Psychosocial Influences on Pain and Depression

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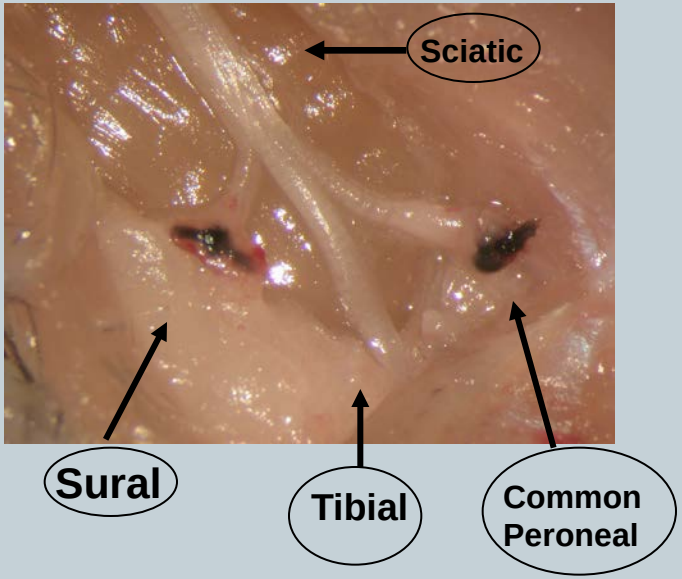
Research Goal

To determine the physiological mechanisms through which psychosocial factors alter the risk of pain and affective disorders after nerve injury.

General Methods

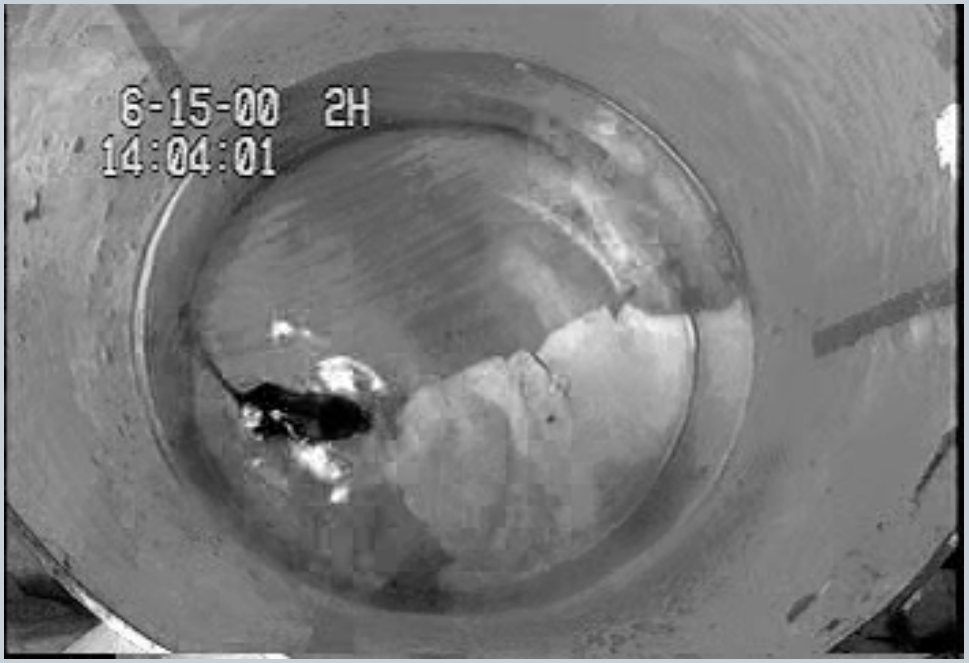
Adult male mice

Spared nerve injury



Ligation, followed by transection and resection, of right sural and common peroneal nerves

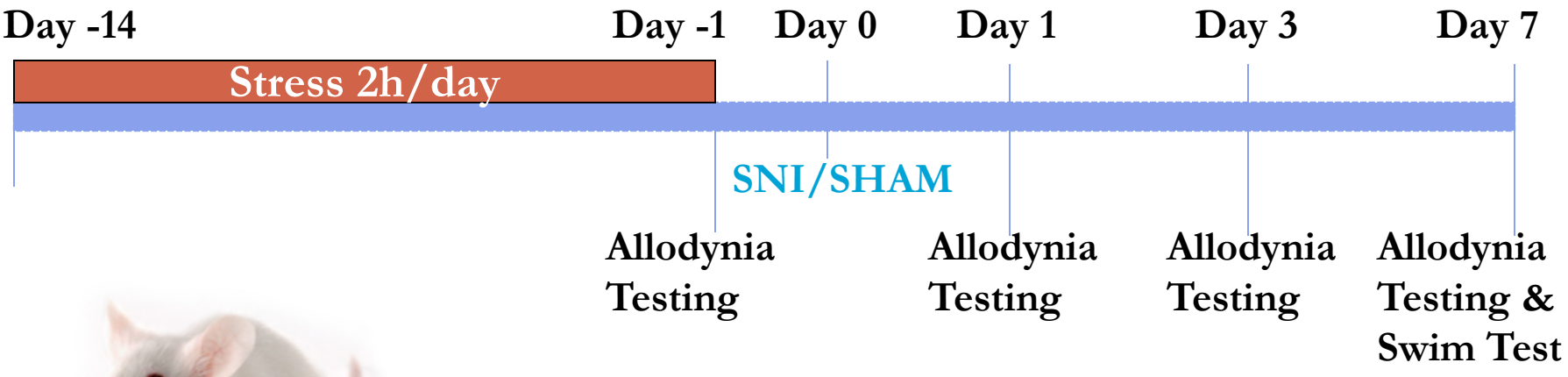
General Methods



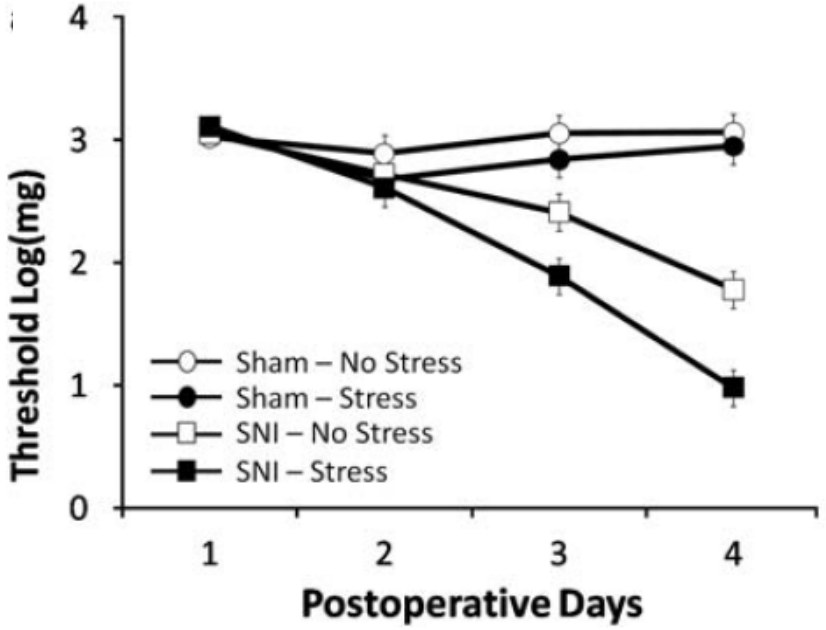
Mechanical allodynia: von Frey monofilaments
Depressive-like behavior: Forced swim test

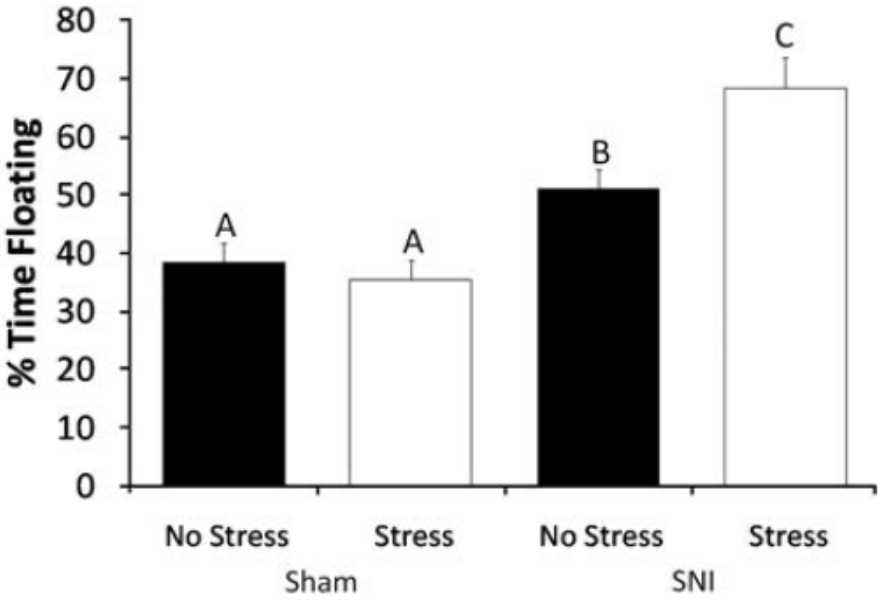
Hypothesis: Stress Exacerbates Allodynia and Causes Depressive-like Behavior After SNI

Experimental Design:



Stress Exacerbates Allodynia and Depressive-like Behavior After SNI

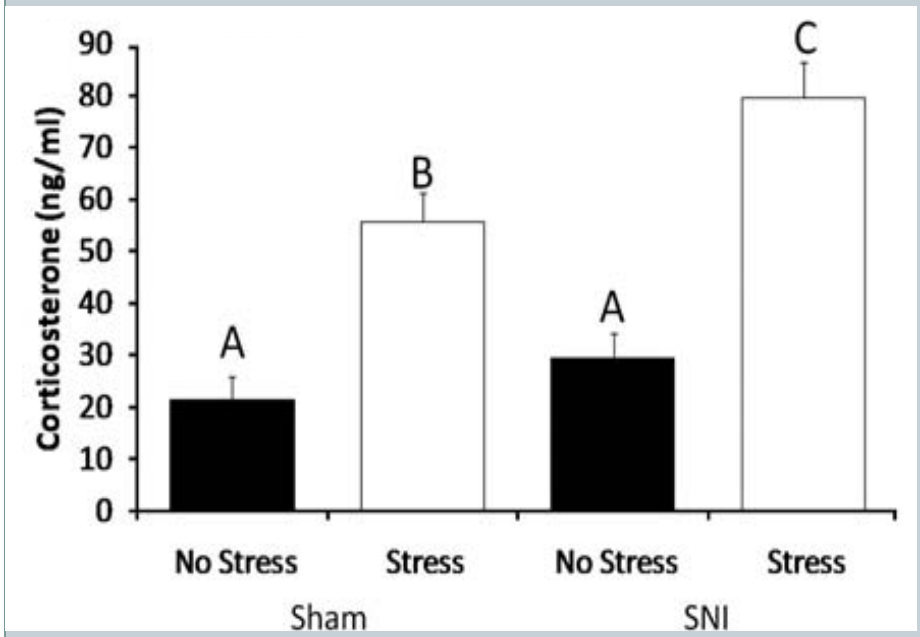




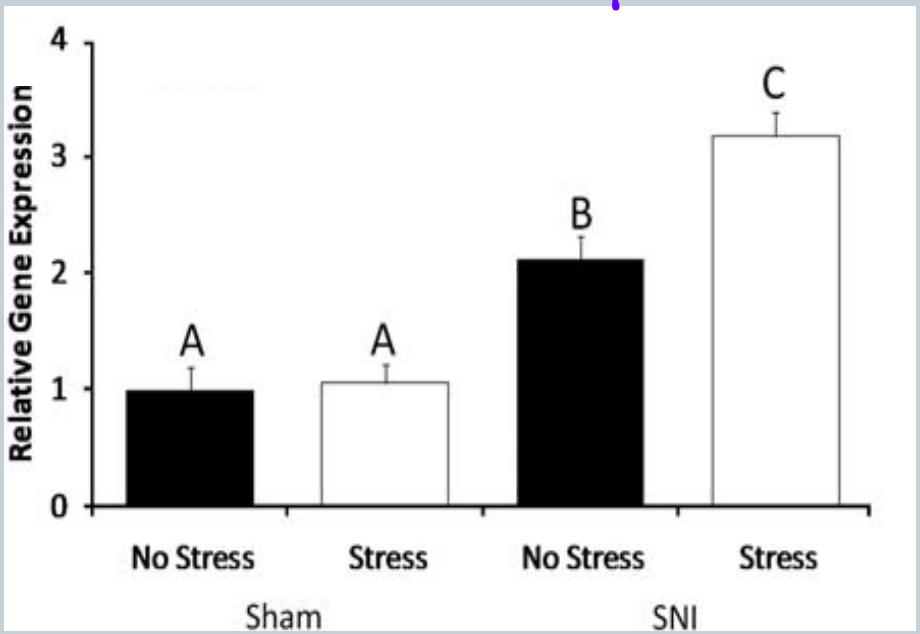
Norman et al., *Molecular Psychiatry*

Possible Physiological Mechanisms

Serum Corticosterone

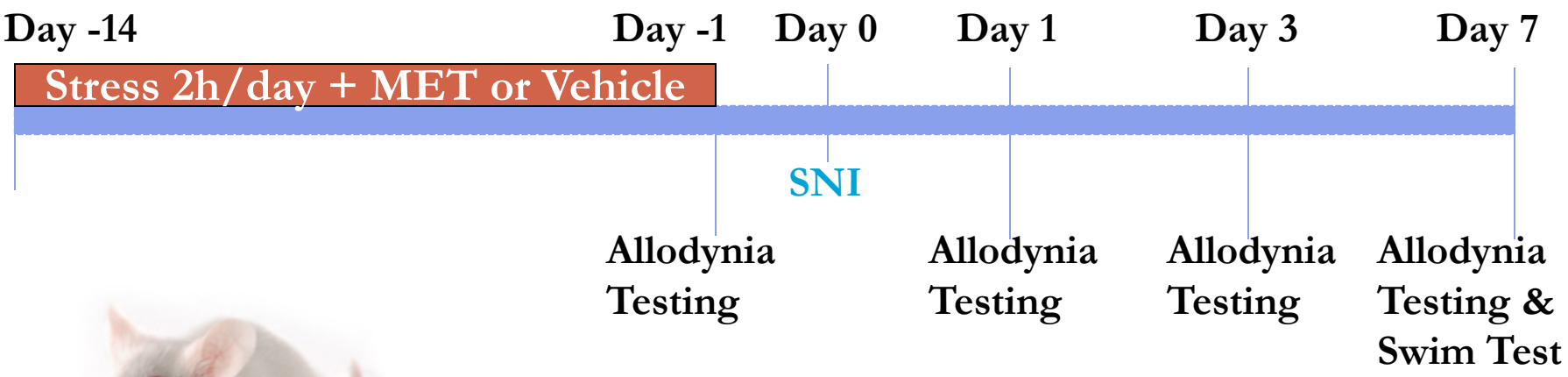


Cortical IL-1β



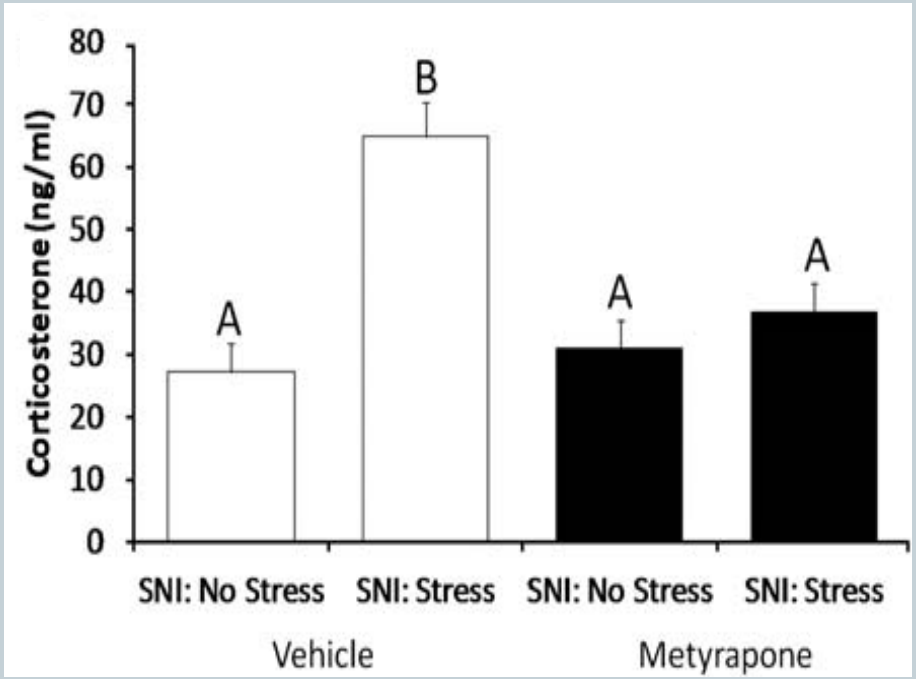
Hypothesis: Corticosterone Mediates the Effects of Stress on SNI-Induced Neuroinflammation and Behavior

Experimental Design:

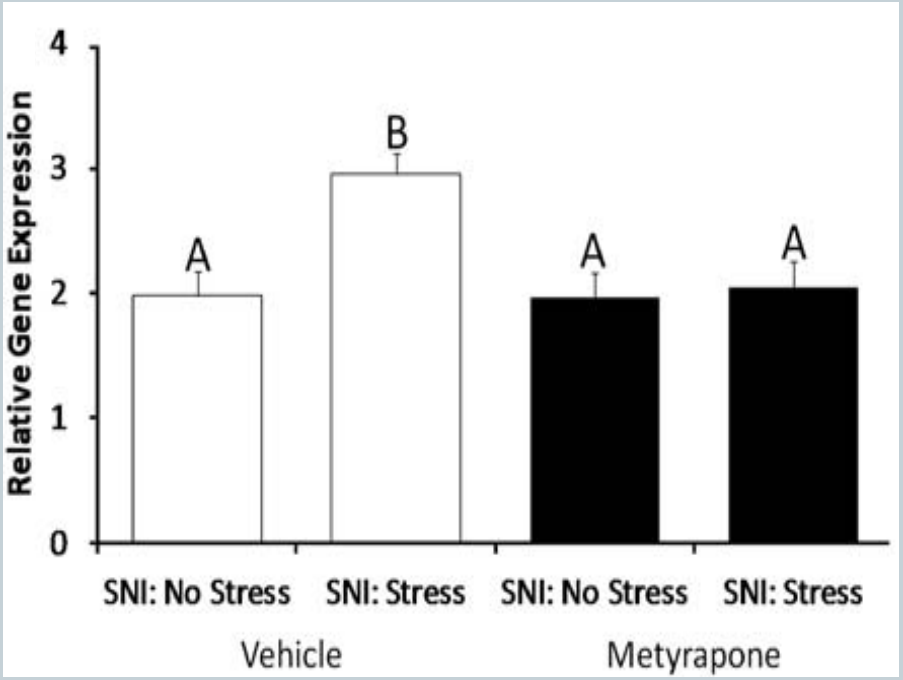


Role for Stress-Induced Corticosteroids

Serum Corticosterone

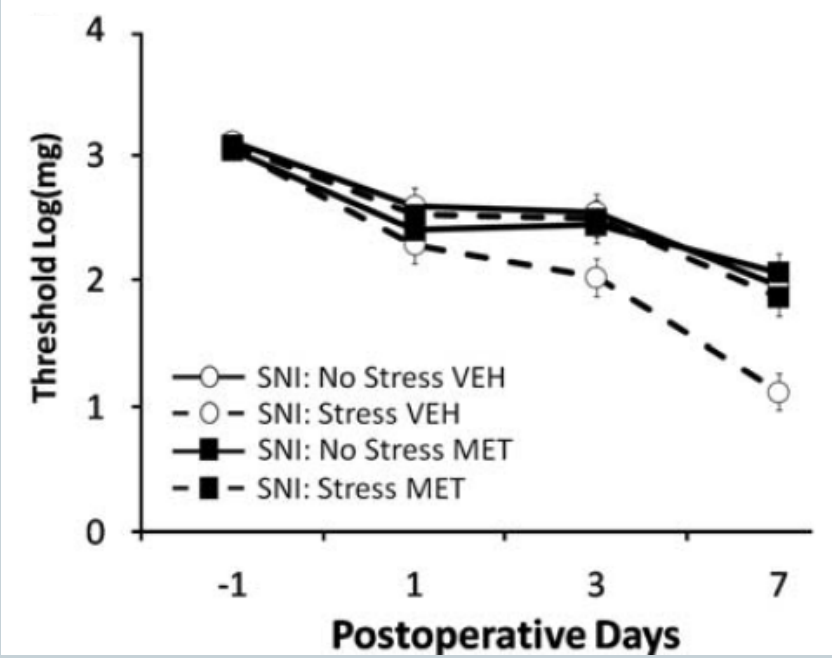


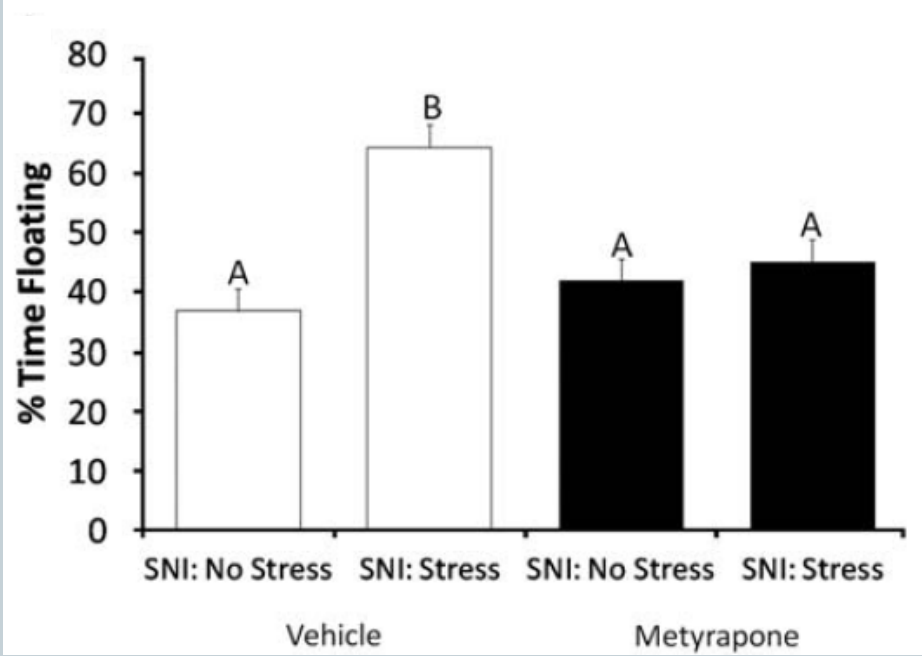
Cortical IL-1β



Metyrapone is a corticosteroid synthesis inhibitor that maintains basal corticosteroid concentrations during stress

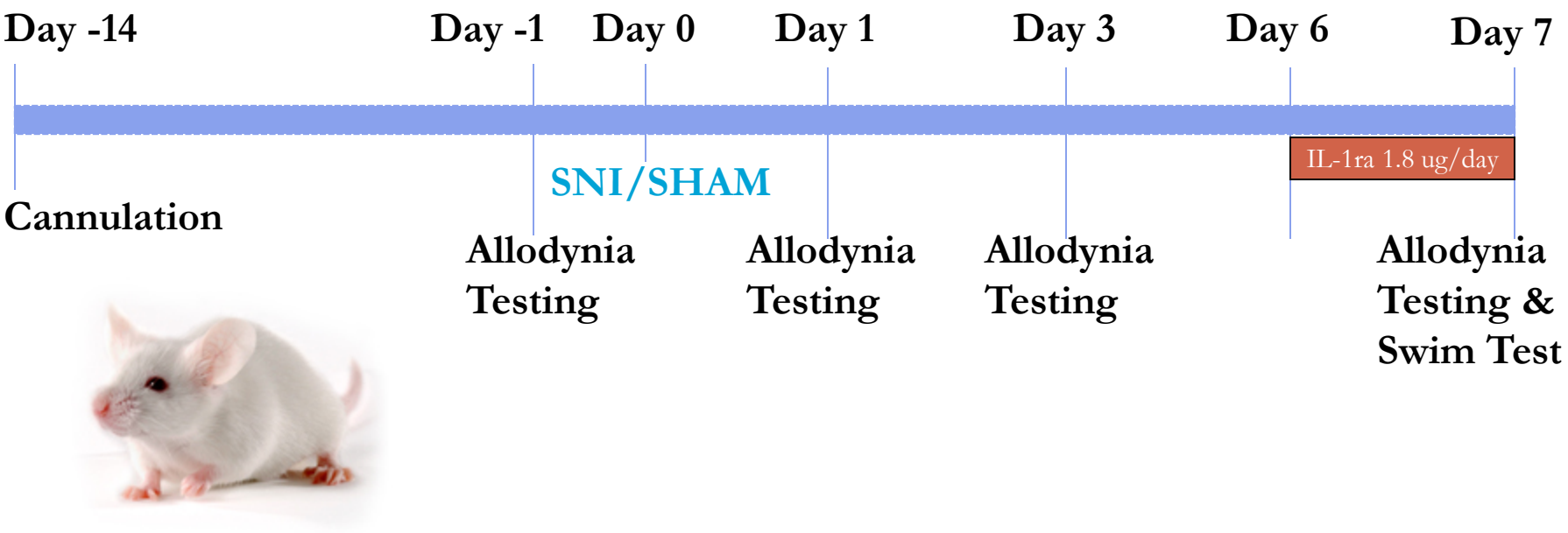
Metyrapone Ameliorates the Effects of Stress on Allodynia & Depressive-like Behavior After SNI



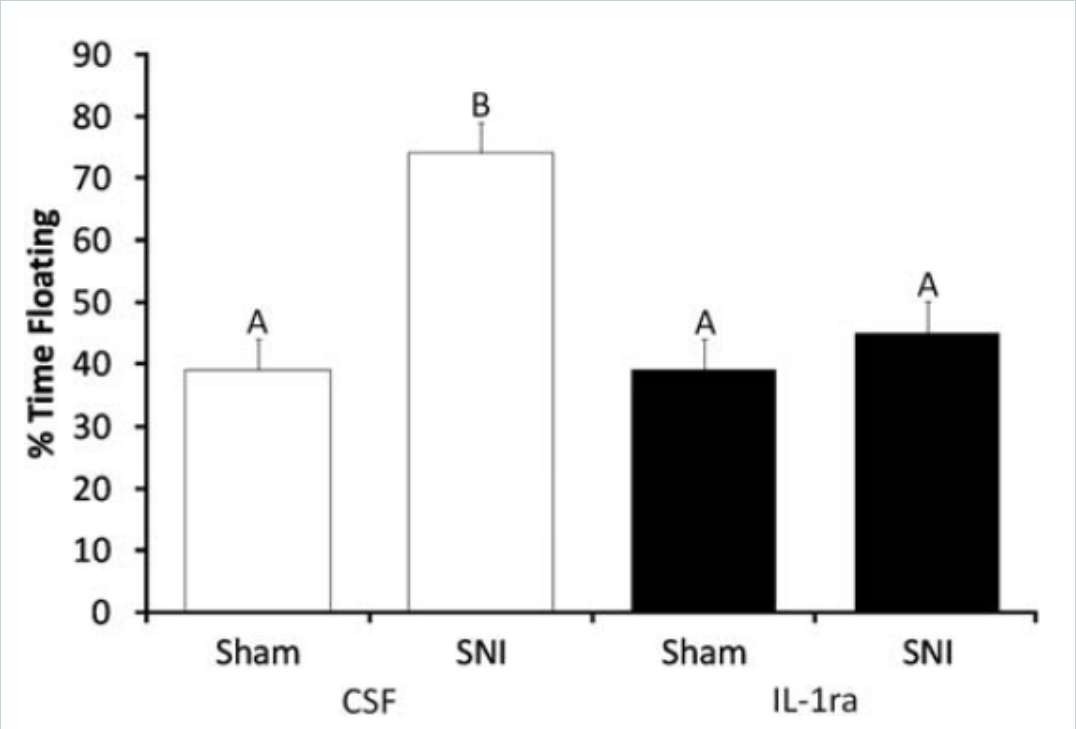


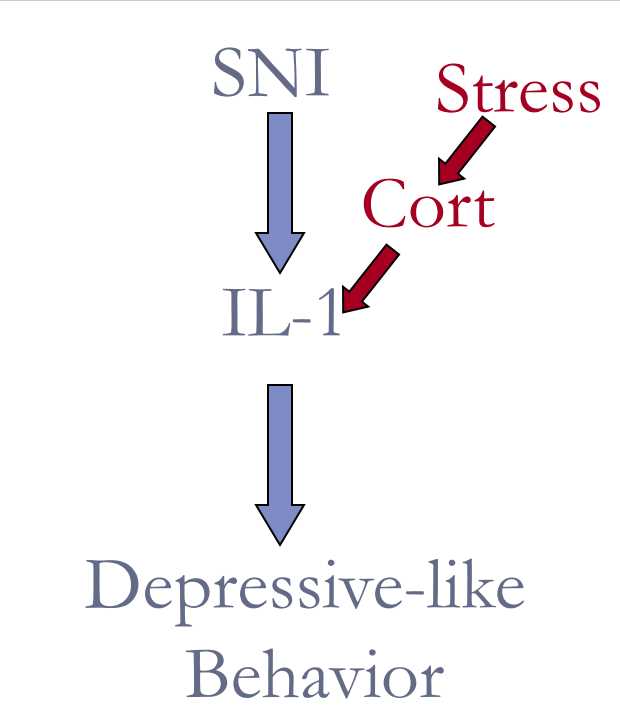
Hypothesis: IL-1ra Will Prevent SNI-Induced Depressive-like Behavior

Experimental Design:



IL-1ra Prevents the Expression of Depressive-like Behavior After SNI





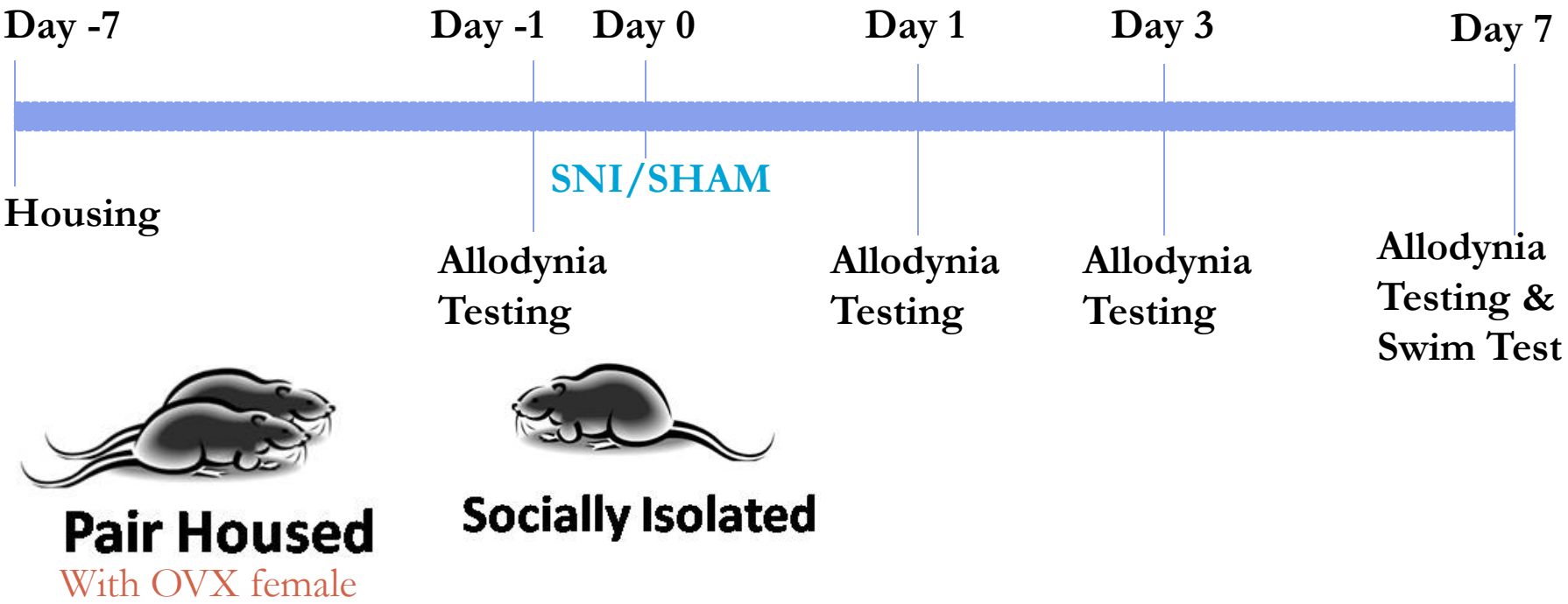
IL-1ra: IL-1 receptor antagonist

Interim Conclusion

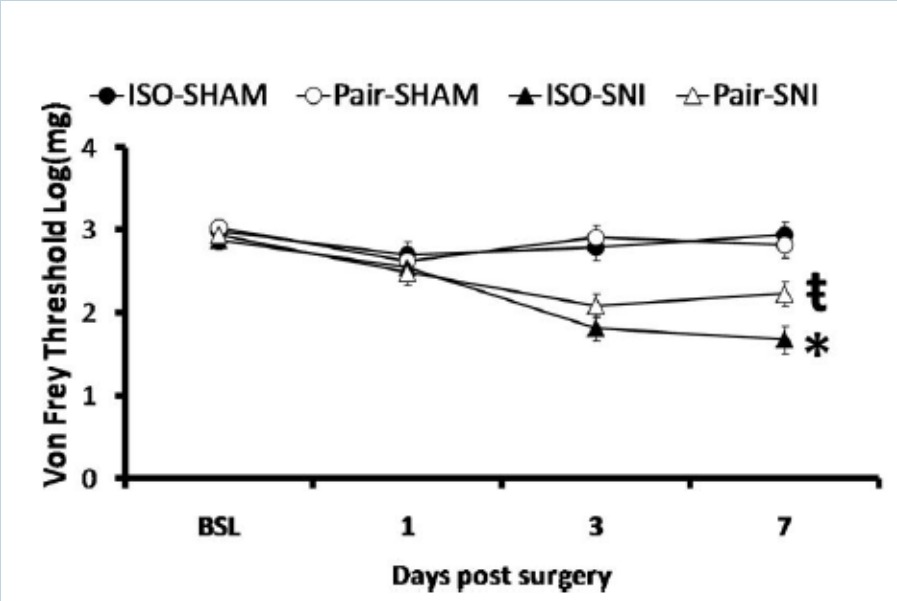
Nerve injury causes neuroinflammation which in turn contributes to the development of depressive-like behavior. Both allodynia and depressive-like behavior are exacerbated by prior exposure to stress.

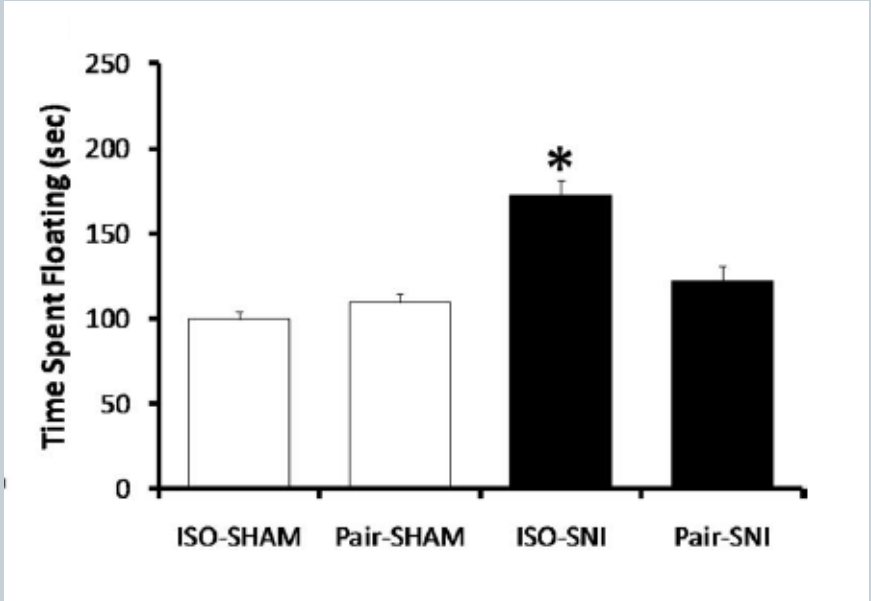
Hypothesis: Affiliative Social Behavior Will Reduce SNI-Induced Depressive-like Behavior

Experimental Design:

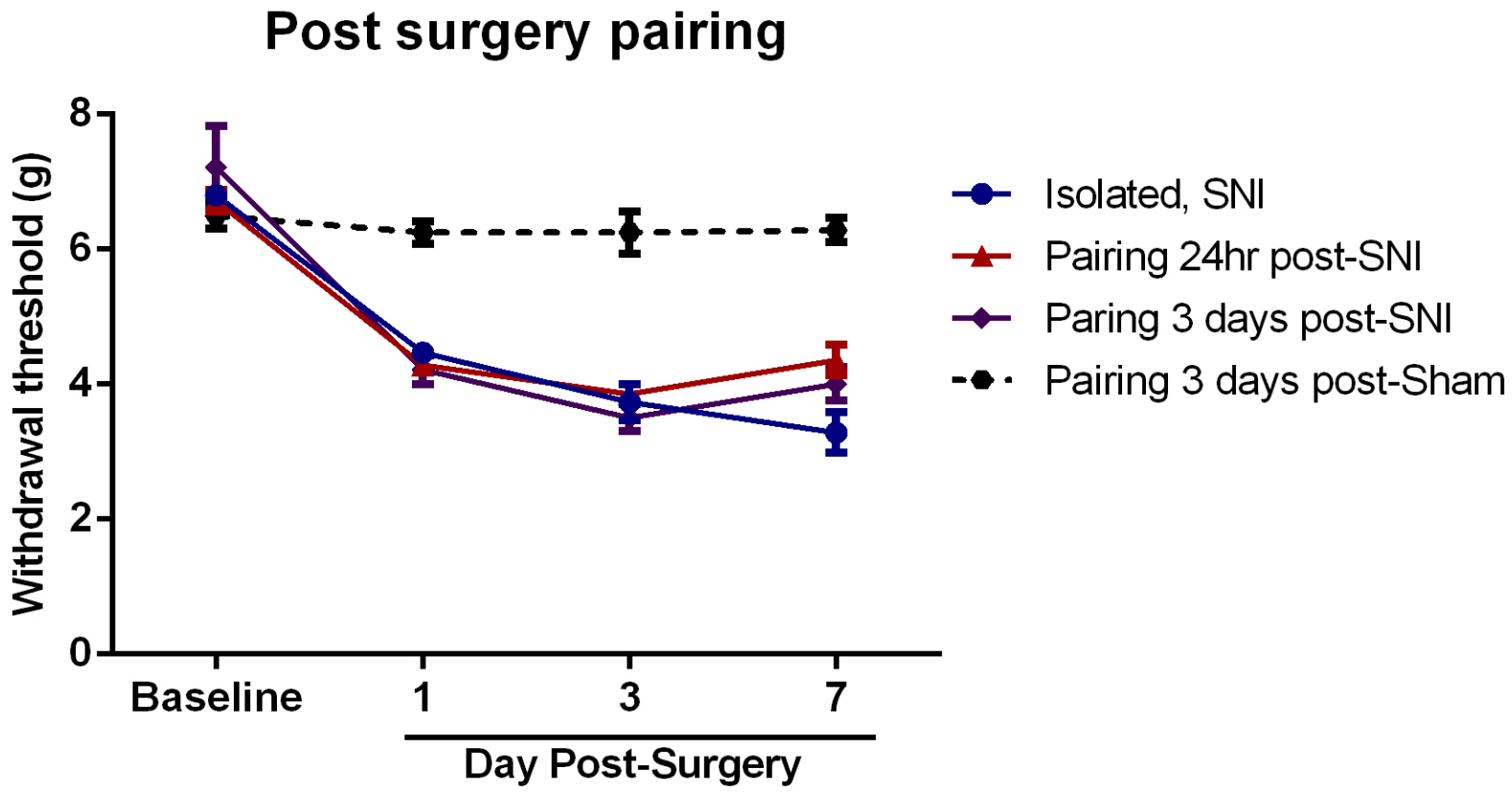


Social Interaction Reduces Allodynia and Eliminates Depressive-like Behavior After SNI



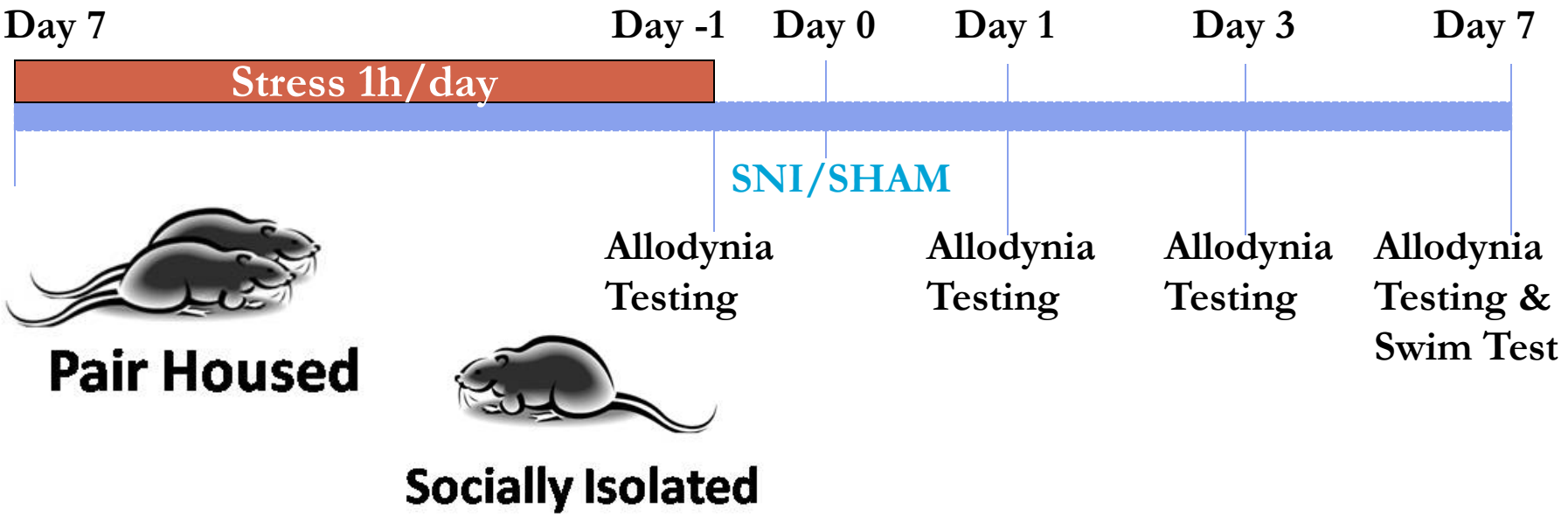


Social Pairing After Nerve Injury Also Is Effective at Reducing SNI-Associated Allodynia

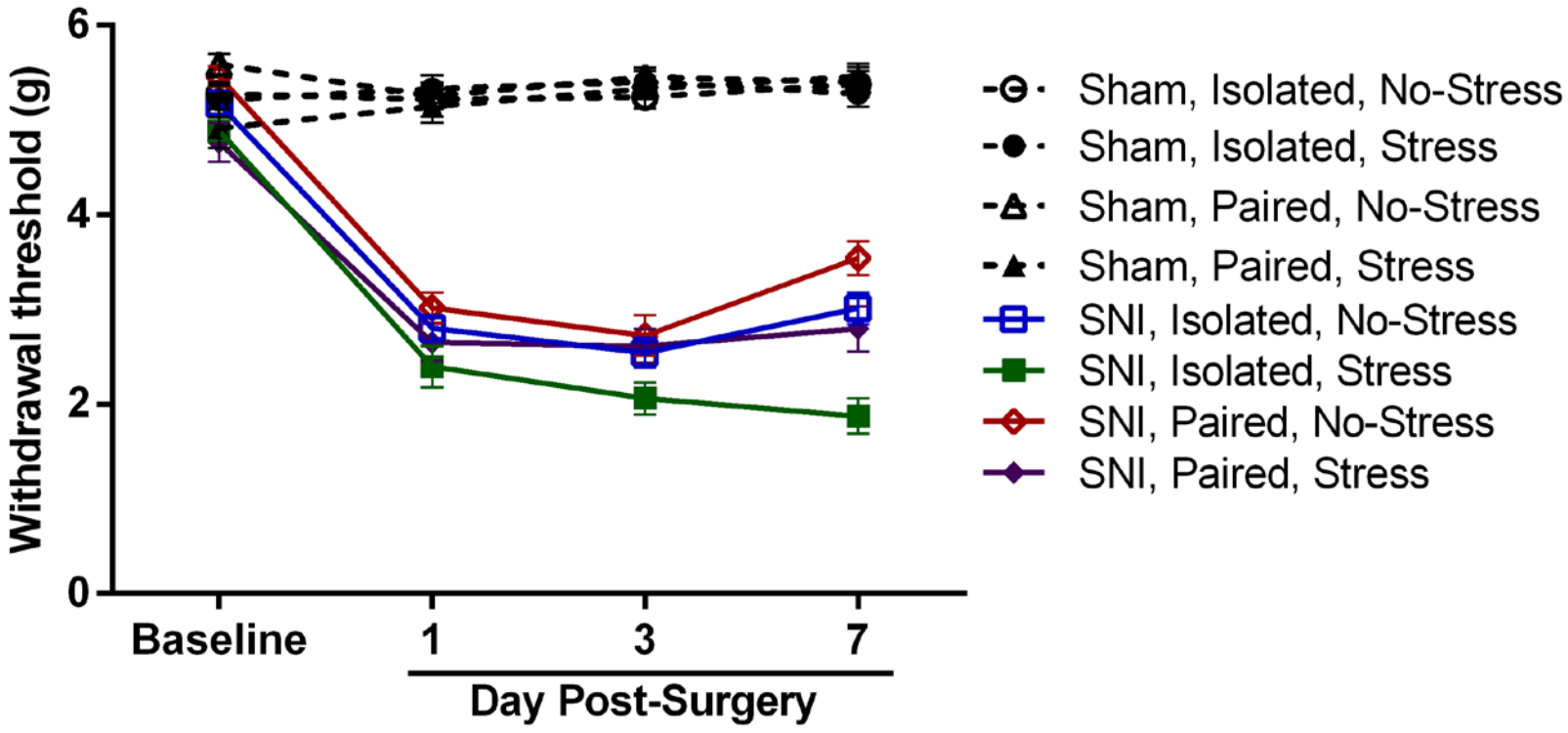


Hypothesis: Social Interaction Reduces the Effect of Stress on Allodynia After SNI

Experimental Design:

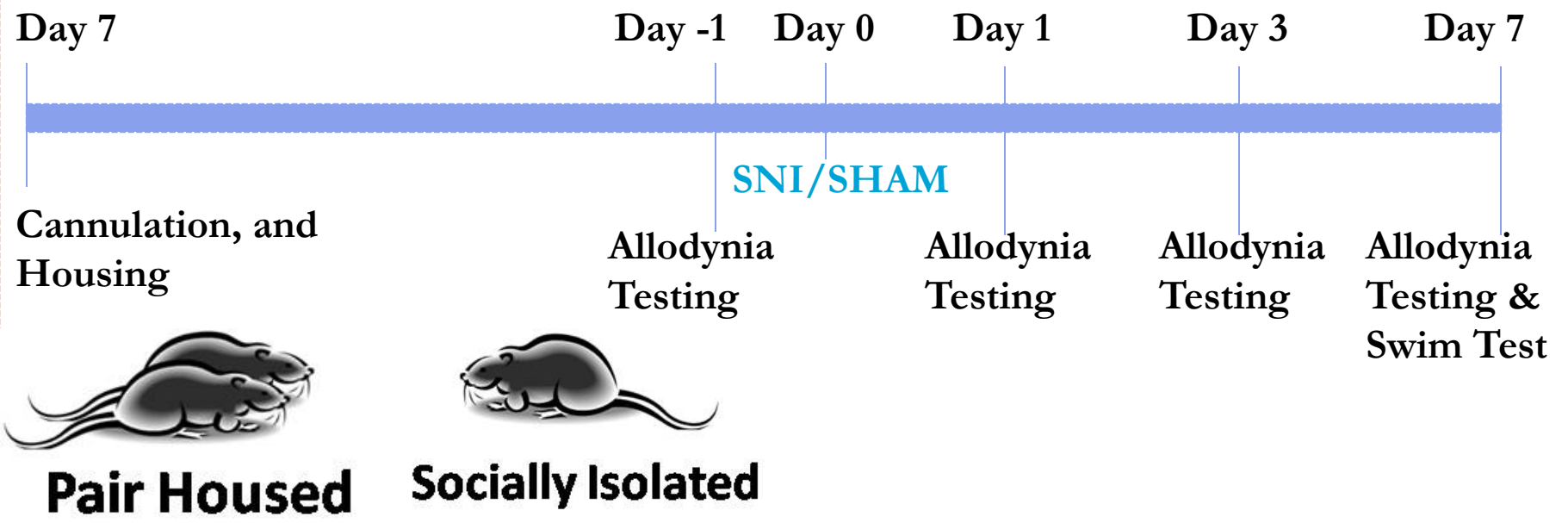


Social Interaction Improves SNI-Related Allodynia But Does Not Eliminate The Effects of Stress

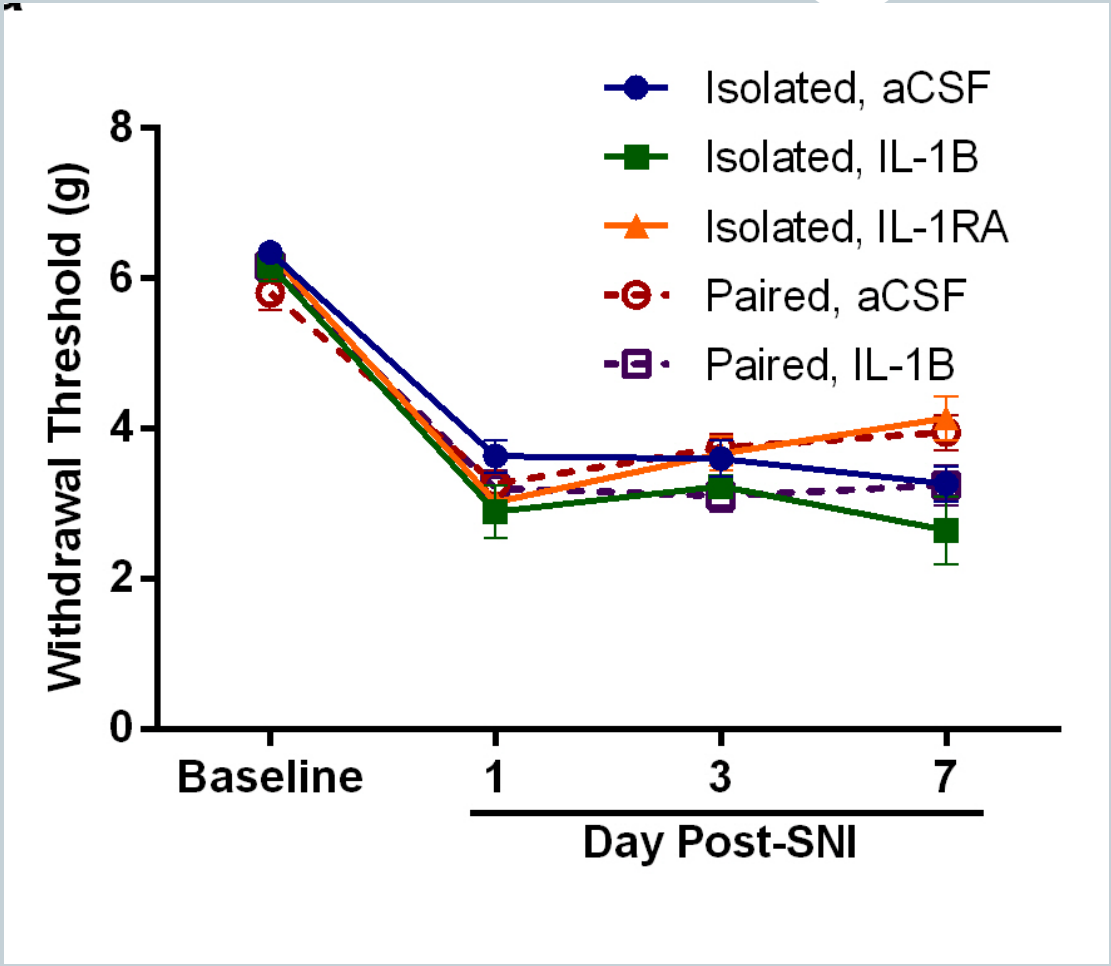


Hypothesis: The Protective Effects of Social Interactions on SNI Are Due to the Suppression of IL-1

Experimental Design:



IL-1 Mediates the Effects of Social Interaction on Allodynia



- Giving IL-1 to paired mice increases allodynia
- Giving IL-1ra to socially isolated mice reduces allodynia

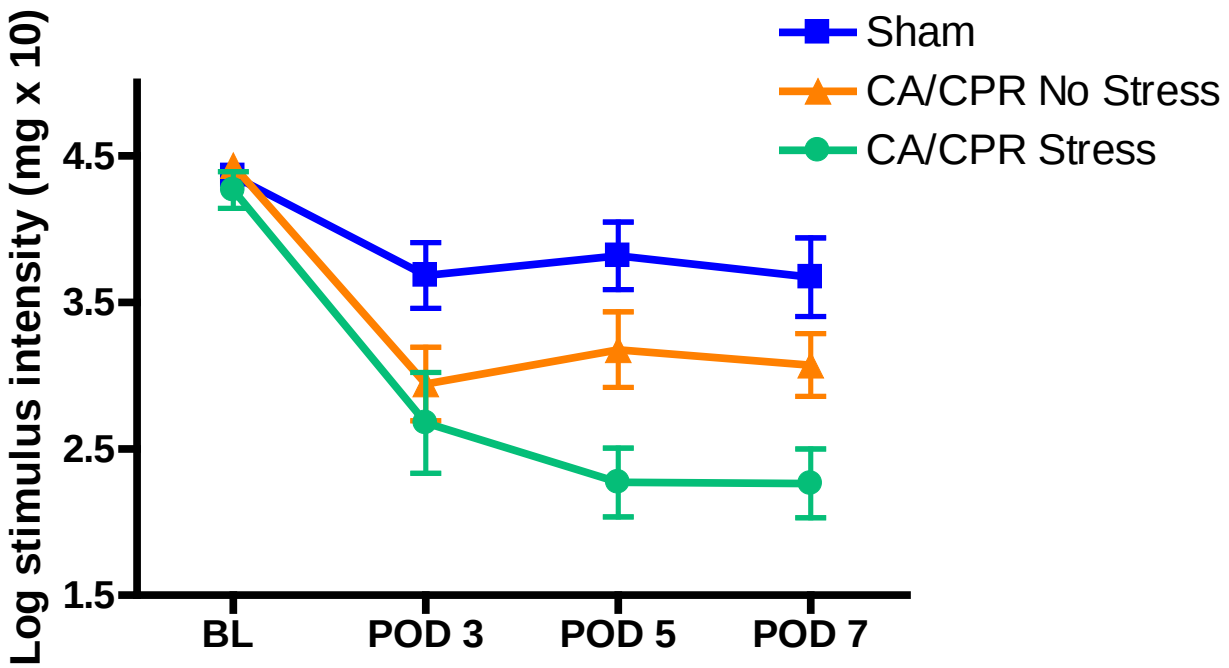
Summary

- SNI causes neuroinflammation which in turn promotes the development of depressive-like behavior
- Stress exacerbates neuroinflammation, allodynia and depressive-like behavior through a corticosteroid mediated pathway
- Social interaction reduces SNI-associated neuroinflammation, allodynia and depressive-like behavior.

Take Home Message

Environmental factors that increase neuroinflammation after nerve injury exacerbate allodynia and depressive-like behavior, while environmental factors that decrease neuroinflammation after nerve injury reduce allodynia and depressive-like behavior.

Last Thought: The Same Relationships Among Neuroinflammation, Stress, Depression, and Allodynia May Exist For Other Forms of Neuropathic Pain



CA/CPR: Cardiac Arrest/CPR

Thanks

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