Presentation 2 – Tom Findley

Chemical Sensitivities

Fiedler 1996

- Persian Gulf Registry 1995
- 200 NE vets with, 228 w/out fatigue as medical complaint mail questionnaire
- 89% 63% fatiguing illness
- 39% 30% report chemical sensitivity
- 33 19% car exhaust
- 20 11% Perfume

Past Gulf War Research

Thomas Findley, M.D., Ph.D
WRIISC Associate Director for Research

Medical Evaluation of Vets With Fatigue, Chemical Sensitivity

Pollet 1998

- Medical exam of 72 complaints of fatigue, chemical sensitivity
  - Excludes self report of manic/depressive, schizophrenia, eating disorder, head trauma, age over 57
- 4 medical reasons for fatigue (3 focal weakness, 1 lyme)
- 15 psychiatric diagnoses (4 etoh, 7 mania, 3 schizo, 1 eating)
- 33 (62%) CFS
- 4 idiopathic CFS
- 14 cfs/mcs
- 6 mcs

- Veterans vs civilians with CFS,
  - Gradual onset (92 vs 21%)
  - Able to work (87 vs 54)
  - CFS severe (25 vs 61%)
  - Bed day/month (2 vs 3.5)
  - MCS also (29 vs 13%)

Prevalence of Chronic Fatigue and Chemical Sensitivity
Kipen 1999

- 68,000/700,000 GW vets in VA registry
- 2,011 randomly selected from 7 states; excluded persons in other major studies
- DE, IL, NJ, NY, NC, Ohio, PA
- 1161 (60%) response rate; 1000 answered CFS MCS questions (10% female)
- 34% CFS symptoms
  16% no other cause for fatigue
- 36% chemical sensitivity
  13% ≥ 3 lifestyle change
  OR 2 in women and African American

- No case definition for Gulf War Syndrome
- 16% VA gulf war registry meet CFS case definition
  - **Minimum 6 month fatigue**
  - **Substantial decrease in activity**
  - **At least 4 symptoms:**
    - Impaired memory or concentration
    - Sore throat
    - Tender lymph nodes
    - Muscle/multi joint pain
    - Headaches
    - Unrefreshing sleep
    - Postexertional malaise

Symptom Patterns
Hallman 2003

- 1161 responses
- 981 self reported medical problem due to gulf service
- Cluster analysis
- Mild illness in 60%
- Severe illness in 40%

- Factor analysis
- Mood memory fatigue – depression, anxiety, sleep
- Musculoskeletal - pain numbness in muscle or joint
- GI - abdominal pain, gas, diarrhea, nausea vomiting
- Throat breathing problems

Medical Followup

Natelson 2001

- **76 with CFS/ICF examined**
  - 34 axis I psychiatric illness beginning before GW
    - 31 continued after GW
  - 42 no axis I before
    - 21 developed axis I after
- **2 year followup**
  - 44 returned questionnaire
  - 13/26 came for repeat exam
  - symptom, symptom severity, job impact unchanged

Quantitative Sensory Testing

Peckerman 2000

- 29 GV with 1994 CDC CFS
  - 24% smokers
- 31 healthy GV
  - 3% smokers
- Vibration no difference
- Thermal no difference
- Tactile elevated in GV CFS compared to GV healthy;
- Both higher than civilian CFS healthy
- Higher tactile – self reported exposure to PB, burning human waste

Cardiovascular Response

Peckerman 2000

- 51 GV with CFS/ICF; 42 healthy GV
- Forehead cold pressor no difference
- Speech stressor
- Arithmetic stressor
- CFS GV little change in total peripheral resistance with cognitive stress
- Sedentary persons show heightened response to stress

Cardiovascular CFS and PTSD

Peckerman 2003

- **Subjects**
  - 55 GV with CFS (ICF)
    - 16 PTSD
    - 39 no PTSD
  - 47 healthy GV
- **Forehead cold pressor**
- **Speech stressor**
- **Arithmetic stressor**
- **Tilt table**

Aerobic Capacity

Nagelkirk 2003

- Background
  - No case definition for Gulf war Syndrome
  - Used CDC CFS case definition
  - CFS exercise capacity inconsistently reported – low or low normal
- Subjects
  - 15 GV with CFS (3 female, 12 male)
  - 19 control sedentary GV

- Procedure
  - Bicycle ergometer
- Results
  - Both CFS and controls in 10th percentile
  - Ve/O2 and Ve/CO2 at 0 watts higher in controls (lower O2 by 15%)
  - Ventilation at peak higher in controls (30%)
  - Trend to higher RER, workload (10%), HR (5%)

Perceived Exertion

Cook 2003

- Background
  - Perceived Exertion during exercise elevated in CFS
  - Lower maximum capacity
  - No elevation in RPE in exercise as a percent of peak capacity
  - VO2 max and VE same
  - 15 GV with CFS
  - 19 healthy GV

  - RPE elevated in GV CFS at both absolute and relative intensity
  - VO2 max similar, but ventilation VE 20% lower in CFS (-1 SD)

Muscle Function and EMG

Unpublished Data

- Background
  - Inconsistent nerve conduction and strength findings
  - Our finding of elevated sensory thresholds
  - 34 GV with muscle symptoms
  - 25 normal GV

- Decreased speed up and down stairs; walking
- EMG abnormalities 7/33 (21% vs 0%)
- 10 decreased interference pattern at maximum
- 5 increased polyphasic
- 6 decreased recruitment with increase in recruitment frequency
- 20% decrease in CSA in those with EMG change (similar to immobilization)

Fatigue and ACE Polymorphism

Vladutiu 2004

- Background
  - Myoadenylate deaminase (AMPD1)
  - Carnitine palmitoyltransferase (CPT)
    - Myopathies with pain, fatigue after exercise
  - I/D polymorphism in intron 16 of ACE gene (DCP)
    - I allele – decreased ACE activity, enhanced endurane
    - D allele – increased MI, CAD, LVH
      - DD 71% triple vessel, 54% single vessel CAD

- Study Population
  - 61 nonveterans with CFS (mostly female)
  - 49 veterans with ICF or CFS
  - 45 healthy Nonveterans
  - 30 healthy veterans

- Results
  - AMPD1, CPT – no difference or trend between groups
  - DCP
    - 85% D allele, 78% DD in veterans with ICF, CFS
    - 50% D allele in normal veterans, CFS and normal non veterans

Psych Diagnoses

Lange 1999

- 47 healthy
- 100 fatigued GV from 10 states, GW registry

- 17 medical cause for fatigue
- 19 Etoh, schizo, mania eating disorder

- 53 CFS, ICF, MCS
- 42 healthy

- CFS 62% Axis I – 36% depression, 21% PTSD, phobias
- CFS 40% more than one DX
- Healthy 14%

PTSD

Natelson 2001

- 76 CFS, ICF GV

- 50% PTSD

- PTSD
  - Kang 2003
  - 11,000 GV
  - 9,000 non GV

Stressors

Fiedler 2000

- 164 vets with fatigue examined
- 45 healthy GW Vet
- 35 CFS with psych
- 23 CFS no psych

- CFS vs healthy
  - More stressors during and after the war
  - More negative coping strategies
  - More neuroticism, defensiveness

- Self reported stressors

Cognitive Function

Lange 2001

- 39 healthy
- 48 GW vet with fatigue
  - 27 CFS
  - 17 CFS MCS
  - 4 MCS
  - 42% Major depressive disorders
  - 29% Anxiety disorders
  - 21% PTSD

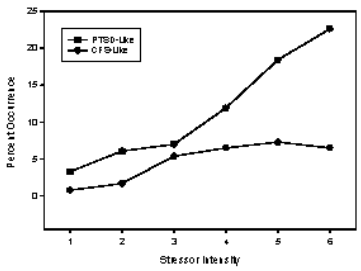
- 25% increase simple reaction time
- 10% increase complex reaction time
- Digit span backwards
- PASAT
- Trail making test

- Effect of mental disorders
- Depression – decreased simple and complex reaction time, PASAT
- Anxiety – PSAT
- PTSD – not related
- GWI still associated with simple reaction time; not complex or PASAT

PTSD

Kang 2003

- 700,000 deployed to gulf
- 800,000 not deployed to gulf
- Sampling stratified by sex, active/reserve/natl guard, branch of service
- 15,000 deployed GW vets
- 15,000 non gulf vets
- 70% response rate



- CFS 5.6% vs 1.2%
- PTSD 12% vs 4.3%
- Combat exposure – chemical gear or alarm, witness death, actual combat
- PTSD increases with increased combat
- CFS does not
- Both increase if national guard activated or deployed to gulf

Immune Function

Zhang 1999

- 43 GW vet with CFS (31 Axis 1)
- 34 healthy GW vet (6 axis 1)
- 68 civilian with CFS (33 axis 1)
- 53 healthy civilian (0 axis 1)

- No changes in civilians with CFS
- Veterans with CFS show type 1, inflammatory response
  - More total and % T cell
  - More total and % MHC II+ T cell
  - Less percent NK cells
  - Higher IL-2, IL-10, IFN-gamma, TNF-alpha
  - Trend to higher IL 4, LI 6, LI 12

Immune and Cognitive Function

Brimacombe 2002

- 40 GW vet with CFS
- 33 health GW vet
- 28 civilian with CFS
- 31 healthy civilian

- Immune function related to CFS
- Reaction time higher in GW and civilians with CFS
- Only lymphocytes significant (.06) when reaction time included in model
- Education and reaction time most significant

- SF36 general health, physical function, mental health, social function
- Education and reaction time highly related in veterans with CFS
- Only reaction time in civilians for all but mental health
- TH2 and lymphocytes related to SF36 in vets
- Only lymphocytes remain when reaction time included