

# Evaluating Neuropathic Pain: Where are we now and where are we going?

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# Workshop Objectives

- To discuss the newly proposed definition and evaluation of neuropathic pain and the role of QST
- To review the neurophysiology of QST and its clinical relevance
- To demonstrate bedside quantitative sensory testing and set the stage for a discussion of future regarding the usefulness of this tool in clinical practice

# Disclosure

- Received honoraria or consultation fees from the following companies:

Janssen Ortho, Paladin, Biovail,  
Lobopharm, Pfizer, Purdue, Ortho Biotech,  
Bayer, Valeant, Ortho McNeil, Merck  
Frosst, Proctor and Gamble & GSK

# Where have we come from: neuropathic pain measurement.

1998: (*Pain and Suffering in History: Narratives of Science, Medicine and Culture*," which took place 13-14 March 1998. Darling Biomedical Library UCLA)

- McGill Pain Questionnaire
- Facial expressions
- Happy/sad face graphic pain scale used with pediatric patients
- Analog scale for patient self-assessment

2008

- McGill Pain Questionnaire (and many more specific to age/culture)
- Multiple NeP pain scales (screen and quantify)
- VAS/NRS/Facial expressions (pictures/photos)
- Multiple standardized tools to assess the biopsychosocial experience of pain

# Where have we come from?

- Evolving definition of neuropathic pain

# Definition of Terms

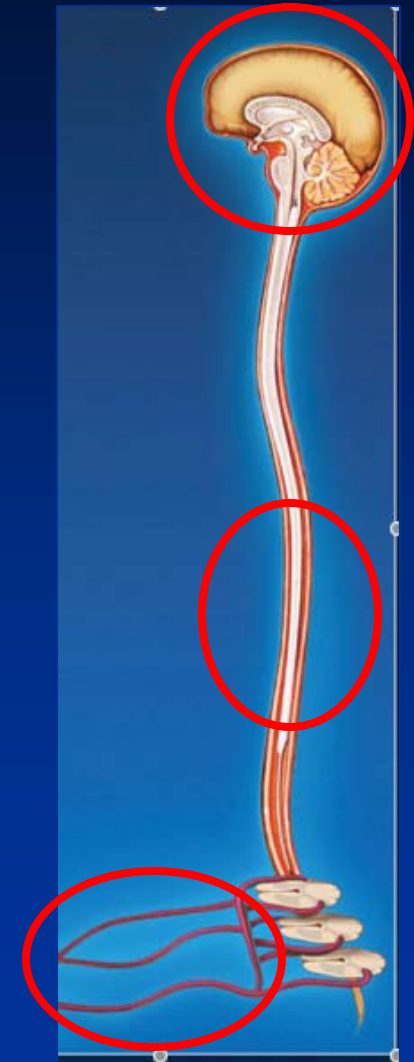


- Neuropathic Pain:1994

“Pain initiated or caused by a primary lesion or dysfunction in the nervous system”

Merskey H, Bogduk N, eds. *Classification of*  
2nd ed. Seattle, Wash: IASP Press; 1994:209-214

*Chronic Pain.*



# Problems with current definition of neuropathic pain

“Pain initiated or caused by a primary  
lesion or dysfunction in the nervous  
system”

1. What is a dysfunction?
2. Which disease?

# Definition of Terms



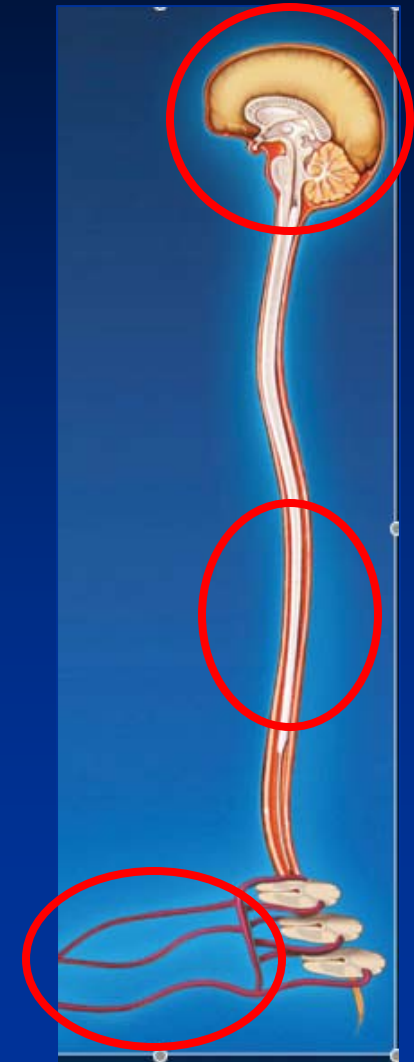
- Neuropathic Pain:

“Pain initiated or caused by a primary lesion or dysfunction in the nervous system”

Merskey H, Bogduk N, eds. *Classification of Chronic Pain*. 2nd ed. Seattle, Wash: IASP Press; 1994:209-214

“Pain arising as a direct consequence of diseases affecting the somatosensory system”

IASP NeuP SIG 2007 – Treede RD, Jensen TS, et al. Neuropathic pain: redefinition and a grading system for clinical and research purposes. *Neurology*. 2008 Apr 29;70(18):1630-5. Epub 2007 Nov 14.



# Challenges in Diagnosing Neuropathic Pain

- Diverse symptomatology<sup>1</sup>
- Multiple mechanisms<sup>1</sup>
- Difficulties in communicating and understanding symptoms
  - Patients may find it difficult to articulate their symptoms clearly
  - Physicians may find it difficult to interpret some of the terminology patients use to describe their symptoms
- Variable response to treatment<sup>2</sup>

1. Woolf CJ, Mannion RJ. Lancet. 1999;353:1959-64

2. Bonezzi C, Demartini L. Acta Neurol Scand Suppl. 1999;173:25-3

# NeuPSIG Recommendations

Grading System:

Definite

Probable

Possible

(Unlikely)

# Grading System

## Criteria to be evaluated for each patient:

1. Pain with a distinct neuroanatomically plausible distribution
2. A history of a relevant lesion or disease affecting the peripheral or central somatosensory system
3. Demonstration of the distinct neuroanatomically plausible distribution by at least one confirmatory test
4. Demonstration of the relevant lesion or disease by at least one confirmatory test

## Grading of certainty for the presence of neuropathic pain:

<b>Definite</b> neuropathic pain	all (1-4)
<b>Probable</b> neuropathic pain	1 and 2 plus either 3 or 4
<b>Possible</b> neuropathic pain	1 and 2 without confirmatory evidence from 3 or 4

# Grading system: Criterion 1

1. Pain with a distinct neuroanatomically plausible distribution.

A region corresponding to a peripheral innervation territory or to the topographical representation of a body part in the central nervous system

Suggested tool: pain diagram drawn by the patient

# Coloured Pain Drawing

Pain drawing key

dull aching -yellow

sharp - red

tingling - green

burning - blue



# Grading system: Criterion 2

2.A history of a relevant lesion or disease affecting the peripheral or central somatosensory system

The lesion or disease is reported to be associated with pain, including a temporal relationship typical for the condition.

Suggested tool: medical history +/- neuropathic pain scales

# SCALES



## Differentiate between NP and non-NP pain

- Leeds Assessment of Neuropathic Symptoms and Signs (LANSS)
- Neuropathic Pain Questionnaire (NPQ)
- Neuropathic Pain Diagnostic Questionnaire (Douleur Neuropathique en 4 questions, DN4)
- ID-Pain

## Measure characteristics of NP

- Neuropathic Pain Scale (NPS)
- Neuropathic Pain Questionnaire (NPQ)
- Neuropathic Pain Symptom Inventory (NPSI) (French)

# Grading system: Criterion 3

3. Demonstration of the distinct neuroanatomically plausible distribution by at least one confirmatory test

As part of the neurological examination, these tests confirm the presence of neurological signs concordant with the distribution of pain.

Suggested tools:

Clinical neurological exam

**Quantitative sensory testing (evidence of sensory loss or gain in the area of pain)**

Electrophysiology

- electroneurography (sensory nerve conduction)
- evoked potentials (SEP, LEP)

# Grading system: 4

4. Demonstration of the relevant lesion or disease by at least one confirmatory test

As part of the neurological examination, these tests confirm the diagnosis of the suspected lesion or disease. Which tests depends on which lesion or disease is causing neuropathic pain.

Confirmatory tests:

IHS criteria for trigeminal neuralgia

CSF analysis

MRI

Electrophysiology (motor/sensory electroneurography)

Intraoperative neuroanatomical evidence

Biopsy

# Sensory Examination Goals

- To test each type of nerve fiber looking for evidence of damage or dysfunction
- Determine the pattern of loss
  - Nerve fibers
  - Distribution - radicular loss/ gloves and stocking / peripheral neuropathy etc..
- To evaluate for both sensory loss AND sensory gain
- To help delineate disease mechanisms

# Limitations of QSPT

- No gold standard for comparison
- Testing at one site cannot determine the neuroaxial level of dysfunction
- Cold hypoalgesia, heat hypoalgesia and mechanical hyperesthesia difficult to diagnose as the confidence limits are close to the limits of the possible data range
- Paradoxical heat sensation and dynamic mechanical allodynia are unimodal parameters (both signs are normally absent so they cannot be reduced)
- Need an unaffected body part to provide normal reference data

# *How is Quantitative Sensory Pain Testing different that what I am doing now?*

- Offers a standardized approach to sensory testing and evaluates all the sensory fibers
- Evaluates and quantifies both sensory loss and sensory gain
- Allows mapping of affected areas which helps to determine pattern of loss
- The Question?
  - Should this be a standardized exam with standardized tools for consulting pain physicians?

# QSPT as a diagnostic and a monitoring tool

- Identify loss of function in A Beta (touch and vibration)
- Identify loss of function in A Delta and C (Thermal and pinprick)
- Assess efficacy of lidocaine infusions

# Conclusions

- We still don't know (or can't define) what neuropathic pain really is.
- We still can't really measure it.
- Treatment outcomes have been slow to improve.
- Quantitative measurements of symptoms and signs offer an opportunity to improve our measurement of neuropathic pain
- Adoption of simple bedside techniques to evaluate sensory signs of neuropathic pain can lead to improved diagnosis of neuropathic pain

Thank You!

# Neurophysiological Basis of QST and its Clinical Relevance

Canadian Pain Society  
Victoria, BC  
May 29<sup>th</sup> 2008

Serge Marchand, Ph.D.

Université de Sherbrooke, Faculté de médecine, Neurochirurgie



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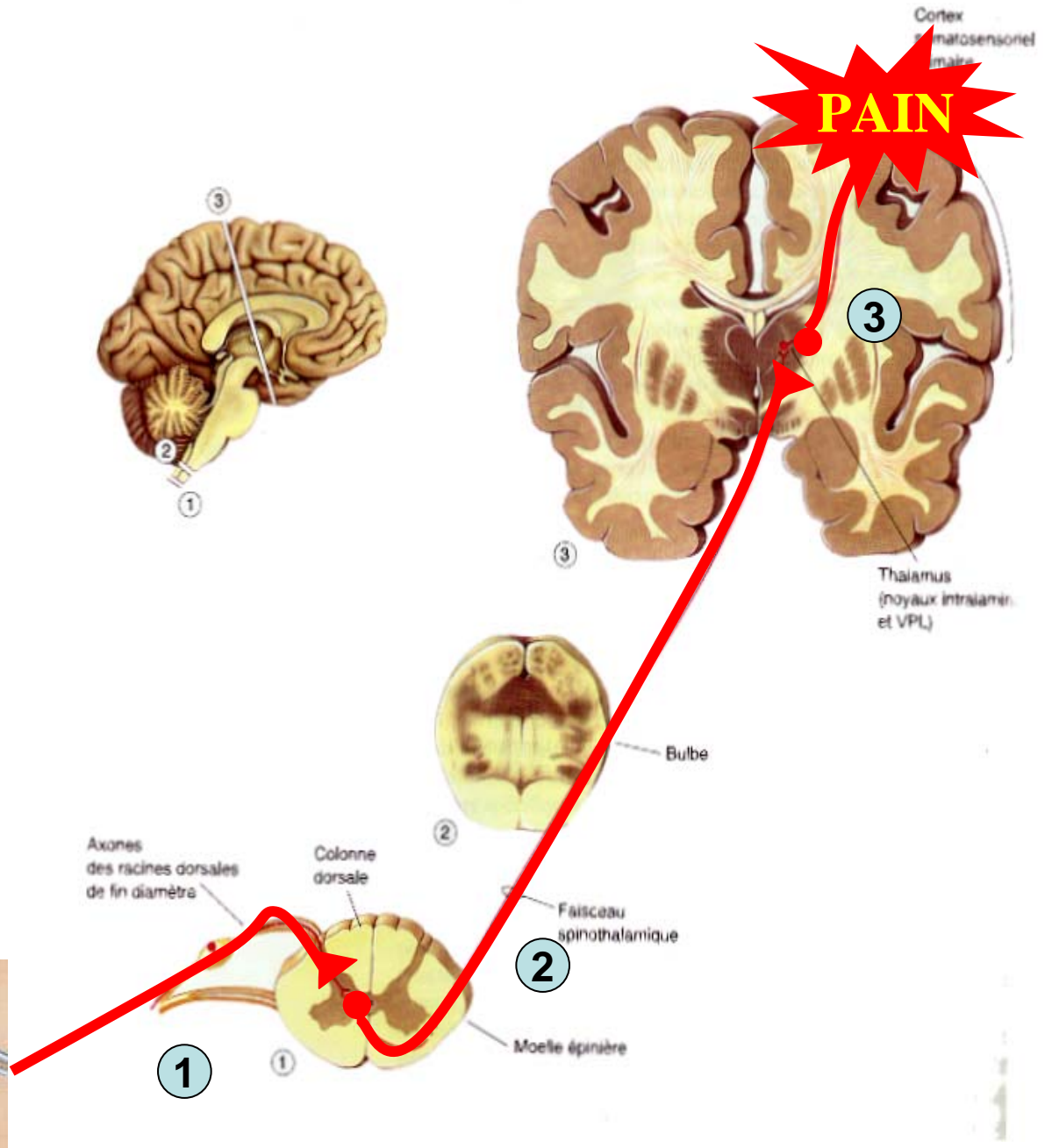
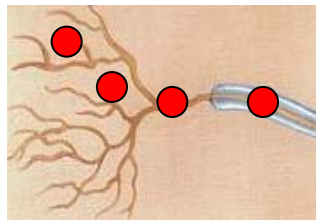
# Objectives

- To review the neurophysiology of QST and its clinical relevance
- Review the basis of mechanistic approach to pain treatment based on QST

Université de Sherbrooke, Faculté de médecine, Neurochirurgie

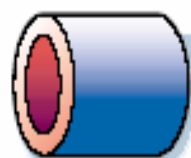


# From Nociception to Pain



# Primary afferent axons

Primary afferent axons



**A $\alpha$  and A $\beta$  fibres**

Myelinated  
Large diameter  
Proprioception, light touch

Thermal threshold

None



**A $\delta$  Fibre**

Lightly myelinated  
Medium diameter  
Nociception  
(mechanical, thermal, chemical)

~ 53 °C Type I

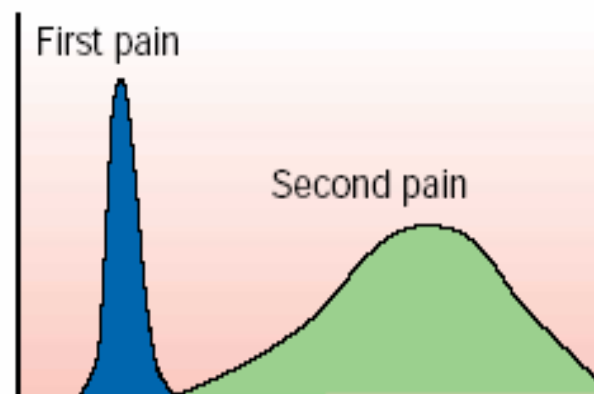
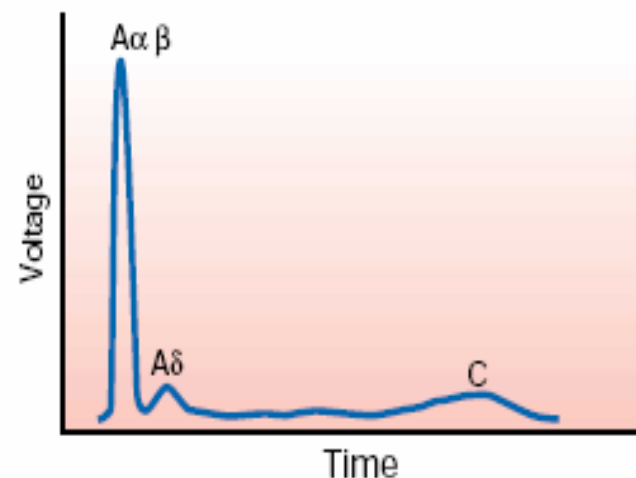
~ 43 °C Type II



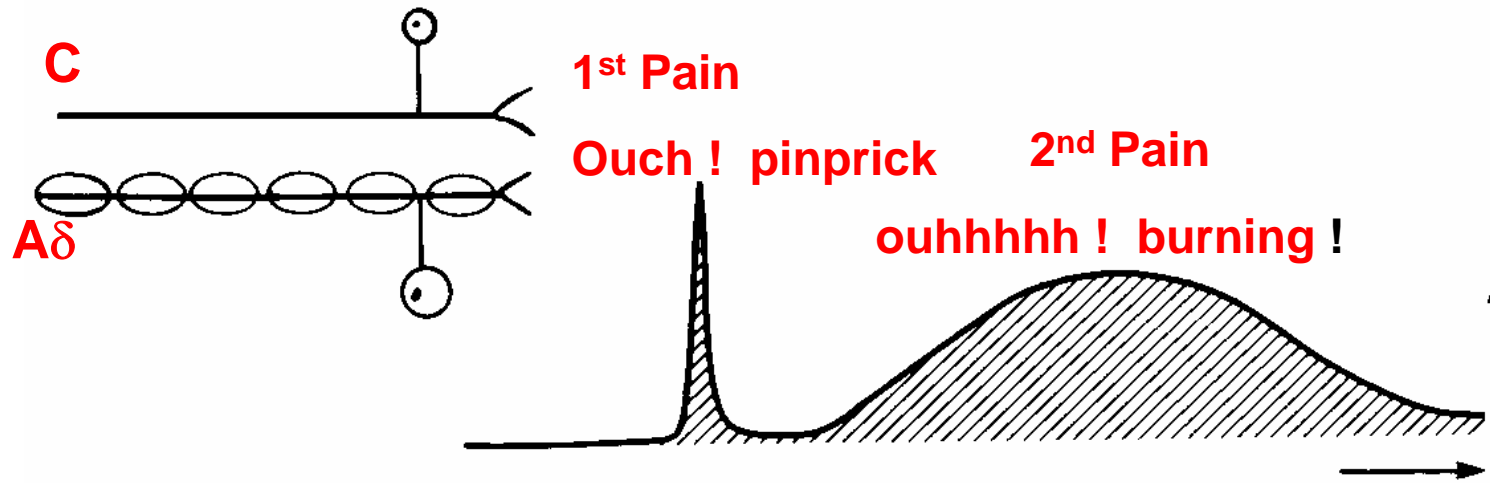
**C fibre**

Unmyelinated  
Small diameter  
Innocuous temperature, itch  
Nociception  
(mechanical, thermal, chemical)

~ 43 °C



# First and Second Pain



# QST testing of peripheral fibers

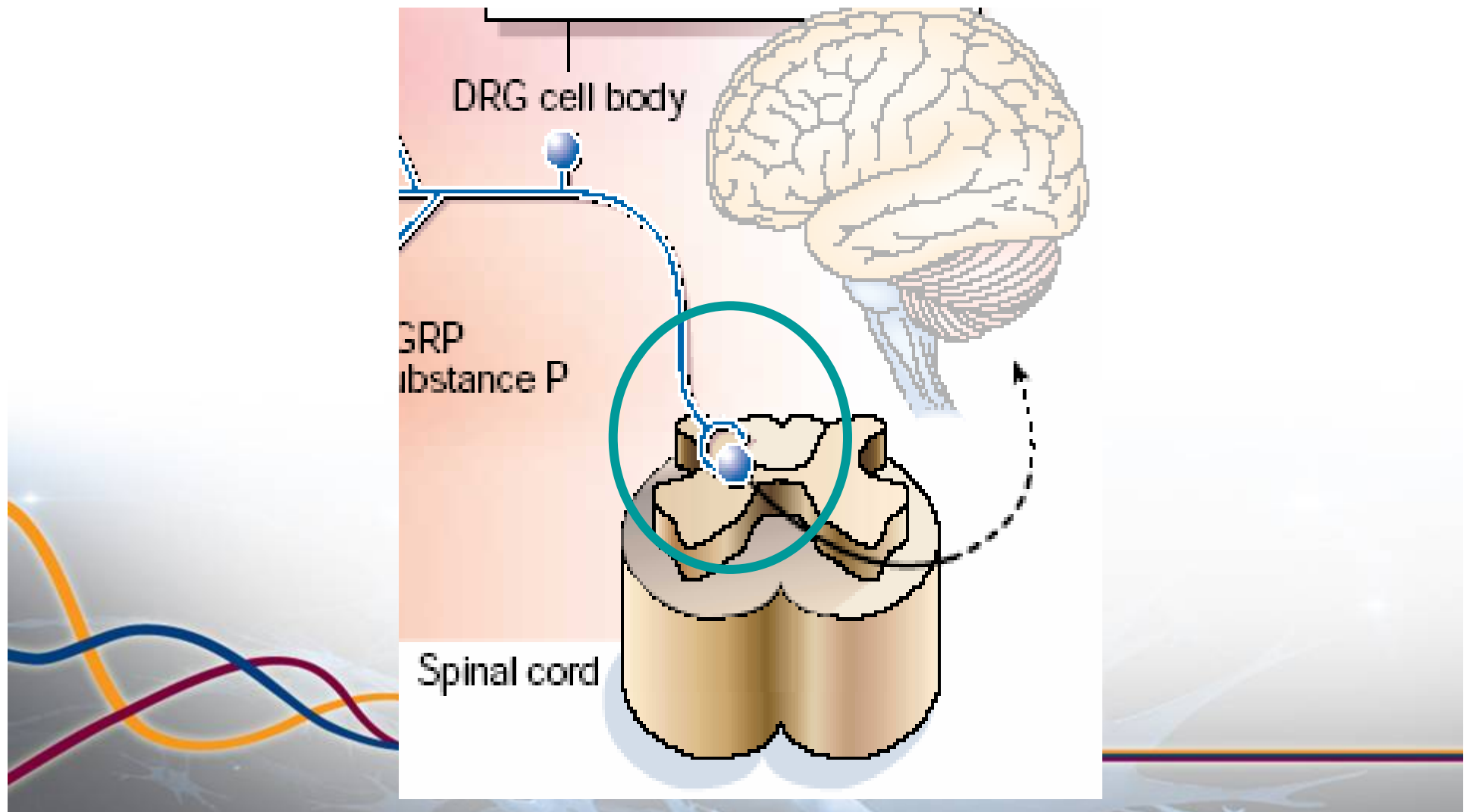
A- $\beta$  : Vibration detection threshold

A- $\delta$  : Cold detection threshold

C: Heat and Heat pain detection

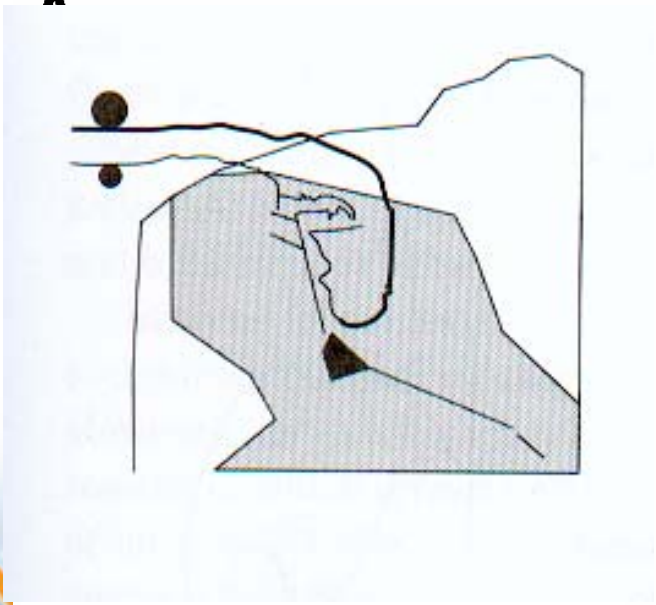


# Secondary nociceptors: Dorsal Horn

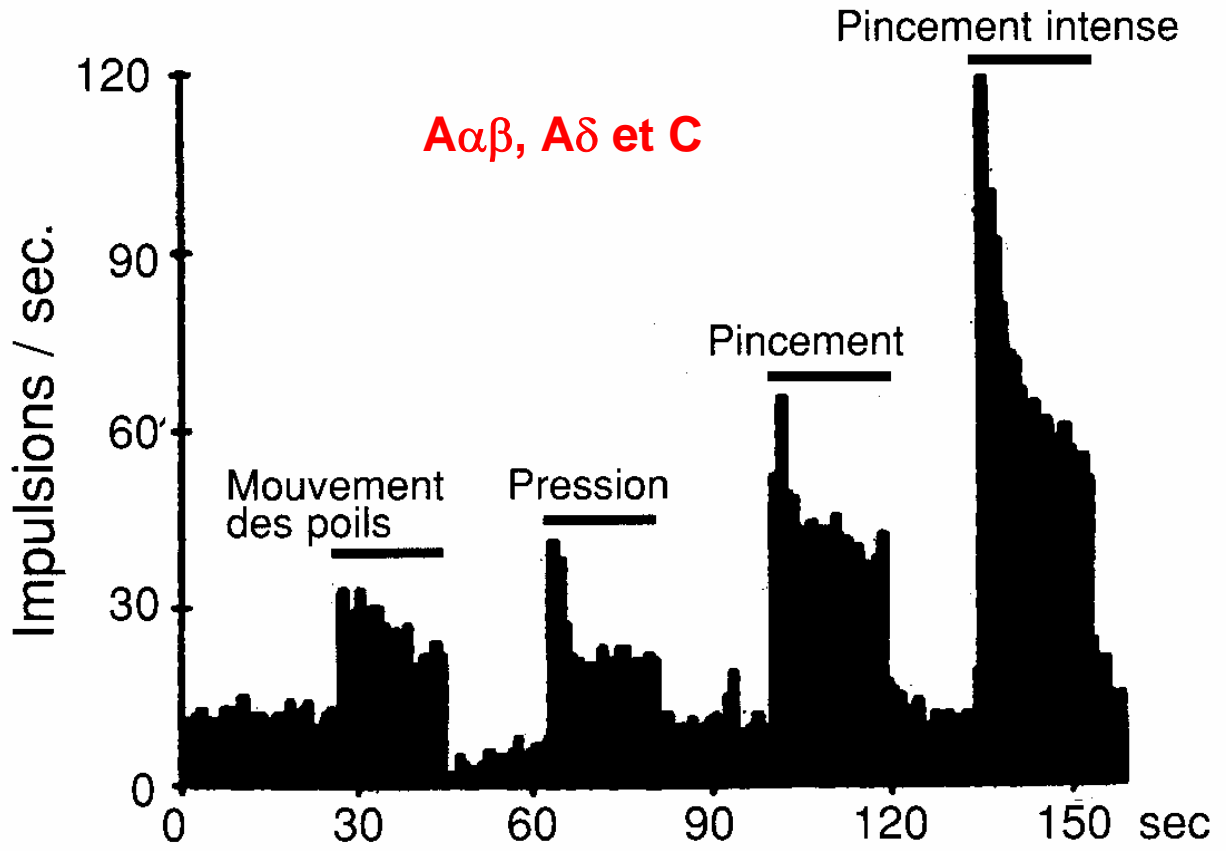


# Secondary nociceptive neurons

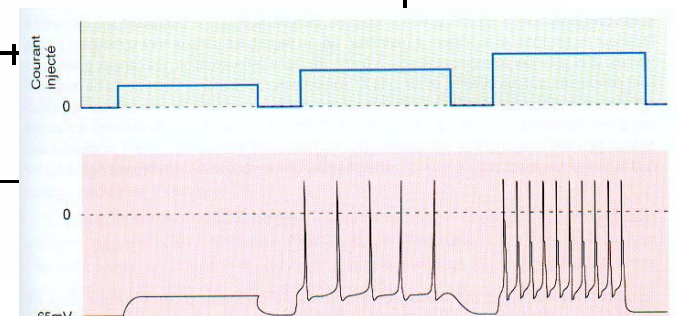
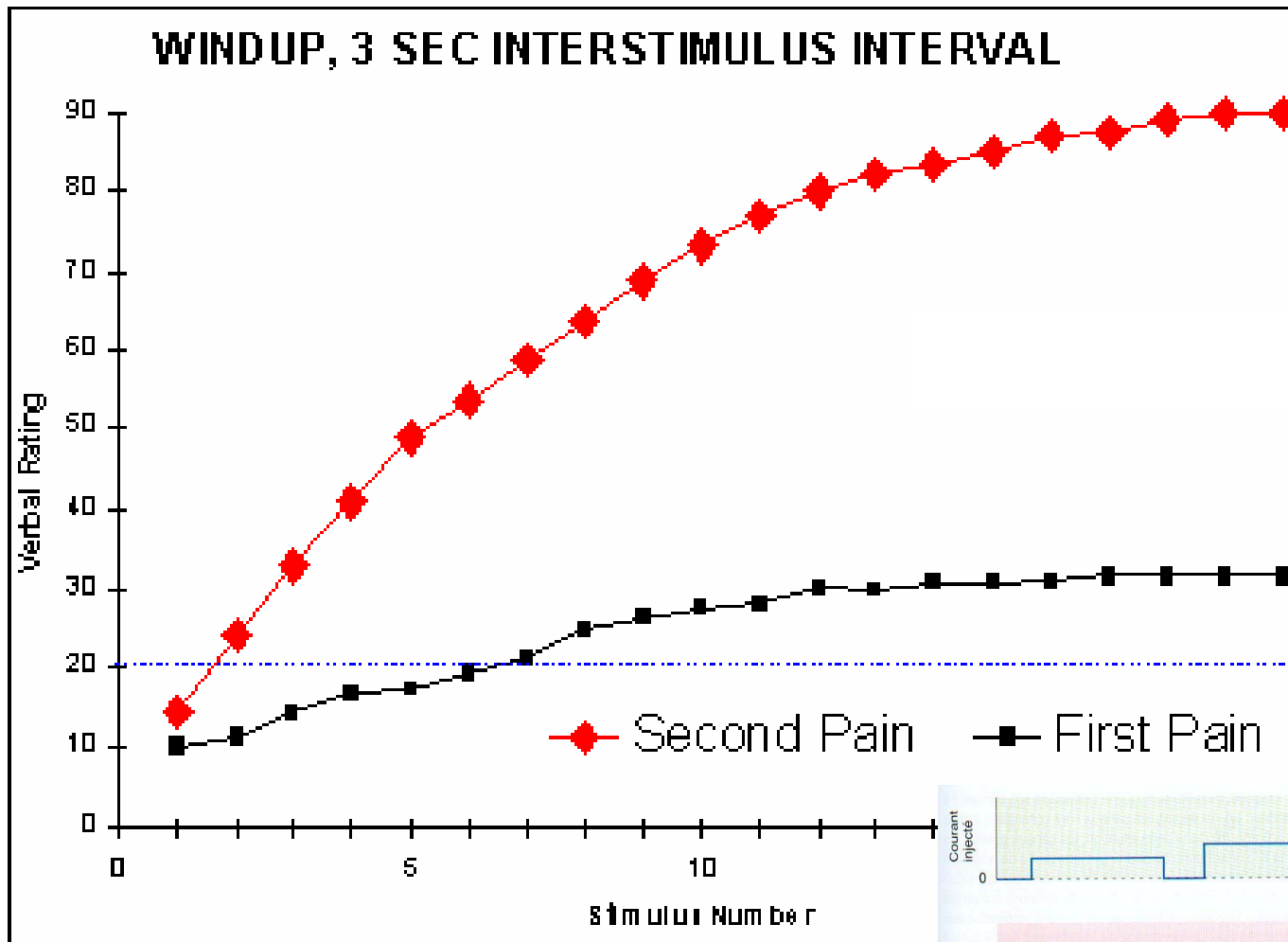
## Wide Dynamic Range



Wide dynamic range neuron activity

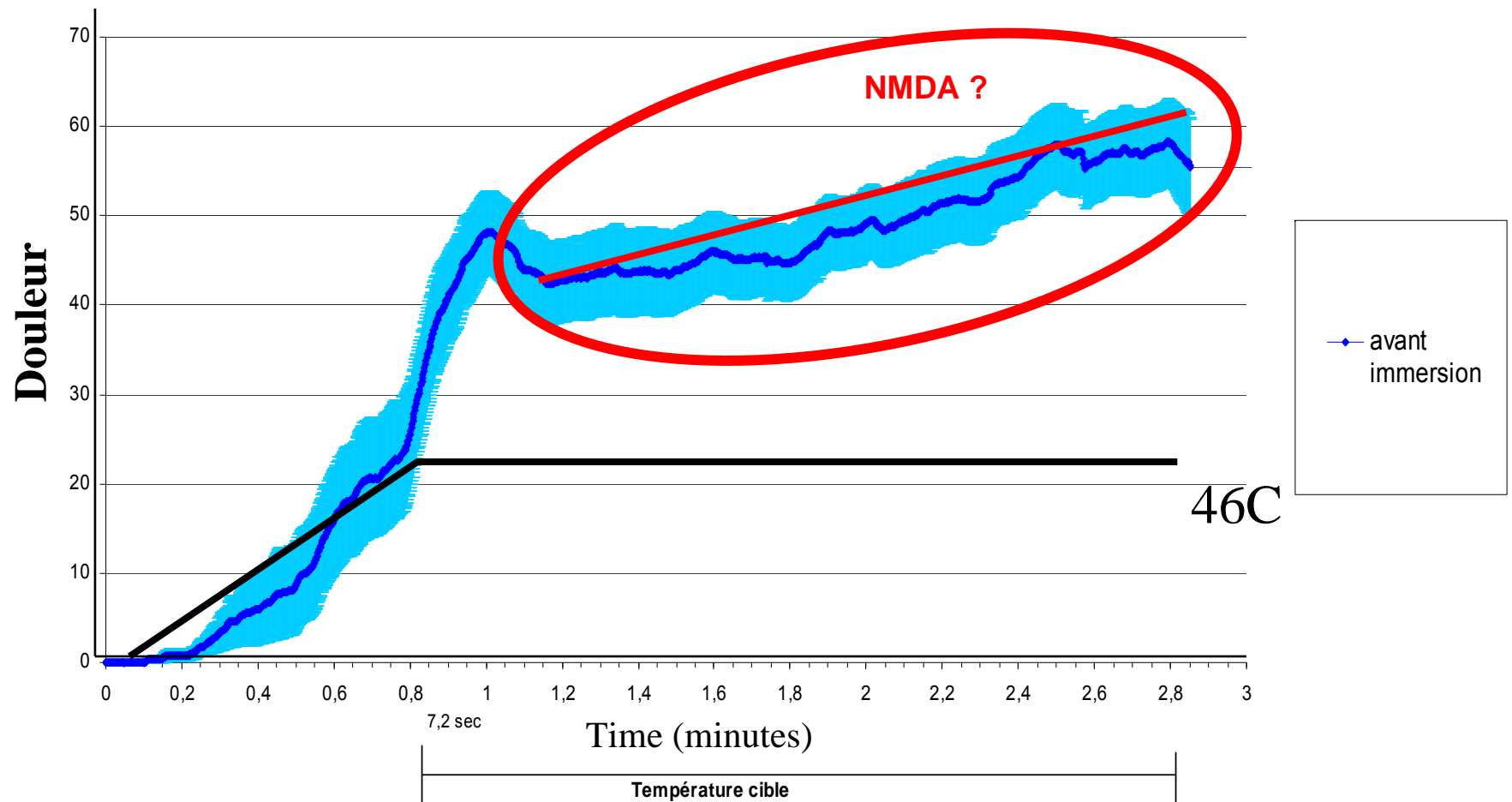


# Temporal summation





# Temporal Summation Healthy Subjects



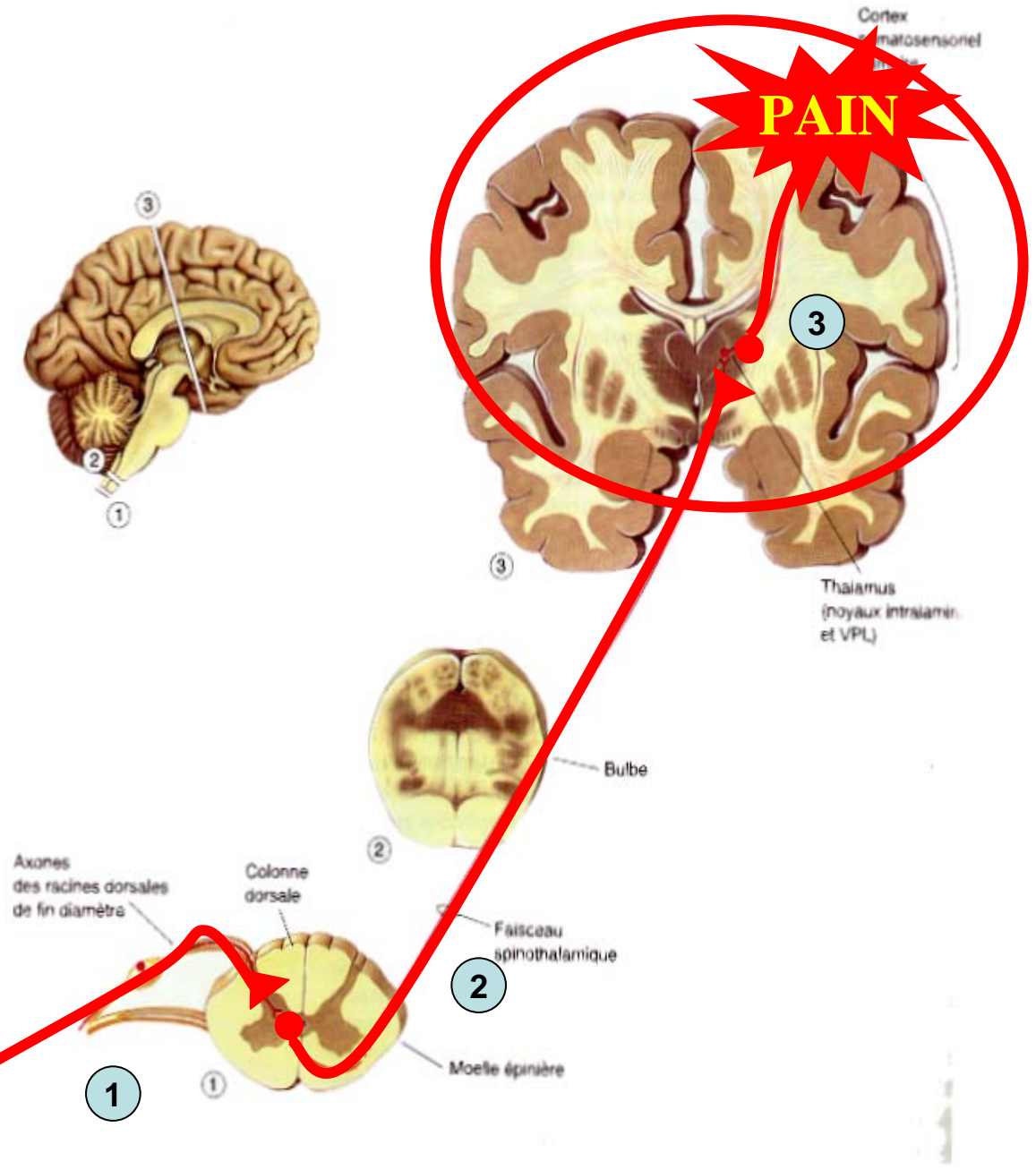
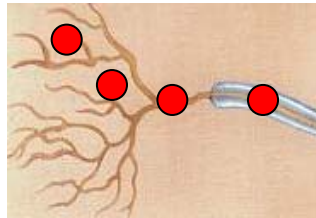
# QST of central sensitization

## Temporal sommation:

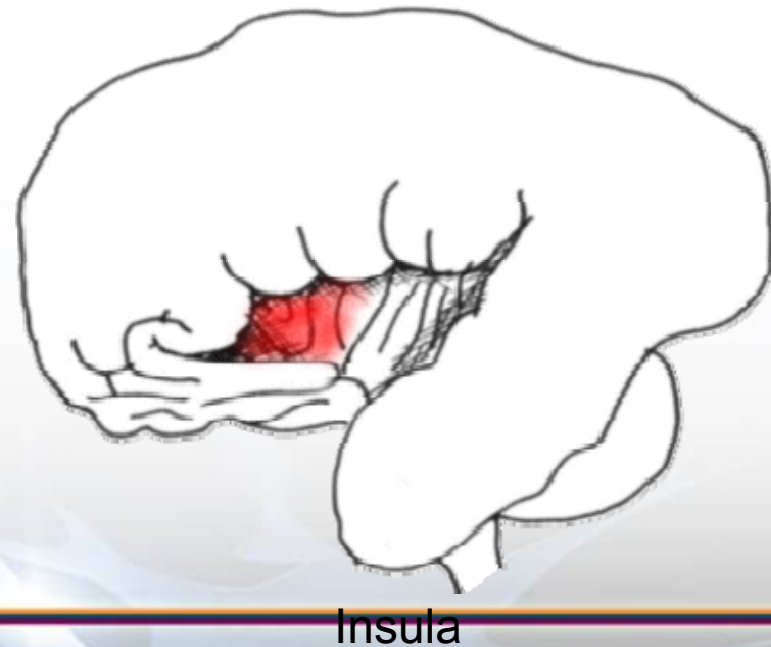
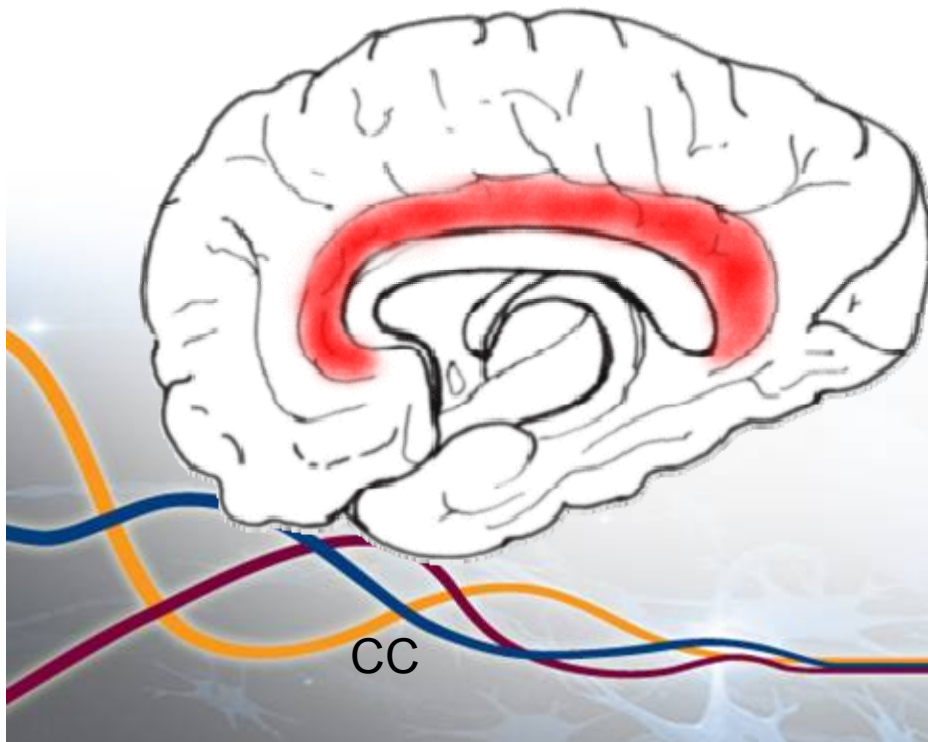
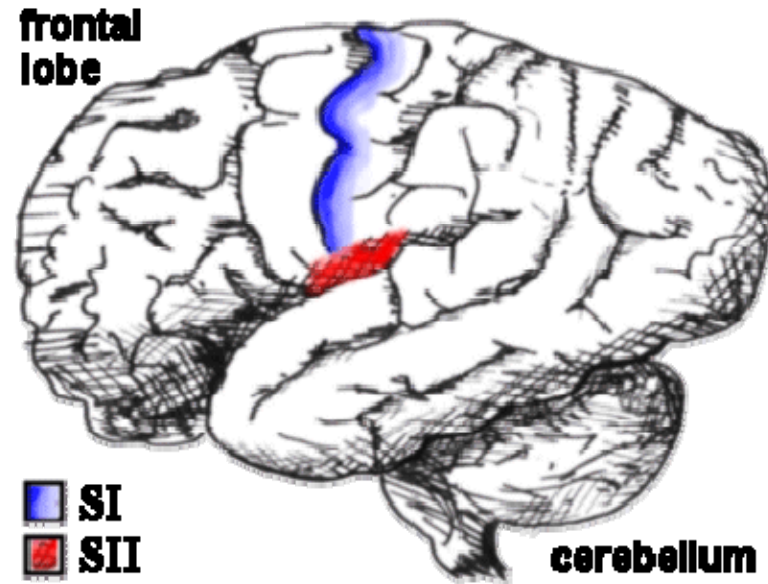
- Repeated stimulation (pin prick or thermal st) will produce escalating pain
- Persistent pain after the stimulation



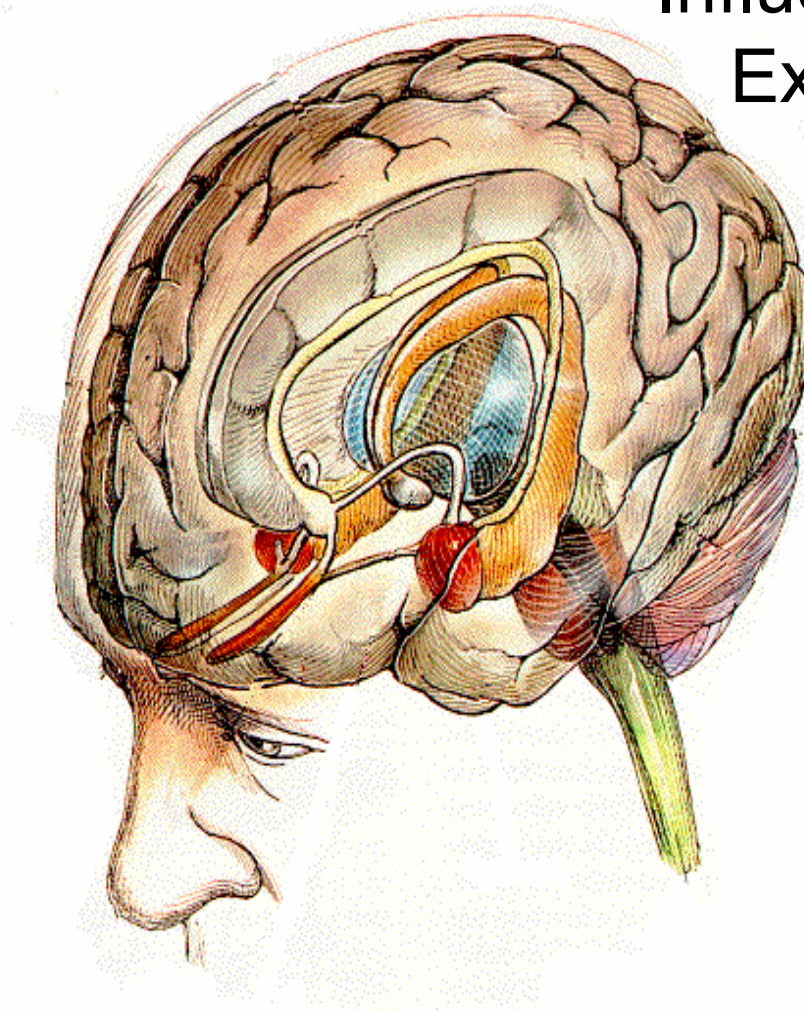
# From Nociception to Pain



# Four major regions activated by pain



# Limbic System



Influences of :  
Expectation  
Emotions  
Anxiety  
...

# Pain mechanisms and their disorders

*British Medical Bulletin* 2003; 65: 83–93

**AKP Jones\***, **B Kulkarni\*** and **SWG Derbyshire<sup>†</sup>**

*\*Human Pain Research Group, University of Manchester Rheumatic Diseases Centre, Hope Hospital, Salford, Manchester, UK and <sup>†</sup>Department of Anaesthesiology, University of Pittsburgh, Pittsburgh, Pennsylvania, USA*

. . . The brain does not share the construct . . . that the medical profession would like to impose on it.

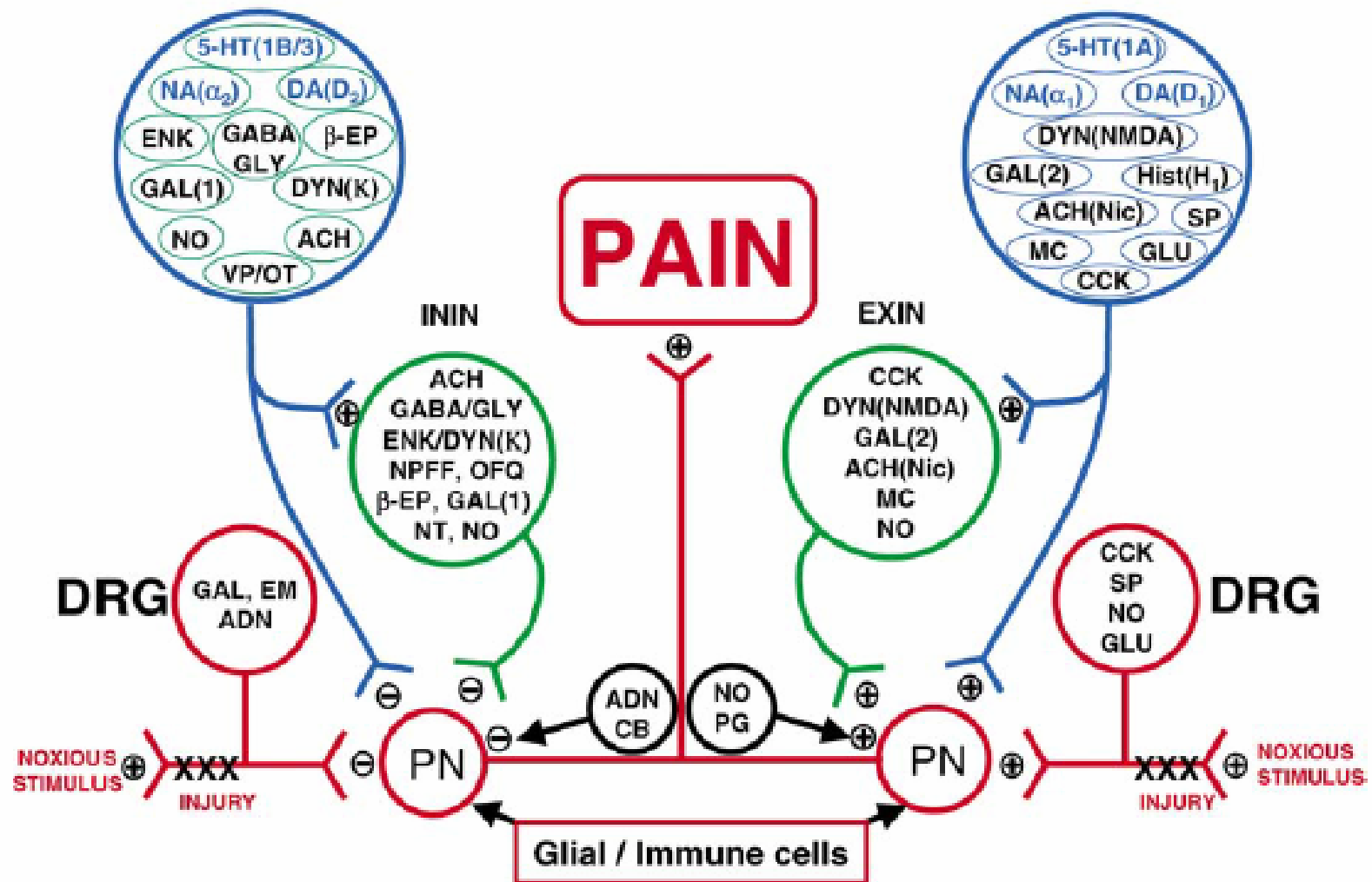
. . . it is likely to be simpler . . . with greater emphasis on the psychological context of the pain and the pathophysiological mechanisms resulting in its maintenance.



# Inhibition vs facilitation

## INHIBITION OF NOCICEPTION

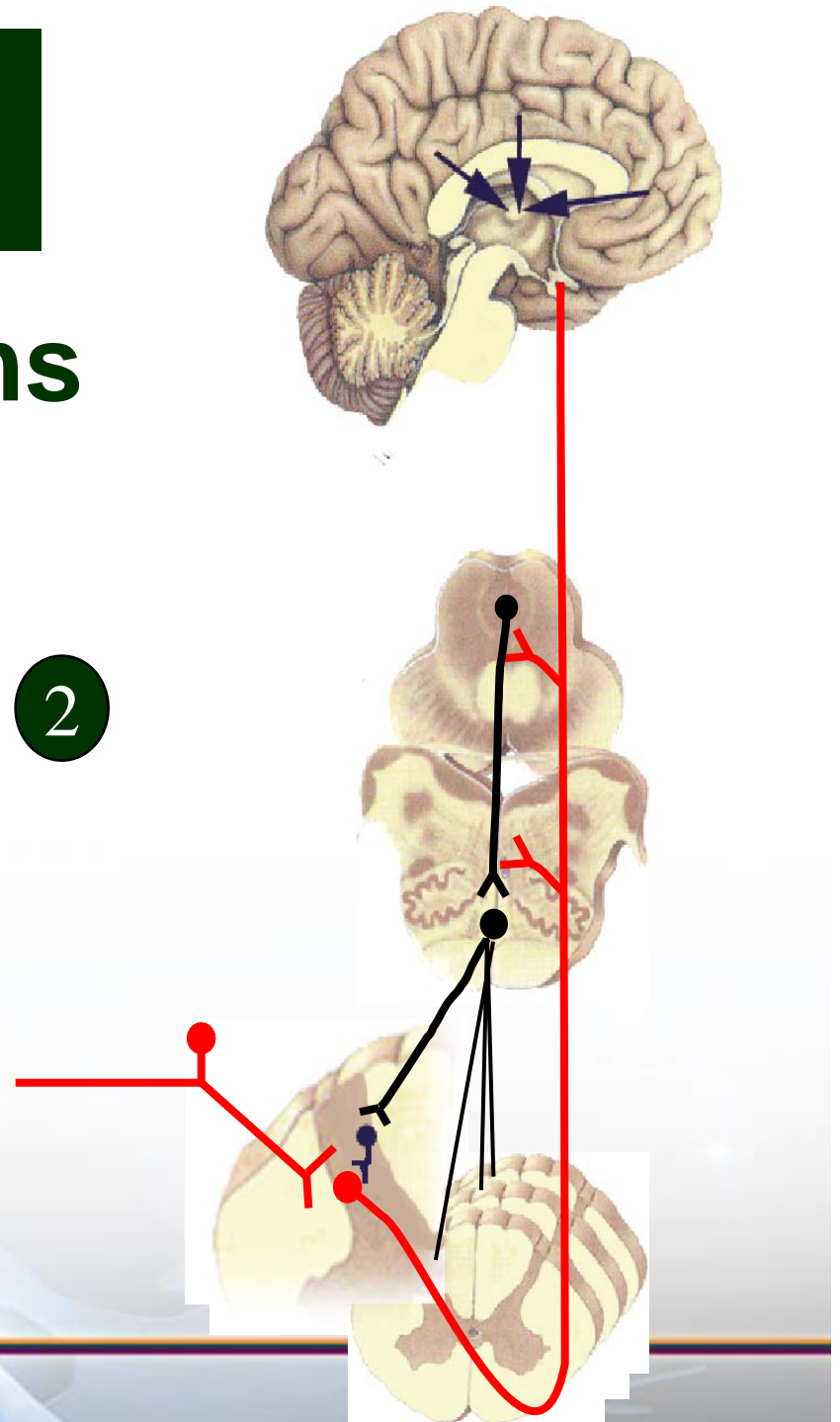
## FACILITATION OF NOCICEPTION



# Endogenous Pain Inhibition

## Descending Systems

### Diffuse Noxious Inhibitory System





Pain 114 (2005) 295–302

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**PAIN**

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[www.elsevier.com/locate/pain](http://www.elsevier.com/locate/pain)

## Widespread pain in fibromyalgia is related to a deficit of endogenous pain inhibition

Nancy Julien<sup>a</sup>, Philippe Goffaux<sup>b</sup>, Pierre Arsenault<sup>b</sup>, Serge Marchand<sup>a,b,\*</sup>

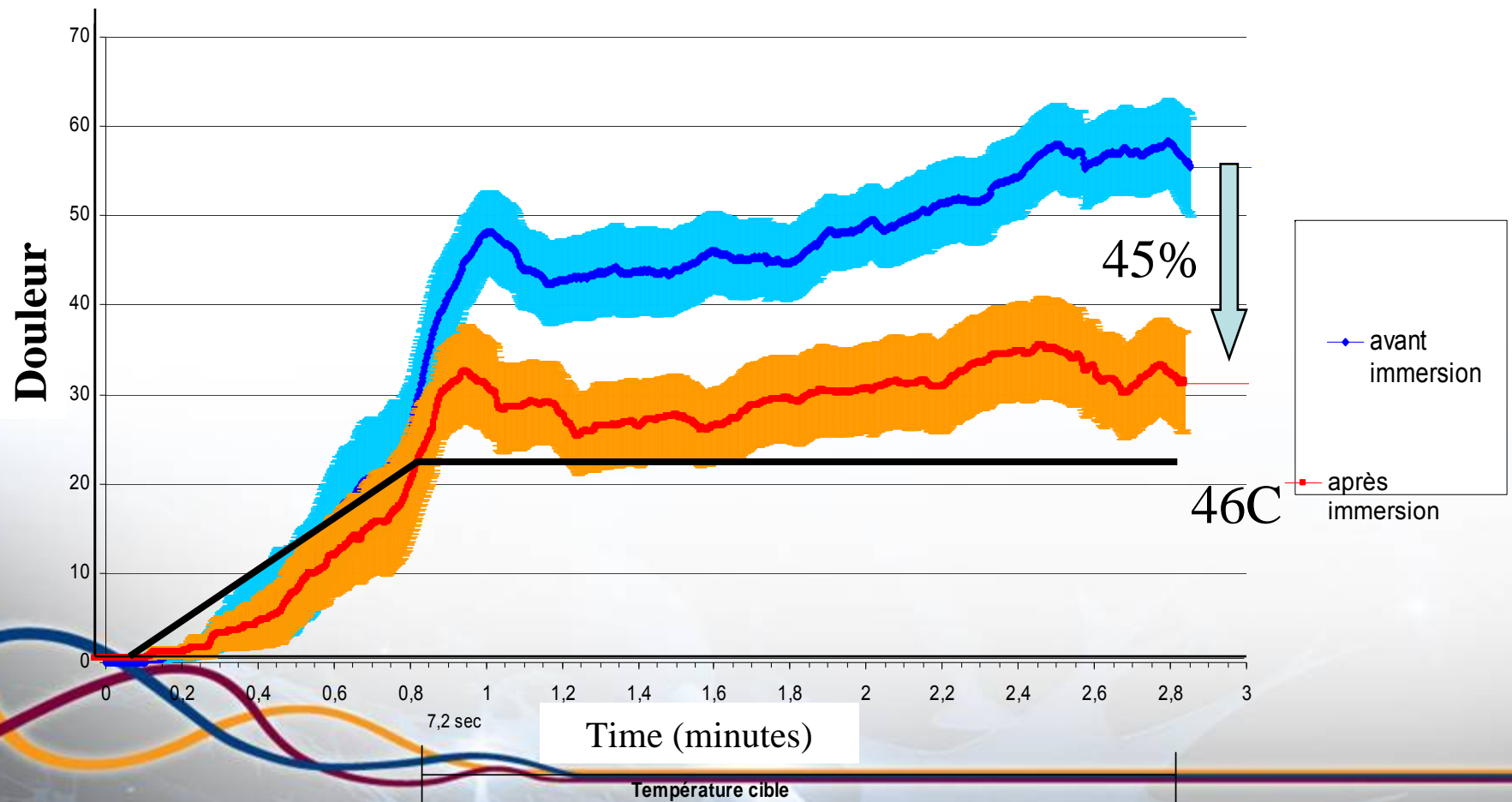
<sup>a</sup>*Département des Sciences de la Santé, Université du Québec en Abitibi-Témiscamingue, Rouyn-Noranda, Que., Canada*

<sup>b</sup>*Faculté de Médecine, Université de Sherbrooke, 3001, 12e Avenue Nord, Sherbrooke, Que., Canada J1H 5N4*

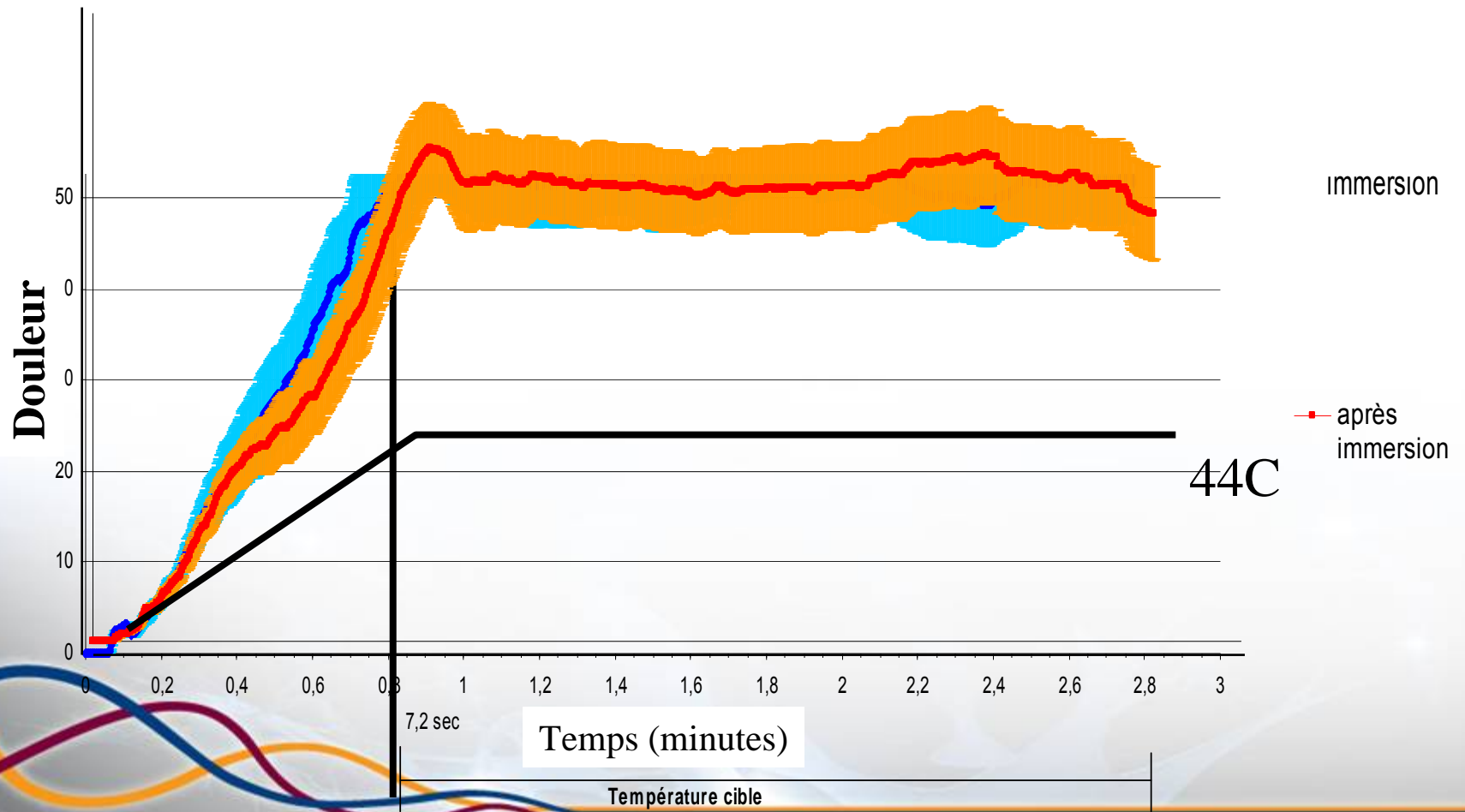




# Temporal Summation Healthy Subjects



# Temporal Summation in Fibromyalgia



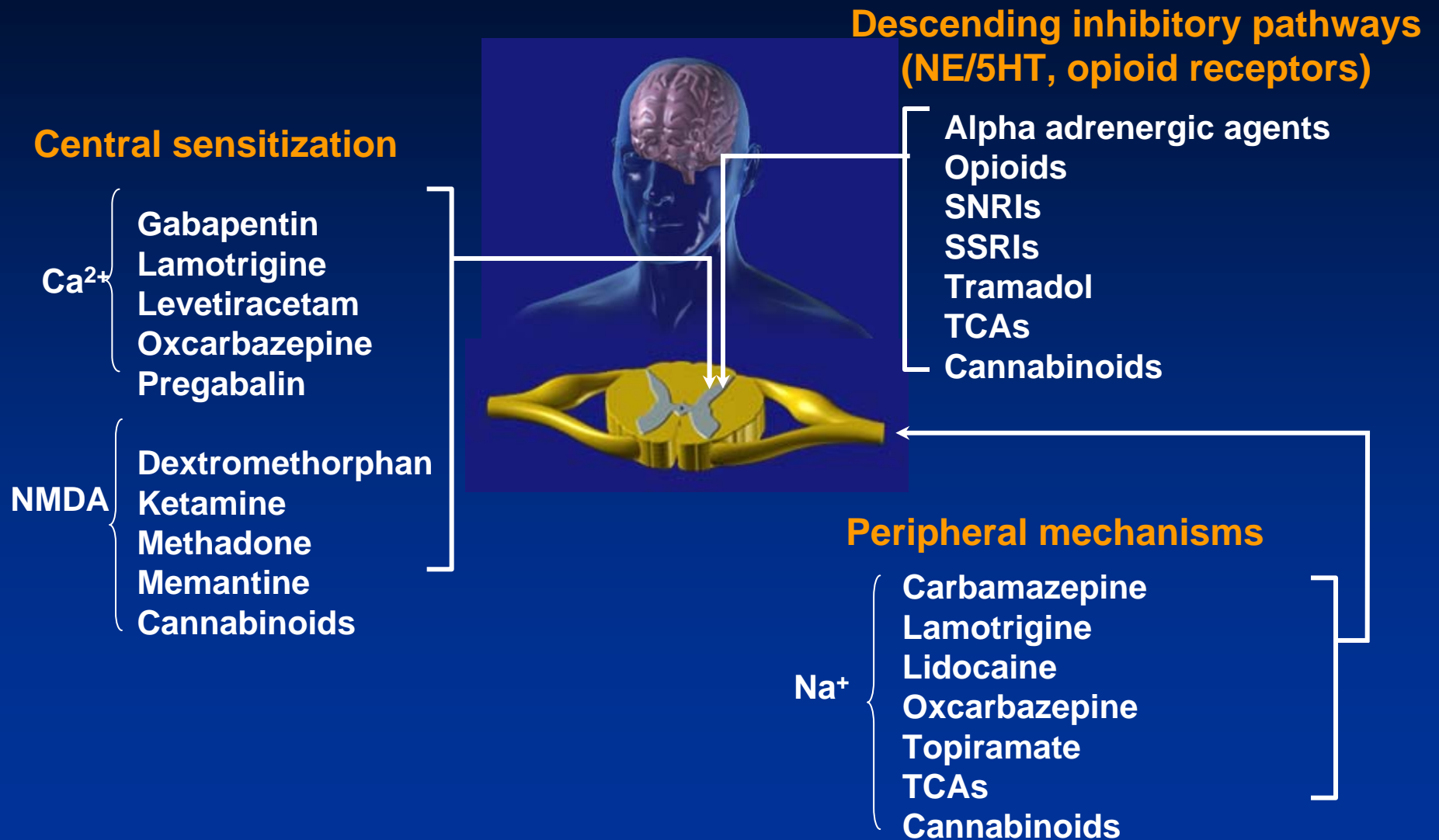
## Dysfunction of DNIC :

# Is it a generalized effect of all chronic pain conditions ?

- Deficits of DNIC in Tension-Type Headache (Pielsticker, PAIN 2005)
- Deficits of DNIC in IBS (Wilder-Smith,C.H., GUT 2004)
- No deficit of DNIC in Low Back Pain (Julien et al., PAIN 2005)



# Medications for neuropathic pain



NE: norepinephrine; 5HT: 5-hydroxytryptamine; NMDA: N-Methyl D-Aspartate;

SNRI: selective norepinephrine reuptake inhibitor; SSRI: selective serotonin reuptake inhibitor; TCA: tricyclic antidepressants

Review

## The clinical picture of neuropathic pain

Troels Staehelin Jensen<sup>a,\*</sup>, Hanne Gottrup<sup>a</sup>, Søren Hein Sindrup<sup>b</sup>, Flemming Winther Bach<sup>a</sup>

<sup>a</sup> Department of Neurology and Danish Pain Research Center, Aarhus University Hospital, Norrebrogade 44, DK-8000 Aarhus C, Denmark

<sup>b</sup> Department of Neurology, Odense University Hospital, Odense, Denmark

### Symptoms and findings in neuropathic pain

Symptom/finding	stimulus	Clinical presentation	Mechanism	Pharmacol. modulation
Static hyperalgesia	Gentle mechanical pressure	In area of injury (primary hyperalgesic zone)	Sensitised C-nociceptors	Systemic and topical lidocaine, opioids
Punctate hyperalgesia	Pinprick stimuli	In area of injury and outside (primary and secondary zone)	Sensitised A $\delta$ nociceptors and central sensitisation	Systemic and topical lidocaine Opioids?
Dynamic hyperalgesia	Light brush stimuli	In area of injury and outside (primary and secondary zone)	Central sensitisation due to increased input; due to loss of input	Systemic NMDA antagonists and lidocaine systemically Opioids?
Cold hyperalgesia	Cool stimuli (acetone, alcohol)	Nerve injuries, neuropathies and central pain	Central disinhibition because of loss of input	None?
Heat hyperalgesia	Radiating heat	In area of injury (primary hyperalgesia)	Sensitised C-nociceptors	Systemic and topical lidocaine, opioids
Wind-up like pain	Light brush or pin prick > 3Hz	Evoked pain by repetitive stimulation in and surrounding injury	Central sensitisation due to increased input	Systemic NMDA antagonists and lidocaine systemically
Chemical hyperalgesia	Capsaicin topical Histamine topical	Evoked pain/itch or vasodilatation	Sensitised mechanoinsensitive VR1/histamine receptors	Topical lidocaine
Aftersensations	Any stimulus	In and outside injury zone	Central sensitisation	?
Sympathetic maintained	Sympathetic stimulation or blockade	Present in nerve injuries	Sympathetic hyperactivity	Stimulation: Noradrenaline Blockade: stellate block

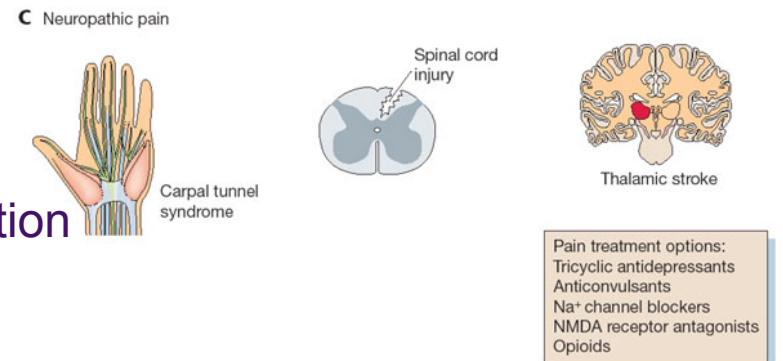
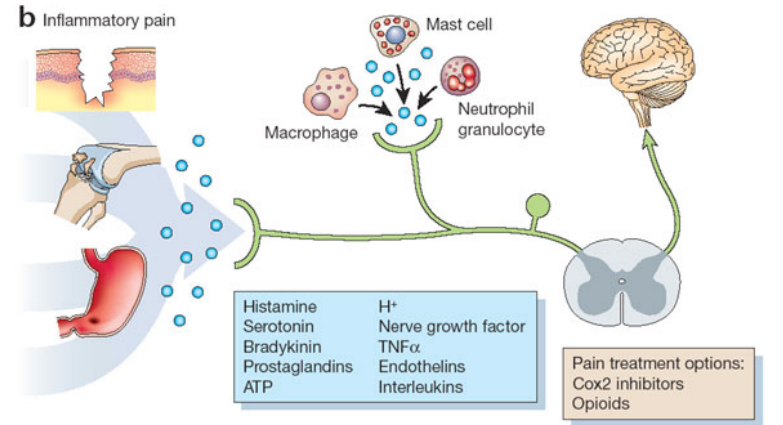
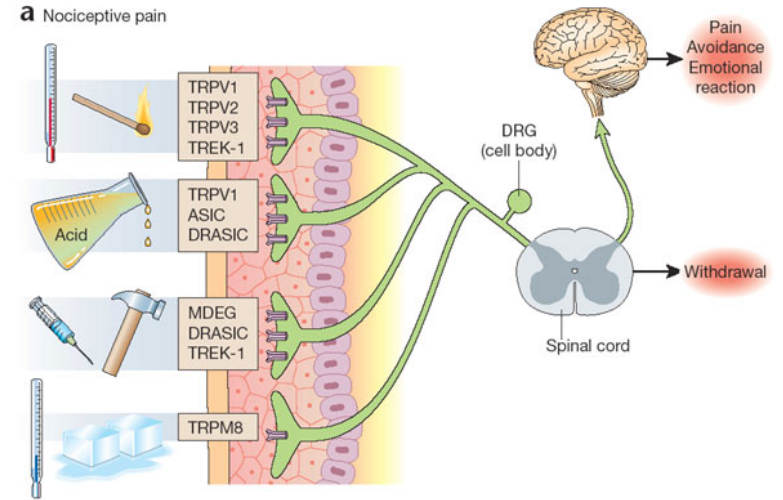
# Types of Pain

**Nociceptive:** somatic, visceral

**Inflammatoire:** somatic, visceral

**Neurogenic:** peripheral, central

**Functional:** hyperactivity, lost of inhibition



## Mechanistic classification of Pain

Marchand S  
 The physiology of pain mechanisms: from the periphery to the brain.  
**Rheumatic Disease Clinics of North America (In Press): 2008.**

Type of Pain		Characteristics	Mechanisms	Example of pharmacological treatments
Nociceptive	<b>Somatic</b> (tissue injury)	Superficial (skin) or deep pain (muscle, fascia, tendon)	Mechanical, thermal or chemical stimuli	Acetaminophen Na <sup>+</sup> blockers NSAID, steroids, opioids
	<b>Visceral</b> (Irritable bowel, cystitis)	Constant or cramping, poor localization. Autonomic responses	Visceral distension	NSAID, Antispasmodics
	<b>Inflammatory</b> (musculoskeletal)	Localized or diffuse pain hyperalgesia, allodynia.	Associated with localized inflammation	NSAID, steroids
Neurogenic	<b>Causalgia</b> (neuralgia, radiculopathy, CNS lesions)	Spontaneous, paroxysmal pain. allodynia, hyperalgesia.	Peripheral or CNS lesions	Anticonvulsivants, opioids, antidepressants
	<b>Functional</b> (FM, thalamic syndromes, Irritable bowel syndrome)	Diffuse deep pain, hyperalgesia, allodynia	Dysregulation of excitatory or inhibitory mechanisms in CNS	Antidepressants, anticonvulsivants, opioids, cannabinoids.

# Individual differences

Genetical predisposition  
Environmental factors

## QST !

### Peripheral neuropathy

- Cold hyperalgesia: C
- Hot hyperalgesia: A $\delta$

### Central sensitization

- Temporal summation
- Persistent/spontaneous pain

### Disinhibition

- Widespread pain (?)

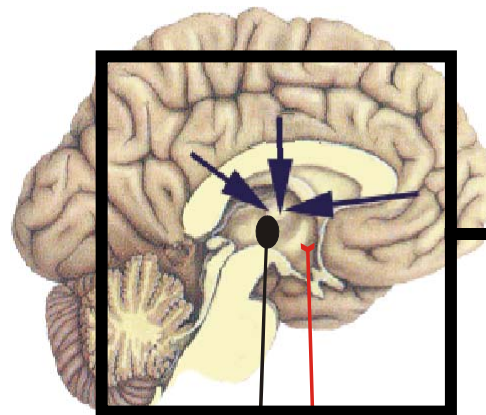


# Current Pain Therapeutics Approaches

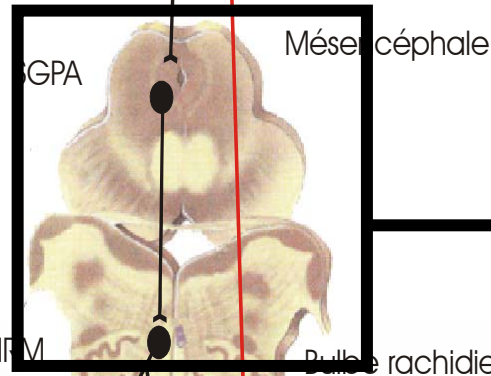
- ◆ **AINS (COX-1 & COX-2)**
- ◆ **Opiacés (mu agonists)**
- ◆ **Anticonvulsants (GABA)**
- ◆ **antidépresseurs (5HT, NA),**
- ◆ **Ketamine, dextorphan, ... (NMDA)**
- ◆ **Cannabinoids (...)**
- ◆ **Combinations (opioids + ....)**

**Need for an Algorithm !**

# Mechanistic Based Treatment

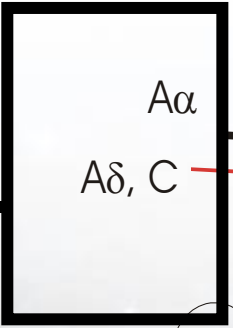


Antidepressants  
Opioids  
...



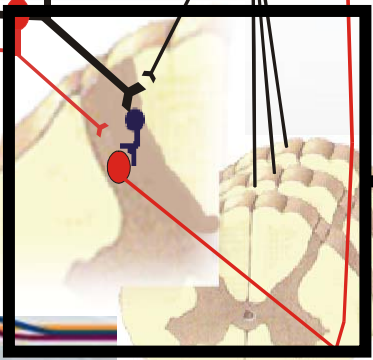
Antidepressants (IR, SS, IRSA, tricyclics)  
Opioids  
...

2



AINS  
COXIB  
Steroids  
capsaicine  
Opioids  
Cannabinoids

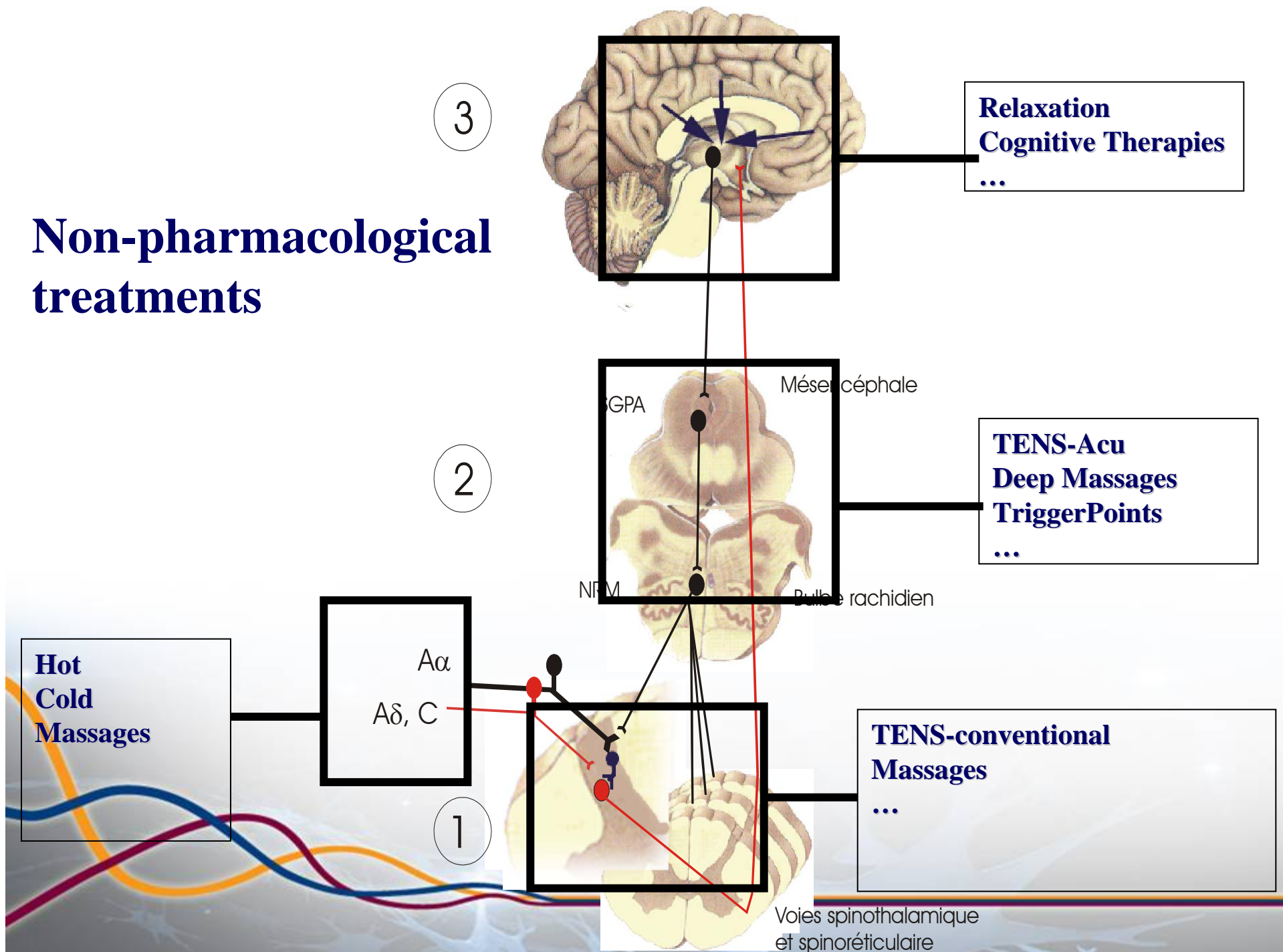
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Anticonvulsifs antiarythmiques  
Antagonist -NMDA  
AINS, COXIB  
Opioids  
Tricyclics Antidepressants  
Cannabinoids

Voies spinothalamiques  
et spinoréticulaires

# Non-pharmacological treatments





### Étudiants

Philippe Goffaux  
Stéphane Potvin  
Nancy Julien  
Isabelle Gaumond  
Yannick Tousignant-Laflamme  
Juliana B .De Suza  
Guillaume Léonard  
Stéphanie Pagé  
Marie-France Spooner  
William Redmond  
Geneviève Leduc  
Émilie Paul-Savoie  
Édith Normand  
Patricia Robichaud

### Collaborateurs

Patricia Bourgault  
Christian Cloutier  
Sylvie Lafrenaye  
Pierre Rainville  
Gilles Lavigne  
Philippe Sarret

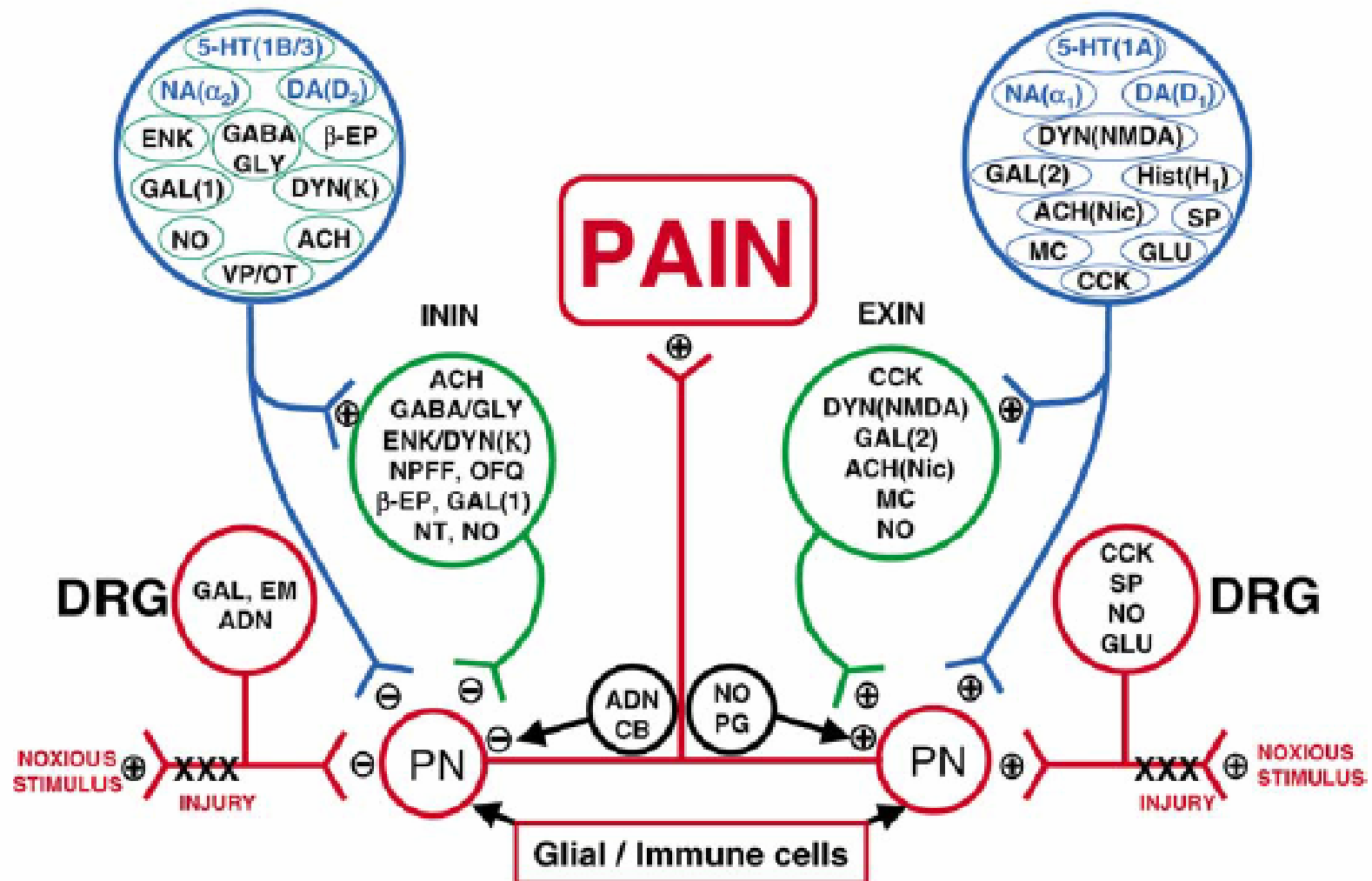
### Support

Instituts de recherche en santé du Canada (IRSC)  
Fonds de recherche en santé du Québec (FRSQ)  
Réseau de recherche en douleur (FRSQ)  
Réseau de recherche sur le placebo (IRSC)  
American Fibromyalgia Syndrome Association (AFSA)

# Inhibition vs facilitation

## INHIBITION OF NOCICEPTION

## FACILITATION OF NOCICEPTION



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QST in clinical practice:  
a practical demonstration and  
feasibility discussion

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# Disclosure

- Grant support from Pfizer for development of QST protocols to Pain Centre and honoraria for CME activities

# Objectives

- Review bedside use of QST procedures
- Discussion of clinical implications
- Utility of QST in research
  - German Research Network on Neuropathic Pain (DFNS, Germany)
  - Neuropathic Pain Research Consortium (NPRC, USA)
  - Not yet subject to formal validation

# Background

- Sensory examination is routine part of neurological examination
  - Pattern of neuro abnormalities
  - Part of complete physical exam
- Testing for allodynia and hyperalgesia is not part of formal neurological exam training for med students at McGill
- Formal QST requires specialized equipment
  - Results in measurable thresholds
- Bedside sensory testing is easy to do
  - Results in “qualitative” or binary (yes/no) result

# Constellation of terms

- Sensory gain or loss?
  - Hypo-
  - Hyper-
  - Para-
  - Dys-
  - An-
- Nature of sign
  - -esthesia
  - -algisia (-dynia)
  - -pathia
- Nature of stimulus
  - Tactile/mechanical vs thermal vs pressure vs vibration
  - Static vs dynamic

# Equipment list

- Touch
  - Cotton ball
  - Brush: foam or bristle, Somedic
  - **QST: Von Frey hairs**
    - Single fibre
    - Full set of monofilaments
- Pain
  - IV needle, toothpick, safety pin, open paperclip (sharp/dull)
  - **QST: Neuropen (large diameter von Frey hair)**
- Vibration
  - Tuning fork (C: 125Hz)
  - **QST: “Vibrometer”, Rydel-Seiffer tuning fork**
- Temperature
  - Alcohol on cotton swab
  - Warm and cool test-tubes of water or tuning fork end
  - Thermal rollers (“Rolltemp” by Somedic)
  - **QST: Medoc Thermal analyser (TSA II)**
- Pressure
  - Finger (!)
  - **QST: Algometer**

# Technique

- General guidelines:
  - Ask about sensitivity first! (history, drawings)
  - No leading questions
  - Tell them what you are going to do
  - “Close your eyes”
  - Establish normal side first
  - Start from unaffected area and move in toward affected area
  - Start with least painful stimulus
  - Watch for nonverbal clues (e.g. grimace, twitch)
  - Check for sensory gain or loss (“Do you feel this more, less, or the same”)
  - Record findings in chart (and on patient?)
    - Use manikin to see changes over time

# Temporal summation

- 10 repetitive stimuli
- Pinprick
- 1 per second
- Baseline and end of test VAS
- Tests for *central sensitization*
  - Presence of aftersensations
  - Wind-up

# Light touch

- Single touch stimulus (no movement)
  - Verify touch sensation on normal area
  - Then touch contralateral (affected) side:
    - “is this more, less or the same”
    - If more, is it painful?
    - Pain response → *static mechanical/tactile allodynia*
    - If increased but not painful → *static dysesthesia*
    - A- $\beta$ -fibre mediated



# Light Brush

- Most studies use the technique described by LaMotte:
  - each stroke at a velocity of - 5 cm/s over a distance of 1-2 cm
  - strokes to normal skin and then to region of hyperalgesia.

LaMotte RH et al. Journal of Neurophysiology 1991
- A -  $\beta$  mediated



# Light Brush Interpretation



- Increased but not painful = brush dysesthesia : mechanism = sensory pathway spontaneous activity (usually spontaneous activity in A-Beta afferents)
- Painful = brush allodynia : mechanism = central sensitization and /or central disinhibition

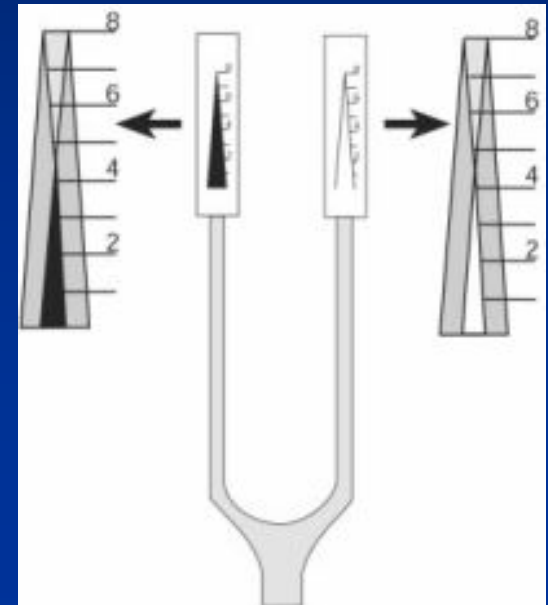
# Pressure

- Gentle increases in pressure with fingertip pad over muscle belly
- Feel for tight bands
  - Trigger points radiate
  - Tender points do not
- Stop pressure at single smooth arc of nailbed pallor
- Pain response → *static tactile allodynia*



# Vibration

- Test of A -  $\beta$  function
- Test over bony prominences?
  - Tibial tuberosity, medial malleolus, 1st MTP joint
  - Or test affected area
- Ask subject to describe sensation (and when it stops)
- Test devices:
  - tuning fork (128 Hz)
  - Rydel-Seiffer (64 Hz)
  - Vibrometer (Somedic)



# Vibration Interpretation

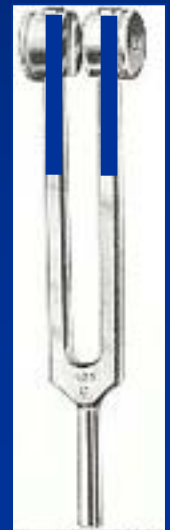


- Increased but not painful = vibration dysesthesia : mechanism = peripheral sensitization
- Painful = vibration allodynia : mechanism = central sensitization

# Cool and Cold Pain



- Nerve fiber: Cool = A -  $\delta$  Cold pain = A Delta and C
- Test:
  - QST uses Medoc TSA system
    - Cold detection and cold pain thresholds
  - Medoc Thermoroller
  - no standardized tool for bedside
  - Ask to compare normal to affected
    - “more, less or same”



# Cool and Cold Pain Interpretation

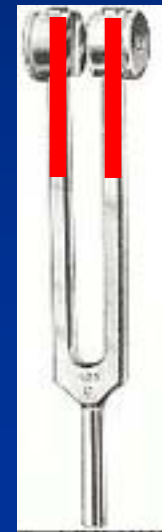
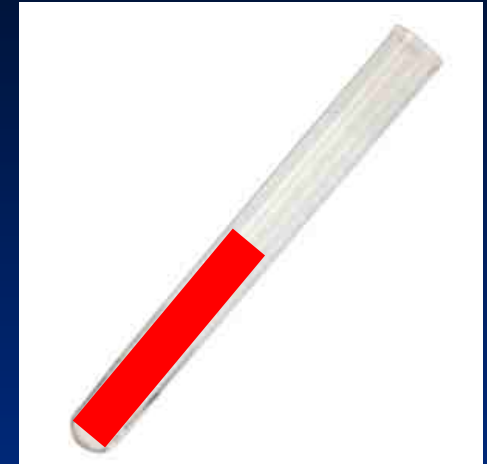


- Cool testing (A Delta)
  - Increased but not painful = cool dysesthesia : mechanism = sensory pathway damage or dysfunction and/or central sensitization
  - Painful = cool allodynia : mechanism = central sensitization
- Cold pain testing (A Delta/C)
  - Increased and painful = cold hyperalgesia : mechanism = If there is only loss of the A delta specific fibers then patients develop loss of cool sensation (cold hypoesthesia) which is mediated by these fibers. Paradoxically the threshold for cold-pain, which is mediated by polymodal C-nociceptors decreases (cold hyperalgesia). The pain is stimulated by cold but is described by the patient as hot and burning. Central sensitization may also play a role.

# Warm and Hot Pain



- Test:
  - QST uses Medoc TSA system
    - Heat detection and heat pain thresholds
  - Medoc Thermoroller
  - no standardized tool for bedside
  - Ask to compare normal to affected
    - “more, less or same”
- If pain detected compared to normal



# Warm and Heat Pain Interpretation



- Warm testing (C fiber)
  - Increased but not painful = warm dysesthesia : mechanism = not yet defined
  - Painful = warm allodynia : mechanism = central sensitization
- Heat pain testing (C and some A Delta)
  - Increased and painful = heat hyperalgesia : mechanism = peripheral sensitization

# Pinprick Evaluation

- Evaluation of different tools used to produce a sharp stimulus demonstrated that if one examiner tests with a probe tip of 0.4mm at an angle  $<120^\circ$  then 10gms of pressure is perceived as sharp and 40gms is perceived as painful. If the probe tip is 0.2mm and held at the same angle then 20gms of pressure is perceived as painful 90% of the time.

# Pin Prick Pain (Punctate Mechanical)



- Probe size and shape matter

Greenspan and McGillis, Somatosens Motor Res 1991

- Keep force applied constant, single touch only
- A -  $\delta$  and C fiber mediated



# Pin Prick Interpretation



- Decreased = mechanical hypoalgesia : mechanism = sensory pathway damage or dysfunction of small fibers
- Increased = hyperalgesia : mechanism = peripheral sensitization of C fibers (if associated with heat hyperalgesia which is also transmitted by C fibers ) otherwise - central sensitization / central disinhibition
- Summation and after sensation indicates central sensitization

# Clinical implications

- Pain validation
- Pain diagnosis
- Insurance claims
- Therapeutic choice
  - Rx for neuropathic pain
  - Are there subtypes of NP?
- Issues
  - Standardization of examiners
  - Predictive value of bedside test

Thank you!

# Acknowledgements

- **NPRC**
  - Misha Backonja U of Wisconsin
  - David Walk - U of Minnesota
  - Ajay Wasan - Harvard U
  - Charles Argoff - NorthShore U Hospital NYC
  - Gordon Irving - Swedish Hosp, Seattle
  - Mark Wallace and Toby Moeller - UC San Diego
  - Nalini Sehgal - U of Wisconsin

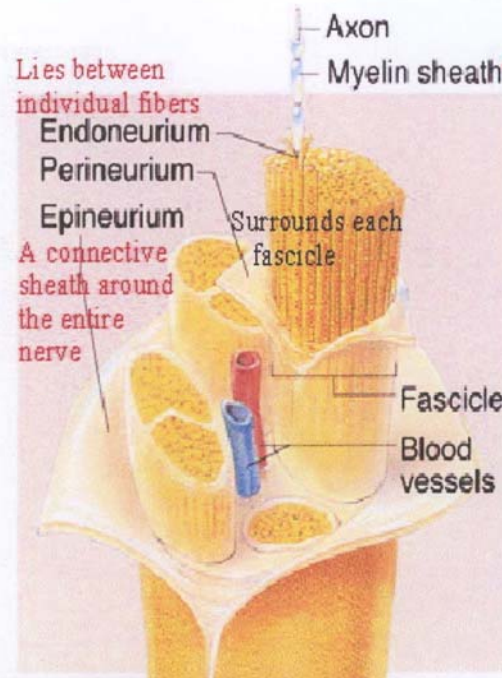
# Nerve Fibers



Nerve Type	Velocity (m/s)	Function
A - $\alpha$	70-120	motor
A - $\beta$	30-70	touch pressure vibration
A - $\delta$	12-30	pain (pinprick) Temperature (cold threshold)
B	3-15	autonomic fibers
C	0.5 - 2	Pain (H/C/P) temperature (heat threshold)

# Structure of a Nerve

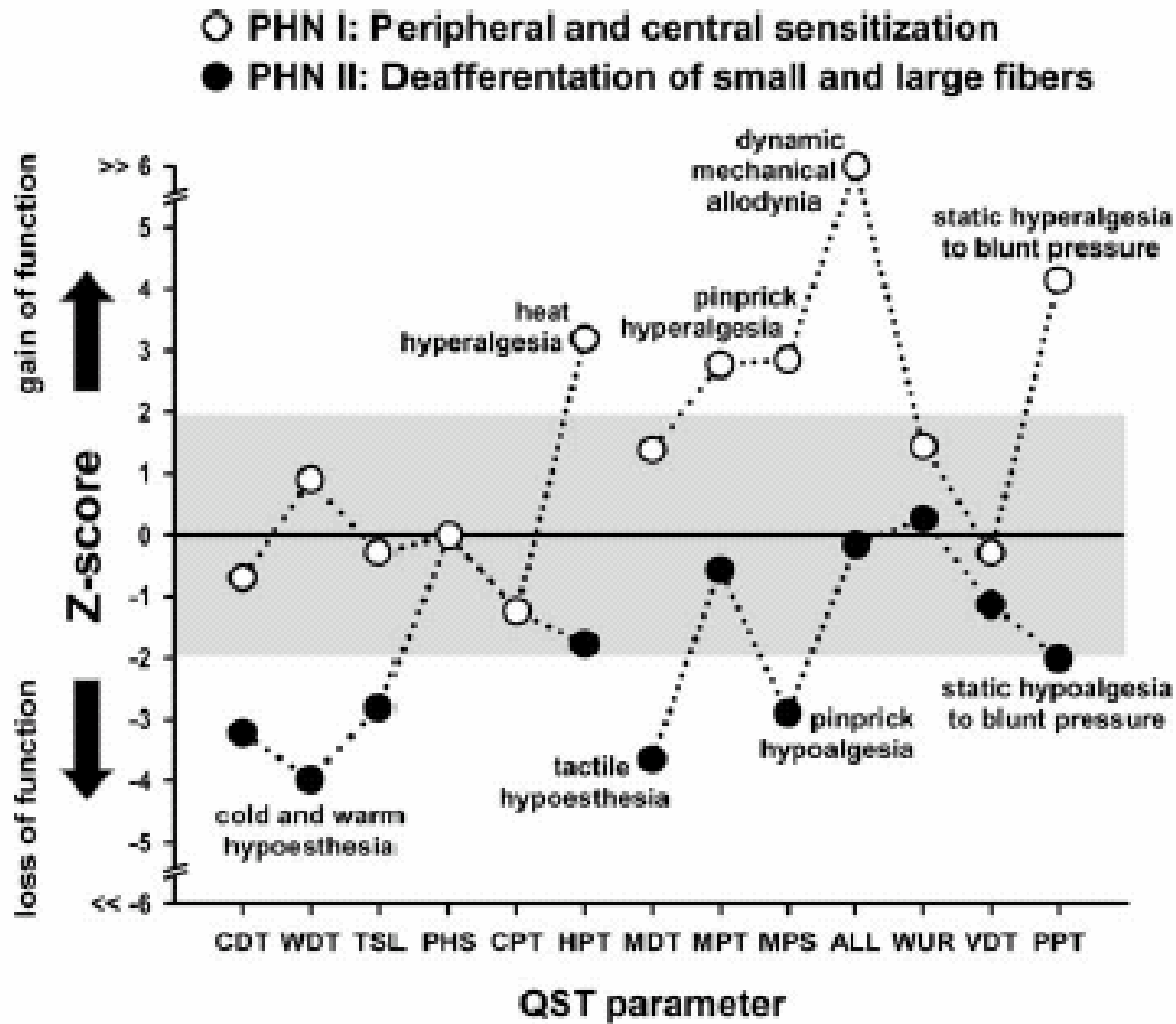
## Structure of a Nerve



Consists of a continuous series of Schwann cells wrapped around the fiber.

A nerve is a group of axons (nerve fibers) outside the CNS. These fibers are bundled together with connective layers. Many of the fibers are myelinated, which means they have a covering made from successive wrappings of Schwann cells.

# QST Profiles as z-Scores



# Electroneurography

- Electroneurography, also known as nerve conduction studies (NCS), nerve conduction velocity (NCV), or stimulation myelographic study (SMS), is used to detect the presence of a neuropathy in a particular nerve. Anatomically, there are three conditions that significantly decrease nerve conduction velocities:
  - \* demyelination (loss of myelin covering of the nerve)
  - \* conduction blocks (damage that stops continued movement of nerve impulse)
  - \* axonal loss (nerve cell death)

# Electroneurography

- Evaluates the large sensory fibers (pain and vibration) and the motor fibers
- Predominately evaluates loss of function (motor and sensory)
- Cannot evaluate the individual fibers in a nerve

# Somatosensory Evoked Potentials (SEP)

- Measure the electrical signal generated by a sensory stimuli
- Stimuli used = electrical
- Transduced by the mechanical receptors and transmitted by the large A beta fibers dorsal columns, medial lemniscus and their thalamo-cortical projections
- Provide a more objective measurement of touch and vibration abnormalities

# Somatosensory Evoked Potentials (SEP)

- The problem:

Large fibers (touch/vibration) = large amplitude waves

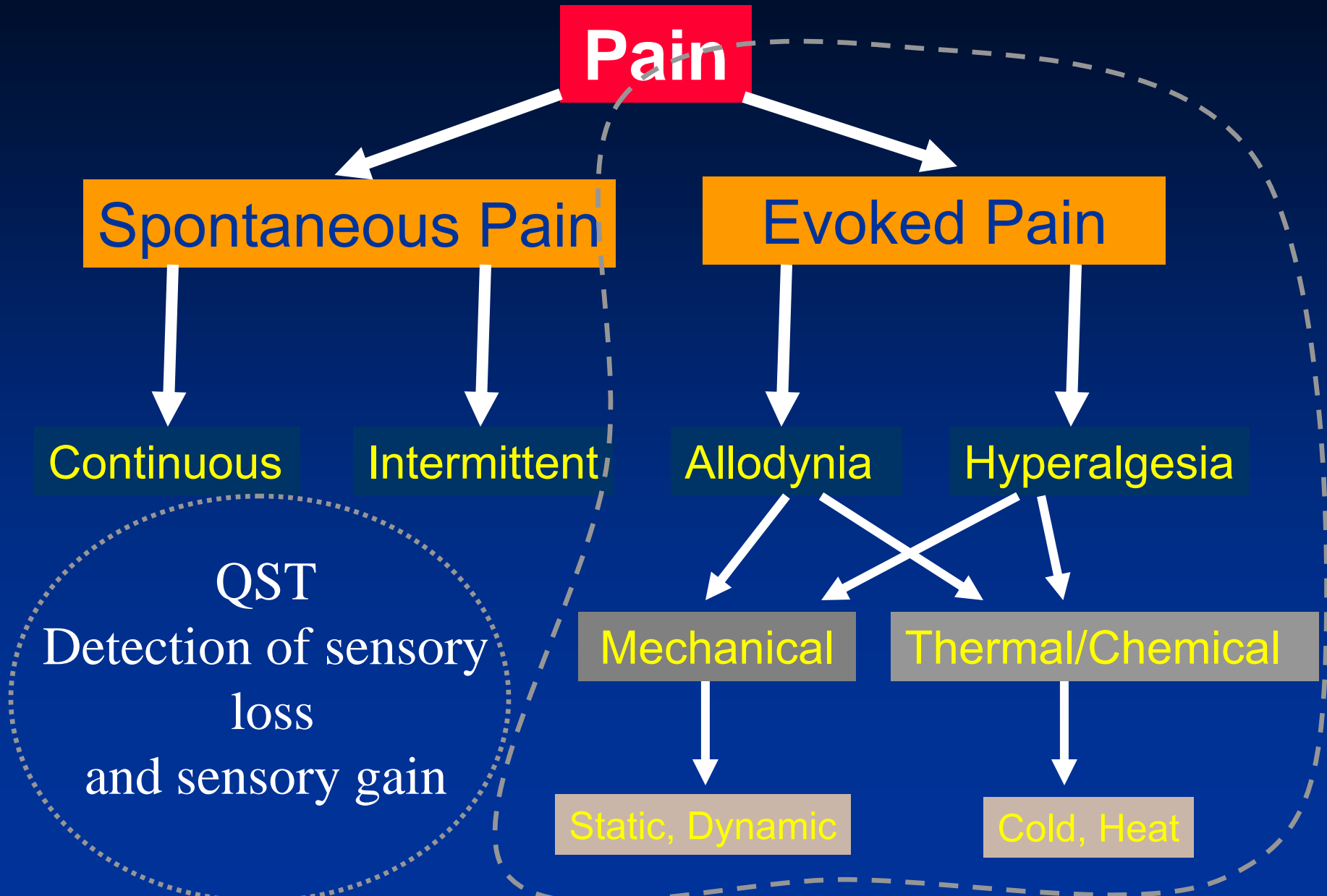
Obscure the waves coming from the small fibers

If only the small fibers are damaged the waveforms will look normal

# Laser Evoked Potentials (LEP)

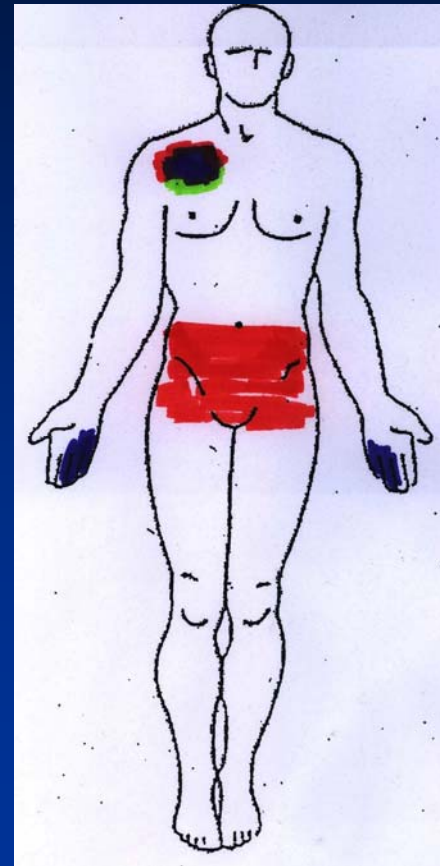
- Infra red laser pulses stimulate the small pain and temperature fibers
- Measures loss of function in the small fibers, spinothalamic tract, lateral brainstem and thalamo-cortical projections
- Most useful for assessing loss of pain sensation (hypoalgesia)
- QST more useful for evaluating hyperalgesia and related pain mechanisms
- Takes 1-2 hours, device is expensive, reimbursement issues.....

# Definition of Terms



# Multiple Pain Symptoms in a Patient with Neuropathic Pain

- Red-burning
- Blue-numbness
- Green-tingling
- Black-aching



# Where have we come from: treatment outcomes.

- 1998: Neuropathic pain patients Tx with WHO guidelines: mean pain intensity rating (NRS) 70/100 at admission-28/100 after 3 days (Grond S et al. Pain 1999)
- 2000: “Efficacy of pain treatment was good in 70%, satisfactory in 16% and inadequate in 14% of patients.”  
(Meuser T et al. Symptoms during cancer pain treatment following WHO-guidelines: a longitudinal follow-up study of symptom prevalence, severity and etiology.  
Meuser T, Pietruck C, Radbruch L, Stute P, Lehmann KA, Pain 2001)
- 2007: IASP NeuPSIG; “despite following best practice guidelines with sequential trials of therapy pain will be unrelieved or inadequately relieved in 40-60% of patients with neuropathic pain.” (Dworkin RH., Pharmacologic management of neuropathic pain: evidence-based recommendations. Pain. 2007 Dec)