Stress-induced hippocampal damage following noise trauma

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BACKGROUND

When a person is exposed to noise trauma on a daily basis, they are increasingly prone to damage in various parts of the brain. Previously, we demonstrated that a single unilateral noise exposure reduced neurogenesis within the hippocampus, a brain region important for learning and memory, 10 weeks after exposure (Kraus 2010). However, the underlying mechanisms of this reduction in neurogenesis are unknown.

RATIONALE AND HYPOTHESIS

One potential mechanism for this reduction in neurogenesis is the activation of the hypothalamic pituitary adrenal axis (HPA) which regulates the bodily stress response. High levels of stress hormones are known to cause a reduction in hippocampal neurogenesis.

The HPA axis (Hypothalamic pituitary adrenal axis)
- Feedback loop that includes the hypothalamus, pituitary and the adrenal glands.
- Main hormones involved are: corticotropin-releasing factor (CRF), adrenocorticotropic hormone (ACTH) and cortisol.
- Loop completed by feedback regulation of cortisol on the hypothalamus, pituitary, hippocampus and amygdala.

This project involved looking at the difference in expression between the glucocorticoid (GR) and mineralocorticoid (MR) receptors within the brain, both of which regulate activity of the HPA axis. Specifically, we analyzed changes of expression of these receptors in the hippocampus. GR and MR receptors in the brain help to regulate the activity of the HPA axis by binding to basal and reactive stress hormone levels due to the differential affinity of the GR and MR receptors for cortisol.

METHODS

Adult male Sprague Dawley rats (2-3 months) exposed to: unilateral noise exposure (narrowband noise, 12 kHz, 126 dB, 2 hour under isoflurane anesthesia) or control (2 hour under isoflurane anesthesia).

Immunohistochemistry was used to immunolabel tissue sections containing the hippocampus. Sections are incubated with the primary antibody for glucocorticoid receptor and mineralocorticoid receptor and DAB was used for visualizing the receptor changes.

Figure 3- (a) Basic immunolabeling methodology. (b) Cresyl violet stained coronal section through the rat brain depicting the hippocampus

Staining was quantified using NIH ImageJ software by measuring relative optical density

OBJECTIVE: To determine if changes in GR and MR receptor expression in the hippocampus underlie the reduction in hippocampal neurogenesis following noise exposure

RESULTS

**Glucocorticoid Receptor Expression**

![Graph](Image)

(a) Compared to control, unilaterally noise exposed animals had a significant increase (~2 fold) in glucocorticoid receptor expression in the dentate gyrus of the hippocampus. Student’s T-test, P < 0.05 (n = 4).

(b) The immunolabeling for the GR receptor shows a significant increase in expression in unilateral-noise exposed rats.

(c) In the MR receptor staining there is little to no difference in the immunolabeling.

CONCLUSION

1. Our studies show a significant increase in glucocorticoid receptor expression and little to no change in the mineralocorticoid receptor expression in the hippocampus following unilateral noise exposure.

2. The increased GR expression may result in greater sensitivity of the hippocampus to stress hormones, which may underlie the reduction of neurogenesis following noise exposure.

FUTURE DIRECTIONS

1. Image J software will be used to quantify changes in mineralocorticoid receptor expression following unilateral noise exposure.

2. In the current study, we only assessed changes in GR and MR expression at 10 weeks after noise exposure. We plan to look at additional time points after noise exposure in order to determine the time course of changes in receptor expression.

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REFERENCES