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Mechanistic Insights into Spinal Cord Stimulation for Pain Modulation: A Systematic Review of Animal Studies

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ADMINISTRATIVE INFORMATION

Support - N/A.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202540047

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 15 April 2025 and was last updated on 15 April 2025.

INTRODUCTION

Review question / Objective Population: Animal models used in experimental studies examining spinal cord stimulation and pain mechanisms. Studies included rodents and other animals where spinal cord–level cells were evaluated. Brain cells were excluded.

Intervention: Spinal cord stimulation, including different stimulation paradigms, applied to animals in experimental models to investigate mechanisms of pain alleviation.

Comparison: Control or sham-stimulated animals, or untreated conditions, were used as comparators to assess the effects of SCS on pain pathways and mechanisms.

Outcome: Identification, classification, and summary of mechanisms of pain modulation by SCS in animals — particularly spinal cord-level mechanisms such as gate control, segmental inhibition, dorsal horn modulation, neuroglial responses, and plasticity.

Study Design: Experimental (in vivo and computational) studies with quantifiable outcome measures and defined control vs. intervention groups. Systematic reviews, human studies, and studies without mechanistic focus were excluded.

Condition being studied Chronic neuropathic pain. Using animal models, we investigate the underlying biological mechanisms at the spinal level that contribute to SCS-induced pain relief.

METHODS

Search strategy The search strategy involved a comprehensive literature review using major electronic databases including PubMed, MEDLINE, Google Scholar, ScienceDirect, BMJ databases, and Cochrane databases.

Participant or population Non-human animal subjects, specifically rodents and mice.

Intervention The intervention being evaluated in this review is spinal cord stimulation (SCS) as applied in preclinical animal models of pain.

Comparator N/A.

Study designs to be included Animal studies with clearly defined control vs experimental groups, quantifiable outcome measures, and spinal cord cellular targets.

Eligibility criteria Inclusion criteria addressed in the PICOS section. Exclusions are human studies or systematic reviews, studies involving brain regions or brain cells, studies assessing different frequencies of SCS without describing pain mechanisms, studies lacking clear mechanistic or pain-focused outcomes, and non-animal studies.

Information sources PubMed, MEDLINE, Google Scholar, ScienceDirect, BMJ databases, and Cochrane databases.

Main outcome(s) Identify, categorize, and summarize the mechanisms by which spinal cord stimulation alleviates pain in animal models.

Quality assessment / Risk of bias analysis The SYRCLE's Risk of Bias tool was used. The SYRCLE Risk of Bias tool is an adaptation of the Cochrane Risk of Bias tool for human studies. The SYRCLE risk of bias tool assesses 10 domains covering different types of biases including selection, performance, detection, attrition, reporting, and other biases.

Strategy of data synthesis Data analysis was performed using a narrative synthesis approach due to the heterogeneity of experimental models, interventions, and outcome measures across included studies. Extracted variables include Author(s), Year of publication, Species used. Cell types involved, Pain model used , and study conclusions. Studies were then categorized based on their proposed mechanism of action.

Subgroup analysis N/A.

Sensitivity analysis N/A.

Country(ies) involved USA.

Keywords Spinal Cord Stimulation, Pain mechanims, Animal Studies.

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