycle, pulse duration, and skull-dependent energy transmission vary substantially across studies, limiting direct comparison and standardization [81,82].

3.3 Wireless and Self-Powered Neuromodulation

Long-term neuromodulation introduces a practical challenge that is less prominent in acute intervention: how to maintain stable treatment over weeks or months without increasing device burden. Conventional implantable stimulators depend on batteries, repeated charging, or external power-delivery hardware, all of which complicate prolonged use [83–87]. Wireless and energy-harvesting systems offer a different route by reducing dependence on conventional implanted power sources while preserving sustained access to autonomic targets.

Zhou et al. developed a wireless self-powered optogenetic platform for long-term cardiac sympathetic modulation in ambulatory canines after MI (Fig. 5a). A triboelectric nanogenerator (TENG) harvested biomechanical energy from body motion and supported optical stimulation, while the fully implantable battery-free configuration enabled prolonged modulation of the left stellate ganglion. Repeated treatment reduced MI-associated sympathetic hyperactivity and remodeling, improved ventricular function and electrophysiological stability, and lowered susceptibility to ventricular arrhythmias (Fig. 5b) [88]. This work extended cardiac optogenetic neuromodulation beyond short-term proof-of-concept experiments, although the need for genetic sensitization and an implanted optical interface remains a major translational barrier.

A different strategy is to supply energy from outside the body while retaining an implanted neural interface. An ultrasound-driven piezoelectric nanogenerator was designed to convert externally applied acoustic energy into electrical output for vagus nerve stimulation. In post-MI animals, repeated stimulation improved ventricular function and was accompanied by reduced inflammation, fibrosis, and sympathetic remodeling [89]. Unlike TENG-based systems, which rely on spontaneous biomechanical input, ultrasound-powered stimulation provides a controllable external energy source while maintaining local access to a defined nerve.

Less invasive approaches have also been explored. Piezoelectric nanogenerator-assisted transcutaneous auricular vagus nerve stimulation was used to modulate post-MI heart–brain signaling without direct implantation of a vagal electrode (Fig. 5c). In this model, treatment attenuated cardiac and heart–brain remodeling and reduced neuroinflammation in the central amygdala [90], with corresponding improvements in myocardial and vascular pathology (Fig. 5d).

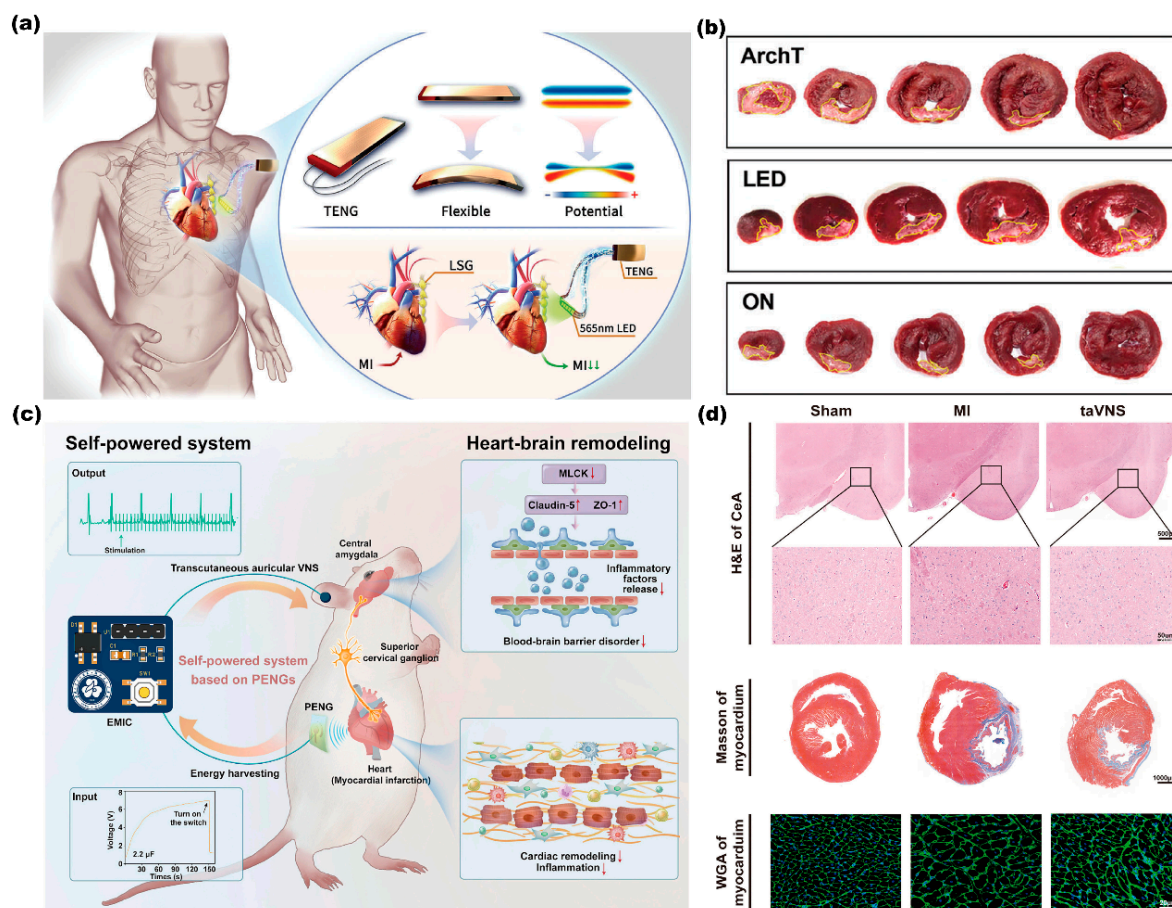


Figure 5: Wireless and self-powered platforms for sustained neurocardiac modulation. (a) TENG-based self-powered optogenetic system for sympathetic neuromodulation. (b) Representative myocardial findings after optogenetic intervention. (c) PENG-assisted transcutaneous auricular vagus nerve stimulation for post-MI heart–brain modulation. (d) Representative histological assessment of cardiac and vascular remodeling after treatment. Panels (a,b) reproduced and rearranged from Zhou et al. [88] under the terms of the Creative Commons Attribution 4.0 International License (CC BY 4.0). Panels (c,d) reproduced from Xu et al. [90] under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives License.

These platforms illustrate different trade-offs between target specificity, invasiveness, and energy autonomy. TENG-based optogenetics offers relatively precise sympathetic control but requires genetic and optical interfaces; ultrasound-powered vagus nerve stimulation retains direct access to a defined peripheral nerve but remains implant-based; and piezoelectric nanogenerator (PENG)—assisted auricular stimulation reduces procedural burden at the expense of less selective neural recruitment. Importantly, wireless or self-powered operation primarily improves energy delivery and the duration of neuromodulation; it does not by itself make a system responsive or adaptive. In most current systems, stimulation remains largely predefined, while long-term performance is still constrained by interface stability, encapsulation, energy-transfer efficiency, and chronic tissue responses [91–94]. The next step is therefore likely to depend on integrating durable power delivery with physiological sensing and adaptive control rather than on energy harvesting alone.

4 Translational Challenges and the Path toward Adaptive Control

Despite rapid technical progress, programmable neuromodulation after MI remains largely preclinical. One of the main difficulties is that the therapeutic target is neither biologically uniform nor stable over time. Functionally distinct neuronal populations can coexist within the same autonomic ganglion or central nucleus [11], while macrophages, microglia, vascular cells, and local neural circuits further influence the cardiac response [12,18,95]. The dominant neurocardiac substrate also changes during the course of MI. Sympathetic activation and electrical instability are most prominent early after infarction, whereas neuroinflammation, abnormal reinnervation, and persistent central and peripheral remodeling become more important during subsequent repair. Anatomical localization alone is therefore unlikely to be sufficient. A neural pathway that is appropriate for intervention at one stage may not remain the optimal target throughout recovery. Single-cell and spatial profiling may help identify disease-associated neuronal or neuroimmune populations [11,95], but the timing of intervention will be just as important as the identity of the target itself. Accordingly, rapid suppression of sympathetic overactivity may be more relevant during the early arrhythmogenic phase, whereas interventions targeting neuroinflammation or neural remodeling may be better suited to later stages of repair.

A second challenge is the lack of comparable dosing frameworks across platforms. Photothermal neuromodulation depends on wavelength, irradiance, local temperature, and exposure duration [66,67], whereas ultrasound-based approaches vary in frequency, acoustic pressure, duty cycle, pulse duration, and targeting strategy [81,82]. Nanomedicine introduces additional variables, including dose, biodistribution, tissue retention, and clearance [58,62,65]. These differences become even more important when moving across species, because tissue depth, skull properties, autonomic anatomy, and device geometry can all alter energy delivery and biological response. Small-animal models are useful for mechanistic studies, whereas large-animal models are more informative for evaluating device scale, energy delivery, and chronic neural interfaces under conditions closer to clinical application. More consistent reporting standards, independent validation, and studies in clinically relevant large-animal models will be needed before different programmable platforms can be compared reliably [96].

Long-term translation will also require attention to material clearance and repeated-exposure safety, as well as the durability of implanted neural interfaces. For sonogenetic and self-powered systems, viral delivery, long-term device stability, and reproducibility of energy output remain additional practical barriers.

The next step is to connect programmability with physiological state. Most current systems are still open-loop: local pathological signals may regulate drug release, external energy can switch treatment on or off, and wireless devices can sustain stimulation, but the therapeutic output remains largely pre-

determined [97]. Recent proof-of-concept work suggests that this limitation can be overcome. In 2026, closed-loop direct-current block of the paravertebral sympathetic chain was evaluated in chronically infarcted pigs using real-time norepinephrine measurements as the feedback signal (Fig. 6a) [98]. Here, cardiac norepinephrine served as the sensed input, a fuzzy-logic controller processed the feedback signal, and direct-current sympathetic block constituted the therapeutic output. A fuzzy-logic controller adjusted the degree of sympathetic block to achieve predefined reductions in cardiac norepinephrine release, with corresponding improvement in left ventricular systolic pressure recovery after ventricular pacing. Together with other emerging closed-loop systems [99–102], this study shows that physiological feedback can be used not only to trigger neuromodulation, but also to regulate its intensity.

Even so, such systems are still some distance from routine clinical use. Direct norepinephrine sensing is invasive [103], the available evidence remains limited, and controller performance has largely been evaluated under controlled experimental conditions rather than the variable physiological states encountered in patients. More practical early systems may therefore need to rely on signals that are easier to acquire continuously, such as ventricular ectopy, heart-rate variability, or validated markers of sympathetic activation [42,55,104]. The challenge is not simply to add a sensor, but to identify a signal that is reliable enough, fast enough, and biologically meaningful enough to justify changing treatment in real time. Conceptual closed-loop architectures illustrate how electrophysiological, autonomic, or inflammatory inputs could ultimately be linked to therapeutic output (Fig. 6b). This transition from programmable to adaptive neuromodulation will depend as much on the quality of the feedback signal as on the sophistication of the stimulation platform itself.

5 Conclusion

Programmable neuromodulation is extending post-MI autonomic therapy beyond fixed stimulation by adding greater control over when, where, and under what biological conditions treatment is delivered. Responsive biomaterials, nanotransducers, ultrasound-based approaches, sonogenetic strategies, and self-powered bioelectronics each contribute a different form of controllability, ranging from microenvironment-responsive release and remotely triggered stimulation to cell-selective and sustained bioelectronic modulation. Their value therefore lies less in replacing established neuromodulatory therapies than in making them more selective, timely, and better matched to the evolving post-infarction state. The field, however, remains largely preclinical. Progress toward translation will depend on clearer definition of therapeutic targets and treatment windows, more comparable dosing and reporting standards, and feedback signals that are reliable enough to guide treatment in real time. The longer-term goal is not simply to make neuromodulation more technically sophisticated, but to make it responsive to the biological state of the patient. Achieving that shift from programmed intervention to adaptive neurocardiac control may ultimately determine whether these emerging technologies become clinically meaningful after myocardial infarction.

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