The Impact of the Local Neuroma Environment on the Development of Pain

AE Halevi, MD, I Wood, BS, J Wang, BS, L Schellhardt, BS, MD Wood, PhD,
SE Mackinnon, MD, AM Moore, MD

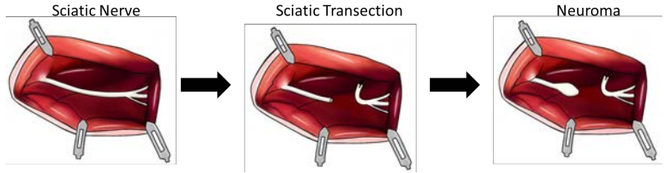
Washington University School of Medicine, Division of Plastic and Reconstructive Surgery

INTRODUCTION

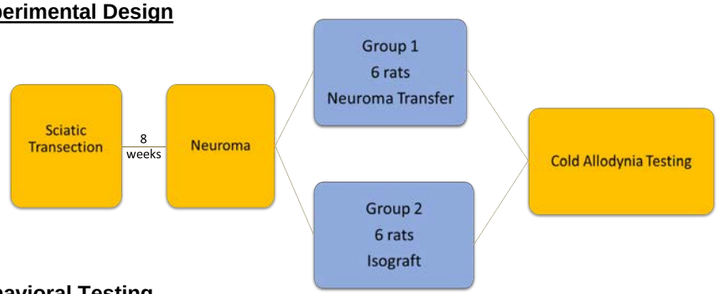
Neuropathic pain and the development of painful neuromas following peripheral nerve injury are poorly understood and unpredictable. Painful neuromas can have a significant effect on quality of life. Current surgical treatments focus on resection of the painful neuroma followed by other surgical modalities, such as transposition, and have variable success. There is currently no clear consensus regarding the optimal approach to treatment, and we have yet to understand the mechanisms that drive the development of pain in patients with painful neuromas. Our study evaluated the effect of the local, both physical and chemical, environment of the neuroma on the intensity and onset of pain in rats using a sciatic nerve transection neuroma model.

METHODS

Injury Model



Experimental Design

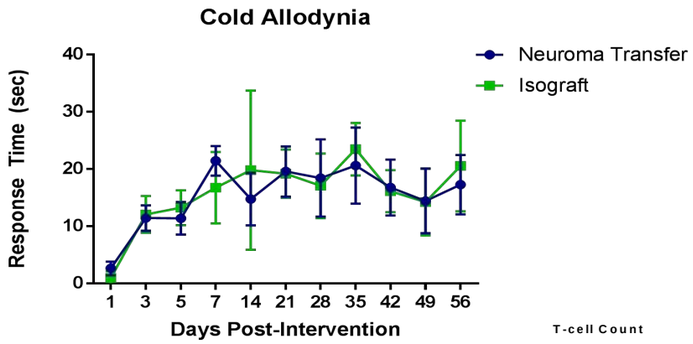


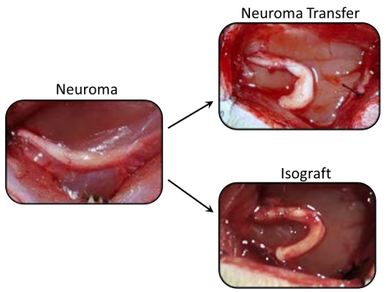
Behavioral Testing

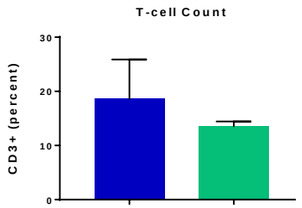
Cold allodynia with acetone application to the affected hind-limb was used for pain-related behavior testing. Licking or non-weight bearing of the limb was consider a positive response, and total response time was measured over 1 minute and average over 5 trials weekly for the duration of the experiment.

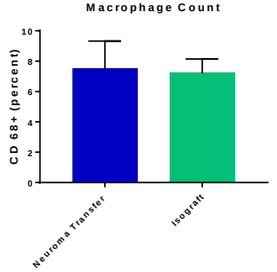
Research Question:
What is the effect of the local environment of a painful neuroma on the intensity and onset of pain?

RESULTS









There was no difference in either the time to onset of pain or the intensity of pain as measured by cold allodynia in the 2 groups. There is histological confirmation that there was axonal ingrowth into the coapted nerve in both groups. Additionally, there were no clear structural differences or variations in inflammatory cell infiltration at the final time point.

DISCUSSION

There were no differences in either onset or intensity of pain in the intervention compared to the control groups, nor any structural or inflammatory cell variations. These data suggest that neuroma pain in the rat model is likely mediated by central changes, either in the DRG or in the brain, and not in the local environment of the neuroma itself. These findings support the use of genetic and proteomic studies focused on the central response to nerve injury in order to identify potential mechanisms for modulating neuropathic pain.

FUTURE WORK

We have shown that there was no difference in the onset or intensity of pain in the neuroma transfer group. This indicates that there is likely a significant effect of central and neuronal responses to injury. We do not have a mechanistic understanding of why this is occurring. Future work will focus on utilizing a similar model, and using qRT-PCR to evaluate differences in regeneration-associated gene expression in the various models to determine what the relationship is between gene expression, central changes, and pain development.

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