DELAYED ONSET OF NEUROPATHIC PAIN IN THE AGED AFTER PERIPHERAL NERVE INJURY

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Abstract

Background and aims

The incidence of neuropathic pain in the elderly is significantly higher than in younger adults and adversely impacts quality of life. Previous studies report exaggerated inflammatory and behavioral responses, as well as differential nociceptor activity after insult in aged animals. Overall, very little is known about how aging alters the onset and development of neuropathic pain after surgery. Therefore we sought to determine the behavioral and inflammatory response following spared-nerve injury (SNI) in aged versus adult animals.

Methods

Young adult (3-6 month) and aged (24-26 month) male FBN rats underwent SNI and the development of neuropathic pain was assessed using mechanical and cold hypersensitivity measures. Behavioral data was collected 3, 5, 7, 10, 14, and every 7 days for 56 days post-surgery. Spinal cords and DRGs were collected either 5 days or 60 days post-surgery to assess gene expression via RT-PCR and immunohistochemistry (IHC) was performed.

Results

Surprisingly, aged animals took significantly longer to develop signs of neuropathic pain than young adult rats as measured by both mechanical hypersensitivity and cold allodynia (21 days aged vs. 5 days young). When we assessed DRG and spinal cord tissue ipsilateral to the injury for inflammatory and ER stress genes we observed an age-and surgery-related upregulation of ATF4, IL-6, and SK2 5-days post surgery. However, there was no difference in behavior or gene expression 60-days post surgery.

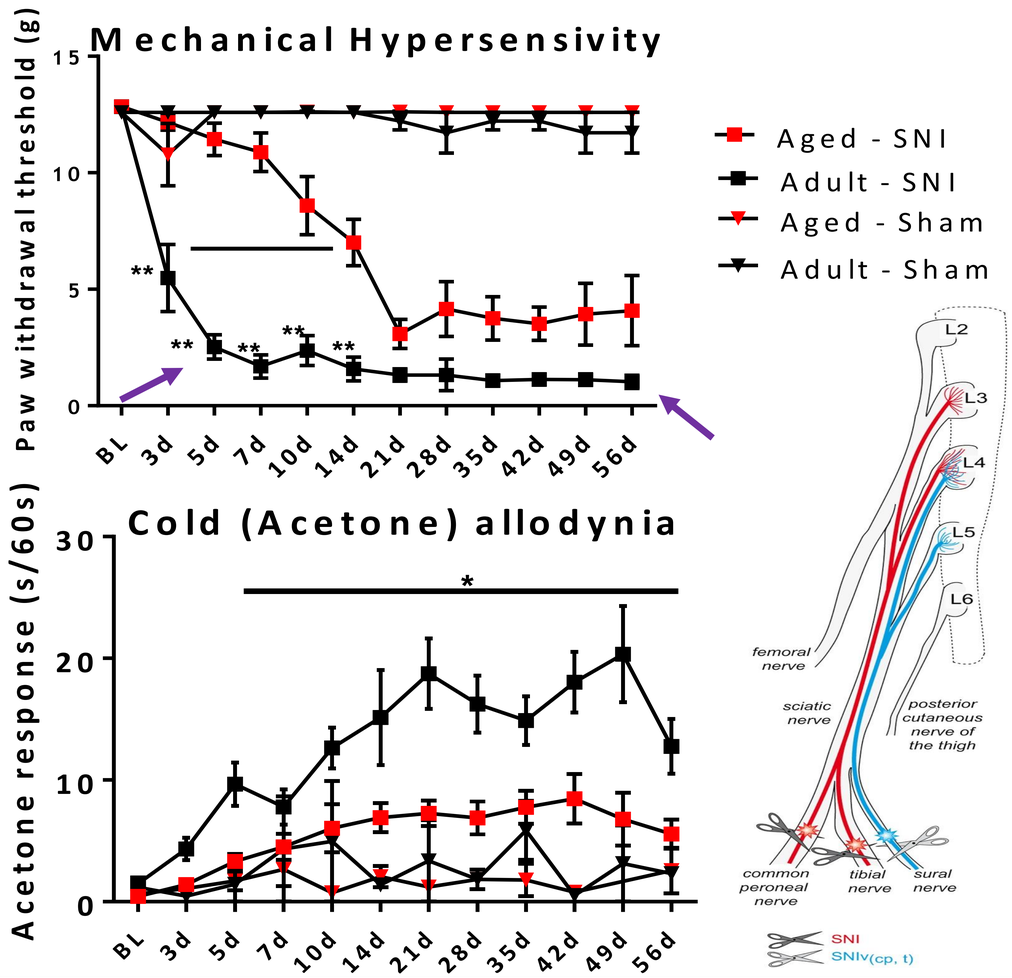
Conclusions

These experiments demonstrate a connection between age, inflammation, ER stress, and pain plasticity. The altered kinetics in the onset of neuropathic pain after injury in the aged hints at potential therapeutic targets in resolution pathways.

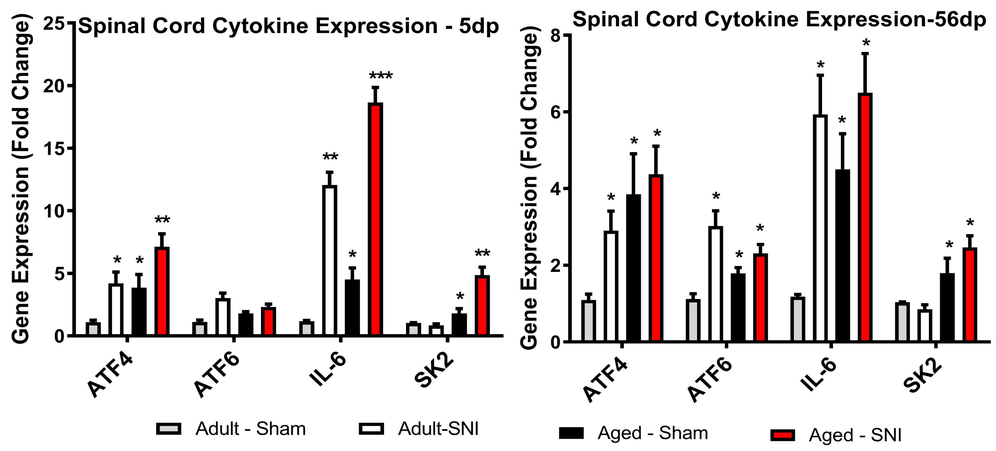
HYPOTHESIS

Aging sensitizes or primes animals to a subsequent stimulus. Neuroimmune interactions yield protracted and exaggerated pain states in an age-related fashion.

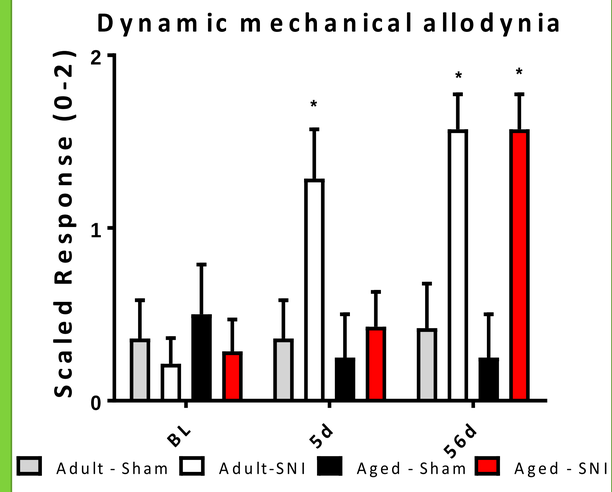
Aging and Nerve Injury – Neuropathic Pain – Evoked Behavior



Aging and Neuroinflammation – Gene Expression



Aging and Dynamic Allodynia



CONCLUSIONS & FUTURE

- Surprisingly, aged animals take longer to develop neuropathic pain post nerve injury.
- This delay could be related to the upregulation of SK2 channel expression.
- Collectively our work demonstrates an age-related mechanism to the development of a chronic pain state.

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