Spinal Cord Injury Pain

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CENTRACARE Health

Objectives

At the conclusion of this session, participants should be able to:

1. Understand the difference between nociceptive and neuropathic pain

2. Understand basic neural tracts involved in spinal cord injury

3. Understand simple guidelines for treating pain after spinal cord injury

There are among us those who haply please to think our business is to treat disease.

And all unknowingly lack this lesson still 'tis not the body, but the man is ill.

S. Weir Mitchell (cited by Schofield 1902)

Silas Weir Mitchell

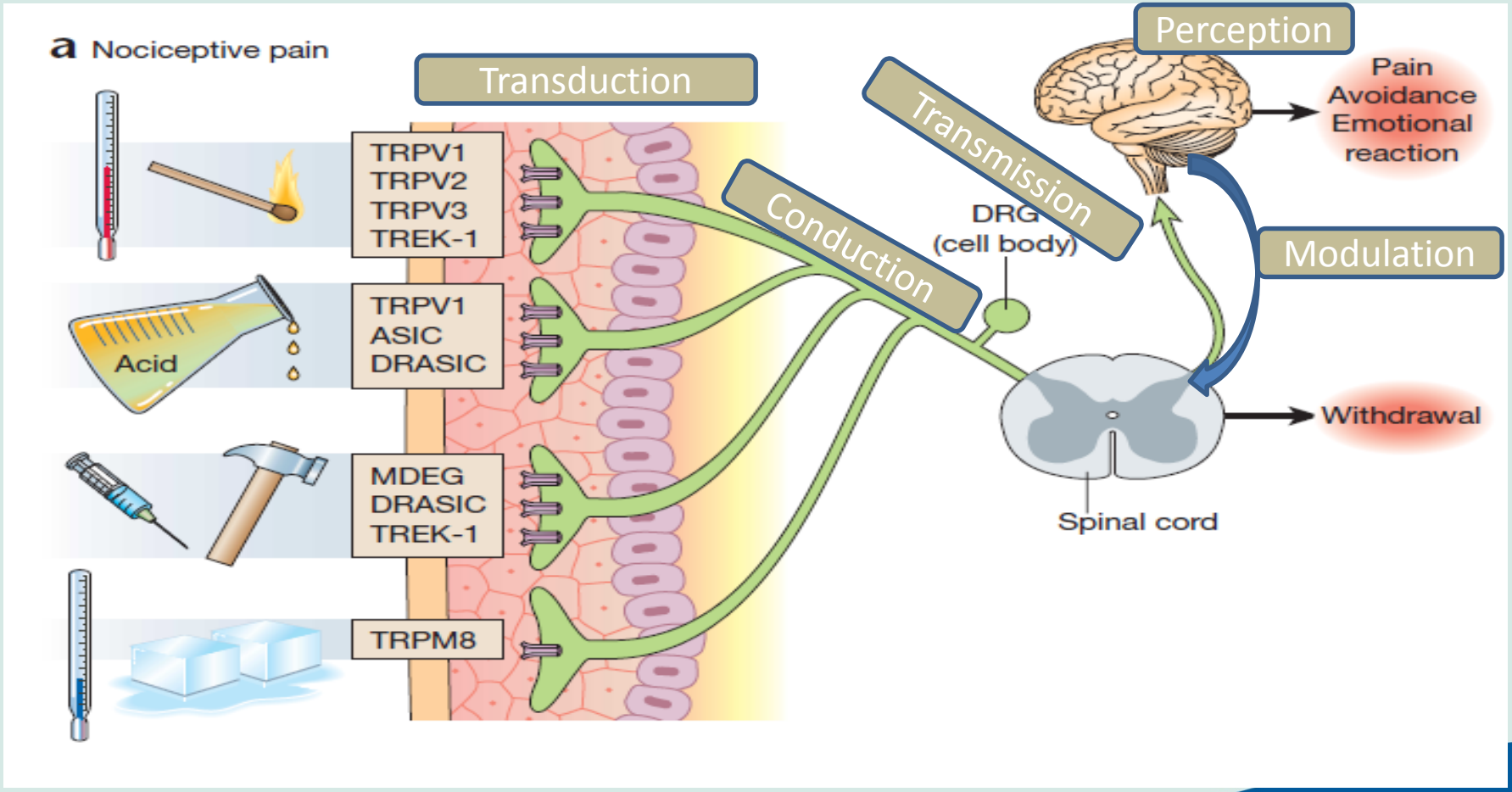
Pain Terminology

- **Pain**: An unpleasant sensory and emotional **experience** associated with actual or potential tissue damage
- **Noxious stimulus**: A stimulus that damages tissue
- **Nociception**: A receptor preferentially sensitive to a noxious stimulus, becomes noxious if stimulus prolonged

Pain Terminology, continued

- **Allodynia**: Pain caused by non-noxious stimulus
- **Hyperalgesia**: An increased response to a noxious stimuli
- **Hyperesthesia**: Increased sensitivity to stimulation
- **Dysesthesia**: An unpleasant abnormal sensation, whether spontaneous or provoked

Nociceptive Pain Processing: Transduction to Perception



Adapted from Scholz J, Woolf CJ, *Nat Neuroscience*. 2002: (5 suppl): 1062-1067

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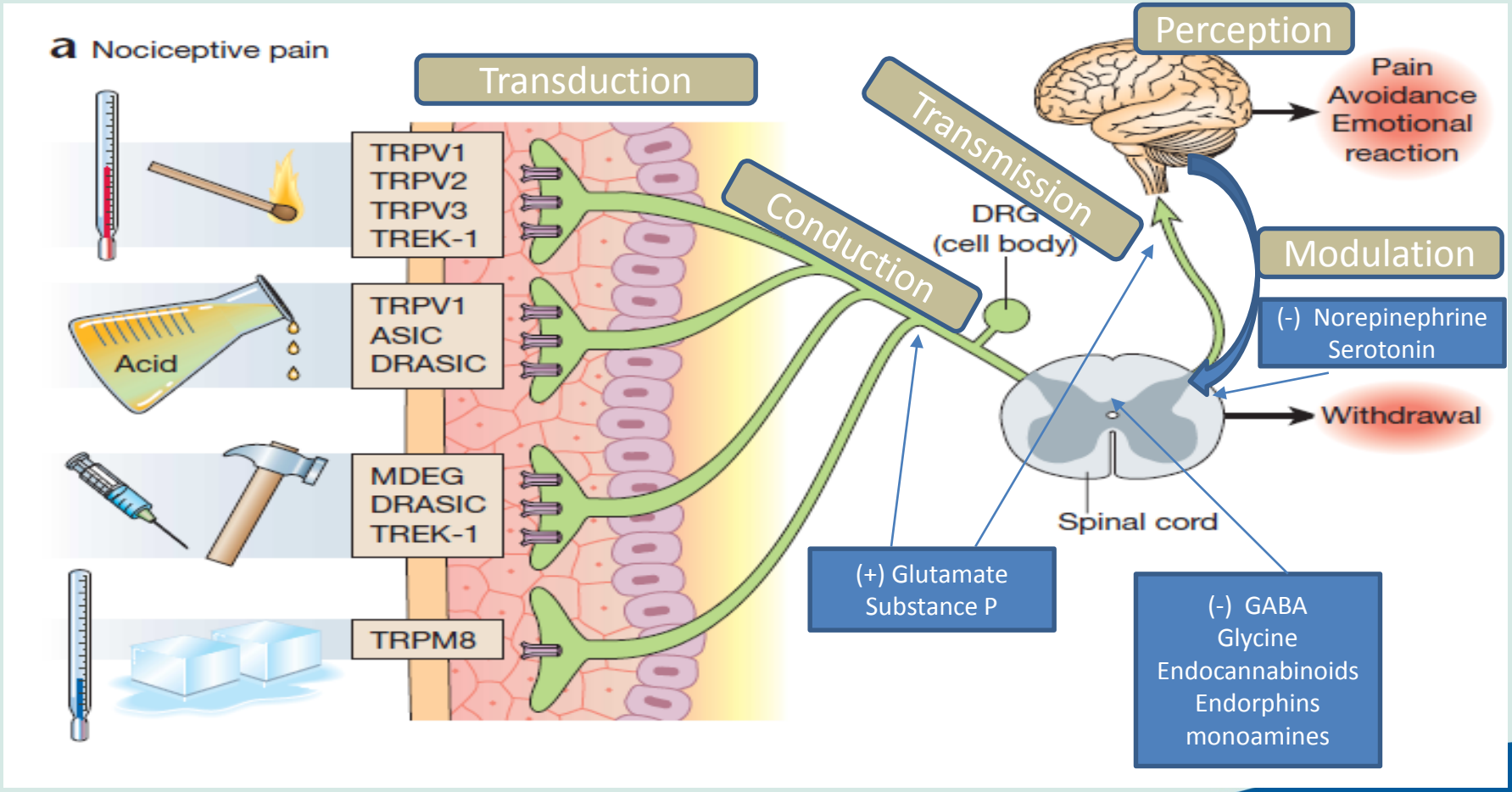

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Peripheral Nerve Fibers

Table 37-4 Nerve Fiber Classification

Sensory and Motor Fibers	Sensory Fibers	Diameter (μm)	Myelinated	Velocity (m/s)	Motor Function	Sensory Function
Aα	Ia Ib	10-20 10-20	Yes Yes	0-120 50-120	α-Motor neurons —	Muscle spindle afferents Golgi tendon organs, touch, pressure
Aβ	2	4-12	Yes	25-100	Motor neurons to intrafusal and extrafusal muscle fibers	Secondary muscle spindle afferents, touch, pressure, vibration
Aγ		2-8	Yes	10-50	Motor neurons to intrafusal muscle fibers	—
Aδ (types I and 2)	3	1-5	Lightly	3-30	—	Touch, pain, and temperature
B		1-3	No	3-15	Preganglionic autonomic fibers	—
C	4	<1	No	0.5-2	Postganglionic autonomic fibers	Pain and temperature

Stanos, et al. "Chronic Pain." *Physical Medicine and Rehabilitation, 5th Ed. 2015*

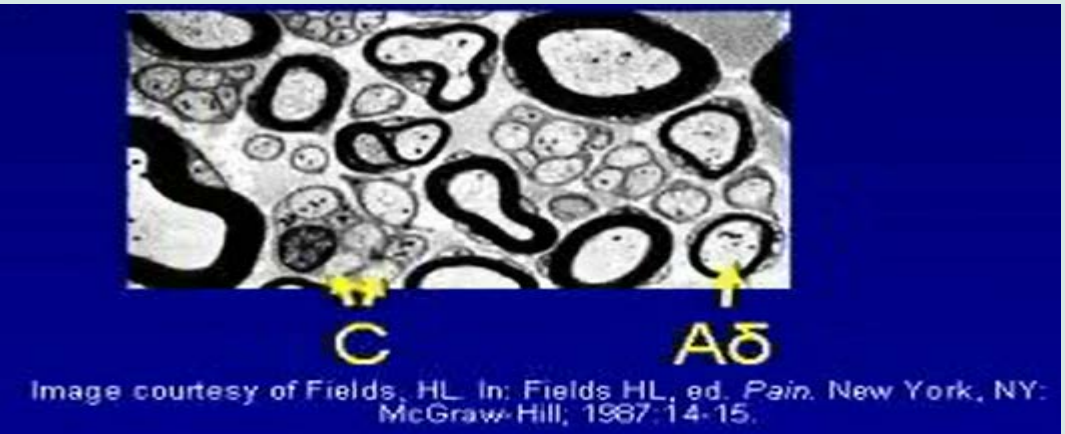


Image courtesy of Fields, HL. In: Fields HL, ed. *Pain*. New York, NY: McGraw-Hill; 1987:14-15.

Normal Sensation

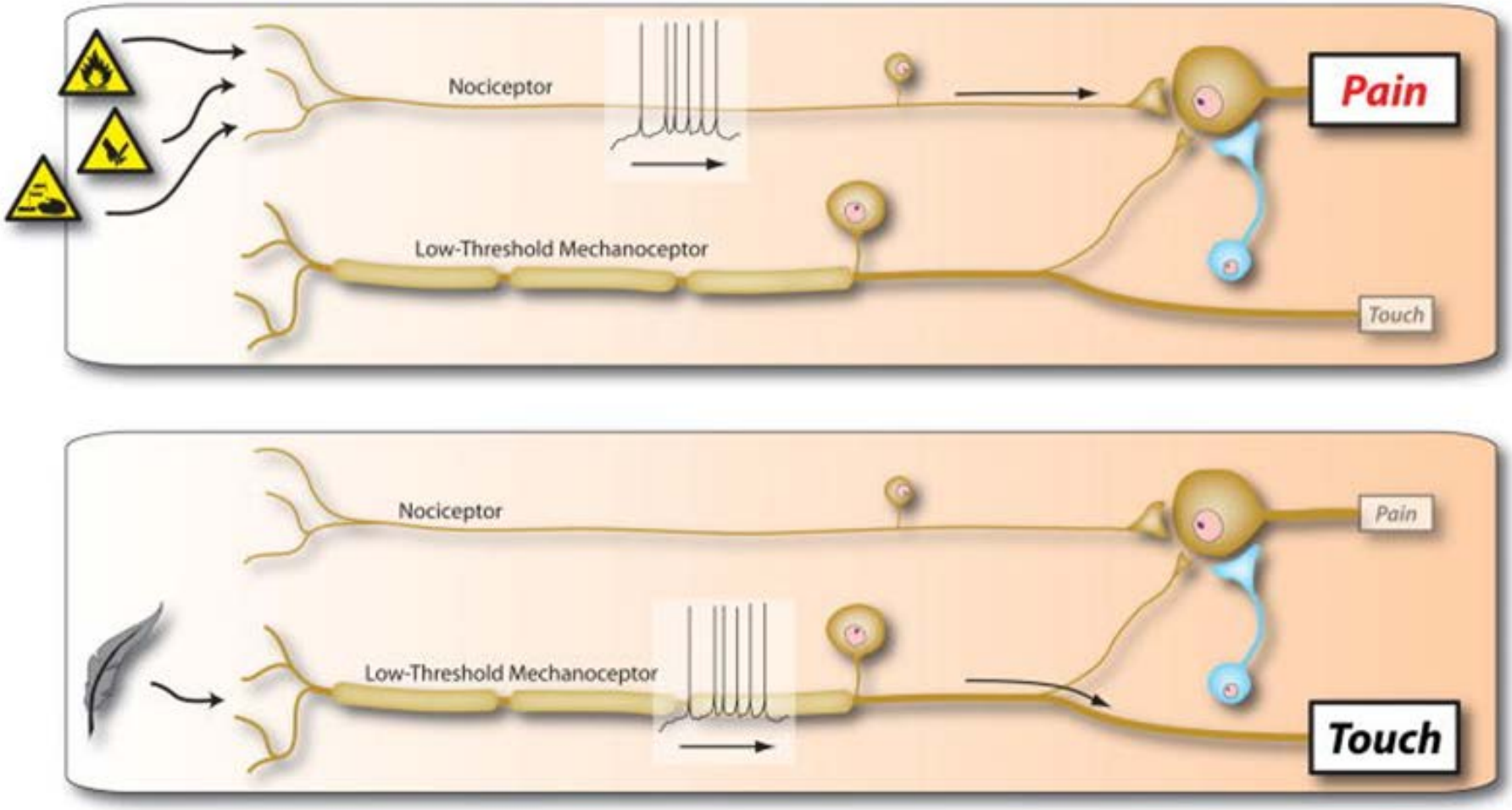


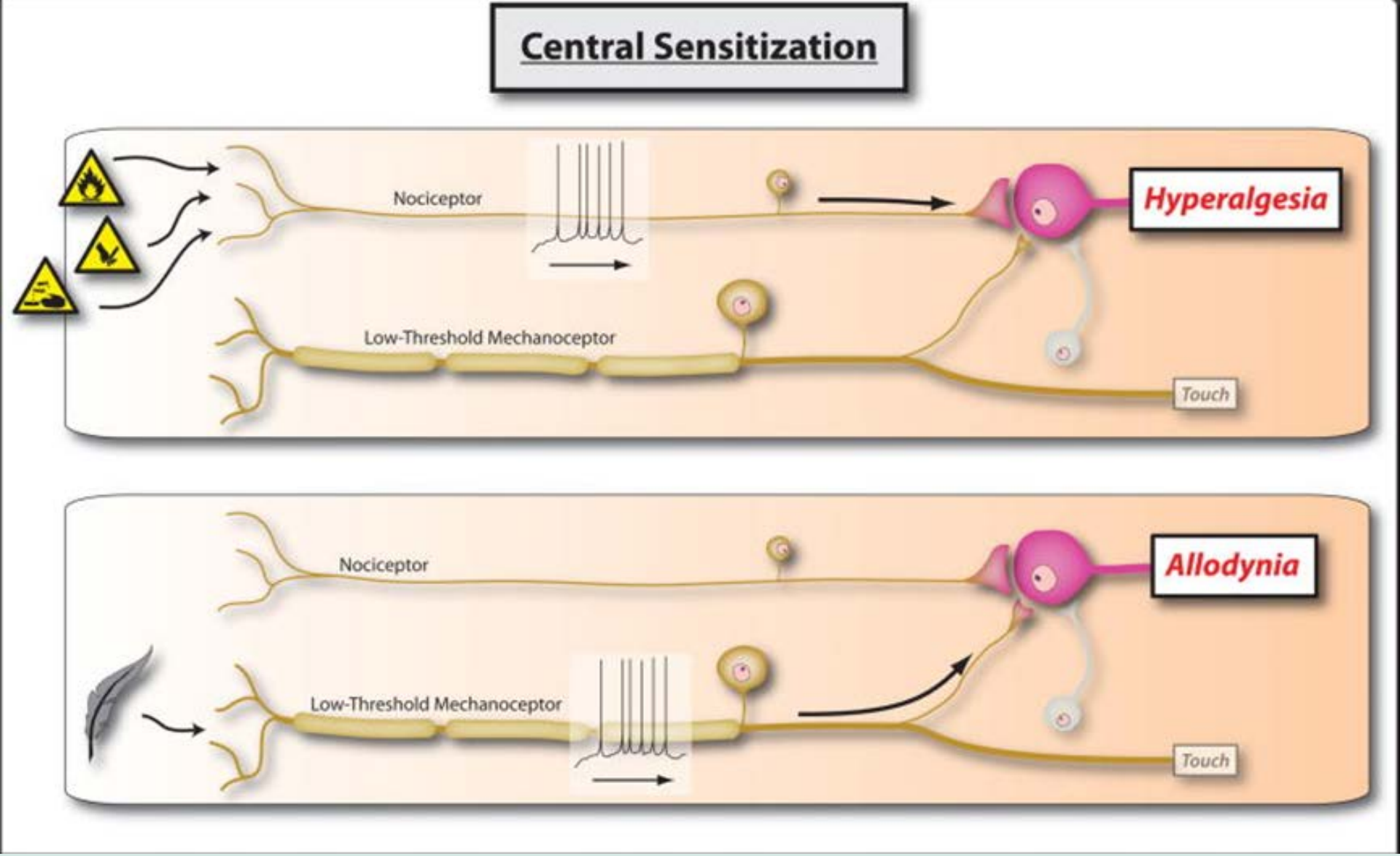
Image courtesy of Woolf CJ. **Central sensitization: Implications for the diagnosis and treatment of pain.** ***Pain*****. 2011 March; 152(3 Suppl):S**

Peripheral Sensitization

- Nociceptors change in response to tissue injury
- Decreased threshold for activation and subsequent evoked pain (hyperalgesia)
- Feed forward loops of sensitization and activation created by nociceptors

Central Sensitization

- Complex changes occurring at dorsal horn, brain stem and higher cerebral sites
- Noxious stimuli not necessary to produce pain
- Increased afferent excitation and reduced inhibition



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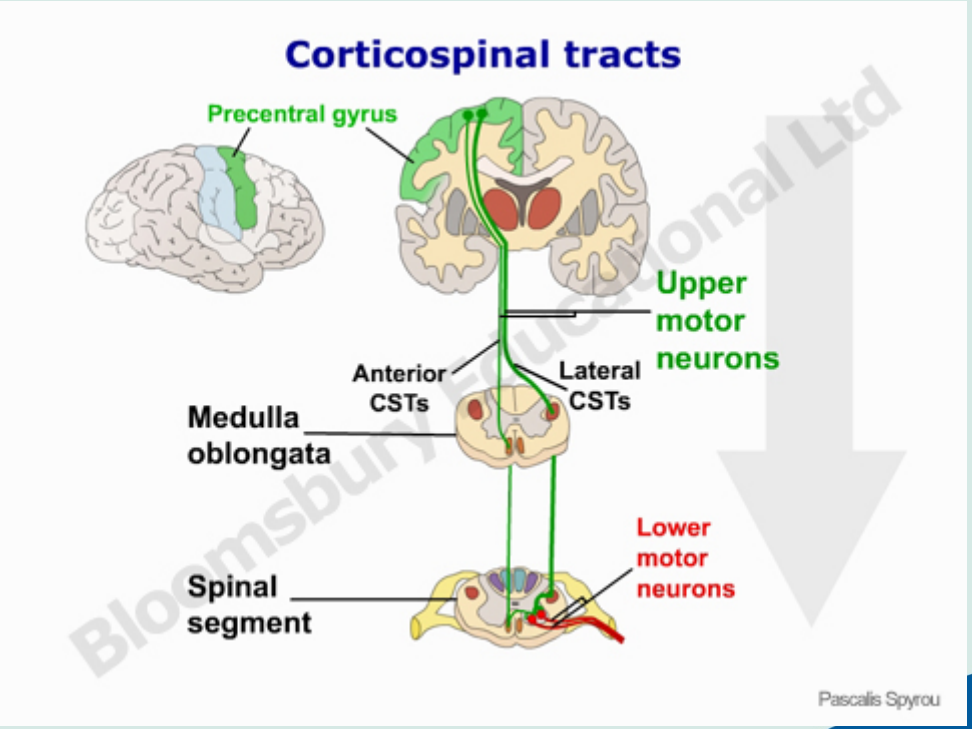
Summary of General Pain Mechanisms

- Several areas of the nervous system contribute to processing of pain signals
- These signals can be normal or pathological processes
- Neuroplastic changes may occur to modulate pain experience

DESCENDING TRACTS

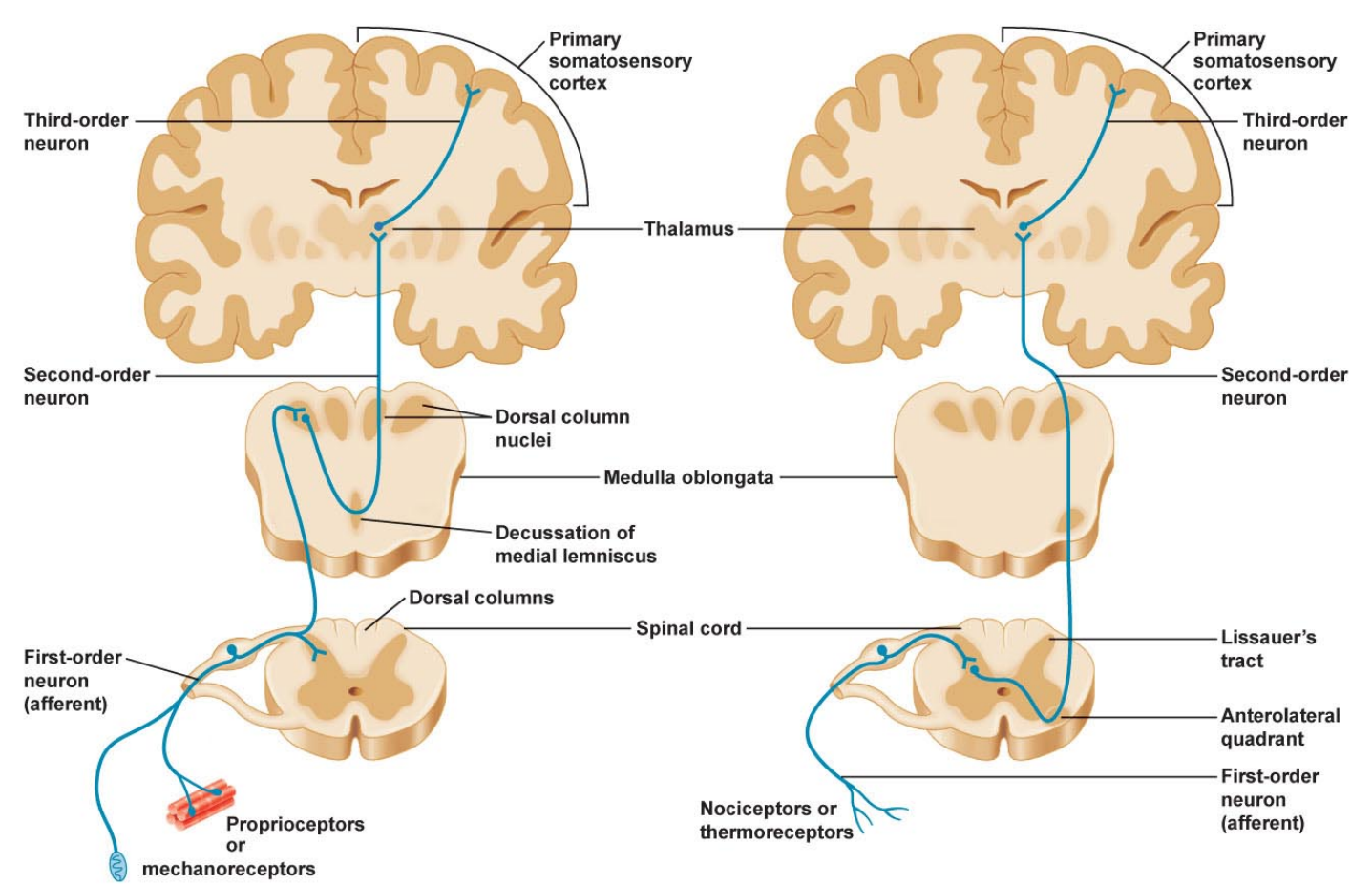
- Corticospinal fibers cross at the medulla to become the lateral corticospinal tract



ASCENDING TRACTS

- Dorsal columns – Cross in the medulla via the medial lemniscus then go to the thalamus

- Spinothalamic – Cross obliquely in the ventral white commisure ascending a level or two



Neuropathic Pain

- IASP definition: "**Pain caused by a lesion or disease of the somatosensory nervous system**"
- Subdivided into **peripheral** and **central**
- Subsets of neuropathic pain may have distinct pathophysiology and present differently clinically
- Different causes of neuropathic pain may explain mixed response to unified treatment paradigm

Neuropathic pain in SCI

- 60-70% of patients
- Usually more severe
- 1/3 have severe disabling pain
- No correlation with injury level or severity
- Correlates with increasing age
  - Peaks in 30-39 age group and then again > age 50

IASP Classification of SCI Pain

- Nociceptive
  - Musculoskeletal
  - Visceral
- Neuropathic
  - Above level
  - At level
  - Below Level

Nociceptive Pain - Musculoskeletal

- Musculoskeletal most common etiology
- Upper extremity most common location (shoulder)
- Shoulder not designed for weight bearing
- Overuse occurs with frequent transfers, WC propulsion, pressure releases
- Pain can also occur at elbow, wrist and hand

Nociceptive pain treatment

- Rest, NSAIDS, analgesics
- Stretching and strengthening exercisese
- Retrain individual on technique for transfers, WC propulsion, etc

Nociceptive pain - Visceral

- May be due to normal afferent input via sympathetics and vagus nerve
- Usually delayed onset
- Aching, dull, cramping
- Treatment aimed at cause if visceral pathology identified

Neuropathic pain in SCI

Fun Fact:

Pain can persist with removal of a section of the spinal cord above the lesion

Mechanisms of Chronic Central Neuropathic Pain after Spinal Cord Injury

- Hulseboscha et al. 2009
- 3 types of central pain from SCI
  1. Above level
  2. At level
  3. Below level

- Spontaneous – Independent of stimuli; numbness, burning, cutting, piercing, electric like
- Perpherally evoked – Response to nonnoxious or noxious stimuli

Above level central pain

- Occurs at dermatomes above level of injury
- Peripheral sensitization contributes to central sensitization
- “Retrograde sensitization” leads to hyperesthesia above level of injury

At level pain central pain (Transitional zone pain)

- Occurs in dermatomes near spinal injury
- Band like pattern around trunk or arms
- Develops shortly after SCI
- Increases in intracellular calcium levels trigger activation of cellular cascades that lead to at level pain

Below level pain central pain

- Localized to dermatomes distal to injury site
- Develops more insidiously than at-level pain
- Classified as a stimulus independent continuous burning pain
- SCI results in sustained hyperexcitability of Dorsal horn
- Microglia thought to be involved, chronically activated at spinal cord

Systematic review and comparison of pharmacologic therapies for neuropathic pain associated with spinal cord injury

- Snedecor et al. 2013
- Pregabalin was the most studied, associated with favorable efficacy for all outcome measures
- Lack of efficacy for other treatments could not be demonstrated

Table 2

Characteristics of studies evaluating medications for the treatment of neuropathic pain in patients with spinal cord injury. All trials were placebo controlled

Study	Country	Design	n	Medication evaluated (maximum daily dose)	Treatment duration	Mean pain duration, months	Mean age, years	Jadad score
Cardenas et al20,[a]	US	Parallel	84	Amitriptyline (125 mg)	6 weeks	168.3	41.4	4
Chiou-Tan et al21	US	Crossover	11	Mexiletine (450 mg)	4 weeks	Not stated	44	2
Finnerup et al22	Denmark	Crossover	30	Lamotrigine (400 mg)	9 weeks	84	49	5
Finnerup et al23	Denmark	Crossover	36	Levetiracetam (3000 mg)	5 weeks	Not stated	52.8	5
Levendoglu et al24,[b]	Turkey	Crossover	20	Gabapentin (3600 mg)	8 weeks	15.8	35.9	4
Norrbrink and Lundeberg25	Sweden	Parallel	35	Tramadol (400 mg)	4 weeks	Not stated	51.3	4
Rintala et al26	US	Crossover	38	Amitriptyline (150 mg) Gabapentin (3600 mg)	8 weeks	91.8	40.8	5
Rintala et al27	US	Crossover	7	Dronabinol (20 mg)	47 days	Not stated	50.1	5
Siddall et al28	Australia	Parallel	136	Pregabalin (600 mg)	12 weeks	121.8	50.1	5
Tai et al29,[c]	US	Crossover	7	Gabapentin (1800 mg)	4 weeks	Not stated	35.9	5
Vranken et al30	Netherlands	Parallel	40	Pregabalin (600 mg)	4 weeks	Not stated	54.5	5
Vranken et al31	Netherlands	Parallel	48	Duloxetine (120 mg)	8 weeks	60 months (median)	50.4	5

Notes:

[a]Excluded due to mixed-pain patient population;
[b]excluded due to prohibition of concomitant analgesic use;
[c]excluded due to no outcomes of interest reported.

Rational polypharmacy

- Amitriptyline
  - 1st generation TCA – Blocks reptake of serotonin and NE (5HT > NE)…also a potent Na channel blocker, mild NMDA antagonist
  - Common SEs: anticholinergic, somnolence, weight gain, orthostatic hypotension
  - Be careful for cardiotoxicity, consider EKG monitoring
- Nortriptyline
  - 2nd generation TCA – More potent NE reuptake than amitriptyline
  - Less side effect profile than amitriptyline

Meds cont…

- Venlafaxine
  - Inhibits NE, 5HT, DA reuptake
- Duloxetine
  - Inhibits NE, 5HT, DA reuptake

Meds cont…

- Gabapentin
  - Binds Alpha-2-delta subunit of calcium channel blocker
  - Decreases release of glutamate, NE, Substance P
  - Nonlinear zero-order absorption…pharmacokinetics less predicable (eg plasma concentrations do not increase propotionally with increasing dose)
  - Maximum plasma concentrations 3-4 hrs
  - Less bioavailability with increased dose
- Pregabalin
  - Same MOA
  - Absorption linear, 1st order (eg plasma concentrations increase proportional to increasing dose)
  - Max plasma concentration within 1 hour
  - Bioavailability >90% irrespective of dose

Other anticonvulsants

- Carbamezapine
- Oxcarbezipene
- Phenytoin
- Clonazepam
- Lamatrigine
- Valproid acid
- topiramate

Topical formulations

- Capsaicin
- Lidocaine
- Diclofenac
- Ketamine

Opioids

- Evidence in oral agents limited
- Side effects limit use (constipation, dependence, etc)
- Tramadol had double blind RCT of tramadol for SCI pain
  - Decreased pain
  - Additional effects: Decreased anxiety, Better global life satisfaction, better sleep quality

(Norrbink et al, Pain 2009)

Cannabinoids (eg Marijuana)

- Marijuana anecdotally reported improved pain
- Efficacy unclear in literature

Other treatments

- Pain psychology
- Integrative therapies
- Intrathecal drug delivery systems
- Surgical procedures
- Chronic Pain Rehabilitation programs

Questions?