

Psychological stress afflicts a considerable portion of the world's population, and is linked, as both a risk factor and potential contributor, to dementia-related brain dysfunction in diseases such as Alzheimer's disease (AD). The brain dysfunction in AD is marked by an increase in amyloid-beta, a protein that accumulates into plaques in the brain, and increased inflammation. The present study aimed to explore how stress may alter inflammation and the production of amyloid-beta. Specifically, we were interested in social isolation as a stressor and its impacts on inflammation-induced amyloid-beta production as well as cognition, and how this may differ in male and female mice.

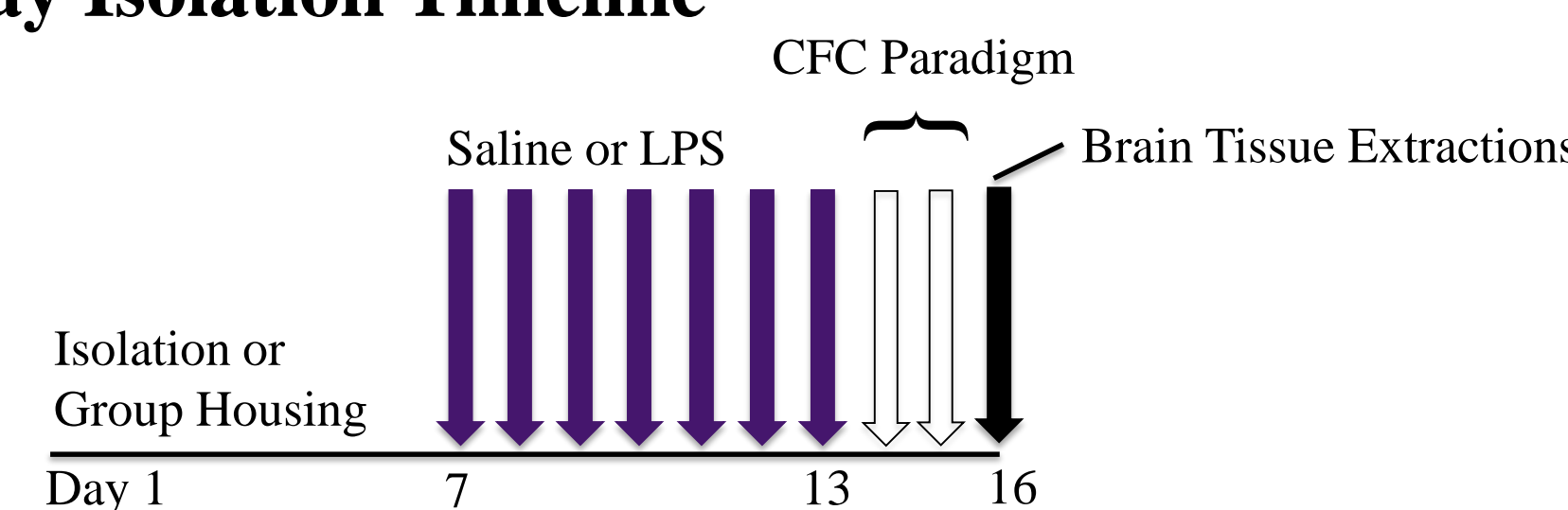
## Introduction

- 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 (A $\beta$ ) 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.

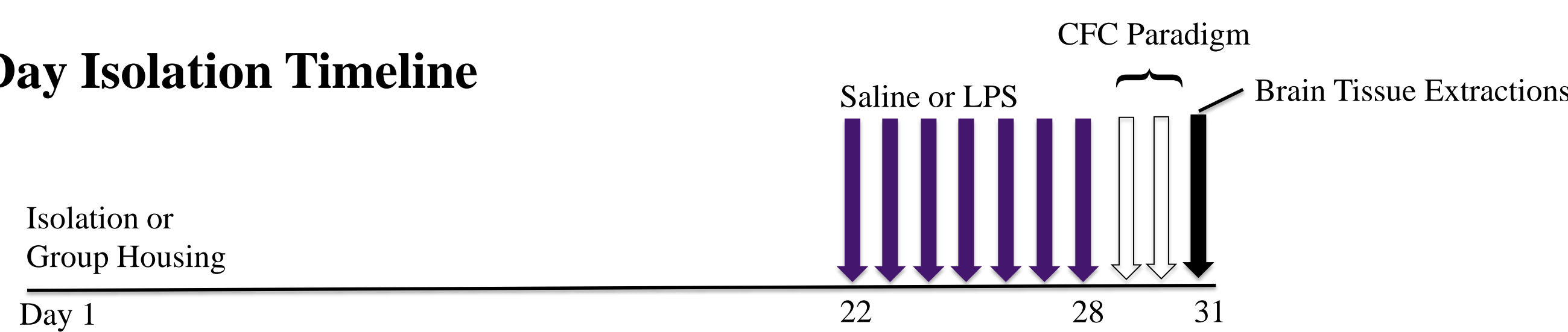
## Methods

- Mice were subjected to acute social isolation (6 days) or chronic isolation (28 days) or control group housing followed by LPS (250  $\mu$ g/kg) or saline injections
- A subset received one injection of LPS or saline and IL-1 $\beta$  levels were assessed
- The remaining mice received 7 total, once daily injections of LPS or saline and then tested for cognition using contextual fear conditioning (CFC).
- CFC measures the freezing response that takes place following pairing of a mild aversive stimulus with a novel context.
- Brain tissues were extracted and A $\beta$  protein levels were assessed.

### 6 Day Isolation Timeline



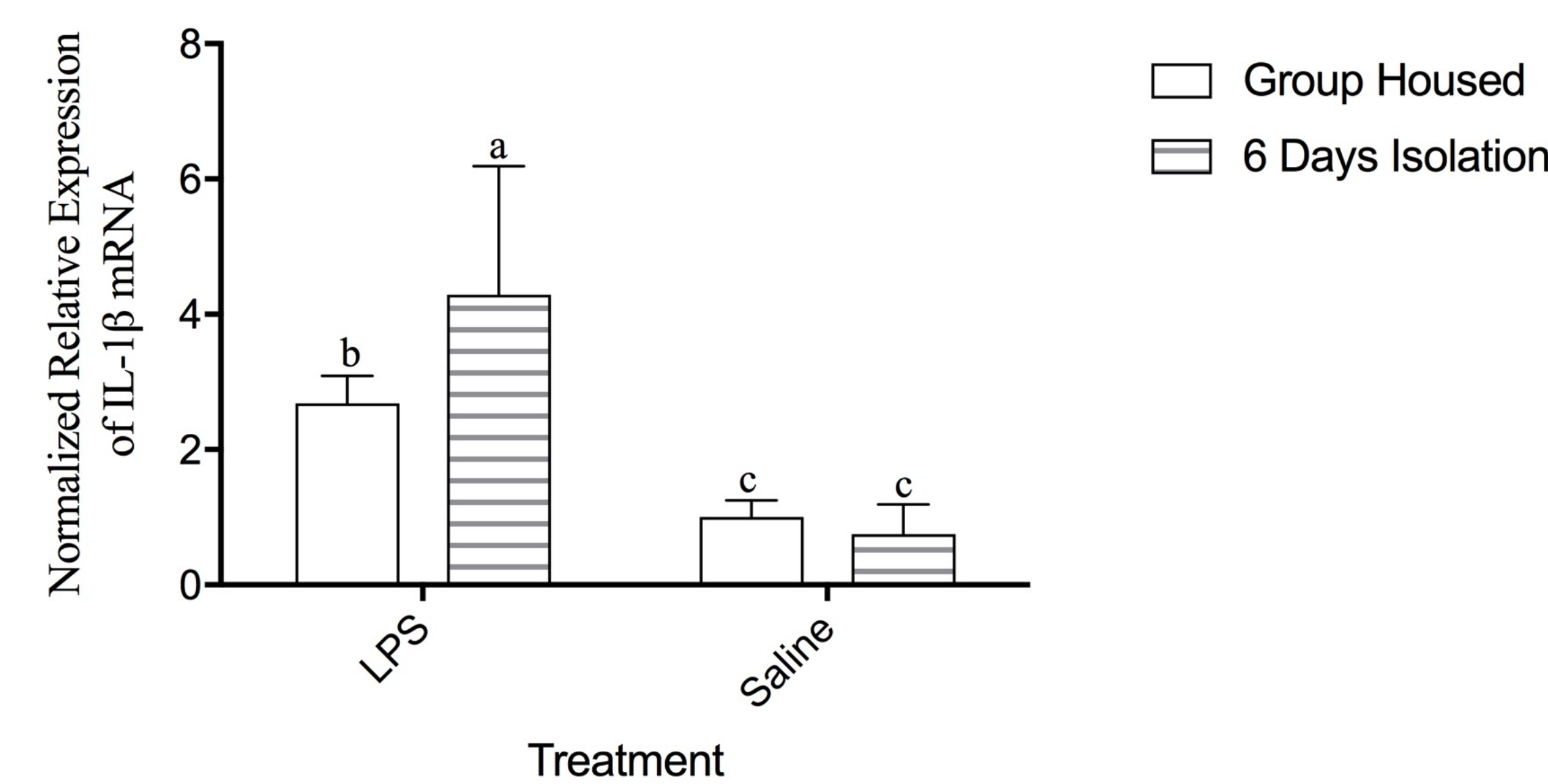
### 21 Day Isolation Timeline



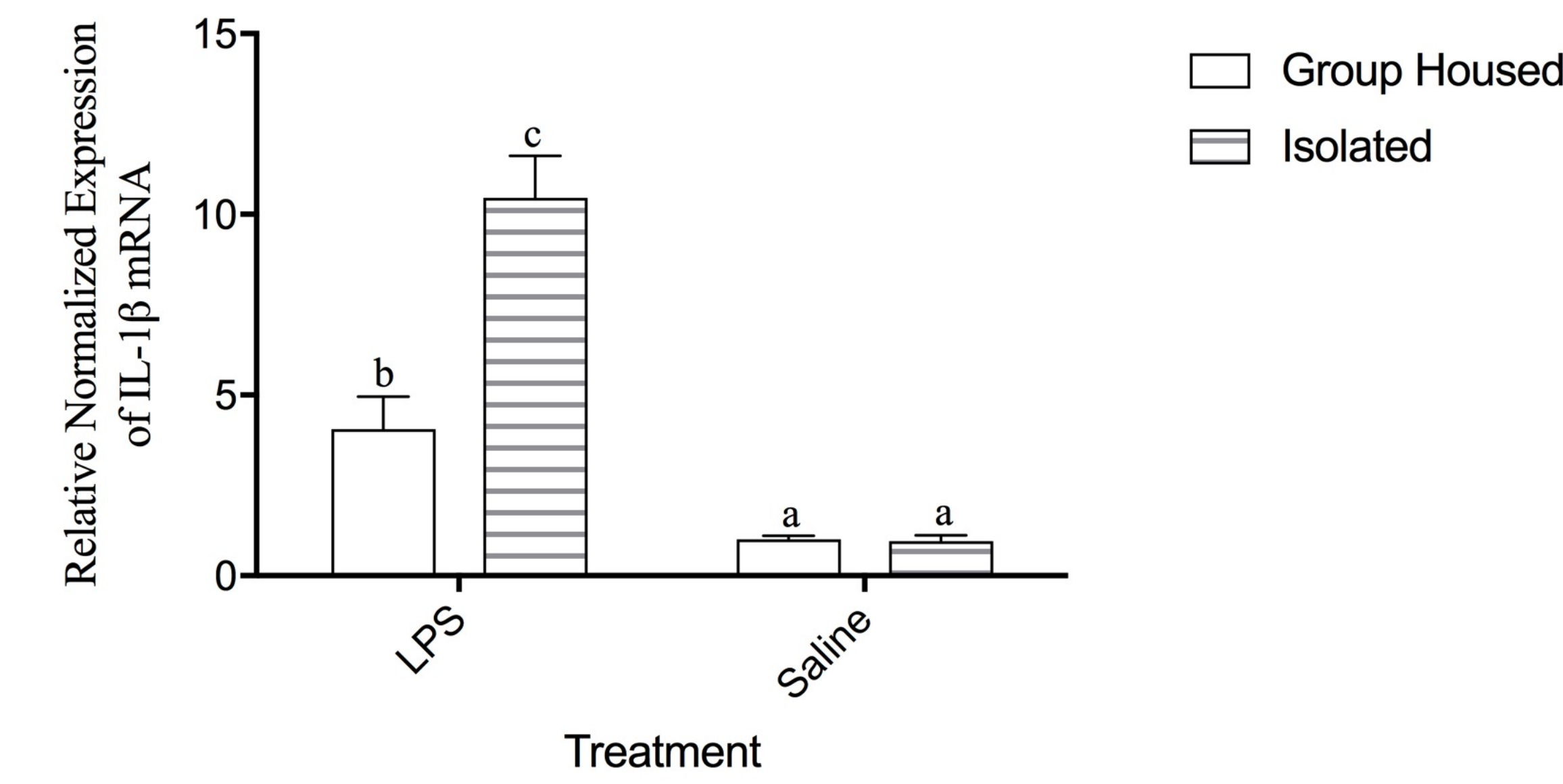
## Conclusion

- Male mice subjected to 6 or 21 days of isolation did not show differences in A $\beta$  levels compared to group-housed mice. This suggests isolation stress did not effect A $\beta$  production in males, despite previous research linking stress and A $\beta$  accumulation (6).
- IL-1 $\beta$  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-1 $\beta$  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 A $\beta$  levels in females will allow us to determine if there is a gender difference in A $\beta$  production following isolation stress.

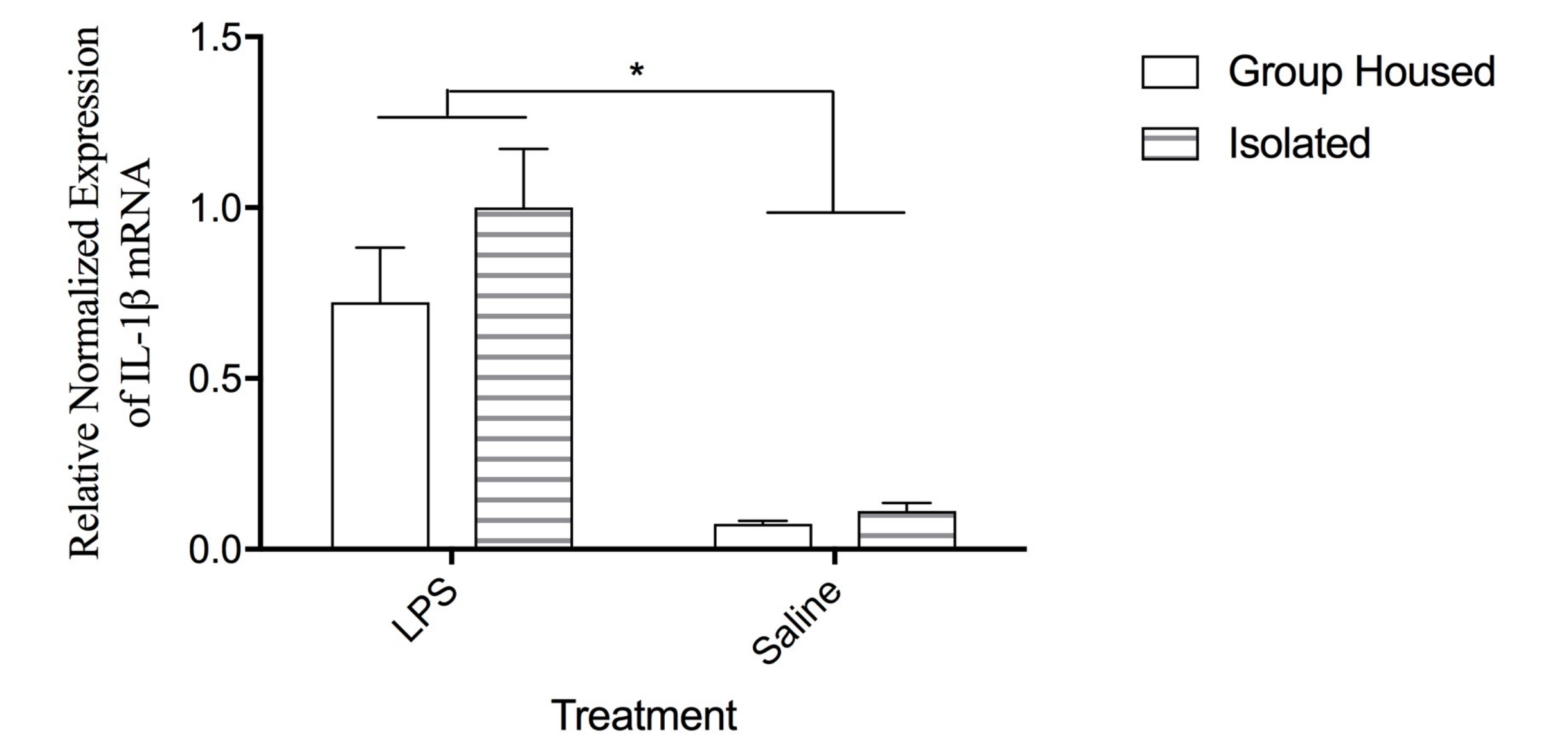
## Results



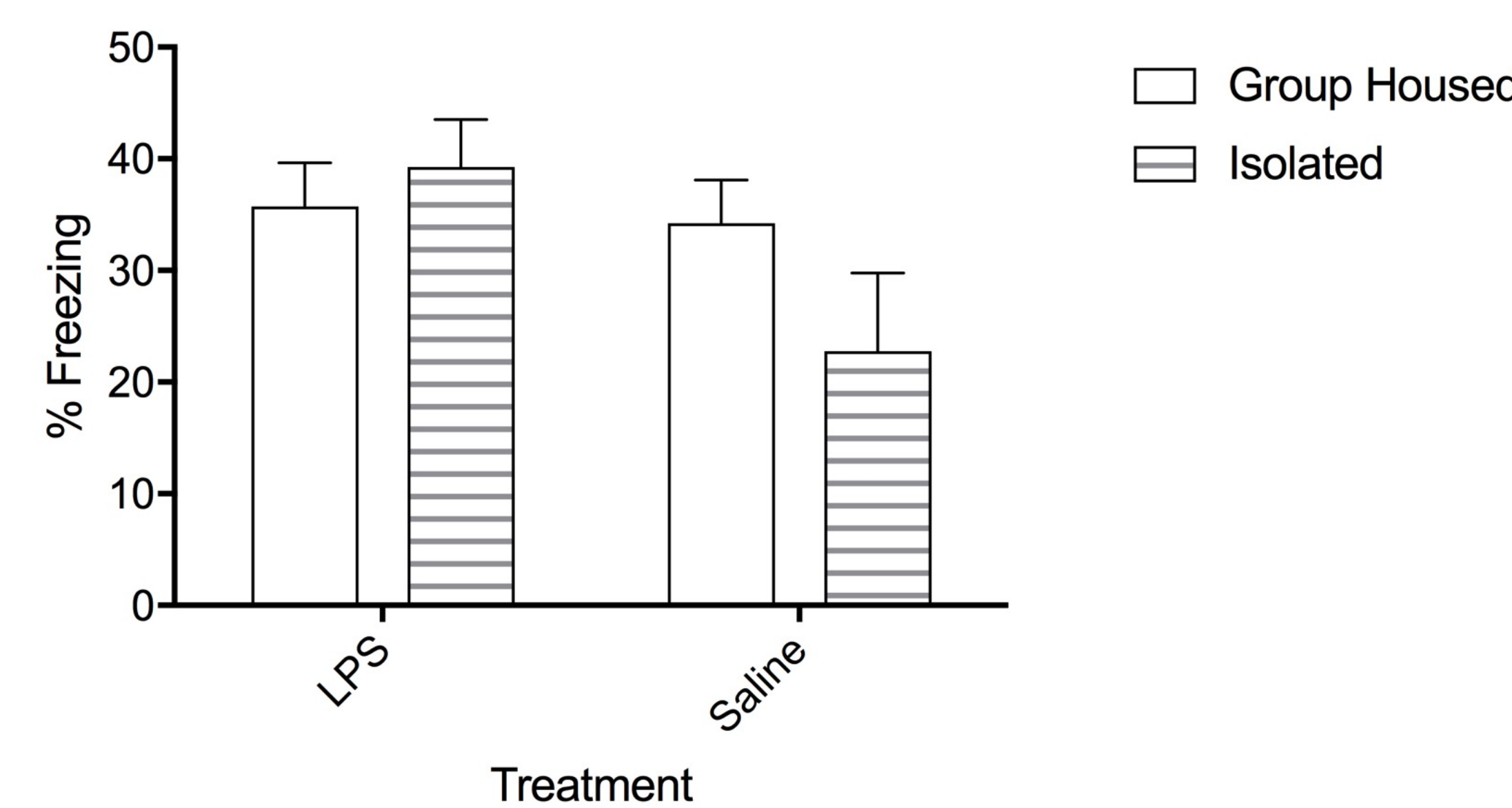
**The Effect of 6 d Isolation and LPS on Hippocampal IL-1 $\beta$  mRNA Expression in Males.** Results from RT-PCR were normalized to  $\beta$ -actin prior to being normalized to our control group (Group Housed/Saline). Different letters (a, b, c) represent significant differences at  $p < .05$ . Bars represent mean  $\pm$  SEM



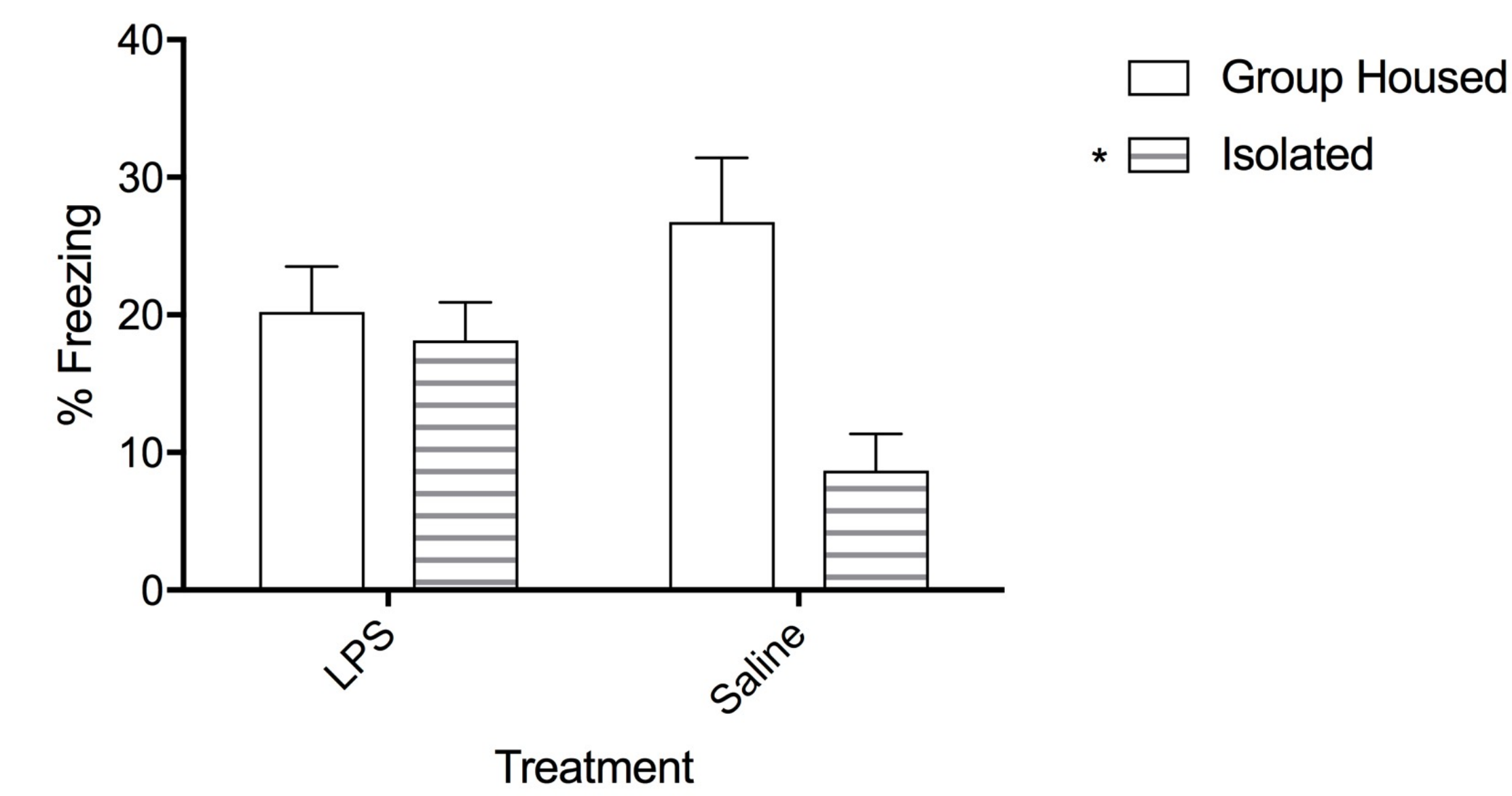
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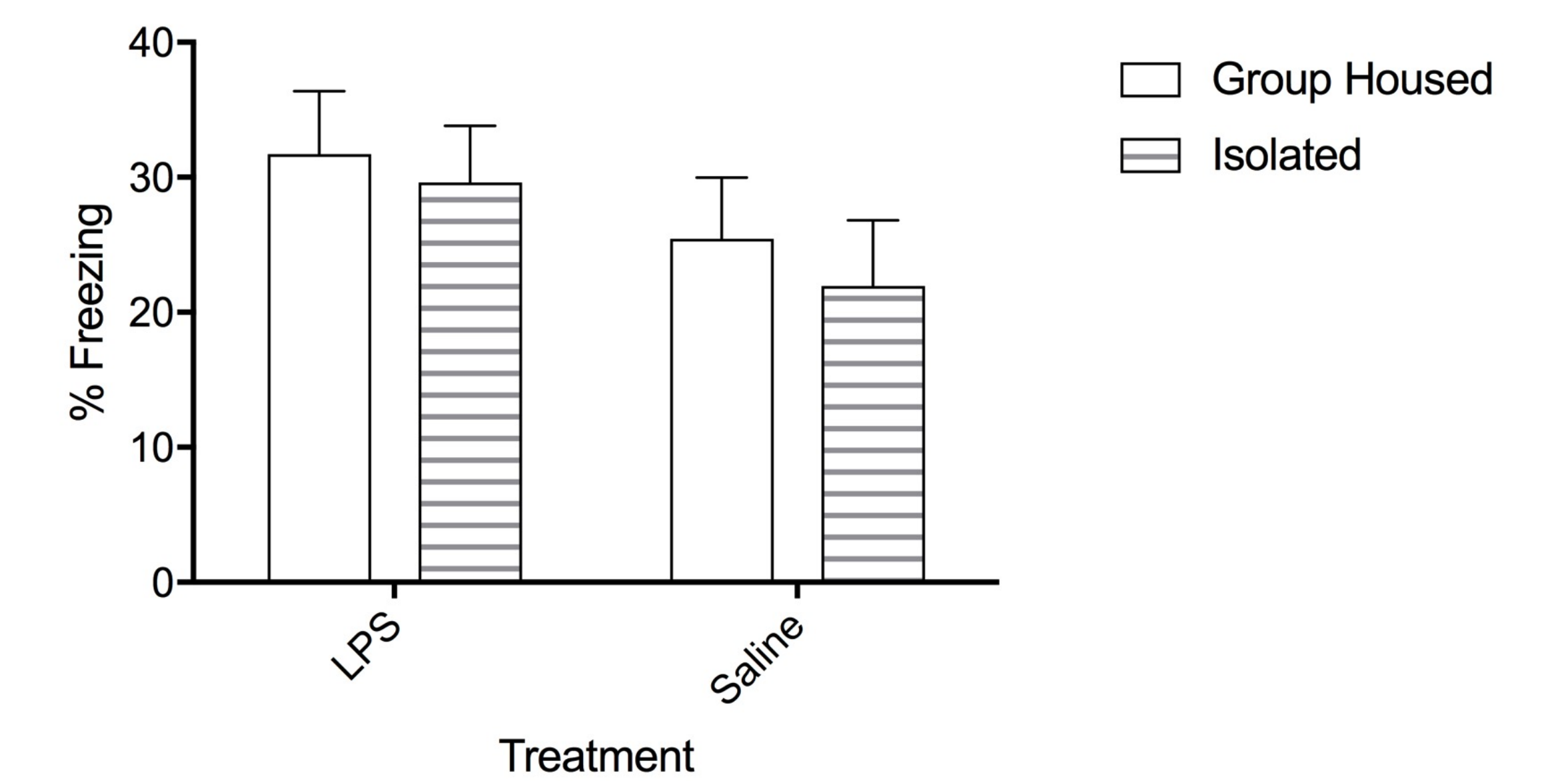
**The Effect of 21 d Isolation and LPS on Hippocampal IL-1 $\beta$  mRNA Expression in Females.** Results from RT-PCR were normalized to  $\beta$ -actin prior to being normalized to our control group (Group Housed/Saline). Different letters (a, b, c) represent significant differences at  $p < .05$ . Bars represent mean  $\pm$  SEM. Ns = 10-12.



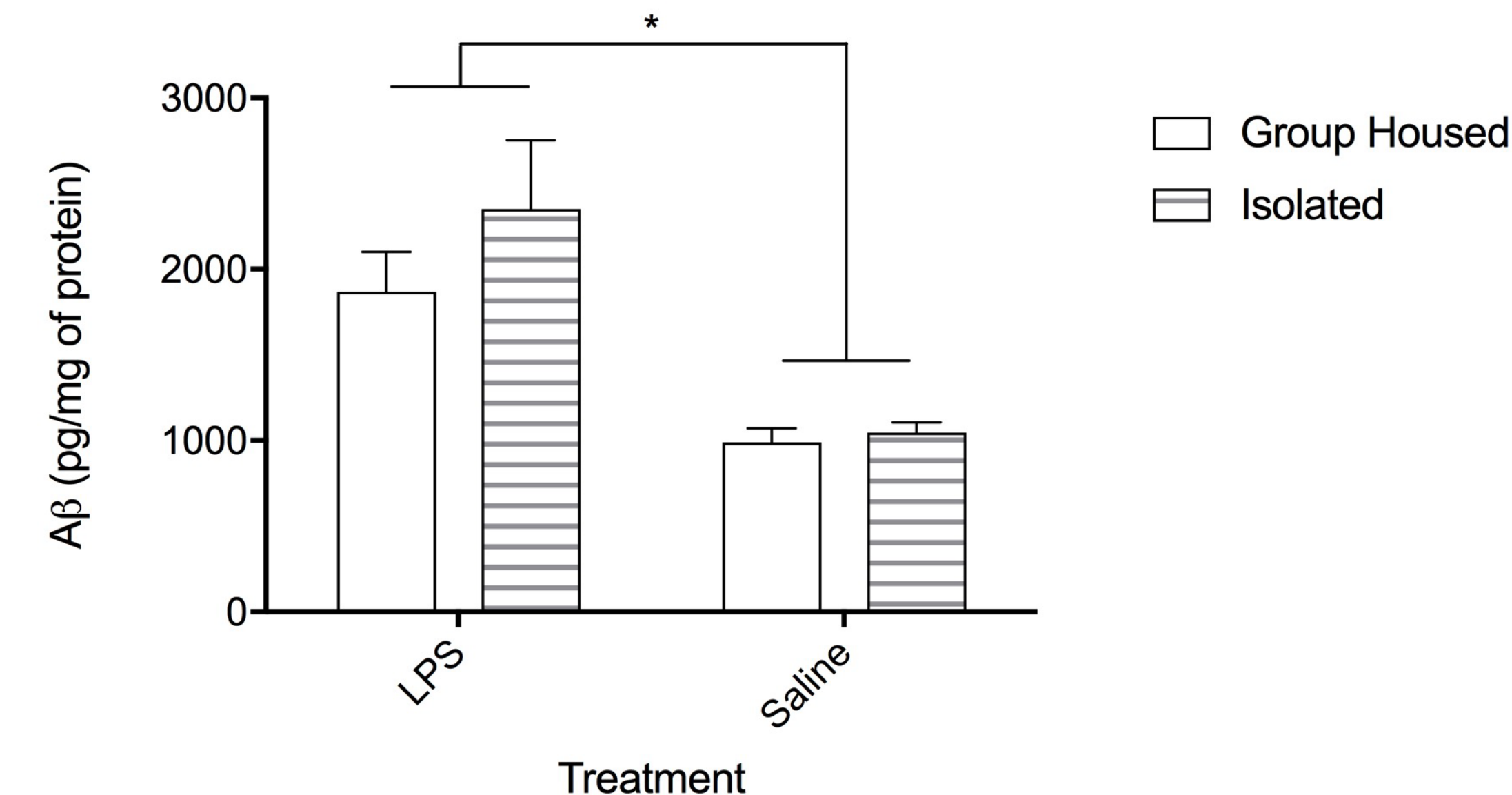
**The Effect of 6 Days of Isolation on Cognition in Males following LPS administration.** Results from CFC analysis demonstrate no significant differences between groups. Bars represent mean  $\pm$  SEM.



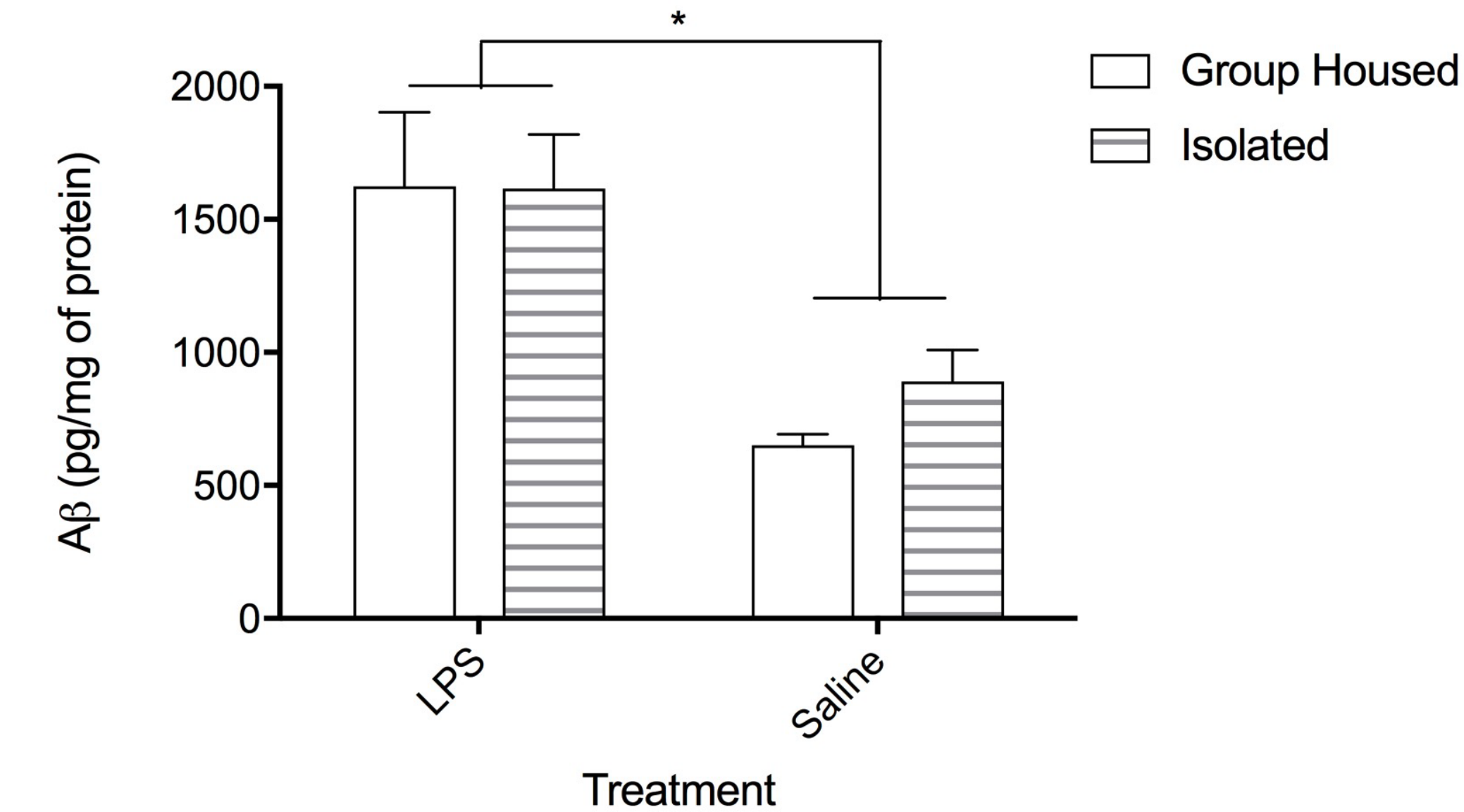
**The Effect of 21 Days of Isolation on Cognition in Males following LPS administration.** Results from CFC analysis demonstrate that isolation significantly impairs freezing behavior. Bars represent mean  $\pm$  SEM.



**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  $\pm$  SEM.



**The Effect of 6 Days of Isolation on LPS-Induced Hippocampal-A $\beta$  levels in Males.** A $\beta$  ELISA reveals 7 d of LPS administration leads to significantly more A $\beta$  compared to Saline-treated controls. Isolation does not exacerbate this effect. Bars represent mean  $\pm$  SEM.



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## References

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