**Acute social defeat-induced neuroinflammation in the vmPFC of Syrian hamsters via microglial activation**

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**Introduction**

- Psychological stress is known to increase neuroinflammation.
- Neuroinflammatory pathways are contributing factors to various stress-related psychopathologies.
- Exposure to chronic stress in rodents results in elevated markers of immune activity, such as activation of microglia, as measured by ionized calcium binding adaptor protein-1 (Iba-1) expression.
- There has been little research investigating the effects of acute social defeat stress on central immune activity.
- Acute stress can prime microglia to exhibit an enhanced proinflammatory response to a subsequent immune challenge (i.e. Lipopolysaccharide).
- The prefrontal cortex (PFC) is a critical brain region for coping with stress-related psychopathologies.
- Neuroinflammatory pathways are contributing factors to various stress-related psychopathologies.

**Methods**

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

**Experiment 1:**
- Social Defeat/No Stress
- LPS/Saline Injection
- Social Defeat
- Euthanasia & Perfusion

1. **Acute Social Defeat:** Subjects were exposed to three, 5-minute aggressive encounters in the home cage of three, separate, larger, aggressive hamsters. Encounters occurred at 5-minute intervals. 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 microglia was assessed by exposure to an endotoxin immune challenge via intraperitoneal (i.p.) injection of 0, 20, 100, and 500 µg/kg lipopolysaccharide (LPS).
3. **Euthanasia:** 4-hours following LPS injection (Exp. 1) or 7 days following defeat (Exp. 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 the prefrontal cortex (PFC) using Rabbit monoclonal anti-Iba-1 antibody (1:10,000; ab178846).

**Figure 1**

- No defeat & Saline
- Defeat & Saline
- No defeat & 20 µg/kg
- Defeat & 20 µg/kg
- No defeat & 100 µg/kg
- Defeat & 100 µg/kg
- No defeat & 500 µg/kg
- Defeat & 500 µg/kg

**Experiment 2:**
- Social Defeat/No Stress
- Euthanasia & Perfusion

1. **Acute Social Defeat:**
   - Subjects were exposed to three, 5-minute aggressive encounters in the home cage of three, separate, larger, aggressive hamsters. Encounters occurred at 5-minute intervals. Control animals were exposed to an empty aggressor’s cage.
2. **Euthanasia:**
   - 7 days following defeat

**Figure 2**

The morphological transformation that occurs in progressive activation states of microglia (Figure adapted from Hinwood et al., 2012).

**Figure 3**

- Iba-1 Immunoreactivity in Infralimbic Cortex
- Iba-1 Immunoreactivity in Prelimbic Cortex

- Microglial Morphology

- 7 Days After Stress (no injection)

**Conclusions**

- These findings indicate that acute social defeat primes microglial activity in the vmPFC following subsequent LPS exposure.
- Acute social defeat appears to “activate” microglia in the vmPFC, as indicated by increased Iba-1 expression and acute changes in morphology.
- Acute social defeat does not appear to contribute to an arrested hyper-ramified state, as discussed in Hinwood et al., 2012.

**Discussion & Future Directions**

- The greatest differences were observed at 20µg/kg, which may indicate a point at which a greater percentage of cells display hyper-ramification.
- The disparity between OD and morphology data at 20µg/kg may be due to low sample size (n=4/group); current efforts are increasing the power of these samples.
- Future work will still for phagocytic microglial activation state marker, CD68.
- Determine the effects of an antibiotic, minocycline, that selectively inactivates microglia on defeat-induced changes in behavior.

**Acknowledgements and References**

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