Investigating the impact of depression on neuroinflammation in Alzheimer's disease

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Summer Research Fellowship (SRF) 2020 for Science Students

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Abstract

Depression is believed to be a risk factor and early symptom for Alzheimer's disease (AD). One possible link which explains the comorbidity could be the inflammation process in both diseases. This project explores the impact of depression on neuroinflammation in AD by the administration of corticosterone in rats. It is found that 21 days of corticosterone administration leads to systemic inflammation and anxiety-like behavior, but no depressive-like behaviors and cognitive alterations were observed. Additionally, no neuroinflammation was observed. Collectively, the 21-day administration of corticosterone is insufficient to impact cognitive function in rats. The objective will be further explored by having longer periods of corticosterone injection.

Introduction

Pathology of Alzheimer's disease (AD)

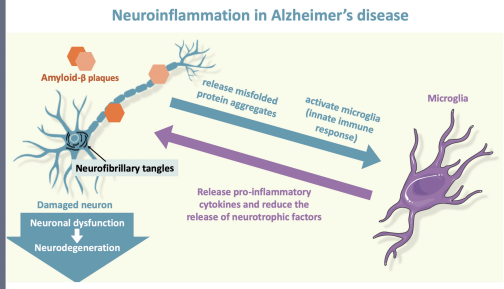

Figure 1. Neuroinflammation process in Alzheimer's disease

aggregation of β-amyloid plaque and neurofibrillary tangles

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activation of innate immune response

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activated microglia releases proinflammatory cytokines and induces neuroinflammation

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neuronal dysfunction and death

Inflammation in Depression

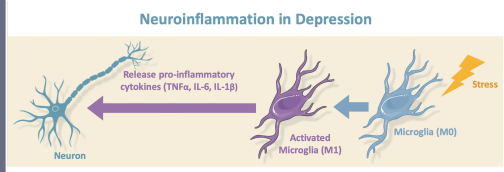


Figure 2. Neuroinflammation process in Depression

Cormobidity of Depression and AD

Studies shown:
- depressed patients had over 50% increased risk for dementia
- 20-30% of Alzheimer's disease patients have depression

It is hypothesized that depression is a risk factor for AD by inducing neuroinflammation.

Results

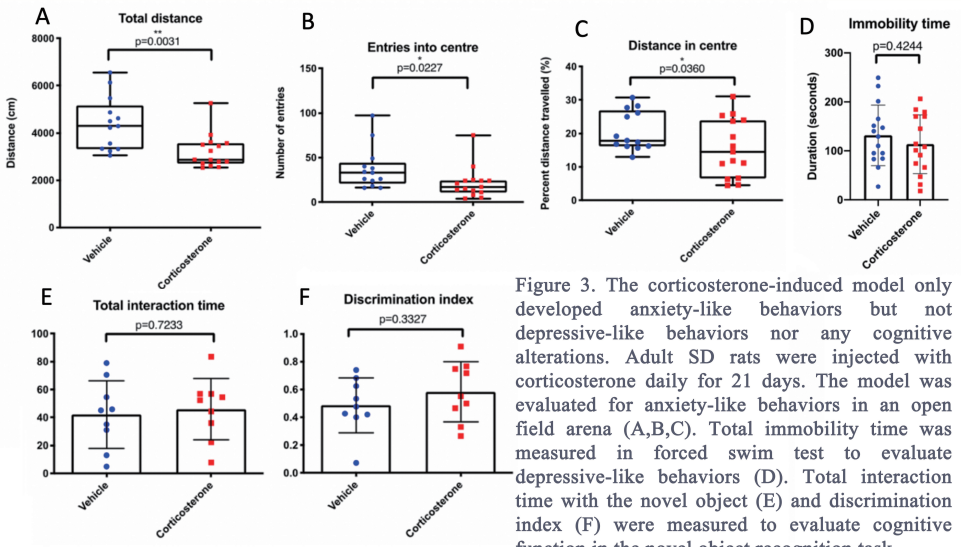


Figure 3. The corticosterone-induced model only developed anxiety-like behaviors but not depressive-like behaviors nor any cognitive alterations. Adult SD rats were injected with corticosterone daily for 21 days. The model was evaluated for anxiety-like behaviors in an open field arena (A,B,C). Total immobility time was measured in forced swim test to evaluate depressive-like behaviors (D). Total interaction time with the novel object (E) and discrimination index (F) were measured to evaluate cognitive function in the novel object recognition task.

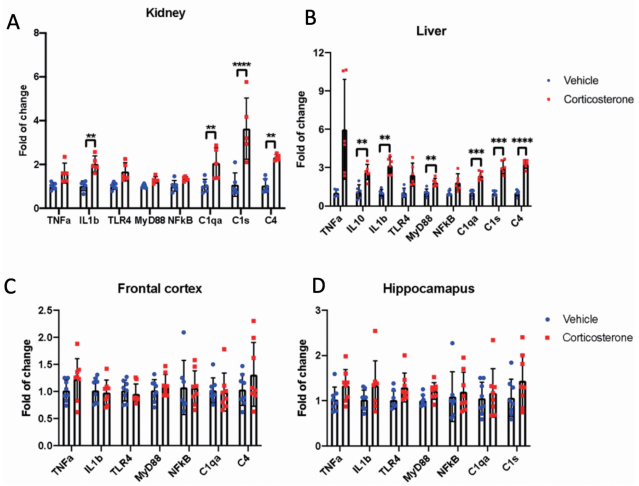


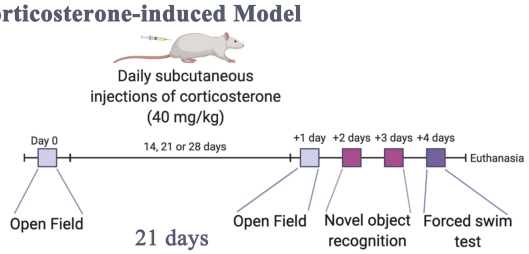
Figure 4. Corticosterone-induced model displayed systemic inflammation but no neuroinflammation was observed. No significant change was observed in the frontal cortex and hippocampus (A,B) while some inflammatory cytokines such as Il1b, C1qa, C1s and C4 increased significantly in the kidney and liver (C,D).

Summary

Corticosterone-induced model:
- anxiety-like behavior was displayed
- no depressive-like behavior or cognitive alterations was observed
- systemic inflammation was observed in kidney and liver
- no neuroinflammation was observed in frontal cortex and hippocampus

Methodology

Corticosterone-induced Model



Under depression, elevated level of glucocorticoid is observed in the bloodstream. While the main glucocorticoid found in human is cortisol, corticosterone is the main glucocorticoid in rodents. For this reason, corticosterone was injected daily into Sprague-Dawley (SD) rats for 21 days to induce depressive behaviours.

Discussion

Many studies have revealed the association between inflammation and depression. For instance, studies have shown that depression frequently accompanies with sickness involving inflammation such as cardiovascular diseases and rheumatoid arthritis. This is consistent with our findings that the injection of corticosterone can lead to systemic inflammation in liver and kidney. However, no neuroinflammation was observed in the corticosterone-induced models, which it is in line with the absence of depressive-like behaviors and cognitive alterations in the model. In comparison, a previous study has shown that 14 days of corticosterone administration was able induce depressive-like behaviors in rodents, though they did not investigate inflammatory changes. Therefore, future studies will focus on different timelines (14, 21 or 28 days) of corticosterone administration to investigate the inflammatory and behavioral changes with different durations of corticosterone administration in the animal model.

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