Evidence That Manual Therapy Favorably Alters Central Sensitization of Nociceptive Input

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Overview

• Pain and the nervous system
• The sensitization era
• Immediate effects of spinal manipulation
  • Summary and future directions

Pain and the nervous system

Pain – A Priority?

• And finally – “We believe pain arises in the nervous system but represents a complex and evolving interplay of biological, behavioral, environmental, and societal factors that go beyond simple explanation”

http://www.iom.edu/Reports.aspx

Gate Theory of Pain

Image from http://faculty.washington.edu/chudler/pain.html
The sensitization era

Sensitization Era

- Pain research has expanded to consider
  - Plastic elements of pain
  - Sensitization of pain
  - Hyperalgesic states

Sensitization Era

- Peripheral sensitization model
  - How clinicians are typically trained
  - Joint and muscle are “source” of pain
    - No changes from peripheral generator to noxious input to reported sensation
    - Nice, predictable linear association

Traditional pain perception models
Sensitization Era

• Central sensitization model
  – Modulation of nociceptive input after entering the central nervous system
  – Variation in
    • Dorsal horn relay
    • Cortical activity
    • Endogenous inhibition
  – Variation from periphery to nociceptive input to reported sensation

Sensitization Era

• Paradigm Shift for Pain
  – Historically viewed as a reflexive/peripheral phenomenon
  – Currently viewed as a plastic/central phenomenon
    • Starts in the periphery
    • Multiple areas for nervous system modulation
    • Pain perception is cortically mediated

Dorsal Horn Central Sensitization

• Wind up
  – Increased frequency of peripheral input
  – Projection neuron amplifies signal to higher centers
  – Can not be directly measured in humans
  – Temporal summation is proximal measure utilized in our lab (and others) for dorsal horn excitability

Temporal Summation (Staahl and Drewes, 2004)

No “wind up”
(central sensitization absent)

“Wind up”
(central sensitization present)

Bialosky et al., Man Ther, 2008
**Temporal Summation**

Temporal summation rates are lower for healthy controls (dark boxes) in comparison to subjects with FM (light boxes) from Staud et al, *Pain* 2002.

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**Hypothesis Generation**

- Manual therapy techniques stimulate many different receptors
- Perhaps their afferent input disrupt nervous system pathways involved with development of chronic pain

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**Central Hypothesis**

- Manual therapy inhibits pain (or development of chronic pain) through suppression of temporal summation (a proximal measure of dorsal horn excitability)

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**Immediate effects of spinal manipulation**

From Cibulka, *Phys Ther*, 1992
10/29/2011

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**Purposes of This Study**

1. Determine if spinal manipulation selectively suppresses temporal summation of pain.

2. Determine if the effect of spinal manipulation is specific to areas innervated by the lumbar spine

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**Study Design**

- **Subjects (n = 60)**
  - Baseline QST
  - Bicycle (n=20)
  - Extension (n=20)
  - SMT (n=20)
  - Follow-up QST

**Results**

- No statistically significant differences in A-delta fiber mediated pain perception (first pain)
- Manipulation is a general counter-irritant for A-delta fiber mediated pain perception, with similar properties as lumbar exercise and general exercise.

(George et al, 2006)

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**Graphs**

- **Inhibition**
  - Change in median pain score (A-delta fiber mediated)
  - Lumbar Innervated Area
  - Cervical Innervated Area

- **Inhibition**
  - Change in temporal summation (C-fiber mediated)
  - Lumbar Innervated Area
  - Cervical Innervated Area

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60 healthy subjects
Mean age: 24.0 years (sd = 3.2)
67% females
Statistically significant differences in C-fiber mediated pain perception (temporal summation).

Manipulation suppressed temporal summation more than stationary bicycle riding ($p < 0.05$) and lumbar extension exercises ($p = 0.10$).

(George et al, 2006)

Follow-Up Study
(Bialosky et al, *Phys Ther*, 2009)

- Study used parallel methods to the first one
- 36 participants with LBP
  - 26 Females (72.2%)
  - Mean age: 32.4 years (sd= 12.6)
  - Mean duration: 221.8 weeks (sd= 365.3)

Hypothesis Supported

- Evidence that spinal manipulation suppressed temporal summation
  - Healthy subjects
  - Patients with low back pain

- End of story?
90 healthy subjects
Mean age: 22.9 years (sd=2.7)
73% females

Thoracic Manipulation Study
(Bishop et al, *Spine J*, 2011)
- Results confirmed specificity to indirect measures of central sensitization (temporal summation)
- Greater reductions with SMT compared to exercise and control conditions
- More widespread effects than the lumbar SMT – detected caudally
“Aren’t You Forgetting Something Else?”

Sensitization Era

Bialosky et al, Man Ther, 2008

Studied Technique

From Cibulka, Phys Ther, 1992

60 healthy subjects
Mean age: 23.1 years (sd = 3.1)
73% females
Study Design

Subjects (n = 60)

Baseline QST

Positive + SMT (n=20)

Neutral + SMT (n=20)

Negative + SMT (n=20)

Follow-up QST

Expectation Manipulation

• Positive
  – “The SMT is a very effective form of manipulation used to treat low back pain and we expect it to reduce your perception of heat pain.”

• Neutral
  – “The SMT is a form of manipulation used to treat low back pain that has unknown effects on perception of heat pain.”

• Negative
  – “The SMT is an ineffective form of manipulation used to treat low back pain and we expect it to temporarily worsen your perception of heat pain.”

Patients Who Believed Manipulation will Help (n=78)

Matched Treatment?

• Recent line of research has identified group of manipulation responders
  – Derivation study - Flynn et al, Spine, 2002
  – Validation study - Childs et al, Annals Int Medicine, 2004
  – Validation #2 study – Cleland et al, Spine, 2010
• Clinical prediction rule that increase probability of favorable responses

Personal communication from Julie Fritz and John Childs
Matched Treatment?

- The clinical prediction rule appears to have strong utility
  - Acute symptoms, lack of leg pain, spinal hypomobility, low psychological distress, and hip internal rotation
- Mechanisms for improvement unknown?
- Could suppression of temporal summation be a player?

Immediate Changes In Temporal Summation

Matched Treatment?

- Mechanisms of clinical prediction rule response may be
  - Related to factors specific to receiving spinal manipulation
  - Related to expectation of receiving spinal manipulation

Immediate Change In Temporal Summation In CPR Positive

Matched Treatment?

- Mechanisms of clinical prediction rule response may be
  - Related to factors specific to receiving spinal manipulation (expected and confirmatory)
  - Related to expectation of receiving spinal manipulation (unexpected and interesting)

Summary and future direction
Central Hypothesis

- Manual therapy inhibits pain (or development of chronic pain) through suppression of temporal summation (a proximal measure of dorsal horn excitability)

Summary

- We have seen consistent evidence that spinal manipulation suppresses dorsal horn excitability in a way that may be specific to chronic pain development
- We have also seen how expectation may contribute (or detract) from this effect

Summary

Spinal Manipulation → Pain Relief

Inhibition of Dorsal Horn Excitability (Temporal Summation)

Activation of Descending Inhibition (Patient Expectation)

Summary

Spinal Manipulation → Pain Relief

Of Course Not the Only Ways…

Future Directions

- Effects of spinal manipulation on cortical processing of pain
- Determining optimal dosage parameters for lasting suppression of temporal summation
- Comparison to placebo conditions
- Clinical relevance
  - Mechanisms for clinical prediction rule responders
  - Precursor of favorable outcomes

Thank You!

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