**Presentation 4b – John Ottenweller**

## Paraoxonase Activity in Gulf Era Veterans

Paraoxonase (PON1) is a plasma protein produced by the liver that degrades a number of organophosphates including pesticides and nerve agents (sarin).

There are common genetic variants that alter the affinity of the enzyme for its substrates.

- A substitution at position 192 (R allele) reduces metabolism and increases toxicity of pesticides.

## Genetic Variants of PON1

We were not allowed to measure the PON1 phenotypes because the consent in the NHS did not allow genetic testing.

Instead we measured activity in the presence of 1 M NaCl, which we found was able to separate phenotypes relatively well.

Lowest PON1 levels associated with QQ phenotype, intermediate levels with QR phenotype and highest levels with the RR phenotype

## Control of PON1 Activity

PON1 activity depends on genetic variants.

PON1 activity depends on enzyme protein levels.

Liver and kidney disease lower PON1 levels.

Smoking and alcohol use lower PON1 levels.

PON1 levels are affected by diet.

## Univariate Analyses of PON1

Those with PTSD had lower PON1 activity.

As PTSD symptoms increased, PON1 activity decreased

Those with more combat exposure had lower PON1 activity.

Lower PON1 activity was associated with poorer mental functioning.

## Summary of PON1 Results

Those with CMI have higher PON1 activity.

- Increase is greater in those with PTSD.
- Increase is less in GVs than NGVs.

Without CMI, increasing PTSD symptoms lead to lower PON1 activity. Decrease greater in those with CMI.

Decrease in PON1 with increasing combat exposure was greater in those with PTSD.

Interactions with education questionable because only 41 veterans had just a high school eduction.

## Conclusions about PON1

Likely genetic influences:

- Non-caucasians are more likely to have R allele.
- Risk of CMI increased in those with R allele
  - However, risk was less in GVs.

Likely environmental influences:

- Aging leads to lower PON1 activity.
- Greater combat exposure and more PTSD symptoms lead to lower PON1 activity.

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