5xFAD Mice Display Cognitive Impairment in a Novel Object Placement Task

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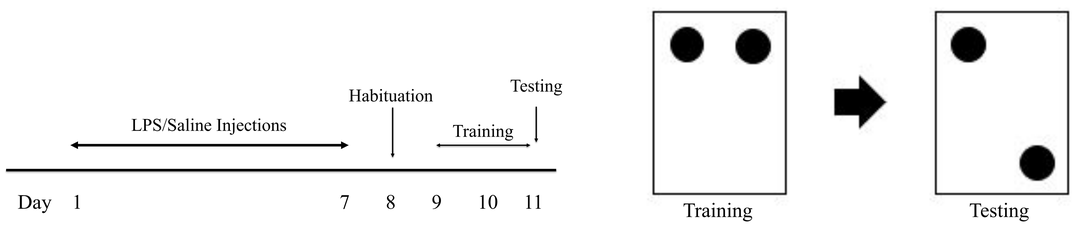
Alzheimer's disease (AD) is the 6th leading cause of death in America, and there is currently no cure or treatment for the disease. Key pathologic features of the disease include amyloid beta plaques and tau tangles that result in severe cognitive decline and ultimately, death. One of the main hallmarks of Alzheimer's disease (AD) is dramatic cognitive decline, including memory loss. Because of this, AD research continually seeks new ways to study the cognitive health of animal models of AD. Researchers have assessed cognitive deficits in AD mice through a variety of behavioral paradigms. The purpose of the present study is to assess if mice with AD-like markers display cognitive deficits in an additional behavioral paradigm, the Novel Object Placement (NOP) task.

Introduction

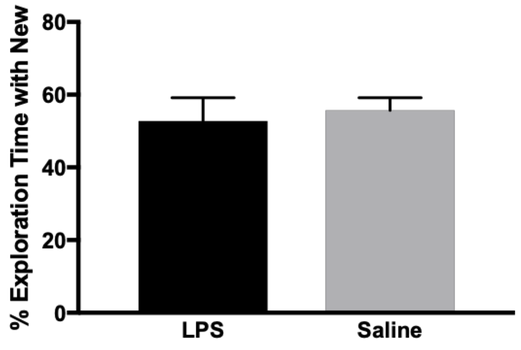
- Alzheimer's disease (AD) is a neurodegenerative disorder that affects nearly 5.5 million Americans, and there is currently no cure.
- AD is characterized by amyloid beta plaques and cognitive deficits.
- 5xFAD mice have genetic mutations that result in the production of a protein, amyloid beta, that is seen in human AD, and is often associated with cognitive deficits.
- Our lab has shown that 7 consecutive days of LPS injections result in an increase in hippocampal expression of amyloid beta along with deficits in contextual fear conditioning.
- Previous research has shown that 5xFAD mice exhibit cognitive deficits in contextual fear conditioning at six months of age.
- This study explores whether cognitive deficits emerge in animals with varying degrees of Alzheimer's-like pathologies in a novel object placement (NOP) task.
- In this task, mice are exposed to two identical objects in an arena for three training sessions, and in a subsequent testing session, one of the objects is moved to a different location in the arena. Cognitively normal mice demonstrate a preference for novelty and spend more time exploring the moved object.
- Pilot data from our lab demonstrates that cognitively healthy, experimentally naïve mice spend more time exploring the object in the novel compared to the old location, indicating intact memory for the old and new locations.
- It is hypothesized that both 5-6 month-old 5xFAD mice and nontransgenic mice that have been administered 7 consecutive days of LPS injections will exhibit deficits in the NOP task.

Methods

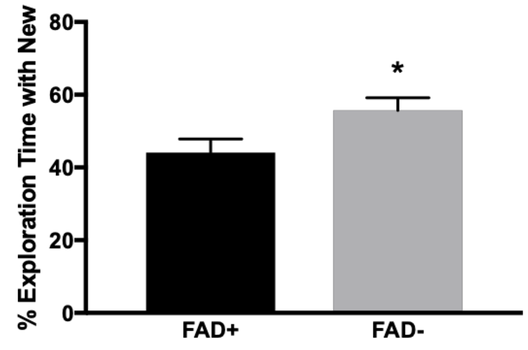


- On Days 1-7, 5-6 month-old, nontransgenic mice were administered LPS or saline for 7 consecutive days prior to the beginning of the novel object training protocol, and 5-6 month old, transgenic 5xFAD mice were administered injections of saline.
- On Day 8 all animals underwent a habituation session in which they were individually placed into the testing arena with no objects for five minutes each.
- On Days 9, 10, and 11 all animals were placed into the arena with two identical objects placed in adjacent corners of the arenas and were allowed to explore for five minutes. Objects remained in the same locations throughout each training session.
- Four hours after training on Day 11, one of the objects was moved to a novel location in the testing arena, and the animals were placed back into the arena for the testing session. Object locations were counterbalanced.
- Object exploration was measured using Noldus EthoVision XT tracking software.
- Learning was calculated as the amount of time the animal spent exploring the object in the new location divided by the total time the animal spent exploring both objects.

Results



Nontransgenic mice. An independent samples *t*-test shows no significant effect of LPS on object location memory *(p* = .697).



5xFAD mice. An independent samples *t*-test shows a significant effect of genotype on object location memory (*p* = .037).

Conclusion

- There was no significant difference in percent exploration time with the new object between the nontransgenic animals that received LPS or saline.
- 5xFAD animals spent less time with the object in the novel location compared to nontransgenic animals, indicating an impairment in identifying the object in the novel location.

Future Directions

- Given these data, our lab plans to repeat this experiment in 5xFAD mice at 4 months of age to investigate at what age cognitive deficits emerge in the NOP task.
- Future studies will also explore the extent to which these observed cognitive deficits are correlated with amyloid beta plaque formation and number.

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