

### Presentation 16- John Concato

ACETYLCHOLINESTERASE ACTIVITY IN GULF WAR  
DEPLOYED AND ERA VETERANS: JUN '04 UPDATE

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#### BACKGROUND

Original proposal (B. Doebbeling, H. Soreq):

Research study to determine whether mood or anxiety disorders are related to serum levels of various enzymes among Persian Gulf veterans

Completed and ongoing analyses (West Haven CERC):

Based on original and additional "exploratory" hypotheses

#### SOURCES OF DATA

Questionnaire responses from Iowa Gulf War Cohort Study

- Wave I: 3,695 veterans of Persian Gulf era, from Iowa
- Wave II: 374 case patients with cognitive dysfunction, depression, or chronic widespread pain; 228 controls without these conditions (N=602 subset of Wave I)

Laboratory analyses of stored sera, at Hebrew University

- Acetylcholinesterase (AChE)
- Butyrylcholinesterase (BChE)
- Paraoxonase, Arylesterase (PON1, AryI)

#### FINAL STUDY SAMPLE FOR CURRENT ANALYSES

<u>Wave II participants:</u>	602
• enzymes not measured	- 25
<u>Full study cohort:</u>	577
• non-white or female veterans	- 89
<u>Final study cohort:</u>	488

ORIGINAL HYPOTHESES

1. Mood and anxiety symptoms are associated with selected blood enzyme levels
2. Deployed (vs. non-deployed) Gulf War veterans have lower capacity to increase blood AChE levels
3. Veterans with (vs. without) symptoms of Gulf War Veterans Illness (GWVI) have lower capacity to increase blood AChE levels under challenge

INTERIM SUMMARY

1. Findings not consistent with original hypotheses regarding association of anxiety or mood disorders and AChE or other enzyme levels in this population
2. Deployment status not associated with AChE or other enzyme levels
3. Symptoms of GWVI were not strongly associated with AChE or other enzyme levels

ADDITIONAL "CANDIDATE" ANALYSES

1. Immunoassays for splice variant of AChE [AChE-R]

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#### ANALYSIS OF AChE-R

Original protocol: *If blinded testing of serum identifies a significant decrease in total AChE activity on the basis of mood and anxiety symptoms, immunoassays for the level of the "readthrough" splice variant of acetylcholinesterase will be conducted.* [No association found]

Revised hypotheses under discussion: approval for analyses given

#### ADDITIONAL "CANDIDATE" ANALYSES

1. Immunoassays for splice variant of AChE [AChE-R]:
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2. Comparison of enzyme activity among veterans v.s. available database of U.S. adults

#### ADDITIONAL "CANDIDATE" ANALYSES

1. Immunoassays for splice variant of AChE [AChE-R]:
  - not yet done, based on results of planned analyses
2. Comparison of enzyme activity among veterans vs. available database of U.S. adults:
  - methodological issues re: sampling, clustering, covariates

#### COMPARISON TO "HEALTHY" POPULATION

##### Methodological problems related to:

- sampling differences (e.g., race, geographic location)
- clustering effects (e.g., siblings, offspring)
- covariates (e.g., age, body mass index, meds, acute illness)

Cogent hypothesis not yet developed

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2. Comparison of enzyme activity among veterans vs. available database of U.S. adults:
  - methodological issues re: sampling, clustering, covariates
3. Examination of self-reported exposures and enzyme levels

ADDITIONAL "CANDIDATE" ANALYSES

1. Immunoassays for splice variant of AChE [AChE-R]:
  - not yet done, based on results of planned analyses
2. Comparison of enzyme activity among veterans vs. available database of U.S. adults:
  - methodological issues re: sampling, clustering, covariates
3. Examination of self-reported exposures and enzyme levels:
  - results presented today

FORMAT FOR CURRENT ANALYSES

- Enzyme levels assigned as outcome variables in multiple linear regression analyses; results presented as difference in values (nmol/min/ml) for exposed vs. non-exposed
- Models done both unadjusted and adjusted for: age, BMI, smoking, acute illness, antidepressant medications, alcohol/drug use, case-control status in original Iowa study

DEMOGRAPHIC AND SERVICE CHARACTERISTICS  
(N=577)

Age ( $\pm$ std dev)	mean 39 ( $\pm$ 9) yrs
Education $\geq$ some college	65%
Employed	90%
Married or living with partner	72%
Gulf Service	
• Regular military	32%
• Guard/Reserve	68%
• Deployed	72%

[87% male, 97% white]

OTHER CHARACTERISTICS  
 (N=577)

Hypertension	13%
Coronary artery disease	2%
Drug abuse/dependence	2%
Alcohol abuse/dependence	6%
Antidepressant use	9%
Antipsychotic use	<1%
Post-traumatic stress disorder:	
• deployed	9%
• non-deployed	3%

OVERALL RESULTS FOR ENZYME LEVELS  
 (NMOL/MIN/ML; N=577 FULL COHORT)

Enzyme	Range	Median	Mean ± sd
AChE	130-2908	839	882 ± 362
BChE	142-11412	5053	5065 ± 1476
PON	3-185	38	43 ± 25
ARYL	0-46	18	17 ± 7

SELF-REPORTED EXPOSURES AMONG DEPLOYED  
 (N=414)

Est. mean (std dev) days in Gulf	154 (±77)
Vaccinations	11 (±19)
Pyridostigmine tabs	25 (±69)
Chemical attack alert	81%
Chemical warfare agents	8%
• nerve gas	9%
• mustard gas/blistering agent	3%
Pesticides	63%
• personal creams, etc.	60%
• clothing or bedding	36%

SELF-REPORTED EXPOSURES AMONG DEPLOYED  
 (N=414)

Petrochemicals/solvents	93%
Smoke/combustion products	95%
Sources of infectious agents	91%
Sources of lead from fuels	88%
Ionizing/non-ionizing radiation	23%
Physical trauma	6%
Heat stress	23%
Psychological stressors	35%

*[OTHER TABLE AND FIGURES BEING CHECKED*

*PRIOR TO PUBLICATION]*

SUMMARY AND CONCLUSIONS

Most self-reported exposures (vs. non-exposures)  
not associated with difference in enzyme levels

Given multiple comparisons and other methodological  
issues, limited evidence exists re: associations  
(e.g., petrochemicals and PON)

Results can help inform future proposals and protocols