Persistent Pain: Pain Without Nociception

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"Sufferers from chronic pelvic pain are the **medical "lepers**" of our patients. They face **misdiagnosis, unhelpful surgeries, and prejudice** as drug seekers. I wish to dedicate this book to our patients who have taught us love and compassion, how to **rise above our own prejudices** and that we must **learn from other disciplines** in order to **deliver hope and relief**. Our aim is to **educate other medical professionals** and to encourage the public to seek out those who have been **called to their care**."

C. Paul Perry
Pelvic Pain, Diagnosis and Management

"I must thank….. my patients, all of whom have taught me so much, **enduring my inadequacies of knowledge** with patience..."

Fred M Howard
Pelvic Pain, Diagnosis and Management

Objectives

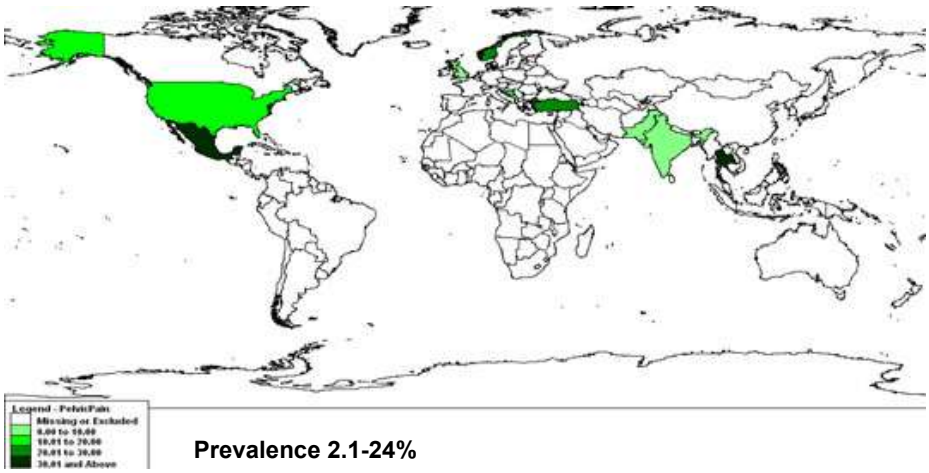
- **The participant will**
  - Learn the neurobiology of nociceptive pain
  - Learn the neurobiology of non-nociceptive pain
  - Identify some of the more common treatments for non-nociceptive pain

Disclosures

- Paid Consultant
  - Patented Medicine Prices Review Board
    - No overlap with the subject matter of this presentation
- Jean Hailes

CPP Scope

- **North American Data**
  - 1 in 10 outpatient gyne visits
  - Indication for
    - 15-50% gyn laparoscopies
    - 12% hysterectomies
    - Direct and indirect costs > 2 billion/yr
- **Prevalence/incidence unknown**
  - **World prevalence** (2009-2012)
    - **5.7-26.6%**
    - Prevalence for women of reproductive age 14-24%
    - 14% of women experience CPP at some point during their lifetime
    - Many countries and regions do not have basic data



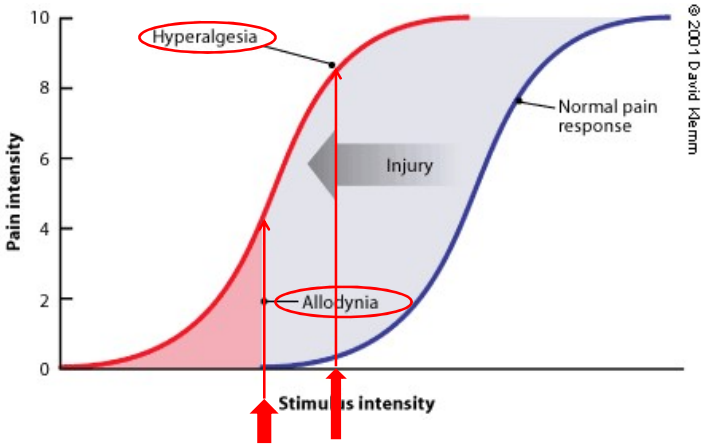
Prevalence 2.1-24%

CPP in Australia and NZ

- **Australia**
  - 60% dysmenorrhea (Ju)
    - 17% chronic
  - >$6 billion direct costs (Evans)
- **NZ three-month prevalence** (Grace)
  - CPP 25%
  - Dysmenorrhea 55.2%
  - Dyspareunia 19.7%
  - Only 1/3 women (34%) reported no pelvic pain

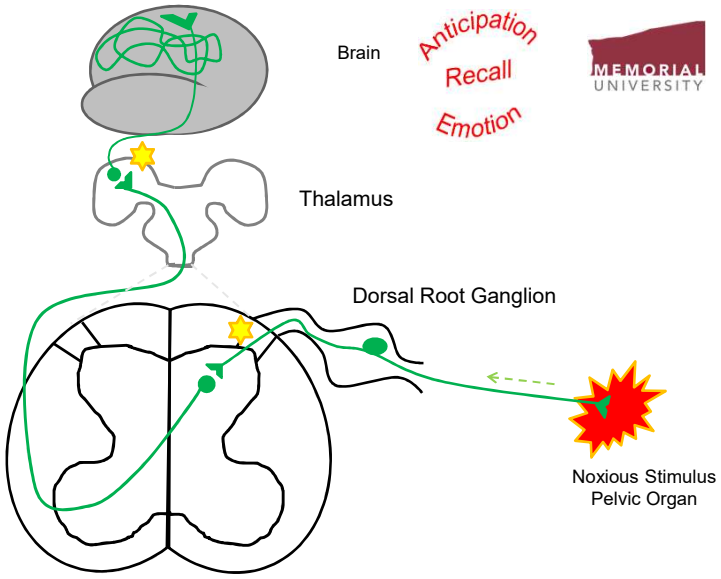
Definitions

- **Hyperalgesia**
  - ❖Excessive sensitivity to pain
- **Allodynia**
  - ❖Pain resulting from a non-noxious stimulus to normal tissue
- **Dysesthesia**
  - ❖An unpleasant sensation produced from a non-noxious stimulus



Neurobiology of Acute Pain

- **Peripheral Activation of Nociceptor**
  - Receptor sensitive to a noxious impulse
- **A △ Nerve fibers**
  - Lightly mylenated
  - Cold and mechanical stimuli
  - Acute sharp fast pain
- **C Nerve Fibers**
  - Unmylenated
  - Warm and mechanical stimuli
  - Slow dull pain



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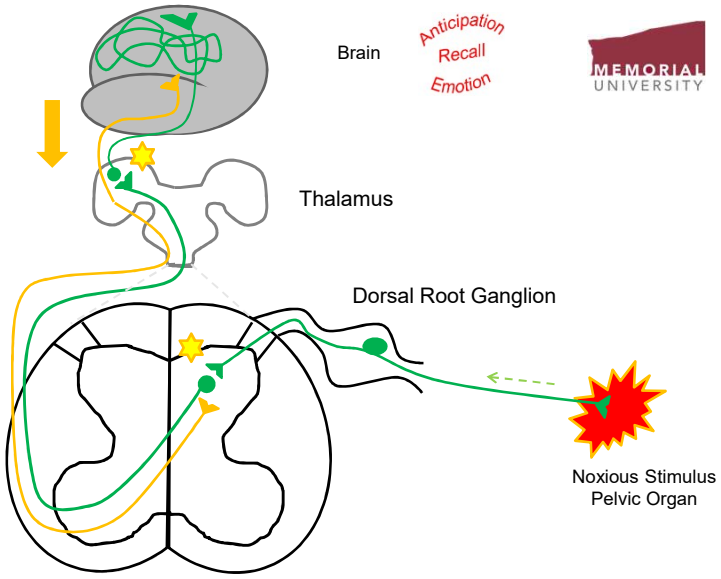
Neurobiology of Acute Pain

- **The "Pain Matrix"**
  - ❖3 domains in the CNS process pain
    - Sensory: location and severity of pain
    - Affective: emotional valence of pain
    - Cognitive: what we think and do about pain



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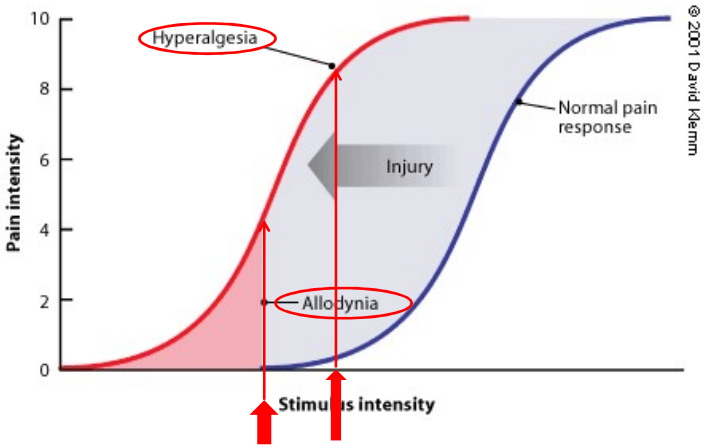
How does nociceptive pain become centralized pain?



Stressors affecting pain sensitivity; Neuroplasticity

Anticipation
Recall
Emotion

- Early life stressors
- Physical trauma (MVA)
- Certain catastrophic events (war but not natural disasters)
- Infections
- Psychological stress/distress

Genetics

Repetitive nociceptive input

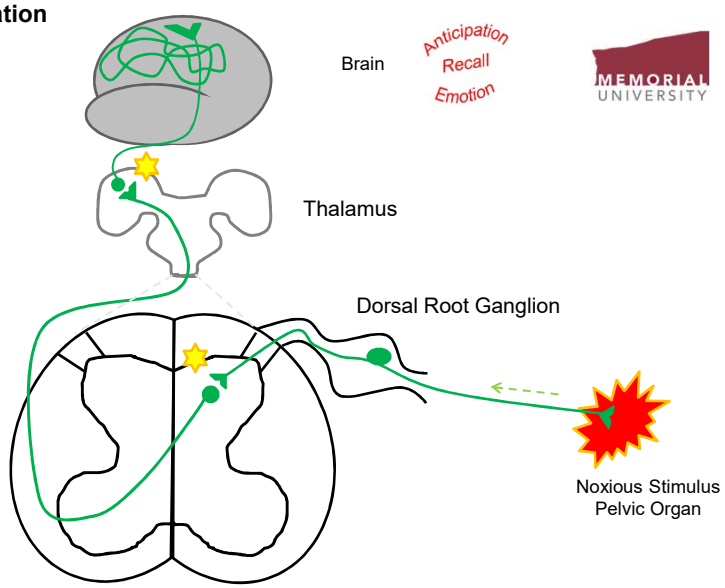
Consequences of being in pain, chronically

- **Neuroplasticity**
  - **Central sensitization**
  - **Convergence**
  - **Antidromic transmission**
    - Neurogenic inflammation
  - **Peripheral sensitization**

Central Sensitization

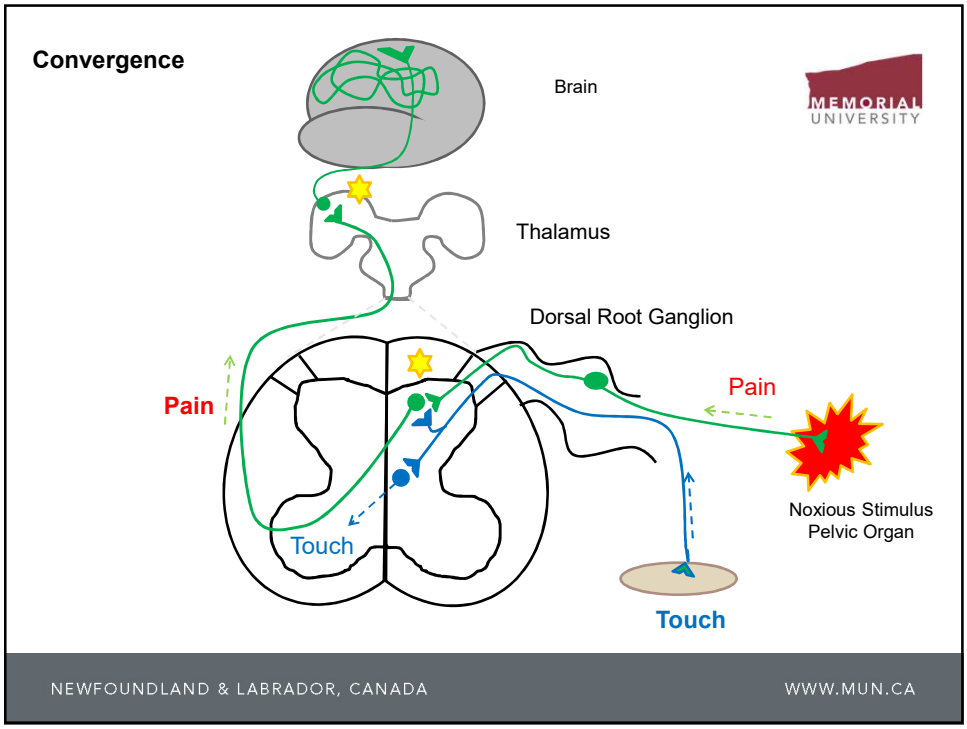
- **Increased excitability of central pain-transmitting neurons**
  - Reduction in pain threshold (allodynia)
  - Increased response to painful stimuli (hyperalgesia)(wind up)
  - Increased duration of pain after nociceptor stimulation has ceased (persistent pain)

Central sensitization



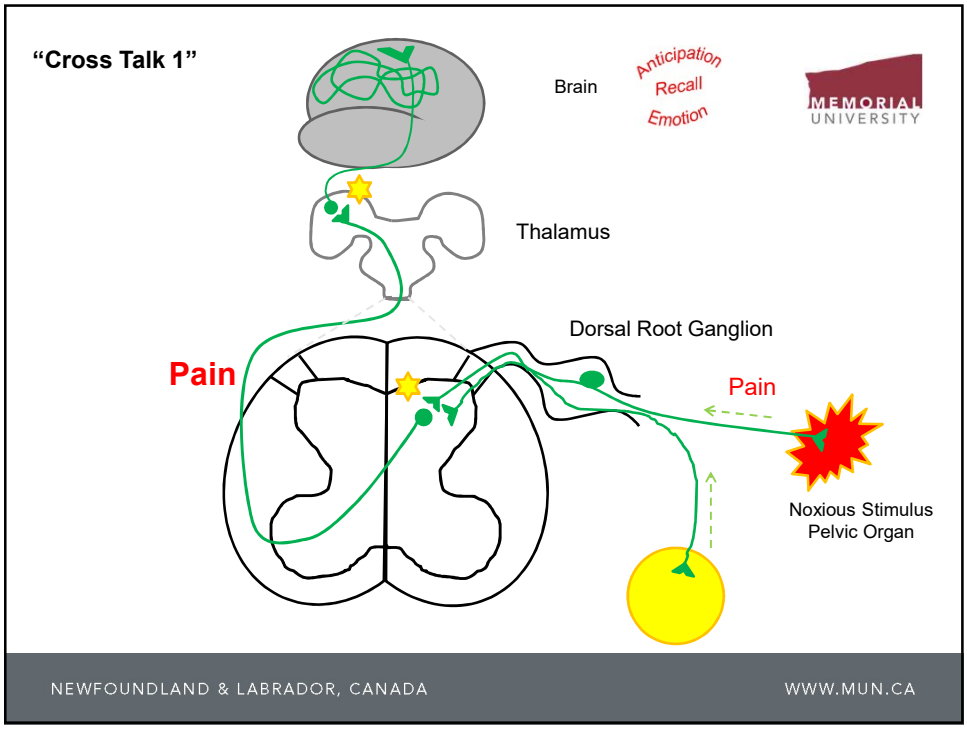
Convergence

- **Convergence**
  - ❖Neural cells sprout new dendrites
  - ❖New synaptic connections in SC
    - Link ascending peripheral touch pathways with ascending nociceptive (pain) pathways (allodynia) (dysesthesia)
    - Pain spreads beyond the original location of injury (expansion of the pain field)



Pelvic Organ "Cross-Talk"

- **Afferent input from a diseased organ and a normal organ converge on the same spinal interneuron sending the pain signal to the CNS**
- **Multiple axons branching to different pelvic structures on the same peripheral afferent nerve**
- **Pelvic organ "cross talk"**
  - Central sensitization = allodynia


"Cross Talk 1"
Brain
Anticipation
Recall
Emotion
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Thalamus
Dorsal Root Ganglion
Pain
Pain
Noxious Stimulus
Pelvic Organ
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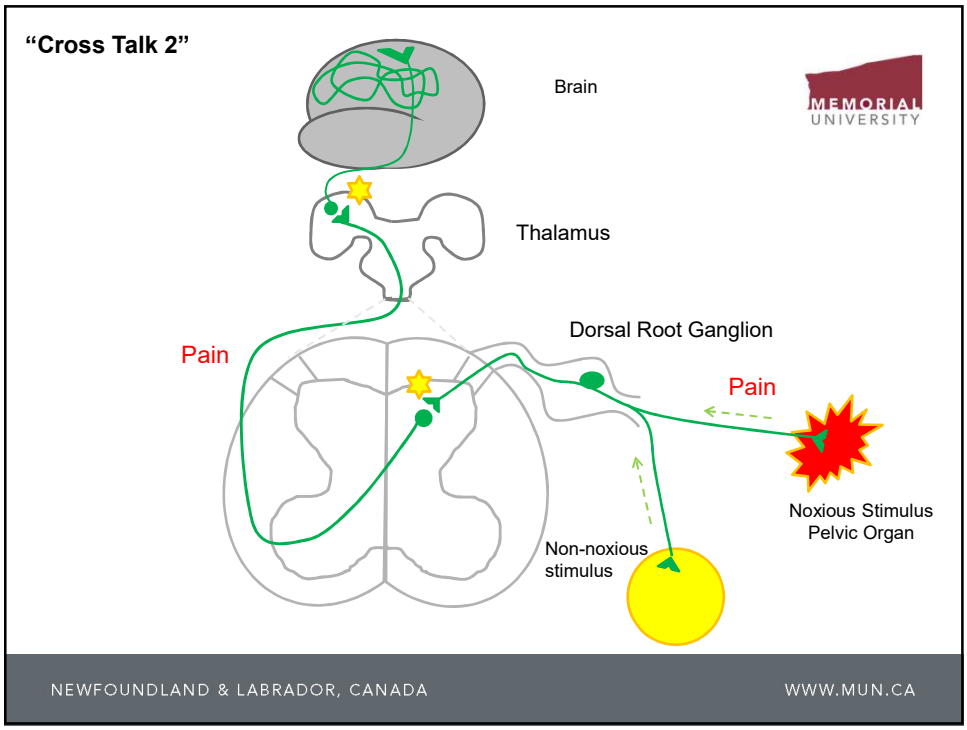
"Cross Talk 2"
Brain
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Thalamus
Dorsal Root Ganglion
Pain
Pain
Noxious Stimulus
Pelvic Organ
Non-noxious
stimulus
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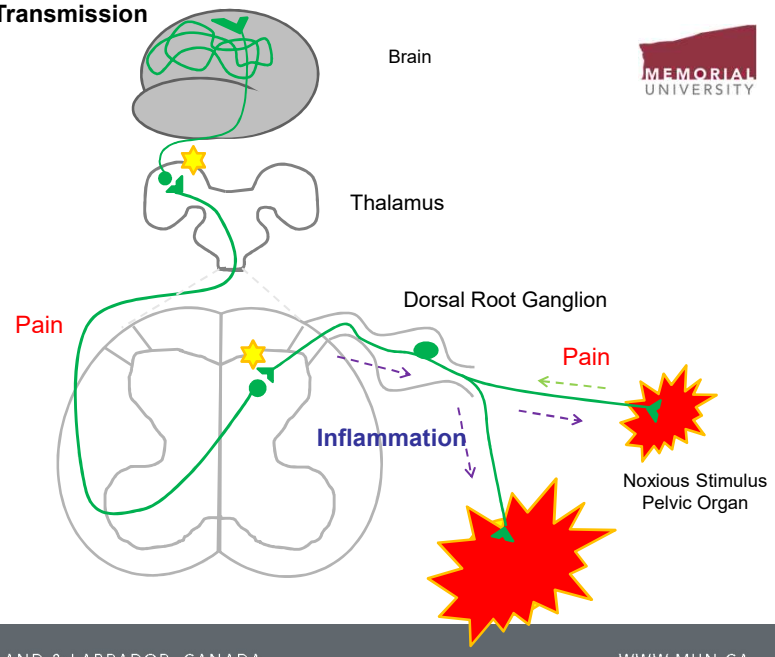
Antidromic transmission

- **Pathologic dorsal root reflex**
  - Afferent dorsal horn neurons release pro-inflammatory chemical mediators at their peripheral terminals
  - Substance P, NGF
    - Mast cell degranulation
  - Results in “neurogenic inflammation” in the periphery
  - Because of “cross talk” this can lead to pathology in other organs

Antidromic Transmission



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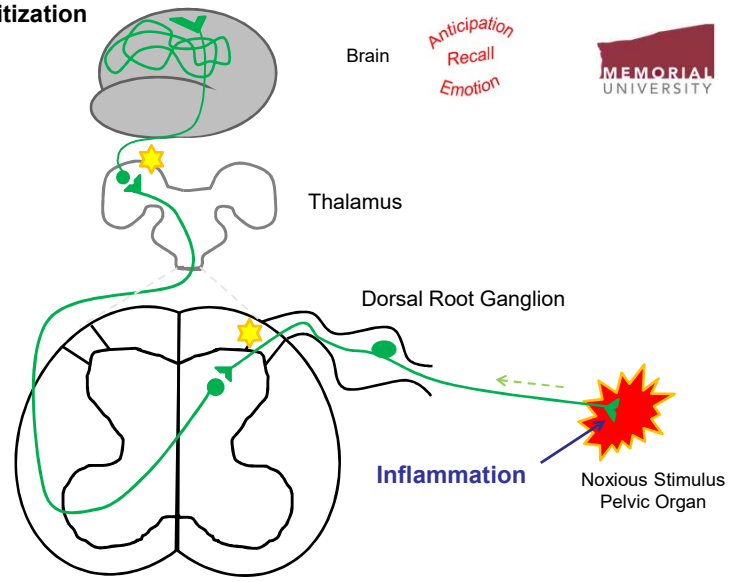
Peripheral sensitization

- **Increased excitability of peripheral nociceptors**
  - Inflammatory mediators stimulate nociceptors
  - Causes altered function and sensitization
  - Amplifies pain signal to CNS
  - Hyperalgesia

Peripheral sensitization



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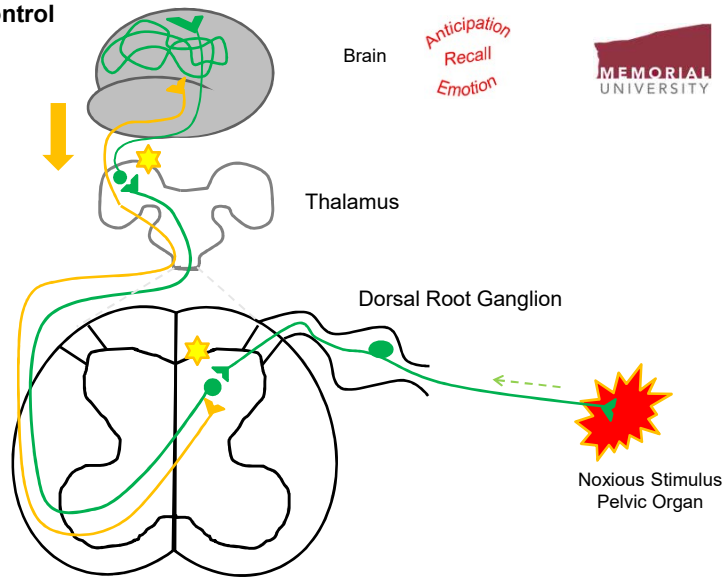
Loss of Pain inhibition

- **Peripheral**
  - ❖Neural mechanisms in DRG “gate”
- **Higher centres in the brain**
  - ❖Process and modulate the pain signal
  - ❖Descending supra-spinal control
- **Descending feedback**
  - ❖Stress, anxiety, sleep
  - ❖Pain persistence and distribution

Anticipation
Recall
Emotion

Supra-spinal control



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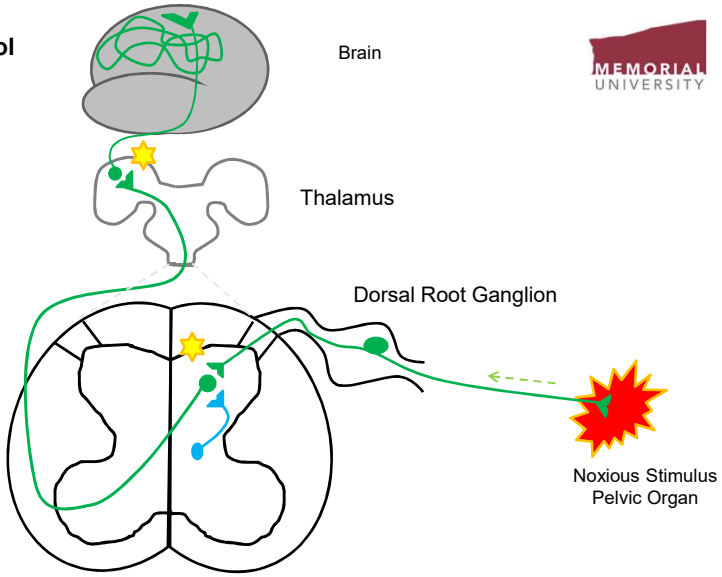
Loss of Inhibitory control



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Pain perception can be **extensively modulated** at **multiple levels** of pain signal processing

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Please note that the next slide refers to guidelines from the Canadian Pain Society, not Australian guidelines.

For information on pelvic pain management, please refer to resources on the Jean Hailes website.

Consensus Guidelines Canadian Pain Society

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Please see the Jean Hailes resources on managing pelvic pain

1st line

- **TCA** (NNT 2.1-2.8)
- **Gabapentinoids** (~4.5)
  (Anti-epileptics)
- **SNRI** (5)

2nd line

- **Tramadol** (5)
- **Opioids** (2.6)

3rd Line

- **Canabinoids** (3.4)

4th Line

- **SSRIs** (7)
- **Methadone**
- **Tapentadol**
- **Other Anticonvulsants**
  - **Lacosamde** (10-12)
  - **Lamotrigine**
  - **Topiramate**
- **Topical Lidocaine**

Nonpharmacological Therapies

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Strong Evidence

- Education
- Aerobic & strength training
- CBT
- Multidisciplinary treatment

Modest Evidence

- Accupuncture
- Hypotherapy
- Biofeedback

Weak Evidence

- Chiropractic
- Manual/massage therapy
- Electrotherapy
- U/S
- Meditative movement
- Mindfulness based stress reduction

No evidence

- Trigger point injections
- Flexibility exercise

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