Effects of social isolation on LPS-induced hippocampal amyloid-beta expression and cognitive dysfunction in C57BL6/J male and female mice

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Introduction

- Alzheimer’s disease (AD) is a neurodegenerative disorder that affects nearly 5.3 million Americans, and there is currently no cure (1).
- AD is characterized by amyloid-beta (Aβ) plaques in the brain (2).
- Neuro-inflammation is known to play a role in the pathogenesis of AD (3).
- Lipopolysaccharide (LPS) induces systemic inflammation and causes cognitive impairment by enhancing beta-amyloid generation (3).
- Systemic inflammatory responses may contribute to the outcome or progression of neurodegenerative disease (4).
- Research has shown that psychological stress is associated with the body losing its ability to regulate the inflammatory response which can promote the development and progression of disease (5).
- Our hypothesis is that isolated animals will demonstrate cognitive deficits in CFC as well as increased brain amyloid-beta following LPS injections.

Methods

- Mice were subjected to acute social isolation (6 days) or chronic isolation (28 days) or control group housing followed by LPS (250 μg/kg) or saline injections.
- A subset received one injection of LPS or saline and IL-1β.
- Brain tissues were extracted and Aβ levels were assessed.

Results

The Effect of 6 Days of Isolation and LPS on Hippocampal Aβ mRNA Expression in Males. Results from RT-PCR were normalized to β-actin prior to being normalized to our control group (Group Housed/Saline). Different letters (a, b, c) represent significant differences at p < .05. Bars represent mean ± SEM.

The Effect of 21 Days of Isolation on Cognition in Females following LPS administration. Results from CFC analysis demonstrate no significant differences between groups. Bars represent mean ± SEM.

Conclusion

- Male mice subjected to 6 or 21 days of isolation did not show differences in Aβ levels compared to group-housed mice. This suggests isolation stress did not affect Aβ production in males, despite previous research linking stress and Aβ accumulation (6).
- IL-1β levels were significantly elevated following isolation stress in male mice given LPS. This demonstrates that isolation stress does increase the inflammatory response in males.
- Female and male mice showed similar trends in IL-1β levels. However, the female isolated and group-housed mice did not show statistically significant differences. Further research is needed to determine if isolation has a greater impact on inflammation in males than females.
- Only 21 day isolation stress in males produced a significant deficit in cognition as assessed by CFC.
- Assessing the IL-1β levels in females will allow us to determine if there is a gender difference in Aβ production following isolation stress.

References


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