Peripherally Induced Reconditioning of the Central Nervous System: Proposed Mechanisms for Sustained Relief of Chronic Pain Following 60-Day Percutaneous Peripheral Nerve Stimulation Treatment

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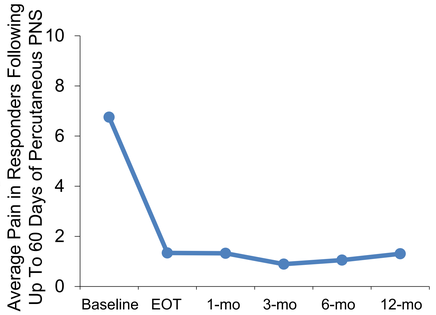
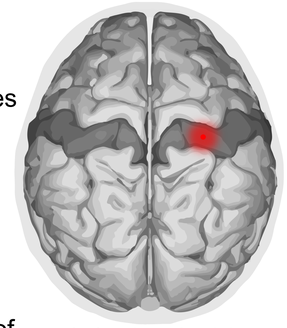
Background

- Peripheral nerve stimulation (PNS) can be an effective tool for the treatment of chronic pain, and recent years have seen the advancement of various PNS features and techniques intended to overcome many of the limitations of conventional PNS.
- **Recent clinical evidence:** significant reductions in pain often persist well beyond the end of treatment (EOT) following up to 60-day percutaneous PNS treatments, outcomes which have not previously been observed with conventional permanently implanted systems.[1-9]



- The primary somatosensory cortex (S1) is dynamic and can substantially change as a result of shifts in afferent input.[10-21] Maladaptive cortical plasticity that contributes to chronic pain can be reconditioned.
- This review summarizes the potential mechanisms by which selective large diameter afferent fiber activation may recondition maladaptive CNS changes associated with chronic pain to induce a prolonged reduction in pain and avoidance of a permanent implant.



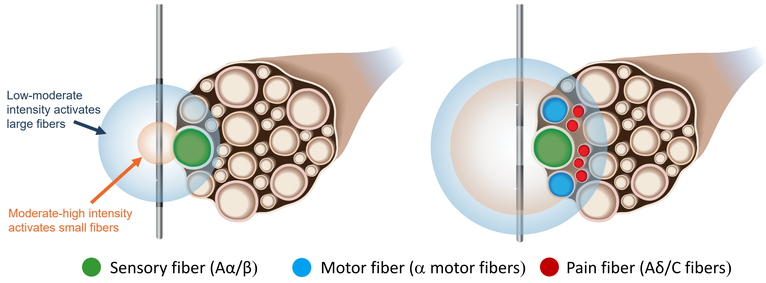
Maladaptive plasticity contributes to chronic pain

Literature Review

- This review is based on searches of published literature on PubMed, Google Scholar, and Web of Science and the authors' familiarity with the published literature in their respective fields, including preclinical and clinical articles related to chronic pain, neurostimulation, peripheral nerve stimulation, and cortical plasticity.

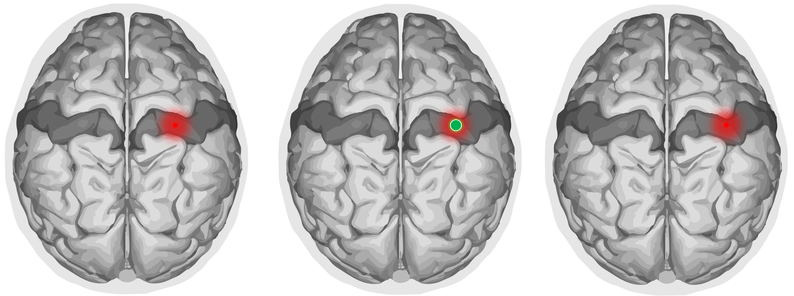
Results & Discussion

Conventional PNS is limited by the use of small electrodes placed in close contact with the target nerve.



- Activation of target fibers nearby the electrode produces comfortable sensations
- Increasing intensity can lead to unintended discomfort (e.g., motor or pain fiber activation)

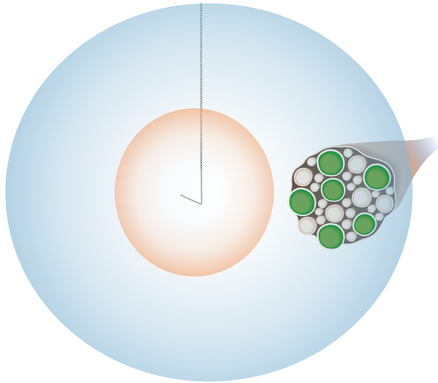
Continuous stimulation is required to support pain relief, necessitating permanent system implantation.



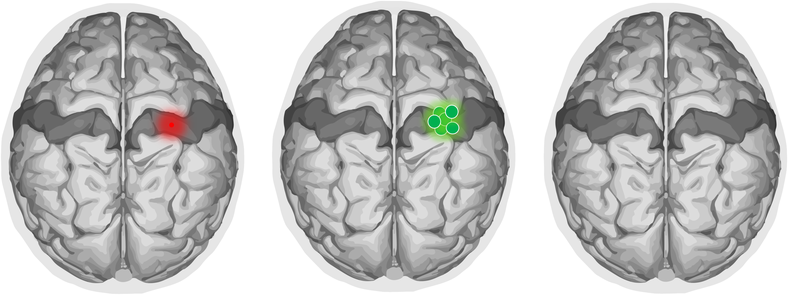
Pre-treatment | Stimulation ON | Stimulation OFF

Remote selective targeting produces focal and robust signals by selectively activating target fibers.

- Capacity for selectively activating targeted sensory fibers increases with a PNS system and leads designed for remote selective targeting.
- Remote selective targeting is a function of multiple factors, including:
  - Large monopolar electrode
  - Waveform design
  - Lead placement remote from the nerve (e.g., 0.5-3 cm)



Generation of focal and robust peripheral signals may enable sustained relief without requiring permanent implantation.



Pre-treatment | During 60-day treatment | Post-60-day treatment

Conclusions

- PNS with remote selective targeting is theorized to generate focal and robust non-nociceptive signals peripherally to enable reconditioning of the cortex to produce sustained relief of chronic pain following short-term (e.g., 60-day) PNS treatment.

References

[1]Rauck et al., 2014; [2]Chae et al., 2013; [3-4]Wilson et al., 2014a, 2014b; [5]Kapural et al., 2018; [6-9]Gilmore et al., 2018a, 2018b, 2019, 2020; [10]Buonomano & Merzenich, 1998; [11]Flor et al., 1997; [12]Flor et al., 2001; [13]Gustin et al., 2012; [14]Hummel & Cohen, 2005; [15]Jenkins et al., 1990; [16]Kuner & Flor, 2017; [17]Maihofner et al., 2004; [18]Mosely & Flor, 2012; [19]Recanzone et al., 1990; [20]Ridding & Rothwell, 1999; [21]Wu et al., 2005.

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