Presentation 6 – Benjamin Natelson

Stress Responses in Gulf War Veterans

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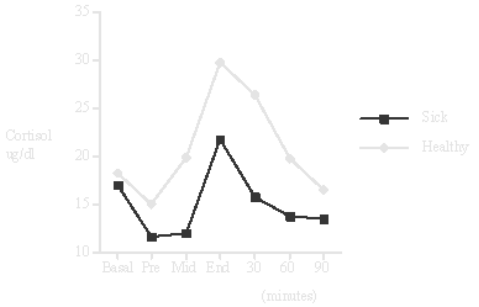
Disorders associated with blunted HPA activity

- PTSD (Yehuda 2002)
- Chronic fatigue syndrome (Gaab 2002)
- Rheumatoid arthritis (Cutolo 2003)
- Chronic pain (Tennant 2001)

Plasma cortisol response to exercise was blunted in GVs with medically unexplained illness



MERIT: Pituitary-adrenal function in GVs with medically unexplained illness

- Study 1: Adrenal volume
  - » Long-term picture of activity of the adrenal gland.
- Study 2: HPA Negative feedback effects
  - » How well are stress responses turned-off?
- Study 3: Activation of the HPA axis
  - » How well are stress responses turned on?

Study 1: Adrenal volume in GVs with medically unexplained illness

Adrenal volumes will reflect the long-term consequences of HPA activity since ACTH stimulates the growth of this gland

- Axial MRI of adrenal glands using 5 mm slices

Study 2: Negative feedback effects of cortisol in GVs

Blunted HPA activity in GVs may result from greater negative feedback effects of cortisol

- Metopirone to shut off adrenal gland followed by hydrocortisone infusion.
- Blood samples assayed for ACTH

Expected results

- Greater suppressive effects of hydrocortisone on plasma ACTH concentrations in sick GVs
- This would provide indirect evidence for altered glucocorticoid receptor density in the brain (i.e.. hippocampus)

Study 3: Central drive on HPA axis

Blunted HPA activity in sick GVs may be caused by reduced activation of the HPA during stress

Insulin induced-hypoglycemia with clamped and stepwise clamped glucose

- Blood samples assayed for ACTH

Expected results

- ACTH responses to insulin-induced hypoglycemia will be lower in GVs with unexplained illness
- This result would suggest impaired centrally-mediated activation of the HPA during stress

Conclusions

- Origins for altered HPA activity can occur at the level of the adrenal gland, hypothalamus, pituitary or higher brain regions.
- This series of studies will test axis function at all levels in an attempt to locate the source of altered HPA activity in GVs with unexplained illness
- These results will improve our understanding of the pathophysiology of the GVs health complaints