The Effects of Inflammation on Dendritic Spine Density

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Alzheimer's Disease (AD) is a neurodegenerative disease that is characterized by deficits in learning and memory. AD pathology is associated with neuronal death through the accumulation of amyloid beta (Aβ) plaques in the synapses. Our lab has previously demonstrated that Lipopolysaccharide (LPS), a component of gram-negative bacteria, induces an inflammatory response that increases Aβ found in the brain. Dendritic spines are projections on dendrites that may or may not be synapsing with an axon. Previous research indicates that there is a correlation between the number of properly functioning synapses and the number of dendritic spines. In this study, LPS was administered to induce inflammation, stimulating Aβ production. We then quantified dendritic spine density in order to compare dendritic spine density in the hippocampus of both LPS- and saline-treated groups. Contrary to our hypothesis, we saw a non-significant increase in dendritic spine density following LPS treatment, when compared to saline controls.

Introduction

- Over 5.5 million Americans suffer from Alzheimer's disease (AD). (1)
- An established feature of AD is a decrease in neuronal activity, associated with decreases in synapses. (4)
- Amyloid-Beta (Aβ) has been implicated in this loss of synapses, and is a key marker in AD pathology. (4)
- Our lab has shown that peripheral inflammation results in an increase in Aβ production. (2)
- Dendritic spines are projections off of neurons that represent sites of communication between cells and are correlated with cell-to-cell communication. (4)
- We hypothesize that inflammation following administration of LPS will lead to an increase in Aβ in the brain and subsequent loss of dendritic spines.

Methods

- 9-month-old mice were randomly assigned to a control group (n=6) and LPS group (n=6)
- Intraperitoneal (i.p.) injections of 250 mg/kg LPS or volume-equivalent saline were administered once a day for 7 consecutive days.
- 4 hours following the final injection mice were sacrificed and brain tissue was collected.
- Brain tissue was processed using the Golgi-Cox staining (5)
- Brains were sliced into thin sections and synapses counted by microscopic examination.
- For each section, dendritic spines were counted on the dendrites of 5 separate neurons in the CA1 region of the hippocampus.
- Dendritic spines must be .05 µm in height in order to be counted
- One-way Analysis of Variance (ANOVA) was conducted between LPS and Saline groups.

Results

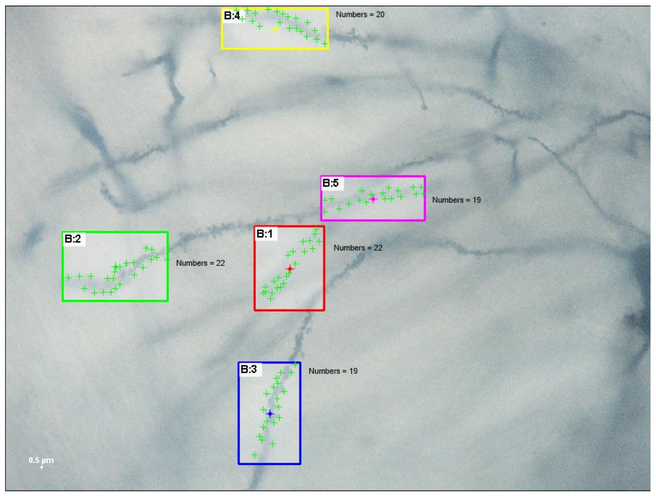

Figure 2. In order to count the dendritic spines, areas 20 µm away from the cell body were measured. Counting started at or slightly after this point and continued for 20 µm. Spines where counted inside of this region. For a spine to be counted, it had to be 0.05 µm in height.

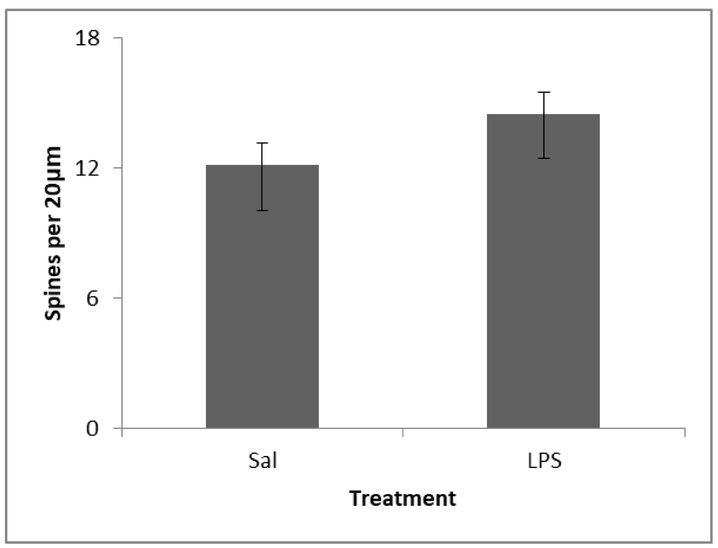

Figure 3. Comparison of dendritic spines per 20 µm in mice that received either saline or LPS for 7 days. A) Mean spine density is not significantly different between groups (1-way analysis of variance [ANOVA]: $F_{1,10}$=2.635, p=0.1355). Error bars represent two times standard error.

Conclusion

- Results were contradictory to our initial hypothesis with a non-significant increase in dendritic spines seen in the LPS-treated group.
- Inflammation my lead to a compensatory increase in dendritic spines as neurons attempt to salvage cell-cell communication.
- To observe a possible Aβ-induced loss of dendritic spines may require a transient period in which the affects of inflammation subside, resulting in a more robust affect of the Aβ produced during inflammation.

Future Directions

- Synaptophysin and PSD95 proteins would be beneficial targets to observe the pre- and post-synaptic cells and thus active synapses.
- Transgenic animals in which some neurons and their dendritic spines fluoresce are soon to be used to repeat these studies and should provide a better method to observe spines and synaptic proteins.

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