Presentation 4a – John Ottenweller

Plasma Cortisol, Paraoxonase and Butyrylcholinesterase in Gulf War Era Veterans

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The National Health Survey of Gulf War Era Veterans and their Families

693,000 Gulf Vets (GVs) and 800,000 non-Gulf Vets (NGVs)

Phases I and II
- Stratifed Random Sample of 15,000 Gulf Vets and 15,000 non-Gulf Vets
- Phase III (1999-2001)
- 5885 random subsample stratified to select veterans close to study sites
- 1996 GVs and 2883 NGVs invited for study

Phase III of the NHS

1061 GVs (53%) and 1128 NGVs (39%) participated

Demographics
- 78% Male
- 78% Caucasian
- 48% Smokers
- 98% had more than a high school education

Phase III of the NHS

Service Characteristics
- 35% Guard/Reserve and 65% Active Duty Troops
- 75% Army and 25% Other Services
- 17% Officers and 83% Enlisted Men

Status for Diseases Tested in Models
- 23% Severe Chronic Multisymptom Illness (CMI)
- 3% PTSD in year before examination

Only 1.6% CFS, so to few to include in model

Data Collected in Phase III But Not in Final Model

CMI

- CMI by itself (univariate analysis) associated with significantly lower cortisol levels

Combat Exposure Scale (Proctor)

Beck Anxiety Inventory

PTSD (CAPS)

Smoking

Summary I

Greater fatigue is associated with lower cortisol levels, but CMI was not in the final model.

At lower BDI scores, more PTSD symptoms lead to higher cortisol levels. At higher BDI scores, more PTSD symptoms lead to lower cortisol levels.

Guard/Reserve veterans have lower cortisol levels than Active Duty veterans.

GVs have lower cortisol levels than NGVs

- Marginally significant interaction between Duty Type and Deployment, so that their main effects are largely driven by lower cortisol levels in deployed Guard/Reserve veterans.

Samples from Case-Control studies involving NJ CEHR, OR EHRC and CDC

Blood samples were collected from GVs with unexplained illnesses or healthy GVs at the East Orange VA, the Portland VA and from the Pennsylvania Air National Guard cohort studied by the CDC (Fukuda).

Summary II

In older GVs, poorer mental functioning was associated with lower cortisol levels.

Lower mental and social functioning were associated with lower cortisol levels, better functioning in either domain was associated with higher cortisol levels.

Cortisol Levels in NJ and CDC Subsample

Only the NJ and CDC datasets (not OR) had physician diagnoses of CFS and Depression.

Summary III

The combination of depression and CFS resulted in much lower cortisol levels than either CFS or depression alone.

Conclusions

Increasing fatigue, and the combination of greater depression and higher PTSD symptoms were associated with lower cortisol levels.

The combination of poorer mental and social functioning was also associated with lower cortisol levels.

Guard and Reserve veterans who were deployed were at greater risk of lower cortisol levels than deployed Active Duty veterans or NGVs

In deployed veterans, the combination of CFS and depression resulted in lower cortisol levels.

Final Message

Something about service in the first Gulf War resulted in lower cortisol levels 8-10 years later, and Guard/Reserve troops were at greater risk.

These lower cortisol levels were associated with increased fatigue, more depressed mood, more PTSD symptoms, and poorer mental and social functioning. Greater allostatic load seemed to be associated with lower cortisol levels.

If low cortisol levels are contributing to some of these symptoms, rather than a result of them,

low-dose glucocorticoid therapy might improve the health and well being of symptomatic veterans with low normal levels of cortisol.

Plasma BuChE in Gulf Era Veterans

BuChE is a plasma enzyme that binds anti-cholinesterases and prevents them from inactivating acetylcholinesterases in synapses and the neuromuscular junction.

Genetic variants with point mutations in the binding site result in lowered affinity.

Reduced activity may result in increased sensitivity to anticholinesterases and neurotoxins.

BuChE Phenotypes

Plasma BuChE activity was measured in the NHS samples from GVs and NGVs.

We were not allowed to measure phenotypes because the consent for the NHS excluded genetic testing.

So we were not able to determine whether BuChE phenotype was associated with illness.

Univariate Analyses of BuChE Activity

Greater fatigue and poorer quality of life were associated with higher BuChE activity.

Better scores on the physical component summary scale of the SF-36 were associated with lower BuChE activity.

Summary of BuChE Analysis

More combat exposure associated with greater BuChE activity.

But an interaction between combat exposure and the physical component summary of the SF-36.

- In those with low combat exposure, lower PCS scores associated with lower BuChE activity.
- In those with high combat exposure, lower PCS scores associated with higher BuChE activity.

Conclusions

We hypothesized that lower BuChE activity would be associated with poorer health in GVs, but it was not.

In nGVs, lower BuChE activity may be associated with poorer physical functioning.

Maybe exposure to anticholinesterases needs to be added to the regression model.