Alzheimer’s Disease is a neurodegenerative disease characterized by decline of cognitive function. This correlates with accumulation of neurofibrillary tangles and Aβ protein fragment plaques, which can initiate an inflammatory response. Injections of LPS can lead to an inflammatory response that stimulates production of Aβ. This project explored whether another series of LPS injections could exacerbate this effect. The animals were given 7 days of LPS or saline injections, a two-week break, and another 7 days of LPS or saline. Contrary to our prediction, Aβ levels were not exacerbated. This was related to a decreased inflammatory response shown by a decrease in IL-1β mRNA in animals given two rounds of LPS. Our lab is now evaluating what mechanism leads to this result.

**Introduction**

- Alzheimer’s disease (AD) is a neurodegenerative disease affecting nearly 5.5 million Americans, and there is currently no cure (1).
- AD is characterized by Aβ plaques of Aβ protein fragments and neurofibrillary tangles of hyperphosphorylated tau protein (pTau) in the brain, predominantly in the hippocampus (2).
- The presence of Aβ plaques has shown to correspond to stimulation of an inflammatory response, predominantly with the release of cytokines (3).
- Our lab has shown that 7 consecutive days of lipopolysaccharide (LPS) injections result in an increase in hippocampal expression of Aβ42 peptides along with deficits in learning and memory (4).
- We hypothesize that the effect of LPS injections will be exacerbated through a second injection series of LPS after a fourteen-day recovery interval, thus modeling multiple, independent, bacterial infections, like that seen in humans.

**Results**

**Experiment 1**

- LPS Injection Schedule
  - Administered two rounds of LPS
  - Second round of LPS injections.
  - β levels were not increased after the second round of LPS injections.
  - phosphorylated tau within the hippocampus.

**Experiment 2**

- LPS Injection Schedule
  - Administered two rounds of LPS
  - Second round of LPS injections.
  - β levels were not increased after the second round of LPS injections.
  - phosphorylated tau within the hippocampus.

**Conclusion**

- 14 days after the last injection, animals administered LPS still have significantly higher levels of Aβ in the hippocampus compared to saline-treated animals. This pattern is not replicated in levels of phosphorylated tau within the hippocampus.
- Contrary to our hypothesis, Aβ levels were not increased after the second round of LPS injections.
- Additionally, the lack of increase of Aβ levels corresponded to a decreased inflammatory response upon secondary administration of LPS, as IL-1β mRNA was significantly lower in the group administered two rounds of LPS.

**References**

1. Fact and Figures

**Future Directions**

- Potential Binding Site on IgM antibody
- Potential Tolerance Mechanism through NFkβ Signaling Cascade

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