Acute social defeat stress induces microglial activation in key limbic regions

Thomas Clarity, J. Alex Grizzell, Matthew A. Cooper
Department of Psychology and NeuroNET Research Center at The University of Tennessee

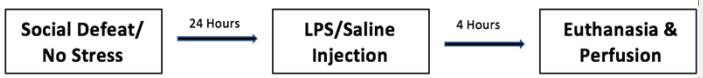
Introduction

- Research suggests a causal relationship between neuroinflammation and stress-related psychopathologies
- Exposure to moderate stress in rodents leads to elevated markers of immune activity, such as microglia
- There has been little research investigating the effects of acute social defeat stress on central immune hyperactivity
- Stress can prime microglia to exhibit a degradative proinflammatory response to a subsequent immune challenge[1]

Methods

Animals: Adult Male Syrian hamsters (*Mesocricetus auratus*)

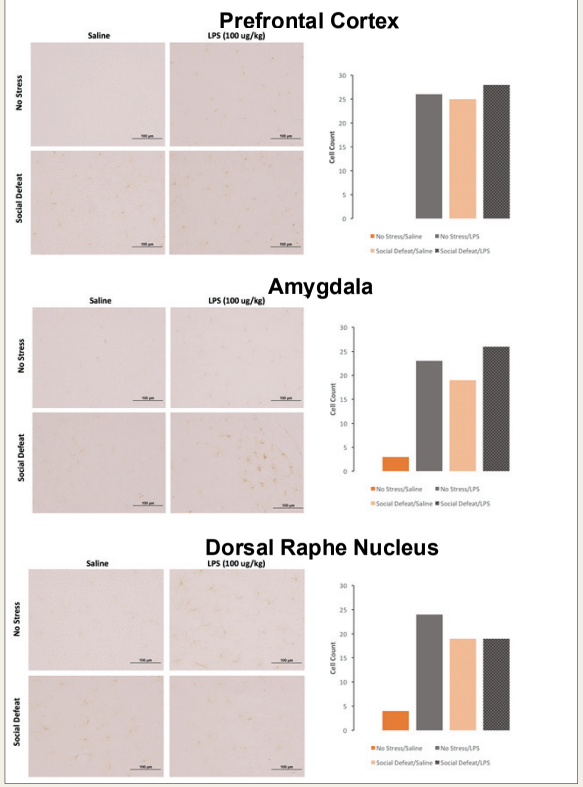
Pilot Study #1:



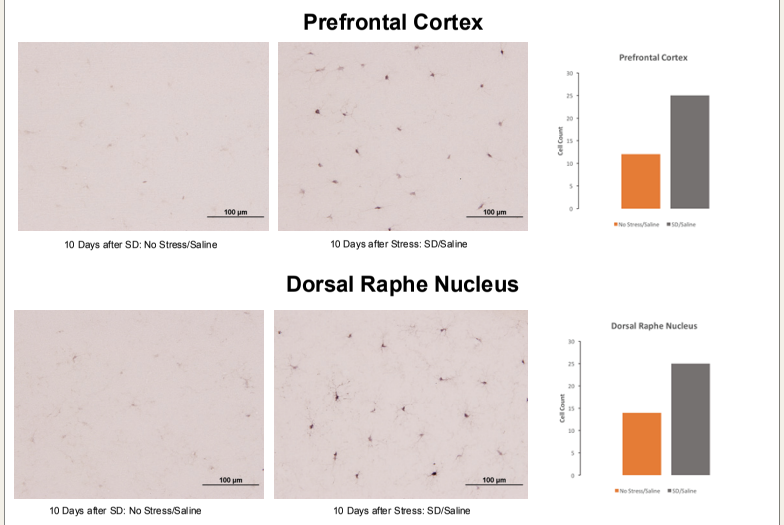
Pilot Study #2:

1. **Acute Social Defeat:** Subjects were exposed to three, 5-minute aggressive encounters in the home cage of three, different, larger, aggressive hamsters with 5-minute between-defeat rest periods. Control animals were exposed to an empty aggressor's cage.
2. **LPS Injection:** 24-hours following social defeat, the effects of stress-induced priming of microglial activation was assessed by exposure to an endotoxin immune challenge via intraperitoneal injection of 100 µg/kg lipopolysaccharide (LPS).
3. **Euthanasia:** 4-hours following LPS injection (Pilot #1) or 10 days following defeat (Pilot #2), hamsters were euthanized and transcardially perfused and brains extracted.
4. **Immunolabeling:** Microglial activation was measured by immunolabeling of *ionized calcium binding adaptor protein-1* (Iba-1) through immunohistochemistry in areas critical for stress processing (i.e. DRN, Amygdala, PFC).

Pilot #1



Pilot #2



Future Directions

- Prolonged activation – How does social defeat activate microglia over time?
- LPS dose response curve – Effects of LPS dosage on microglia activation
- Minocycline – Effects of an antibiotic that selectively inactivates microglia
- Social status model – What is the effect of dominant and subordinate status on microglia?

Conclusions

- LPS injection leads to increased Iba-1 immunoreactivity both in the presence and absence of social defeat stress in the PFC & DRN
- Interestingly, acute social defeat also led to the activation of microglia in these regions in the absence of an LPS injection.
- It appears that all defeated animals, regardless of LPS treatment, maintain microglia activation as much as 10 days following defeat.
- These results demonstrate that acute stress can activate innate immune mechanisms in key brain areas for stress processing, which extends our understanding of cellular mechanisms controlling responses to trauma.

Acknowledgements and References

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