UNITED STATES
DEPARTMENT OF VETERANS AFFAIRS

Psychobiology of Pain and Exercise in Gulf War Veterans with Chronic Musculoskeletal Pain

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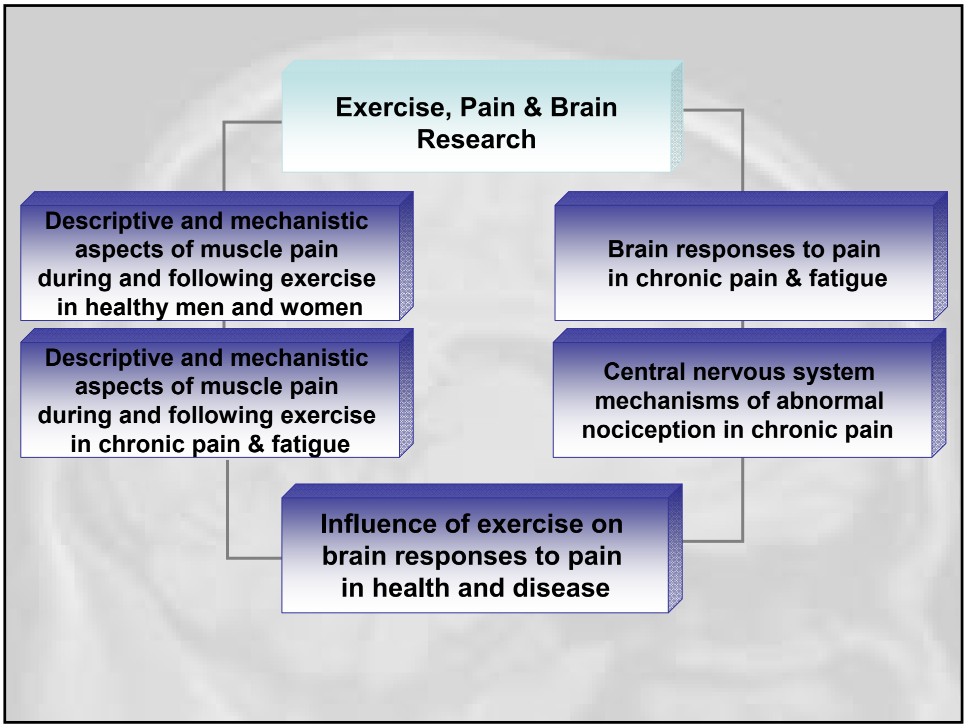
Chronic musculoskeletal pain in Gulf War Veterans

- 15% (100,000 of ~700,000) report chronic muscle pain symptoms (Kang et al., 2000)
- One of three major factors of Gulf War illness (Fukuda et al., 1997).
- Reported twice as frequently (OR=3.06) in Gulf War Veterans (GVs) than non-GVs (Kang et al., 2000; Thomas et al., 2006)
- Estimated 1 in 7 seek health care for war-related concerns and 12% receive disability compensation (Engel et al., 2004; DVA report, 1998; Hodgson & Kipen, 1999; Kang et al., 2000)
- Follow-up data indicate that symptoms have not resolved (Blanchard et al., 2006; Ozakinci et al., 2006; Thomas et al., 2006)



Today's Presentation

- Exercise alters pain sensitivity in Gulf War Veterans (GVs) with chronic musculoskeletal pain (CMP)
  - Follow-up functional brain imaging study
- Functional brain imaging of chronic musculoskeletal pain
  - Past, present and future
- Overview of Merit Review exercise training project
  - Exercise, pain, brain function & structure

Exercise alters pain sensitivity in Gulf War Veterans with chronic muscle pain

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Pathophysiological mechanisms that may maintain CMP

- Fibromyalgia (FM):
  - Chronic musculoskeletal pain disorder
- The mechanism for maintenance of pain and other symptoms in FM is unknown
- Research suggests that FM pain is maintained by abnormal central nervous system regulation of sensory stimuli
  - Behavioral data
    - More sensitive to experimental pain stimuli
    - Altered modulation – DNIC & wind-up
    - **Do not exhibit exercise-induced hypoalgesia (EIH)**

Purpose & Hypotheses

- To determine the impact of an acute bout of exercise on pain sensitivity in GVs with CMP compared to healthy GVs
- **GVs with CMP:**
  - H1: Report lower pain thresholds and higher pain ratings than healthy GVs
  - H2: Rate naturally occurring muscle pain during exercise as more intense than healthy GVs
  - H3: Not demonstrate EIH, but instead become more sensitive to experimental pain stimuli following acute exercise

Methods

- **N = 32 participants (WRIISC)**
  - n= 15 GVs with widespread & chronic muscle pain
  - n= 17 GVs healthy and without pain
- **Testing to occur on 2 separate days**
  - Maximal exercise testing (ACSM)
  - Submaximal exercise testing and pain psychophysics
    - **Psychophysical pain assessment**
    - **Exercise @ 70% of peak oxygen consumption for 30 minutes followed by 3-minute active recovery**
    - **Psychophysical pain assessment**

Method

- **Muscle Pain & Exertion**
  - **Leg-muscle pain (0-10)**
  - **Perceived exertion (RPE – 6-20)**
- **Psychophysical Pain Assessment:**
  - Heat pain thresholds – thenar eminence non-dominant hand
  - Pressure pain thresholds (~3000g), middle digit non-dominant forefinger
  - Supra-threshold heat pain rating (forearm)
    - 14 random stimuli (44-50°C)
    - Descriptor Differential Scales (intensity & affect)

Descriptor Differential Scales

Faint
□□□□□□□□□□ □ □□□□□□□X□ □

Moderate
I □□□□□□□□□□ □ □□X□□□□□□ □

Intense
□□□□□□X□□□ □ □□□□□□□□□ □

Unpleasant
□□□□□□□□□□ □ □□□□□X□□□ □

Distressing
A □□□□□□□□□□ X □□□□□□□□□ □

Intolerable
□□□□□X□□□□ □ □□□□□□□□□ □

Results

Table 1. Demographic, Exercise and Clinical Characteristics for the Final Sample (N = 27)

	CMP (N = 11)	HEALTHY (N = 16)	E.S.
Age (y)	39.4 (±7.4)	40.9 (±7.9)	−.20
Height (cm)	176.2 (±8.6)	174.6 (±9.2)	.19
Weight (kg)	96.5 (±25.8)	90.8 (±14.2)	.30
Resting HR (bpm)	72 (±13)	65 (±11)	.63
Resting SBP (mmHg)	117 (±10)	116 (±9)	.12
Resting DBP (mmHg)	75 (±7)	77 (±7)	−.37
VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$)	28.2 (±7.7)	31.9 (±8.5)	−.47
Peak PO (watts)	169.6 (±45)	204.0 (±53)	−.69
Average PO (Submax)	82.8 (±31)	111.7 (±33)	−.90
Widespread pain complaints	11/11	0/16	—
Pain in 4 body quadrants	9/11	0/16	—
FM diagnosis	3/11	0/16	—
Current pain intensity (0–5)	3.27 (±1.1)	—	—

Abbreviations: CMP, Chronic muscle-pain patients; Healthy, Healthy controls; E.S., Effect size (calculated as Cohen's $d = \frac{\bar{x}_1 - \bar{x}_2}{s_{pooled}}$); HR (bpm), Heart rate (beats per minute); SBP, Systolic blood pressure; DBP, Diastolic blood pressure; VO_{2peak}, Volume of O_2 consumption at peak effort; PO, Power output (Watts attained at peak during maximal exercise and average watts during 30-minute sub-max exercise test).

NOTES. Current pain intensity represents pain felt in muscles and joints at clinical intake; 0 = no pain, 1 = mild pain, 2 = moderate pain, 3 = substantial pain, 4 = severe pain, and 5 = very severe.

Values in columns headed with groups represent means (±standard deviation) or proportions.

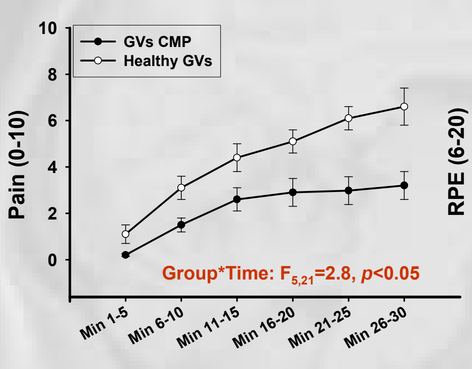
Table 2. Comparison of Pre- and Post-Exercise Heat and Pressure-Pain Thresholds Across Groups

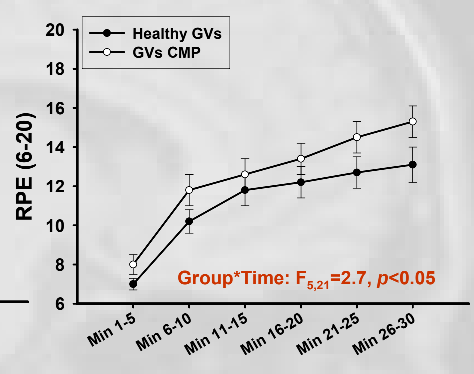
	CMP (N = 11)	HEALTHY (N = 16)	E.S.
Heat-Pain Threshold			
Pre-exercise (°C)	42.9 (±3.3)	44.1 (±3.3)	−.36
Post-exercise (°C)	43.4 (±2.8)	44.8 (±2.8)	−.52
Pressure-Pain Threshold			
Pre-exercise (sec)	22.9 (±16.0)	46.9 (±41.1)	−.75
Post-exercise (sec)	31.5 (±38.3)	49.1 (±38.6)	−.48

Abbreviations: CMP, Chronic muscle-pain patients; Healthy, Healthy controls; E.S., Effect size (calculated as Cohen's $d = \frac{\bar{x}_1 - \bar{x}_2}{s_{pooled}}$).

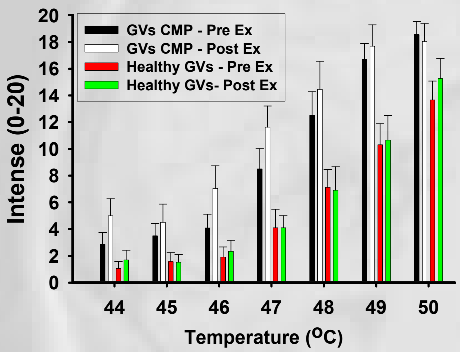
NOTES. Values in columns headed with group names represent means (±standard deviation) for respective variables. The means in this table were compared with a Group × Trial (2 × 2) repeated-measures ANOVA with no significant main effects or interactions found. Effect sizes for the within-group differences across trials (pre- vs post-exercise) were all small (ie, $d < .3$).

GVs with CMP perceive exercise as more painful and effortful than healthy GVs

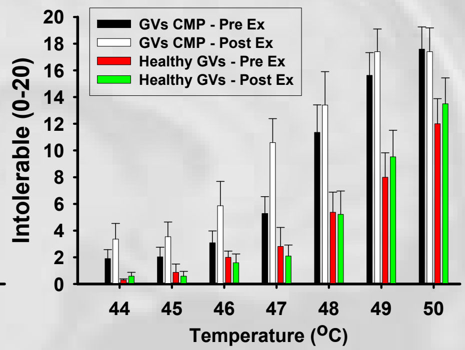




GVs w/ CMP are more sensitive to heat pain than healthy GVs and become more sensitive following acute exercise

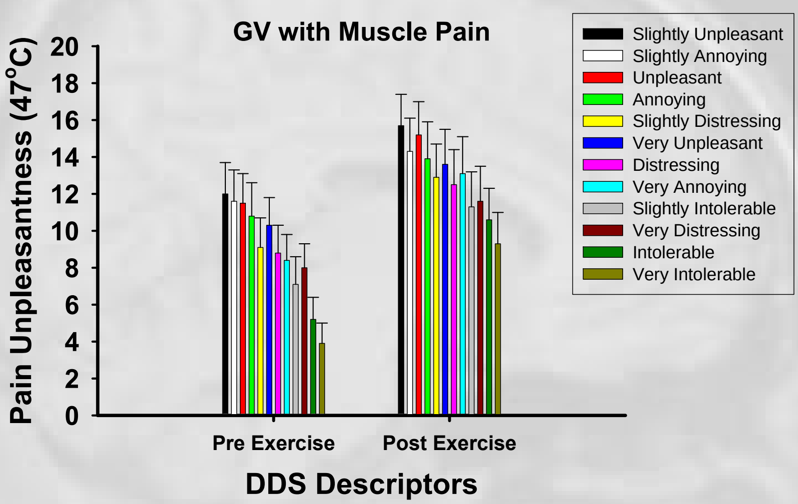


Group*Trials*Time: $F_{6,20}$=2.7, p<0.05



Group*Trials*Time: $F_{6,20}$=5.9, p<0.01

GVs with CMP demonstrated large inceases in affective pain ratings from pre- to post-exercise



Conclusions

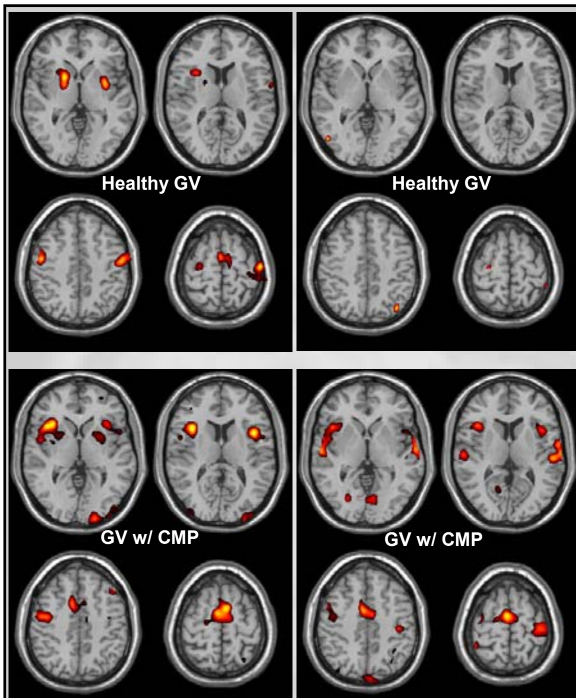
- GVs with CMP:
  - Are more sensitive to experimental heat pain stimuli than healthy GVs
  - Perceive sub-maximal exercise as more painful & effortful than healthy GVs
  - Describe experimental pain stimuli as more intense and more unpleasant following 30 minutes of moderately intense, submaximal exercise

Take Home Point

- Data are consistent with psychophysical & exercise literature for FM & suggest that the central nervous system of GVs with CMP are not properly regulating sensory information.
- GVs with CMP do not exhibit EIH, but instead become hyperalgesic following an acute bout of exercise.

Functional Imaging of Pain in Veterans with Unexplained Muscle Pain

Department of Veteran Affairs Grant:
Merit Review Entry Program Project



Functional MRI data suggesting augmented 'pain-relevant' brain activity to non-painful warm stimuli in GVs with CMP

Take Home Point

- Similar to our work in FM, GVs with CMP exhibit augmented brain responses to both non-painful and painful sensory stimuli.
- It is currently unclear whether this is a result of enhanced processing or decreased regulation of nociceptive information.

Imaging the cognitive modulation of pain in CMP

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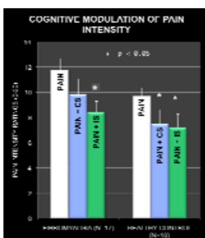
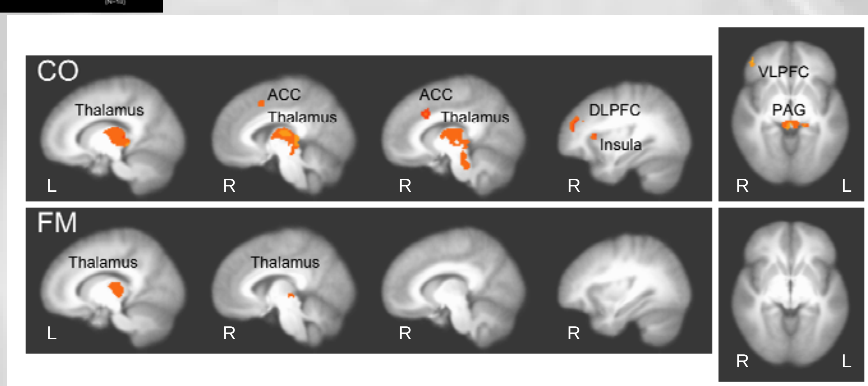
Determine the influence of anticipation & attention on brain responses to pain

- Anticipation manipulated by randomly assigning participants to ‘pain’ and ‘no pain’ conditions
- Attention manipulated by having participants complete the Stroop color-word task while receiving painful stimuli

Results- Incongruent Stroop

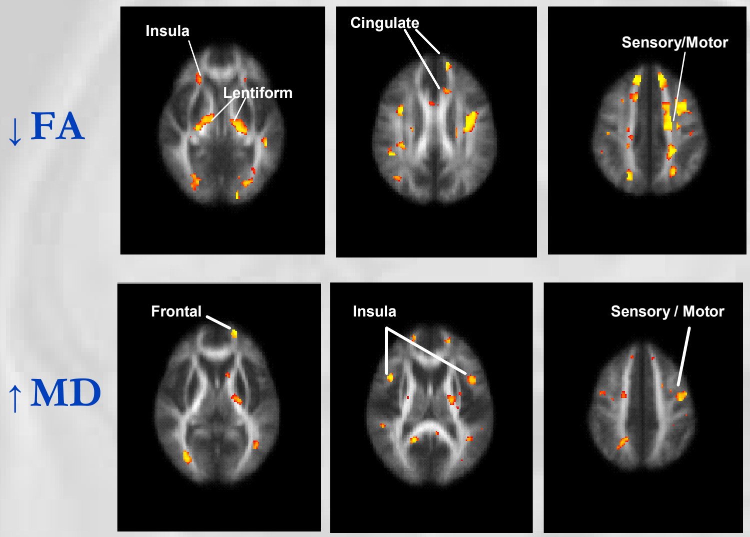


Brain activity associated with the Stroop task during pain accounting for Stroop alone and pain alone



2 groups x 3 tasks repeated measures ANOVA, $p < 0.005$

Diffusion tensor imaging data demonstrating decreased fractional anisotropy and increased mean diffusivity in chronic muscle pain



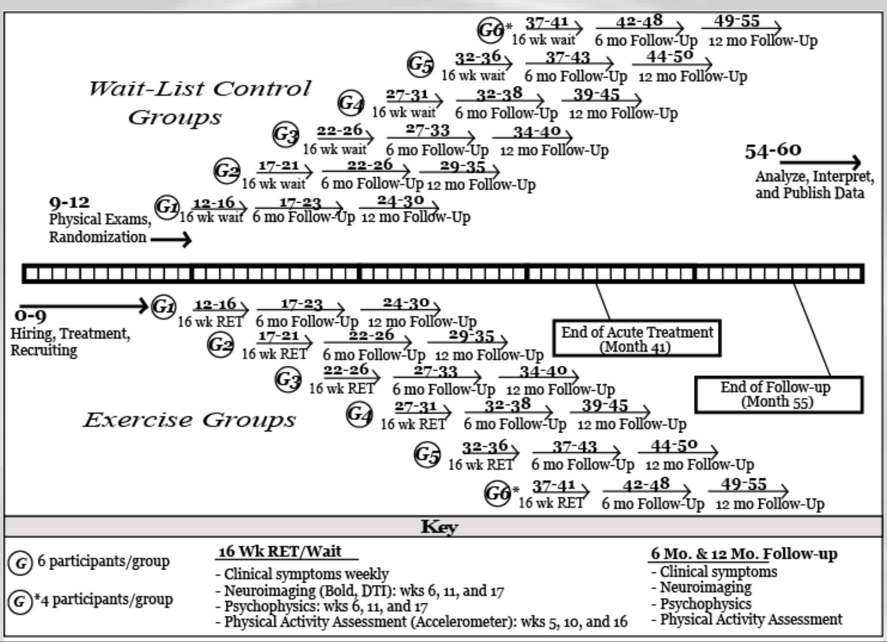
Take Home Point

- It appears that patients with CMP are less efficient at regulating pain.
- This may be in part due to poor communication between brain regions involved in descending pain control.
- Augmented sensory processing and inefficient regulation may be one mechanism through which CMP may be maintained.

The impact of resistance exercise training on pain and brain function in GVs with CMP

Supported by:
Department of Veteran Affairs Merit Review Award

Mechanistic Resistance Exercise Training Trial



Funding Acknowledgement

Thank You