The Effects of Corticosteroids on the Human Brain

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Introduction

➢Corticosteroids: A class of steroid hormones that are produced in the adrenal glands in response to stress.

➢The brain is sensitive to the effects of corticosteroids.

Effects of Corticosteroids

➢ Chronic exposure to high levels of corticosteroids is associated with changes in neurons in the hippocampus and/or with impairment of cognitive performance.

➢Decreases in total brain volume have also been reported.

Significance

- Corticosteroid therapy is significant for illnesses such as asthma, arthritis, transplant rejection, and dermatological disorders.
- Mood disorders, such as major depressive disorder (MDD) or bipolar disorder, in which hypothalamic-pituitary-adrenal(HPA) axis activation and elevated cortisol levels are common.

Hypothesis

We hypothesized that phenytoin would act as a neuroprotective agent against the corticosteroid-induced changes in the human brain.

Purpose

➢ To determine if 3 days of cortisol administration is associated with changes in the brain volume.

➢ To determine whether or not phenytoin acts as a neuroprotective agent against the corticosteroid-induced brain changes.

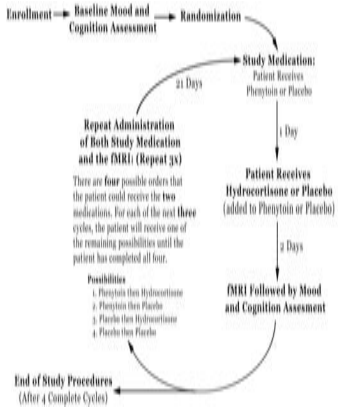
Animal Research

- Rats were pretreated with Phenytoin (40mg/kg).
- Then, the rats were subjected to daily corticosteroid injections (10mg).
- Phenytoin (40mg/kg) pretreatment blocked the effects of daily corticosteroid injections (10mg) in rats.

Study Design

Each participant will receive 4 fMRI scans at separate times in 1 hour imaging sessions with a 21 day washout between each study drug exposure in a crossover design. Hippocampal activation, mood and cognition will be assessed.

- Prior to each scan patient will receive randomly either:
  - Placebo/placebo
  - Phenytoin/placebo
  - Hydrocortisone/placebo
  - Phenytoin/Hydrocortisone



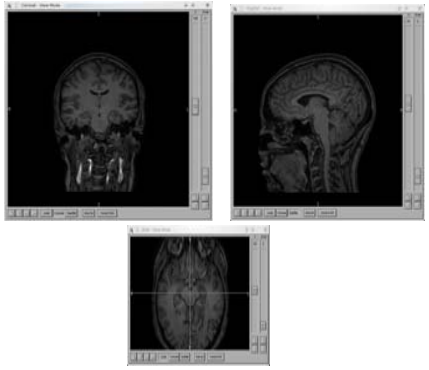
Anatomical Measurements

➢ Brains2 Software was used to measure the volumes

➢The total brain volume, hippocampal volume, and the volume of the amygdala were measured

➢Total Brain volume includes combined volume of the cerebral hemispheres, cerebellum, and the brain stem.

➢The images of the brain are viewed in three sections: Coronal, Sagittal, and Axial views.



Results

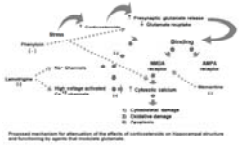
- Phenytoin acted as a neuroprotective agent.
- Improvements in the total brain volume were observed.

Conclusions

➢ The deleterious effects of corticosteroids on the hippocampus appeared to be mediated by glutamate.

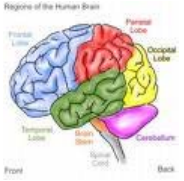
➢Phenytoin modulated glutamate release.

➢Phenytoin pretreatment blocked the effects of corticosteroids (hydrocortisone) on the brain.



Future Plan

Work on more neuroprotective agents



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