Neuropsychological Functioning of U.S. Gulf War Veterans

10 years after the war

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- Harvard Medical School, Psychiatry
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Journal of the International Neuropsychological Society, 2009, 15, 717-729.

National Health Survey of Gulf War Veterans and Their Families

- Congressional Mandate

- VA Cooperative Study #458

- Three Phases:
    - Telephone and Mail Survey (1995)
    - Medical Record Review
    - In Person Examination

Study Principal Investigators

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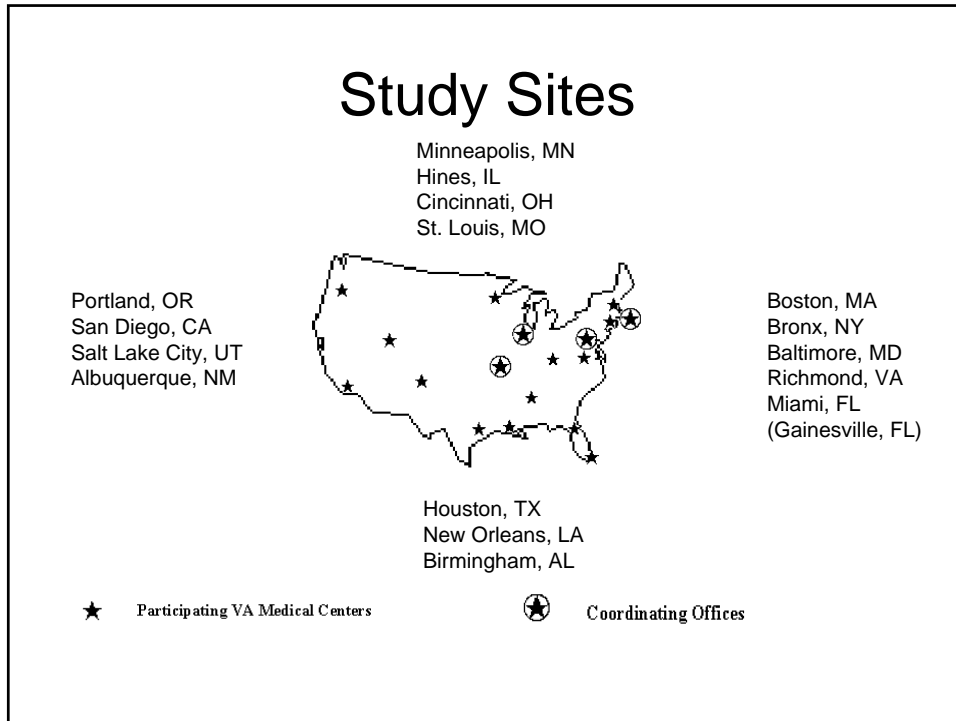 - San Diego VA Healthcare System, UCSD

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Subject Flow

	Deployed Veterans	Non-Deployed Veterans
Target Population	693,826	800,680
Phase 1 Study Population	15,000	15,000
Phase I Participants	11,441	9,476
Phase 3 Study Population	1,996	2,883
Phase 3 Participants	1.061	1,128

Phase 3 Participation

	Deployed Veterans	Non-Deployed Veterans
Recruited	1,996	2,883
Examined	1,061 (53.1%)	1,128 (39.1%)
Refused	680 (34.1%)	1,316 (45.7%)
Could not locate	255 (12.8%)	439 (15.2%)

Study Sites

Minneapolis, MN
Hines, IL
Cincinnati, OH
St. Louis, MO

Portland, OR
San Diego, CA
Salt Lake City, UT
Albuquerque, NM

Boston, MA
Bronx, NY
Baltimore, MD
Richmond, VA
Miami, FL
(Gainesville, FL)

Houston, TX
New Orleans, LA
Birmingham, AL

★ Participating VA Medical Centers   ⍟ Coordinating Offices

Sociodemographic Characteristics

Characteristic	Deployed n = 1061	Non-deployed n = 1128	P-value
Mean Age (SD)	38.9 (8.8)	40.7 (9.6)	0.001
Sex, % Male	78%	78%	0.99
Race, % Cauc.	76.4%	80.0%	0.03
Education, %			0.001
<HS	1.8%	2.0%	
HS	65.7%	56%	
College	19.8%	22.1%	
Postgraduate	12.7%	19.9%	
Mean Income $1,000s (SD)	46.8 (32.6)	52.0 (44.3)	0.003

Military Characteristics

Characteristic	Deployed n = 1061	Non-deployed n = 1128	P-value
Active Duty	7.8	8.5	>0.2
Rank, %			
Enlisted	85.7	80.4	0.001
Officer	14.3	19.6	
Branch			0.22
Army	64.6	62.9	
Navy	12.0	13.6	
Air Force	11.9	13.7	
Marines	11.6	9.8	
Unit, %			
Reserves	36.3	36.9	0.78
Active	35.2	35.9	
Nat. Guard	28.6	27.2	

Neuropsychological Measures

- WAIS-III Digit Span
- Trail Making Test
- Paced Auditory Serial Arithmetic Test
- Continuous Performance Test
- Wisconsin Card Sorting Test
- California Verbal Learning Test
- Rey-Osterrieth Complex Figure Test
- Finger Tapping Test
- Purdue Pegboard Test

- Test of Memory and Malingering
- WRAT-III Reading Subtest

Factor Analysis

- Verbal Memory
- Attention/Working Memory
- Visual Memory
- Executive Functioning
- Perceptual Motor Speed
- Visual Organization
- Motor Speed
- Sustained Attention

Factor Analysis

- Verbal Memory
  - » 9 CVLT variables
- Attention/Working Memory
  - » Digit Span forwards and backwards
  - » PASAT Trial 1 correct
- Visual Memory
  - » Rey Accuracy (IR & DR)
- Executive Functioning
  - » WCST categories & perseverations

Factor Analysis

- Perceptual Motor Speed
    - » Purdue Pegboard, both hands
- Visual Organization
    - » Rey Organization (Copy, IR & DR)
- Motor Speed
    - » Finger Tapping, both hands
- Sustained Attention
    - » CPT sensitivity & mean reaction time

Prevalence of Neuropsychological Impairment -(2SD)

Neuropsychological Impairment	Deployed Veterans	Non-Deployed Veterans	p-value
Verbal Memory	4.1%	3.0%	0.17
Attention/Working Memory	1.8%	0.7%	0.41
Visual Memory	2.2%	4.3%	0.20
Executive Functioning	4.3%	5.9%	0.18
Perceptual Motor Speed	1.8%	2.0%	0.42
Visual Organization	3.0%	5.0%	0.046
Motor Speed	2.6%	1.4%	0.02
Sustained Attention	3.7%	1.7%	0.02

Neuropsychological Functioning
Other Analyses

- Group comparisons on mean factor scores

    - All non-significant

- Group comparisons on individual test variables

    - 4 out of 27 variables where deployed veterans perform worse

        » Trails A time
        » Trails B-A time
        » CVLT List B number correct
        » CPT sensitivity

    - Only Trails B-A result survives Bonferroni correction

Neuropsychological Functioning
Relationship to Psychiatric Symptoms

- Focused on variables capturing worse performance among deployed veterans
    - Factor of motor speed
    - Factor of sustained attention
    - Individual test variable Trails B-A time

- Symptom measures
    - PTSD Symptom Checklist (PCL)
    - Beck Depression Inventory-II (BDI)
    - Beck Anxiety Inventory (BAI)

Neuropsychological Functioning
Relationship to Psychiatric Symptoms

- Regression analyses

- High intercorrelations of PCL, BDI, BAI

- Models tested for all combinations and interactions

Motor Speed	Symptom predictors ns
Sustained Attention	PCL and deployment BDI and deployment
Trails B-A	Symptom predictors ns

Neuropsychological Functioning
Relationship to Deployment Factors

- Logistic Regression Analyses
- Dependent variables
  - Mean score on all 8 neuropsychological factors
- Independent variables
  - Symptoms (PCL, BDI, BAI)
  - Chronic multisystem illness status
  - Khamisiyah exposure status
  - Self-reported exposure to toxic substances
  - Covariates:
    - age, sex, race, education, WRAT-3

Self-Reported Exposure

While in the Persian Gulf, do you believe you were exposed to or did you experience any of the following?

Respondents replied "yes" vs "no"

If "yes", a follow up question assessed of "How many days were you exposed" ($\leq$ 5, 6-30, $\geq$ 31)

Self-Reported Exposure
NOT explaining neuropsychological factors

	Prevalence in Deployed Vets
➤ Smoke from oil well fires	68%
➤ Diesel, kerosene and/ or petrochemical fumes (including tent heater or vehicle exhaust) OR	83%
Skin exposure to diesel or other petrochemical fuel	61%
➤ Burning trash/feces	61%
➤ Depleted Uranium	9%
➤ Microwaves	27%
➤ Ciprofloxacin	16%

Self-Reported Exposure
explaining neuropsychological factors

Prevalence in
Deployed Vets

➢ Chemical Agent Resistant Compound (CARC)　　　　22%
　 OR
　 Other paint or solvent and/or petrochemical substances　　30%

➢ Personal pesticides, including creams, sprays, or flea collars　49%

➢ Nerve gas　　　　　　　　　　　　　　　　　　10%

➢ Ate food contaminated with smoke, oil, or other chemicals　33%
　 OR
　 Bathed in/drank contaminated water　　　　　　　29%

➢ SCUD Missile explosions (air or ground) within one mile　42%

Self-Reported Exposure
explaining neuropsychological factors

Prevalence in
Deployed Vets

➢ Immune Globulin　　　　　　　　　　　　　64%

➢ Pyridostigmine bromide pills　　　　　　　　　49%

➢ Vaccines (any ONE of)
　　 Anthrax　　　　　　　　　　　　　　　44%
　　 Typhoid　　　　　　　　　　　　　　　61%
　　 Botulism　　　　　　　　　　　　　　　15%
　　 Plague　　　　　　　　　　　　　　　　25%
　　 Meningococcus　　　　　　　　　　　　15%

Predictors of mean neuropsychological factor scores

Indep. Variable	Verb. Mem.	Atten./ WM	Visual Mem.	Exec. Func.	PM Speed	Vis. Org.	Motor Speed	Sustained Attention
CMI								X(BDI)
Kham.	X(X)						X(X)	
CARC+			X(X)					
Pest.								X(BDI)
N. Gas								X(BDI)
Contam+								X(X+BDI)
Scud					X(X)			X(BDI)
IG			X(X)					
Vaccines	X(X)				X(X)			
PB								X(BDI)

Summary

- Deployed veterans are more likely impaired on factors of motor speed and sustained attention and an individual variable measuring divided attention

- PTSD, depressive symptoms only explain performance on sustained attention, although deployment remains a significant predictor

Summary

- Deployment factors predict some aspects of neuropsychological functioning that do not differentiate deployed vs. nondeployed, namely memory and perceptual motor speed.

- Symptoms do not explain these relationships.

Summary

- For the neuropsychological factors differentiating deployed and nondeployed:

  - Khamisiyah exposure relates to motor speed

  - Self-reported exposures relate to sustained attention, in combination with symptoms

Discussion Themes

- Objective measurement of cognition

- Whole group vs. subgroup

- "Normal" functioning

- Symptoms as cause or effect

Other Study Findings:
Mental Disorders

Onset of mental disorders in the GW era (1/1/91-7/30/93) were more prevalent in deployed veterans (18.1%) than nondeployed veterans (8.9%). Although depression and anxiety declined over 10 years, they remained higher in the deployed group, who also had more psychological symptoms by self-report and lower quality of life 10 years later.

Toomey et al., 2007
British Journal of Psychiatry

Other Study Findings:
Medical Health

Physical health of deployed and nondeployed veterans was similar. Of 12 conditions assessed, 4 were more prevalent among the deployed: fibromyalgia (2.0 vs. 1.2%), chronic fatigue syndrome (1.6 vs. 0.1%), dermatologic conditions (34.6 vs. 26.8%), and dyspepsia (9.1 vs. 6.0%).

Eisen et al., 2005
Annals of Internal Medicine

Other Study Findings:
Chronic Multisymptom Illness

CMI was more prevalent in deployed veterans (28.9%) than nondeployed veterans (15.8%). CMI manifested similarly in both groups in terms of associated medical and psychological conditions and quality of life.

Blanchard et al., 2006
American Journal of Epidemiology

Other Study Findings:
Pulmonary Functioning

Deployed veterans were more likely to report a history of smoking and wheezing than nondeployed veterans, but there were no group differences in the amount of physician visits in the previous year for pulmonary complaints or performance on pulmonary function tests.

Karlinsky et al., 2004
Archives of Internal Medicine

Other Study Findings:
Neurology Exam

There were no group differences in distal symmetric neuropathy, as measured by electrophysiology, neurological exam, or the two methods combined. Khamisiyah exposed and non-exposed deployed veterans also did not differ from each other.

Davis et al., 2004
Neurology