PERIPHERAL HYPERSENSITIVITY TO SUBTHRESHOLD STIMULI PERSISTS AFTER RESOLUTION OF ACUTE EXPERIMENTAL DISC-HERNIATION NEUROPATHY AND IS MEDIATED BY HEIGHTENED CATION CHANNEL EXPRESSION AND ACTIVITY

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INTRODUCTION / AIM

While acute disc-herniation induced radiculopathy most frequently resolves without clinical sequelae, a fraction of patients experience long-term sensory dysfunction. This study examined chronic sensitivity of the rodent hindpaw following resolution of acute inflammatory neuropathy.

METHODS

C57BL/6 mice underwent mid-thigh sciatic nerve dissection, with either exposure only (control) or placement of nucleus pulposus (NP). Animals were evaluated throughout one, three, and five weeks for mechanical allodynia, thermal hyperalgesia, cold allodynia, and gait stability. At each time point, animals received intraplantar injection of noxious agent or vehicle alone, thereafter the same behavioral testing. Immunohistochemistry was performed of sciatic nerve, dorsal root ganglion (DRG), and spinal cord for inflammatory activation as well as cation channel expression. Ex vivo DRG explants were assessed for by cobalt staining for cation influx upon channel ligand activation.

RESULTS

Upon resolution of acute inflammatory pain, mice at three and five weeks (but not one week) demonstrated profound mechanical allodynia to subthreshold capsaicin compared with sham-operated controls or NP-stimulation animals delivered vehicle only. Conversely, perineural lymphocyte and intraneural macrophage infiltration was only observed at one week. Heightened spinal cord dorsal horn and DRG cation channel expression was seen, and DRG explants derived from NP-treated animals exhibited greater cobalt staining upon ligand-based channel activation compared with controls.

DISCUSSION / CONCLUSIONS

Non-compressive disc herniation sensitizes the sciatic nerve distribution in this animal model, despite resolution of acute intraneural macrophage migration. The demonstrated role of heightened cation channel expression at the DRG may implicated peripherally encoded changes responsible for this neuropathic pain.

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