

Calcitonin Gene-Related Peptide in Pain Beyond Migraine: A Scoping Review

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Introduction

- Calcitonin gene-related peptide (CGRP) is best known for its role in migraine, but recent studies show it also affects other pain pathways.
- It connects sensory nerves and immune cells, promoting inflammation and sensitivity.
- Mapping how CGRP functions across pain conditions may reveal new non-opioid treatment targets.

Methods

- Database:** PubMed (2010-2024)
- Search:** (“calcitonin gene-related peptide” OR “CGRP”) AND (pain OR nociception OR hypersensitivity OR allodynia) NOT (migraine OR headache)
- Included:** 18 studies (13 animal, 5 human)
- Domains:** Orofacial, postoperative, endometriosis, arthritis, neuropathic
- Filters:** English language, free full text, full text, and abstract available
- Analysis:** Narrative synthesis using PRISMA-ScR

Results

- The search identified 1,113 records, with 18 studies meeting inclusion criteria (13 preclinical, 5 human).
- Across models, CGRP consistently enhanced pain signaling by linking immune and sensory pathways.
- Common findings included cytokine release, glial activation, and neurogenic inflammation across multiple pain domains.
- CGRP antagonism (via receptor blockade or antibodies) reduced inflammation, mechanical hypersensitivity, and lesion size.
- Clinical studies demonstrated reductions in postoperative, arthritic, and neuropathic pain, though sample sizes were limited.

Discussion

- If these findings generalize to larger human trials, CGRP may be a shared pain pathway that links inflammation, central and peripheral sensitization.
- This means drugs that block CGRP for migraine could one day help in chronic inflammatory or neuropathic pain.
- Most current evidence is from animal studies; human data remain limited.
- Next steps: clinical studies in endometriosis, arthritis, and neuropathic pain, to explore translational and sex-specific mechanisms or differences.

CGRP amplifies pain through shared neuroimmune pathways across multiple conditions

Emerging evidence shows it’s a shared pain pathway in inflammation, endometriosis, and neuropathy—but clinical data are still limited.

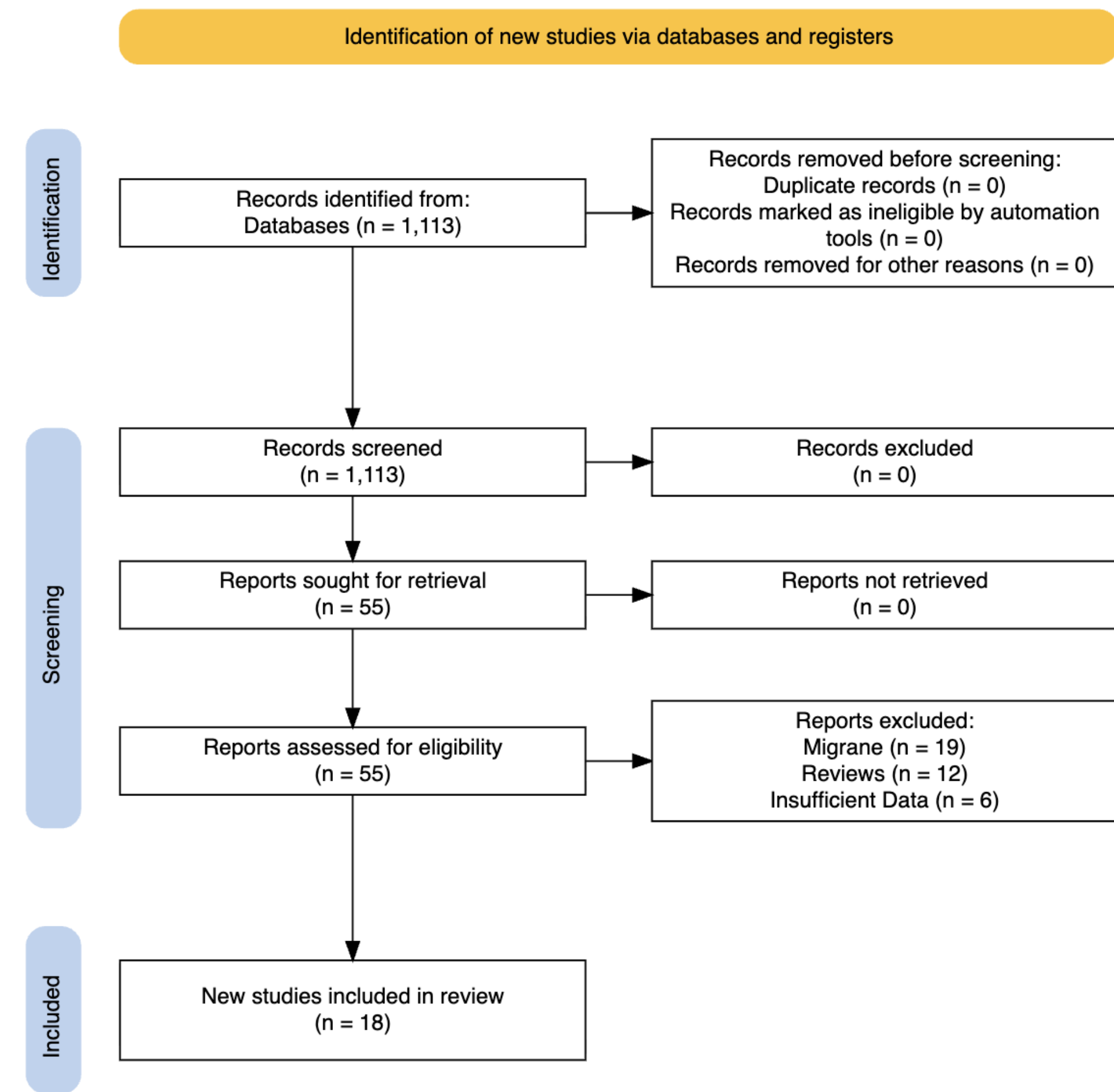


Figure 1. PRISMA-ScR Flow Diagram summarizing the literature search and selection process

Pain Type	CGRP Mechanism	Key Takeaway
Orofacial	Trigeminal neuro-glia signaling → cytokine release → sensitivity	Promotes facial pain and hypersensitivity
Postoperative	Linked to inflammatory, not incisional pain	Receptor blockade reduces inflammatory pain
Endometriosis	CGRP-positive nerve fibers activate macrophages and lesion growth	CGRP-RAMP1 blockade decreases pain and lesion size
Arthritis	CXCL5/CXCR2 → CGRP → TRPA1 → Inflammation	Blocking CGRP lowers swelling and pain
Neuropathic	Increasing spinal CGRP and astrocyte activation	Anti-CGRP antibodies decrease pain and inflammation

Figure 2. Summary of CGRP-related mechanisms and therapeutic targets across pain conditions

References

Scan for full
reference list and
included studies.

