

Joseph L Riley III, PhD | Pain & Aging Pre-Conference Workshop

HOSTED BY: GERONTOLOGICAL SOCIETY OF AMERICA, ANNEBERG CENTER FOR HEALTHSCIENCES

CO-HOST ORGANIZATIONS: AARP, AGING AND DISABILITY, AGING AND HEALTH, NCOA

DISCLOSURE

I have no relevant commercial relationships to disclose.

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Topics

- Pain modulation 101
- Laboratory tests of pain modulation
- Future directions

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Pain is adaptive

- Tissue damage
- Fast vs. slow transmission
- Acute vs. Prolonged
- Chronic pain (beyond normal healing?)

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Early models of pain

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Pain is modulated

16th Century: Descending, top-down modulation; Ascending, bottom-up information.

21st Century: Prior experiences, Attention/expectation, Mood (anxiety, depression), Neurochemical and structural changes, Genetics, Sensitization (Peripheral and Central).

Multiple mechanisms:

- Inhibitory
- Facilitatory

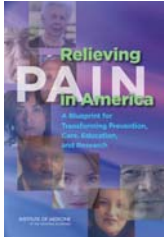
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IOM Report: June 29, 2011

“Pain surpasses its underlying cause to become a disease in its own domains and dimensions.”

“Changes in structure and function of the nervous system”



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Pain modulation becomes dysfunctional

Central Sensitization

- Lower threshold
- Increased sensitivity
- Enlargement of receptive fields
- Increased summation
- Lingering pain sensations

Loss of descending inhibition



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The study of pain modulation

Laboratory (noxious stimuli)

- Single end-points
- Dynamic tests of pain modulation





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Models of pain modulation

<p>Facilitation</p> <ul style="list-style-type: none"> • Temporal summation • Temporal sensitization • Pain after sensations • Prolonged stimulation • REDSTIM 	<p>Inhibition</p> <ul style="list-style-type: none"> • Conditioned Pain Modulation • Offset analgesia • REDSTIM
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Chronic pain populations

- Increased sensitivity
- Enhanced facilitation
- Reduced inhibition

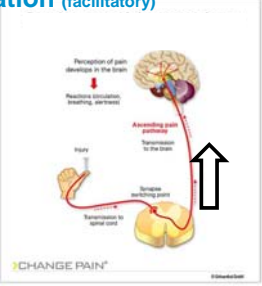
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Temporal summation (facilitatory)

Animal studies

- Short rapid stimulation
- C-fiber specific
- Spinal mechanism
- Central sensitization



CHANGE PAIN™

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Age differences in temporal summation

Participants:

- 88 Younger adults (ages 18-39)
- 48 Middle-aged (40-59)
- 62 Older adults (60-80)

Testing parameters:

- ISI: 2.5-, 3.5-, 4.5-sec
- St: 0.8-sec
- Individualized temperature

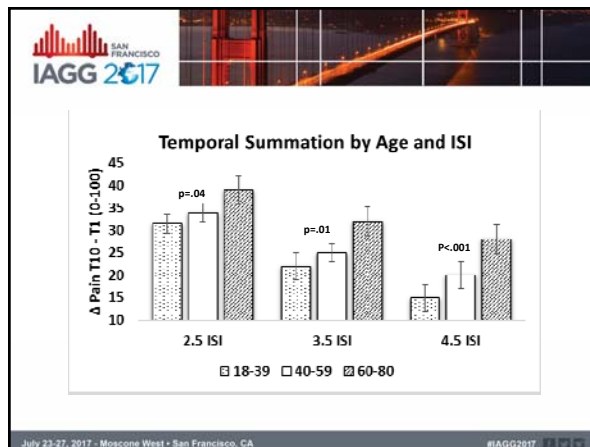
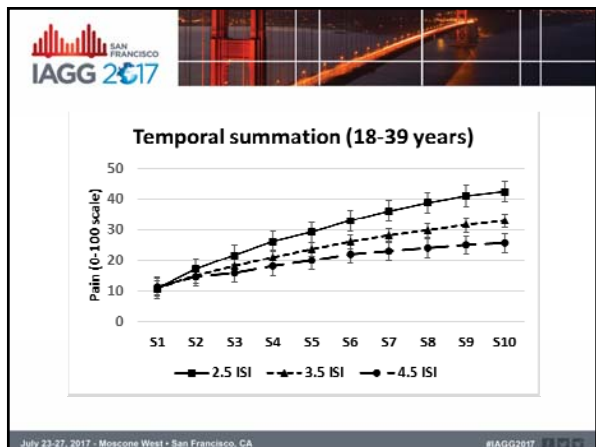


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Rating the delayed sensation

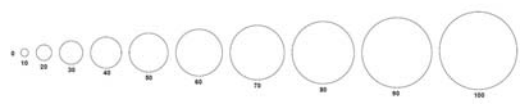


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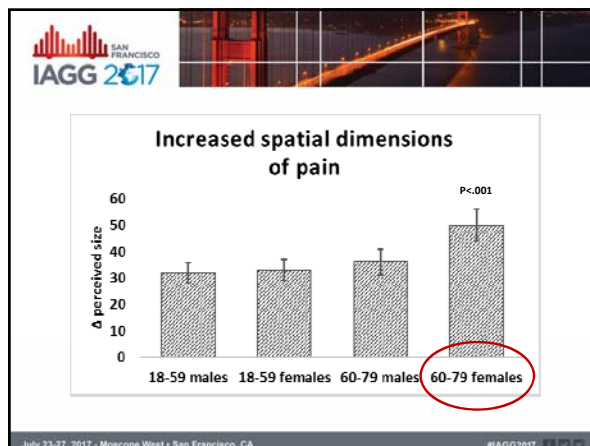
Rated the size percept of the pain

SIZE



Naugle KM, Cruz-Almeida Y, Fillingim RB, Staud R, Riley JL 3rd. Increased spatial dimensions of repetitive heat and cold stimuli in older women. Pain. 2017 May;158(5):973-979.

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Longer acting facilitatory mechanism

Temporal sensitization

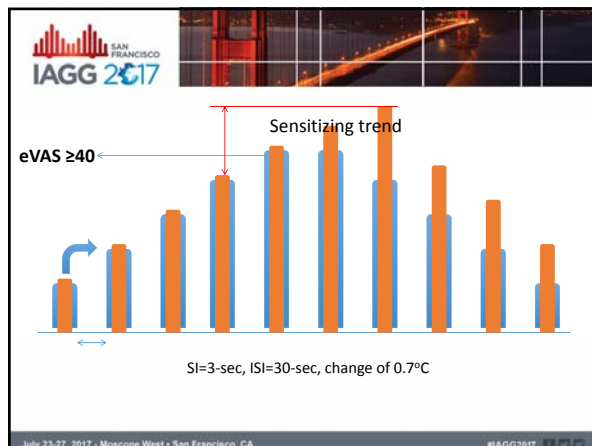
- Asc/dsc S/R curve
(Si = 3.0-sec; ISI = 30-sec)



A WORLD OF PAIN

Vierck CJ, Wong F, King CD, Mauderl AP, Schmidt S, Riley JL 3rd. Characteristics of sensitization associated with chronic pain conditions. Clin J Pain. 2014;30:119-28.

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Conditioned Pain Modulation (CPM)

Pain-inhibits-pain model

Conditioning stimulus

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Conditioned Pain Modulation (CPM)

Pain-inhibits-pain model

- Established in animal models
- Heterotopic
- Eliminated with naloxone

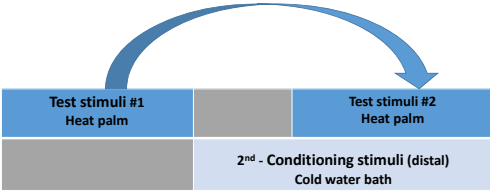
Test stimulus

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CPM

Pain patients have reduced inhibition in tests of CPM



Test stimuli #1 Heat palm

Test stimuli #2 Heat palm

2nd - Conditioning stimuli (distal) Cold water bath

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Conditioned pain modulation

Participants:

- 27 Younger adults (20-44)
- 24 Older adults (56-78)



Riley JL 3rd, King CD, Mauderl AP, Wong F, Fillgrim RB. Differences in pain sensitivity and modulation across the lifespan. Pain. 2010 Jul;150(1):153-160.

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- Model 1. Alternating on 3-minutes (dose response)

	T1	T2	T3	T4	T5
Bath	45-s	45-s	45-s	45-s	45-s
Test	30-s	30-s	30-s	30-s	30-s

- Model 2. Primed (tested duration)

	B1	B2	B3	B4	B5	T1	T2	T3	T4	T5
Bath	45-s	45-s	45-s	45-s	45-s					
Test						30-s	30-s	30-s	30-s	30-s

- Model 3 - Control. No bath - 5 x 30-sec test trials

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Peak pain rating averaged across 5 trials

Large effect for the younger sample, $p. > .001$

Age Group	No bath	Primed	Alt
20-44	~45	~35	~35
56-78	~35	~35	~35

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Peak pain rating averaged across 5 trials

50% the inhibition of the younger group $p. < .05$

Age Group	No bath	Primed	Alt
20-44	~45	~35	~35
56-78	~35	~35	~35

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Response to prolonged stimuli

Participants:

- 36 Younger adults (18-36)
- 28 Older adults (55-78)

Thermal heat at individualized temperature

baseline	20-minute	40-minute	60-minute
120-sec heat trial	120-sec heat trial	120-sec heat trial	120-sec heat trial

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Trial 1 thermal heat

Older group failed to inhibit in the first minute.

Time	18-26 yrs	55-78 yrs
20s	~40	~40
40s	~30	~40
60s	~30	~40
80s	~30	~45
100s	~30	~55
120s	~30	~65

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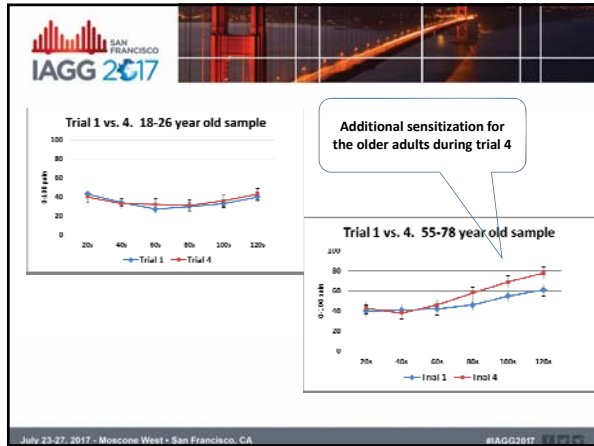
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Trial 1 vs. 4. 18-26 year old sample

Pain profile repeated for younger participants

Time	Trial 1	Trial 4
20s	~40	~40
40s	~30	~30
60s	~30	~30
80s	~35	~35
100s	~40	~40
120s	~45	~45

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- Central sensitivity like effects occurred.
- Loss of inhibition/increased facilitation?

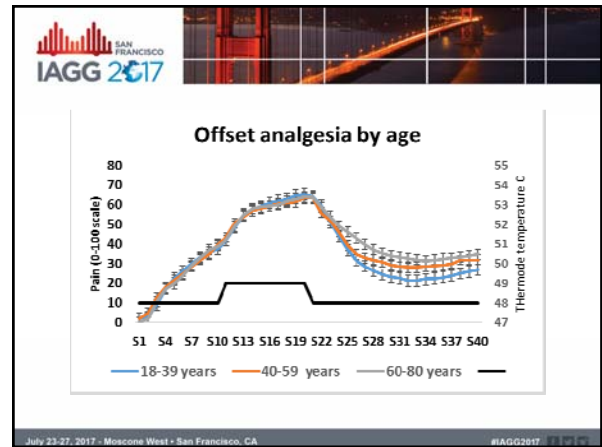
Trial 1 vs. 4. 55-78 year old sample

Offset analgesia (inhibitory mechanism)

Participants:

- 88 Younger adults (18-39)
- 48 Middle-aged (40-59)
- 62 Older adults (60-80)

Phase 1, 10-sec Baseline temperature	Phase 2, 10-sec Offset or baseline temperature	Phase 3, 20-sec Baseline temperature
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Clinical relevance?

Conditioned Pain Modulation

- SF-36 Bodily Pain scale
- Number of Painful Sites
- Disability from Pain
- Physical Activity Level

Temporal Summation

- SF-36 Bodily Pain scale
- Number of Painful Sites
- Disability from Pain

Offset Analgesia

- SF-36 Bodily Pain scale
- Number of Painful Sites

INSIDE EVERY OLDER PERSON IS A YOUNGER PERSON WONDERING WHAT THE HELL HAPPENED.



Future directions

Restoring adaptive pain modulation?

- Central mechanisms
- Plasticity of the CNS
- Exercise restores cognitive functioning
- Exercise programs reduce pain for many pain conditions

Hypothesis: Aerobic exercise program will reset pain modulatory mechanisms in older adults.

time

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UF Pain Research and Intervention Center of Excellence (PRICE)

- Roger B. Fillingim, PhD
- Charles J. Vierck, PhD
- Roland Staud, MD
- Patrick Tighe, MD
- Andre P. Mauderli, DMD, PhD
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- Shannon M. Wallet, PhD
- Nathan Eckert, PhD
- Corey Simon, DPT, PhD and many UF students




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