Appendix A
Presentation 1 - John Concato

ACETYLCHOLINESTERASE ACTIVITY IN GULF WAR

DEPLOYED AND ERA VETERANS: FEB '04 UPDATE

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BACKGROUND RE: 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, Aryl)

RESEARCH 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

OVERVIEW OF CURRENT STATUS

- Transfer of questionnaire data, review of data dictionaries,
  definition and coding of variables completed

- Blood samples shipped; laboratory analyses of AChE, BChE,
  PON1, and Aryl enzymes completed

- Analyses of initial hypotheses conducted; other analyses
  ongoing or under consideration

FINAL STUDY SAMPLE FOR CURRENT ANALYSES

Wave II participants: 602

    • enzymes not measured   - 25

    • non-white or female veterans   - 89

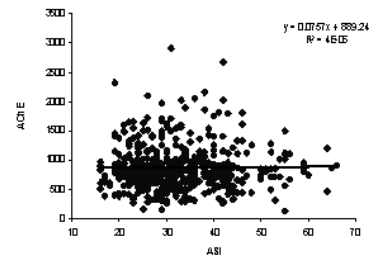   -114

Final study population: 488

FORMAT FOR CURRENT ANALYSES

• Enzyme levels assigned as outcome variables in multiple
  linear regression analyses; results presented as predicted
  least square mean values (nmol/min/ml) for each enzyme

• Models done both unadjusted and adjusted for:
  a) age, BMI, smoking, acute illness
  b) *plus* antidepressant medications or alcohol/drug use
  c) *plus* case-control status in original Iowa study,
     for analyses of deployed vs. non-deployed veterans

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1. ASSOCIATION OF ANXIETY AND ENZYME LEVELS

Stress responses involve several neural pathways, and disease-
  associated changes in AChE and other enzymes
  might be expected among patients manifesting anxiety
  or mood symptoms

Prior work (in a "healthy" population) found a strong
  negative correlation between anxiety measures and AChE

ASSOCIATION OF ANXIETY AND ENZYME LEVELS

CURRENT ('STATE') AND LIFETIME ('TRAIT') ANXIETY

Predicted, adjusted mean enzyme levels (and P values), N=476:

	AChE	BChE	PON1	Aryl
Current:				
Yes	887	5038	45.7	17.0
No	893	5155	41.8	17.6
	(0.88)	(0.48)	(0.16)	(0.49)
Lifetime:				
Yes	884	5042	45.1	17.1
No	895	5162	41.7	17.6
	(0.80)	(0.45)	(0.19)	(0.55)

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2. ASSOCIATION OF DEPLOYMENT AND ENZYME LEVELS

Prior work suggested that external stimuli (e.g., extreme weather, stress, medications) could induce activation of AChE expression and affect enzyme activity

Deployment to the Persian Gulf region could be associated with a decrease in AChE enzyme activity due to enhanced degradation or suppressed production

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ASSOCIATION OF DEPLOYMENT AND ENZYME LEVELS

Predicted, adjusted mean enzyme levels (and P values), N=476:

	AChE	BChE	PON1	Aryl
Deployed				
Yes:	885	5069	42.5	17.2
No:	913	5304	43.3	18.3
	(0.49)	(0.14)	(0.74)	(0.16)

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3. ASSOCIATION OF GWVI AND ENZYME LEVELS

Pertinent symptoms reported at Wave I or II were linked to CDC criteria for GWVI (e.g., involving 2 of 3 axes re: mood-cognitive, fatigue, musculoskeletal symptoms)

GWVI: Definition 1 - onset of symptoms after Gulf War, present at Wave II, regardless of status at Wave I; Definition 2 - onset after Gulf War, present at Wave I and Wave II (subset with longer duration of symptoms)

Analyses of GWVI done for deployed and non-deployed veterans

GULF WAR VETERANS ILLNESS: DEFINITION 1

Predicted, adjusted mean enzyme levels (and P values), N=476:

	AChE	BChE	PON1	Aryl
Deployed				
GWVI	892	5015	42.8	17.4
No GWVI	878	5165	42.2	17.0
	(0.78)	(0.41)	(0.85)	(0.67)
Non-Dpld				
GWVI	890	5107	43.8	18.1
No GWVI	928	5595	41.7	18.4
	(0.61)	(0.14)	(0.72)	(0.85)

GULF WAR VETERANS ILLNESS: DEFINITION 2

Predicted, adjusted mean enzyme levels (and P values), N=474:

	AChE	BChE	PON1	Aryl
Deployed				
GWVI	933	4979	41.4	17.1
No GWVI	854	5129	43.5	17.4
	(0.08)	(0.38)	(0.46)	(0.70)
Non-Dpld				
GWVI	965	5207	35.6	16.5
No GWVI	886	5341	45.1	18.7
	(0.32)	(0.70)	(0.11)	(0.24)

SUMMARY

Findings not consistent with original hypotheses regarding
association of anxiety or mood disorders and AChE
or other enzymes in this population

Deployment status did not affect AChE or other enzymes

Symptoms of GWVI were not strongly associated with AChE
or other enzymes