

The background is a watercolor illustration. It features a silhouette of a person walking towards the right. The person is wearing a backpack. The watercolor washes are in shades of purple, pink, and blue, creating a soft, artistic effect. The title text is overlaid on the purple and pink washes.

KNOW NEUROPATHIC PAIN

A Practical Guide to Understanding,
Assessing and Managing Pain

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This program was sponsored by Pfizer Inc.

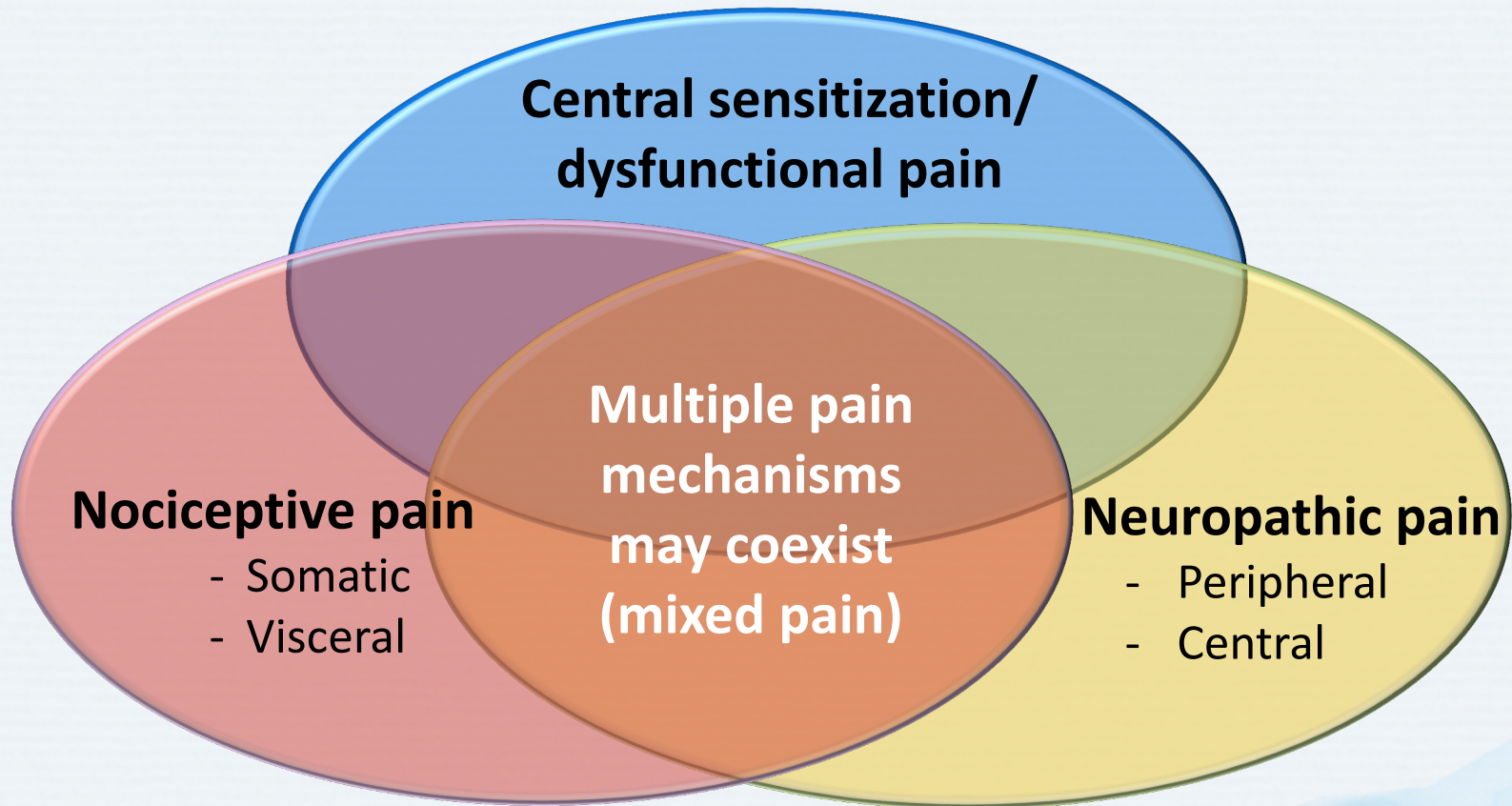
Learning Objectives

- After completing this module, participants will be able to:
 - Explain the pathophysiology of neuropathic pain
 - Discuss the prevalence of neuropathic pain
 - Apply a simple diagnostic technique for the diagnosis of neuropathic pain
 - Understand the impact of neuropathic pain and its comorbidities on patient functioning and quality of life
 - Select appropriate pharmacological and non-pharmacological strategies for the management of neuropathic pain
 - Know when to refer patients to specialists

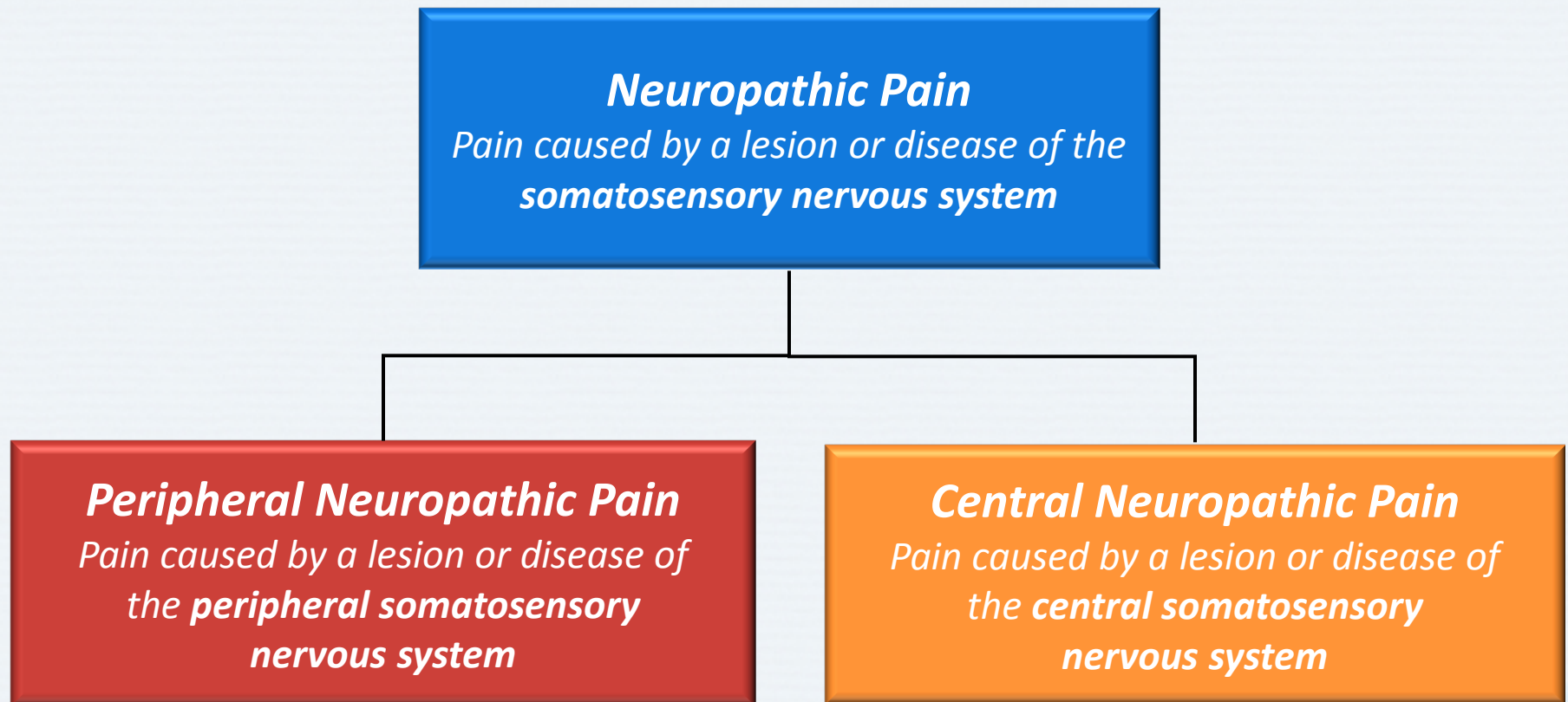
Table of Contents

- What is neuropathic pain?
 - How common is neuropathic pain?
 - How can neuropathic pain be differentiated from nociceptive pain?
 - What is the impact of neuropathic pain?
 - How should neuropathic pain be treated based on its pathophysiology?
- 
- A decorative blue watercolor splash is located in the bottom right corner of the slide, extending from the bottom edge and slightly towards the center.

Pathophysiological Classification of Pain



What is neuropathic pain?



Nociceptive vs. Neuropathic Pain

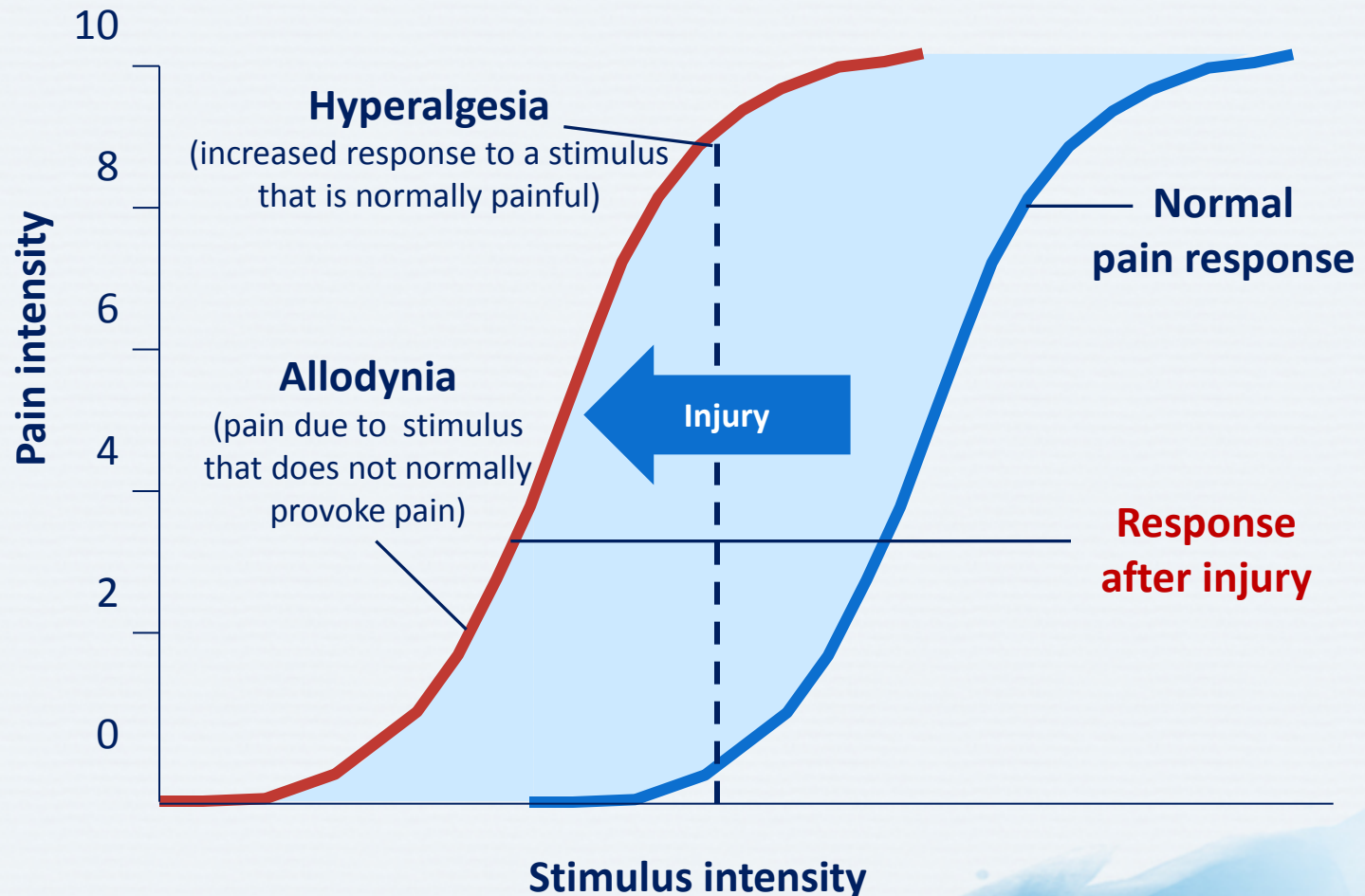
Nociceptive

- Usually aching or throbbing and well-localized
- Usually time-limited (resolves when damaged tissue heals), but can be chronic
- Generally responds to conventional analgesics

Neuropathic

- Pain often described as tingling, shock-like, and burning – commonly associated with numbness
- Almost always a chronic condition
- Responds poorly to conventional analgesics

Neuropathic Pain Is Characterized by Changes in Pain Response to Painful Stimuli



Pathophysiology of Neuropathic Pain

Peripheral mechanisms

- Membrane hyperexcitability
- Ectopic discharges
- Transcriptional changes

Central mechanisms

Hyperexcitability

**Loss of
inhibitory controls**

Reorganization

Sensitization

- Peripheral
- Central

**Neuropathic
pain**

Neuropathic Pain is Prevalent Across a Range of Different Conditions

% affected by peripheral neuropathic pain	Condition		% affected by central neuropathic pain
11–26% ¹	Diabetes	Stroke	8% ⁹
~33% ²	Cancer	Spinal cord injury	75% ¹⁰
35–53% ^{3–5}	HIV	Multiple sclerosis	~55% ¹¹
20–43% of mastectomy patients ^{6,7}	Post-surgical		
Up to 37% ⁸	Chronic low back pain		
7–27% of patients with herpes zoster ¹	Postherpetic neuralgia		

HIV = human immunodeficiency virus

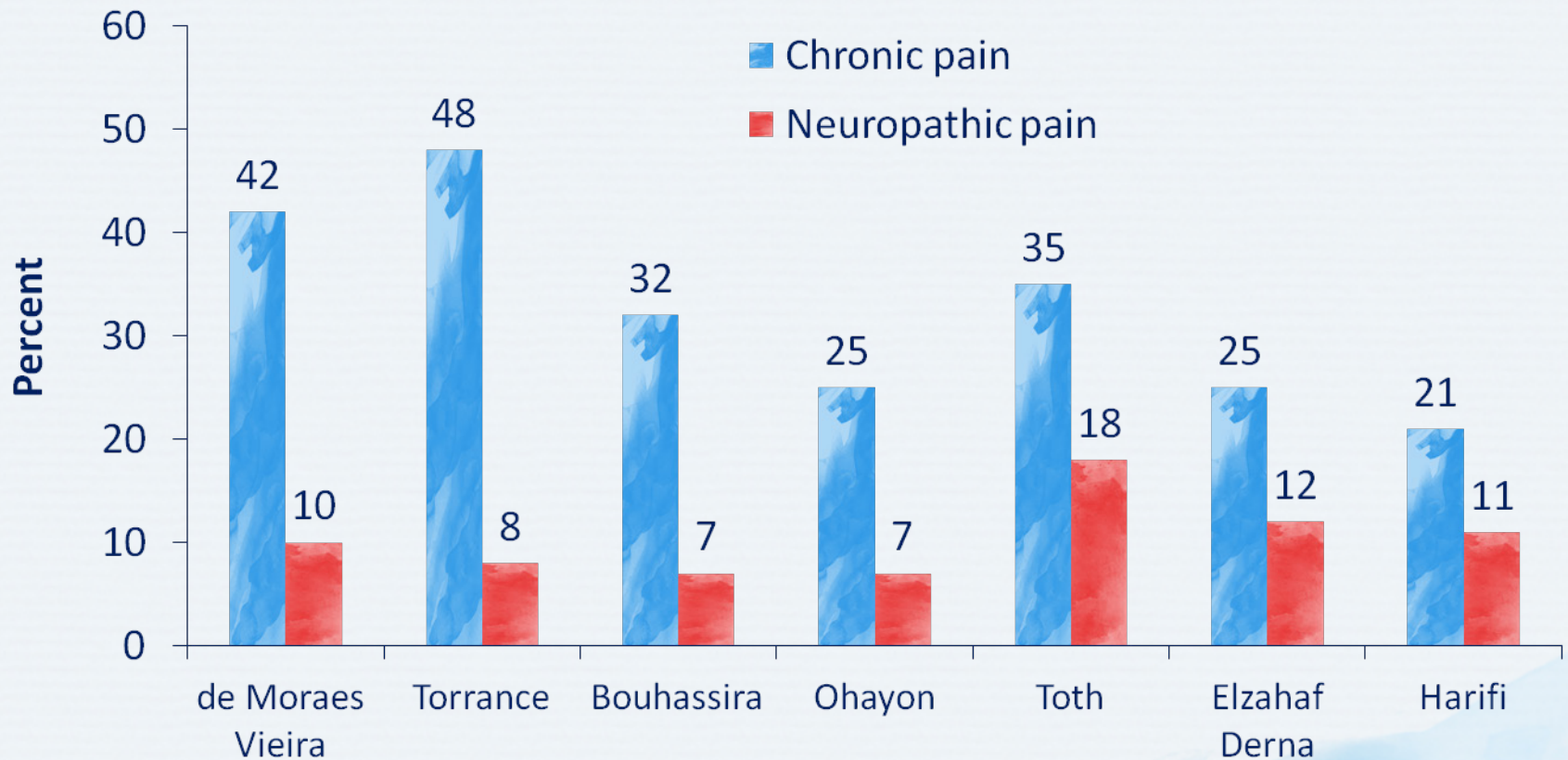
1. Sadosky A et al. *Pain Pract* 2008; 8(1):45-56; 2. Davis MP, Walsh D. *Am J Hosp Palliat Care* 2004; 21(2):137-42; 3. So YT et al. *Arch Neurol* 1988; 45(9):945-8; 4. Schifitto G et al. *Neurology* 2002; 58(12):1764-8; 5. Morgello S et al. *Arch Neurol* 2004; 61(4):546-51; 6. Stevens PE et al. *Pain* 1995; 61(1):61-8; 7. Smith WC et al. *Pain* 1999; 83(1):91-5; 8. Freynhagen R et al. *Curr Med Res Opin* 2006; 22(10):1911-20; 9. Andersen G et al. *Pain* 1995; 61(2):187-93; 10. Siddall PJ et al. *Pain*. 2003; 103(3):249-57; 11. Rae-Grant AD et al. *Mult Scler* 1999; 5(3):179-83.

Discussion Question

**WHAT PROPORTION OF YOUR
PATIENTS SUFFER FROM
NEUROPATHIC PAIN?**

5–20% of the General Population May Suffer from Neuropathic Pain

Summary of Selected Prevalence Studies

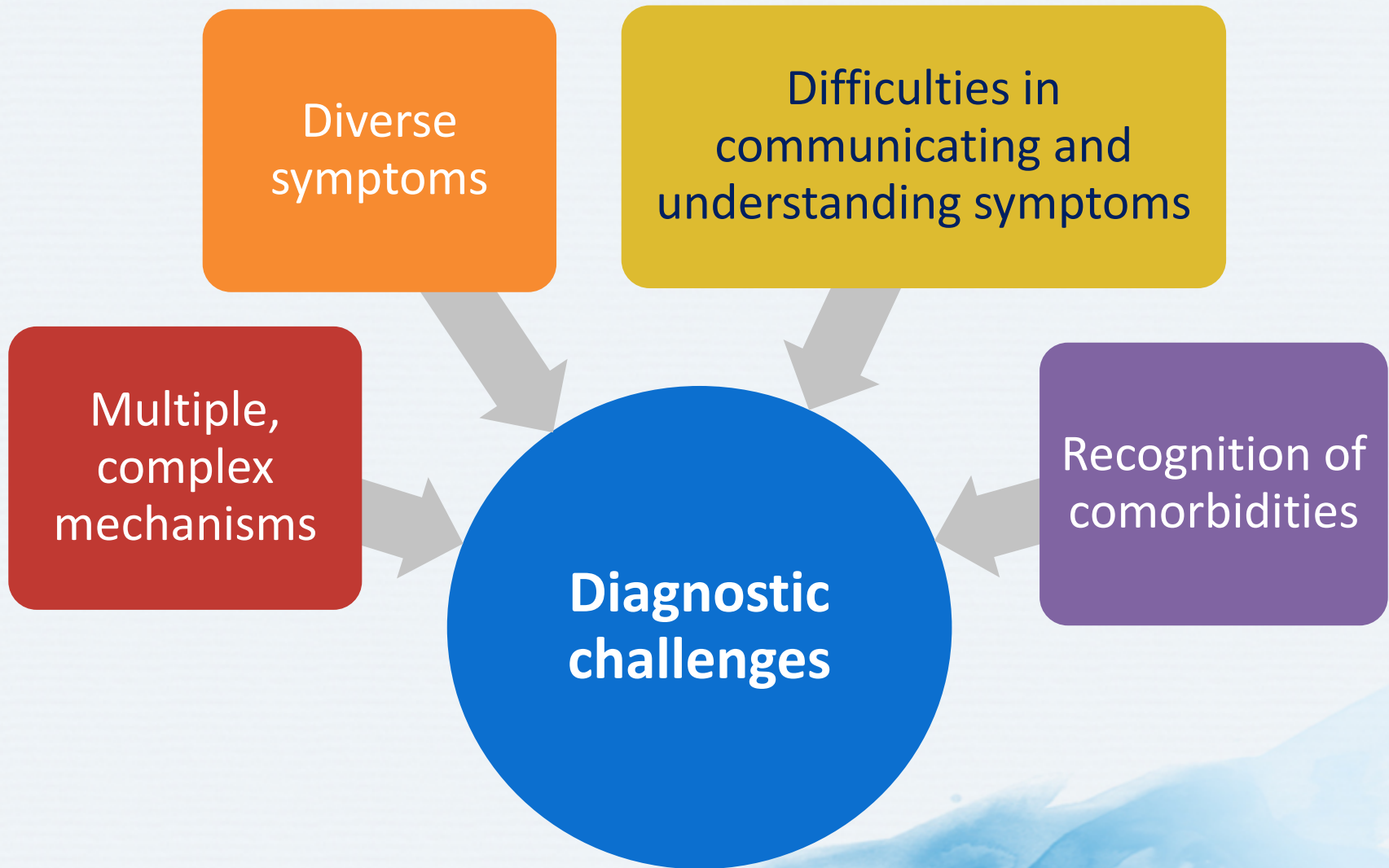


Adapted from: Bouhassira D *et al. Pain* 2008; 136(3):380-7; de Moraes Vieira EB *et al. J Pain Symptom Manage* 2012; 44(2):239-51; Elzahaf RA *et al. Pain Pract* 2013; 13(3):198-205; Harifi G *et al. Pain Med* 2013; 14(2):287-92; Ohayon MM, Stingl C. *Psychiatr Res* 2012; 46(4):444-50; Torrance N *et al. J Pain* 2006;7(4):281-9; Toth C *et al. Pain Med* 2009; 10(5):918-29;

Discussion Question

**WHAT ARE SOME OF YOUR BIGGEST
CHALLENGES IN DIAGNOSING
PATIENTS WITH NEUROPATHIC PAIN?
HOW DO YOU OVERCOME
THESE CHALLENGES?**

Diagnosing Neuropathic Pain Is Challenging



The 3L Approach to Diagnosis¹

Listen^{1,2}

Patient verbal descriptors of pain,
questions and answers

Locate^{1,3}

Somatosensory Nervous
system lesion
or disease

Look^{1,4}

Sensory abnormalities
in the painful area

1. Freynhagen R, Bennett MI. *BMJ* 2009; 339:b3002; 2. Bennett MI *et al. Pain* 2007; 127(3):199-203;
3. Freynhagen R *et al. Pain* 2008; 135(1-2):65-74; 4. Freynhagen R *et al. Curr Pain Headache Rep* 2009; 13(3):185-90.

Listen to the Patient Description of Pain



- **Question** patients about their pain¹
- ***Be alert*** and ask for ***common verbal descriptors*** of neuropathic pain²
- Use analogue or numerical scales to quantify the pain²
- Use screening and assessment tools to distinguish neuropathic pain from non-neuropathic pain³

1. Haanpää ML *et al.* *Am J Med* 2009; 122(10 Suppl):S13-21;

2. Gilron I *et al.* *CMAJ* 2006; 175(3):265-75; 3. Cruccu G *et al.* *Eur J Neurol* 2010; 17(8):1010-8.

Listen: Pain History in Neuropathic Pain

Identify the Following:

- Duration
- Frequency
- Quality
- Intensity
- Distribution and location of pain
- Extent of interference with daily activity

Areas of Further Exploration

- Previous medical history
- Exposure to toxins or other drug treatment (e.g., cancer chemotherapy, radiation)
- Use of pain medications
- Associated psychological and mood disturbance

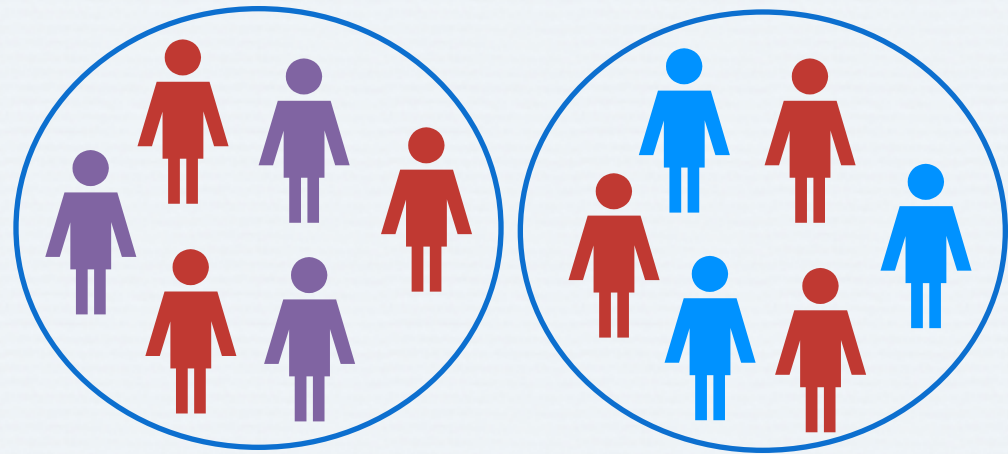
Listen: Neuropathic Signs and Symptoms Can Vary Widely

In One Individual



- Wide spectrum of signs and symptoms often **co-exist** at the same time
- Signs and symptoms **may vary within an individual over time**

Between Individuals



- Signs and symptoms **vary among individuals** with the same underlying etiology
- Signs and symptoms are shared across neuropathic pain states

Listen:

Recognizing Neuropathic Pain

Be alert for common verbal descriptors of neuropathic pain:



Burning



Tingling



Shooting



Electric shock-like



Numbness

Listen: Sensory Symptoms of Neuropathic Pain

Lesion or disease of the somatosensory nervous system

Positive symptoms

(due to excessive neural activity)

Spontaneous pain

Allodynia

Hyperalgesia

Dysesthesia

Paresthesia

Negative symptoms

(due to deficit of function)

Hypoesthesia

Anesthesia

Hypoalgesia

Analgesia

Sensory abnormalities and pain paradoxically *co-exist*

Each patient may have a combination of symptoms
that may change over time (even within a single etiology)

Listen: Positive Sensory Symptoms of Neuropathic Pain

Positive symptom	Definition	Typical verbal descriptors
Spontaneous pain	Painful sensations felt with no evident stimulus	Electric shock-like, burning
Allodynia	Pain due to a stimulus that does not normally provoke pain (e.g., touching, movement, cold, heat)	Vary with stimulus
Hyperalgesia	An increased response to a stimulus that is normally painful (e.g., cold, heat, pinprick)	Vary with stimulus
Dysesthesia	An unpleasant abnormal sensation, whether spontaneous or evoked	Shooting, piercing, burning
Paresthesia	An abnormal sensation, whether spontaneous or evoked	Tingling, buzzing, vibrating

Listen: Negative Sensory Symptoms of Neuropathic Pain

Negative symptom	Definition	Typical verbal descriptor
Hypoesthesia	Diminished sensitivity to stimulation	Numbness
Anesthesia	Total loss of sensation (especially tactile sensitivity)	Numbness
Hypoalgesia	Diminished pain in response to a normally painful stimulus	Numbness
Analgesia	Absence of pain in response to stimulation that would normally be painful	Numbness

Locate the Region of Pain

Correlate the region of pain to the lesion in the somatosensory nervous system*



***Note that in cases of referred neuropathic pain, as can occur for example in some cases of spinal cord injury, the location of the pain and of the lesion/dysfunction may not be correlated**

Gilron I et al. CMAJ 2006; 175(3):265-75; Soler MD et al. Pain 2010; 150(1):192-8; Walk D et al. Clin J Pain 2009; 25(7):632-40.

Look for Sensory and/or Physical Abnormalities

- Inspect the painful body area and compare it with the corresponding healthy area^{1,2}
- Conduct simple bedside tests to confirm sensory abnormalities¹⁻⁴

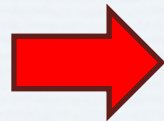


Discussion Question

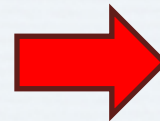
**WHAT BEDSIDE TESTS DO YOU
TYPICALLY USE IN YOUR PRACTICE?
WHY?**

Look: Simple Bedside Tests

Stroke skin with brush,
cotton or apply acetone

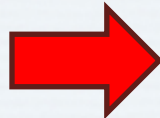


Sharp, burning
superficial pain

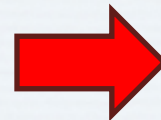


ALLODYNIA

Light manual pinprick with
safety pin or sharp stick



Very sharp,
superficial pain



HYPERALGESIA

Discussion Question

**DO YOU USE A SCREENING TOOL FOR
NEUROPATHIC PAIN IN YOUR PRACTICE?
IF SO, WHICH TOOL AND WHY?**

Neuropathic Pain Screening Tools

	LANSS	DN4	NPQ	painDETECT	ID Pain
<i>Symptoms</i>					
Pricking, tingling, pins and needles	X	X	X	X	X
Electric shocks or shooting	X				
Hot or burning	X				
Numbness		X	X	X	X
Pain described as distinct from other types of pain	X				X
Painful touch					
<div> Select tool(s) based on <i>ease of use</i> and <i>validation in the local language</i> </div>					
<i>Clinical examination</i>					
Brush allodynia	X	V			
Raised soft touch threshold					
Altered pin prick threshold	X				

DN4 = Douleur Neuropathique en 4 Questions (DN4) questionnaire;

LANSS = Leeds Assessment of Neuropathic Symptoms and Signs; NPQ = Neuropathic Pain Questionnaire

Bennett MI et al. *Pain* 2007; 127(3):199-203; Haanpää M et al. *Pain* 2011; 152(1):14-27.

Sensitivity and Specificity of Neuropathic Pain Screening Tools

Name	Description	Sensitivity*	Specificity*
Interview-based			
NPQ	10 sensory-related items + 2 affect items	66%	74%
ID-Pain	5 sensory items + 1 pain location	NR	NR
painDETECT	7 sensory items + 2 spatial characteristics items	85%	80%
Interview + physical tests			
LANSS	5 symptom items + 2 clinical exam items	82–91%	80–94%
DN4	7 symptom items + 3 clinical exam items	83%	90%

Tests incorporating both interview questions **and** physical tests have higher sensitivity and specificity than tools that rely only on interview questions

*Compared with clinical diagnosis

DN4 = Douleur neuropathic en 4 questions; LANSS = Leeds Assessment of Neuropathic Symptoms and Signs;

NPQ = Neuropathic Pain Questionnaire; NR = not reported

Bennett MI *et al. Pain* 2007; 127(3):199-203.

LANSS Scale

THE LANSS PAIN SCALE
Leeds Assessment of Neuropathic Symptoms and Signs

NAME _____ DATE _____

This pain scale can help to determine whether the nerves that are carrying your pain signals are working normally or not. It is important to find this out in case different treatments are needed to control your pain.

A. PAIN QUESTIONNAIRE

- Think about how your pain has felt over the last week.
- Please say whether any of the descriptions match your pain exactly.

1) Does your pain feel like strange, unpleasant sensations in your skin? Words like pricking, tingling, pins and needles might describe these sensations.

a) NO - My pain doesn't really feel like this. (0)

b) YES - I get these sensations quite a lot. (5)

2) Does your pain make the skin in the painful area look like mottled or looking more red or white than the surrounding skin?

a) NO - My pain doesn't affect the colour of my skin. (0)

b) YES - I've noticed that the pain does make my skin look like this. (5)

3) Does your pain make the affected skin abnormally sensitive to touch or pressure? Words like stinging, burning or itching might describe the abnormal sensations.

a) NO - My pain doesn't make my skin abnormally sensitive to touch or pressure. (0)

b) YES - My skin seems abnormally sensitive to touch or pressure. (5)

4) Does your pain come on suddenly and in bursts? Words like electric shocks, jumping or shooting pains might describe these sensations.

a) NO - My pain doesn't really feel like this. (0)

b) YES - I get these sensations quite a lot. (5)

5) Does your pain feel as if the skin temperature is abnormal? Words like hot and burning or cold and numb might describe these sensations.

a) NO - I don't really get these sensations. (0)

b) YES - I get these sensations quite a lot. (5)

B. SENSORY TESTING

Skin sensitivity can be examined by comparing the painful area with a contralateral or adjacent non-painful area for the presence of allodynia and an altered pin-prick threshold (PPT).

1) **ALLODYNIA**

Examine the response to lightly stroking cotton wool across the non-painful area and then the painful area. If normal sensations are experienced in the non-painful site, but pain or unpleasant sensations (tingling, nausea) are experienced in the painful area when stroking, allodynia is present.

a) NO, normal sensation in both areas. (0)

b) YES, allodynia in painful area only. (5)

2) **ALTERED PIN-PRICK THRESHOLD**

Determine the pin-prick threshold by comparing the response to a 23 gauge (blue) needle mounted inside a 2 ml syringe barrel placed gently on to the skin in a non-painful and then painful areas.

If a sharp pin prick is felt in the non-painful area, but a different sensation is experienced in the painful area e.g. none / blunt only (raised PPT) or a very painful sensation (lowered PPT), an altered PPT is present.

If a pinprick is not felt in either area, mount the syringe onto the needle to increase the weight and repeat.

a) NO, equal sensation in both areas. (0)

b) YES, altered PPT in painful area. (3)

SCORING:

Add values in parentheses for sensory description and examination findings to obtain overall score.


TOTAL SCORE (maximum 24)

If score < 12, neuropathic mechanisms are **unlikely** to be contribution to the patient's pain

If score ≥ 12, neuropathic mechanisms are **likely** to be contributing to the patient's pain

- Completed by physician in office
- Differentiates neuropathic from nociceptive pain
- 5 pain questions and 2 skin sensitivity tests
- Identifies contribution of neuropathic mechanisms to pain
- Validated

DN4



Neuropathic Pain Diagnostic Questionnaire (DN4)¹

Patient Name _____

Gender ☐ M ☐ F Date of Birth _____

Date _____ Time _____

Please complete this questionnaire by ticking one answer for each item in the four questions below. A YES score of ≥ 4 is diagnostic of Neuropathic Pain.

Interview of the patient

Question 1. Does the pain have one or more of the following characteristics?

	YES	NO
1. Burning	<input type="checkbox"/>	<input type="checkbox"/>
2. Painful Cold	<input type="checkbox"/>	<input type="checkbox"/>
3. Electric Shocks	<input type="checkbox"/>	<input type="checkbox"/>

Question 2. Is the pain associated with one or more of the following symptoms in the same area?

	YES	NO
4. Tingling	<input type="checkbox"/>	<input type="checkbox"/>
5. Pins and Needles	<input type="checkbox"/>	<input type="checkbox"/>
6. Numbness	<input type="checkbox"/>	<input type="checkbox"/>
7. Itching	<input type="checkbox"/>	<input type="checkbox"/>

Examination of the patient

Question 3. Is the pain located in an area where the physical examination may reveal one of more of the following characteristics?

	YES	NO
8. Touch Hypoaesthesia	<input type="checkbox"/>	<input type="checkbox"/>
9. Pricking Hypoaesthesia	<input type="checkbox"/>	<input type="checkbox"/>

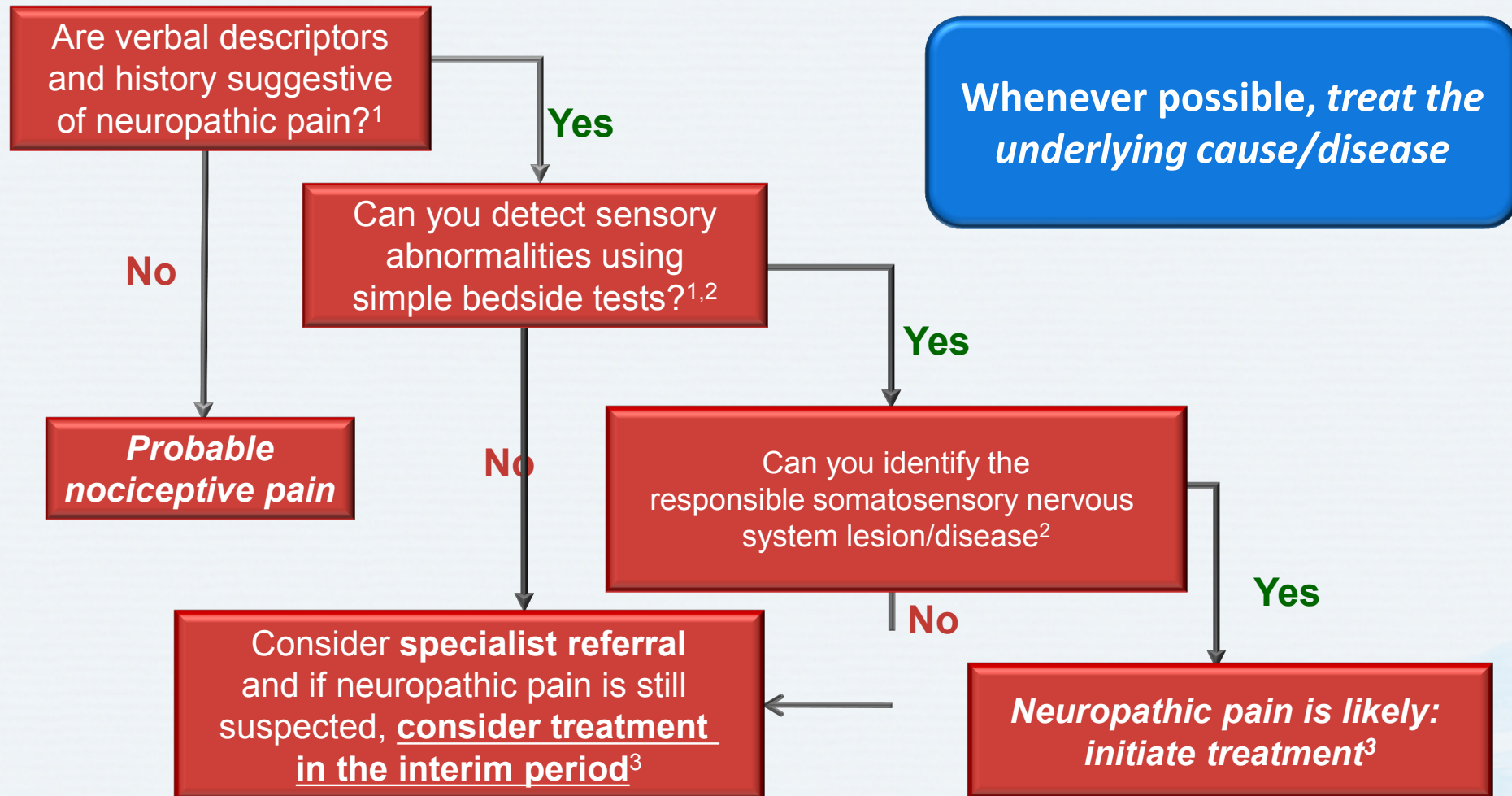
Question 4. In the painful area, can the pain be caused or increased by:

	YES	NO
10. Brushing (e.g. using a Wet Dry brush or brush)	<input type="checkbox"/>	<input type="checkbox"/>


Patient score _____ / 10

- Completed by physician in office
- Differentiates neuropathic from nociceptive pain
- 2 pain questions (7 items)
- 2 skin sensitivity tests (3 items)
- Score ≥ 4 is an indicator for neuropathic pain
- Validated

Clinical Approach to Suspected Neuropathic Pain

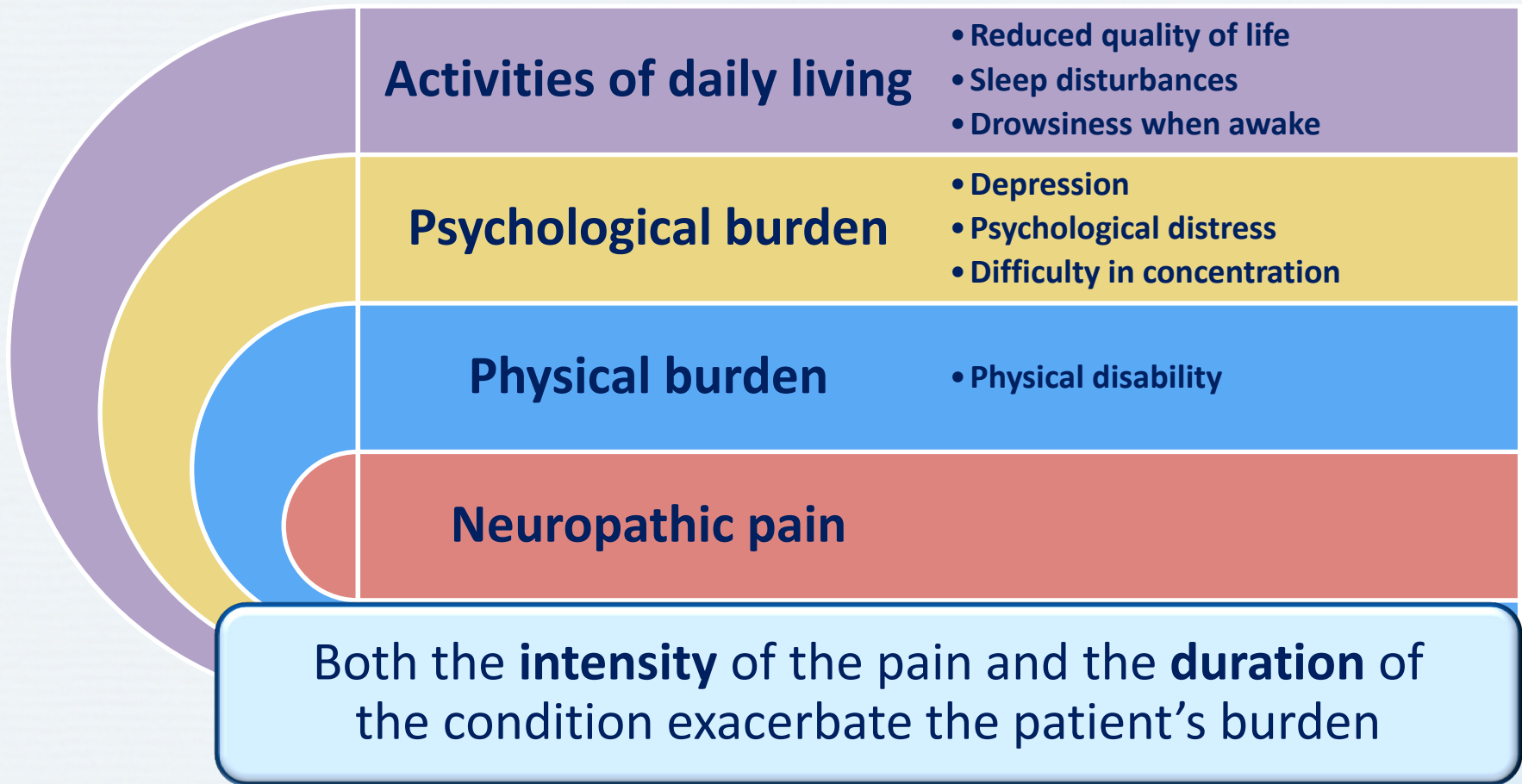


Discussion Question

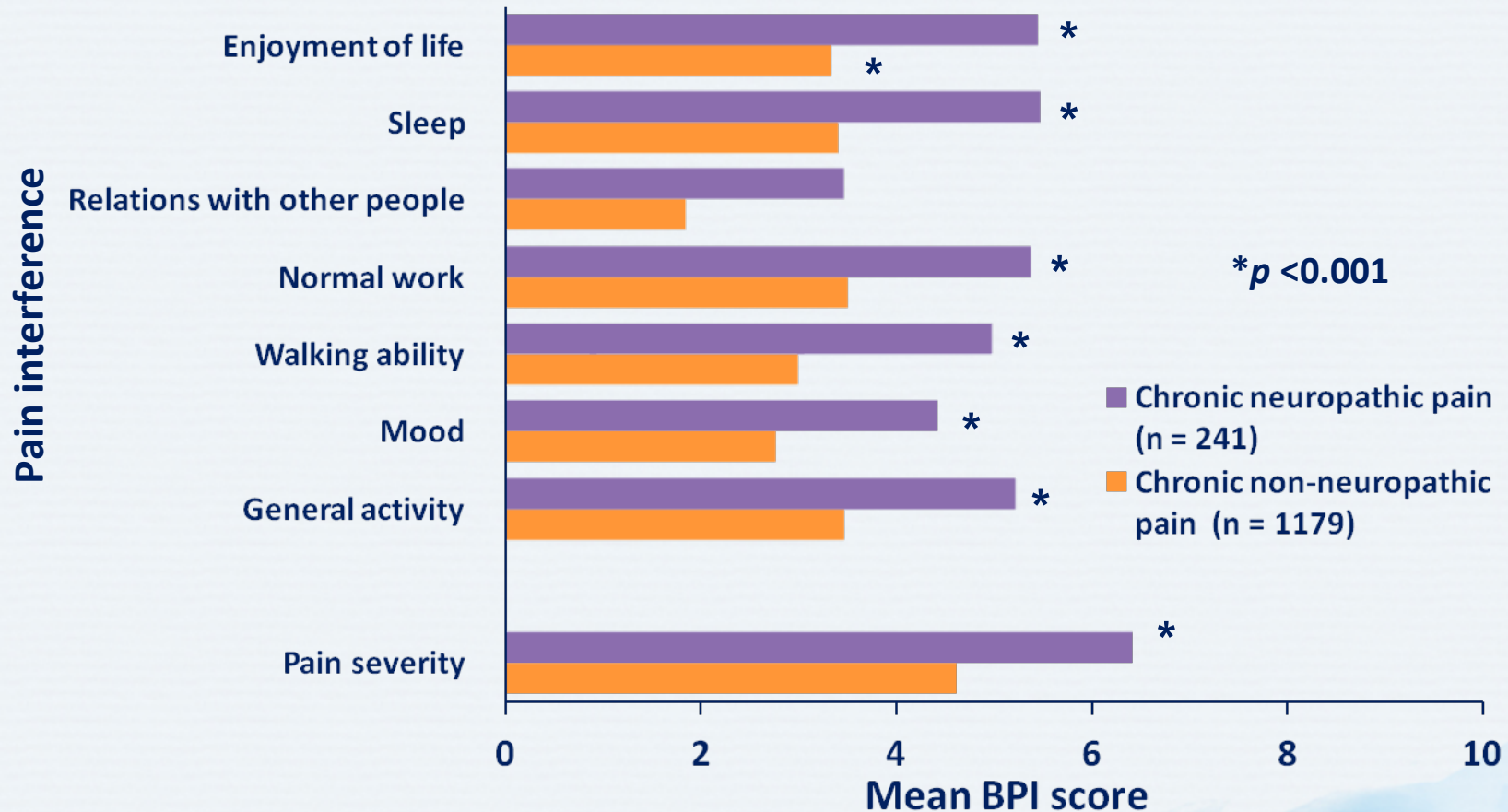


**HOW HAS NEUROPATHIC PAIN
AFFECTED SOME OF
YOUR PATIENTS?**

Patient-Reported Burden of Neuropathic Pain Is Significant



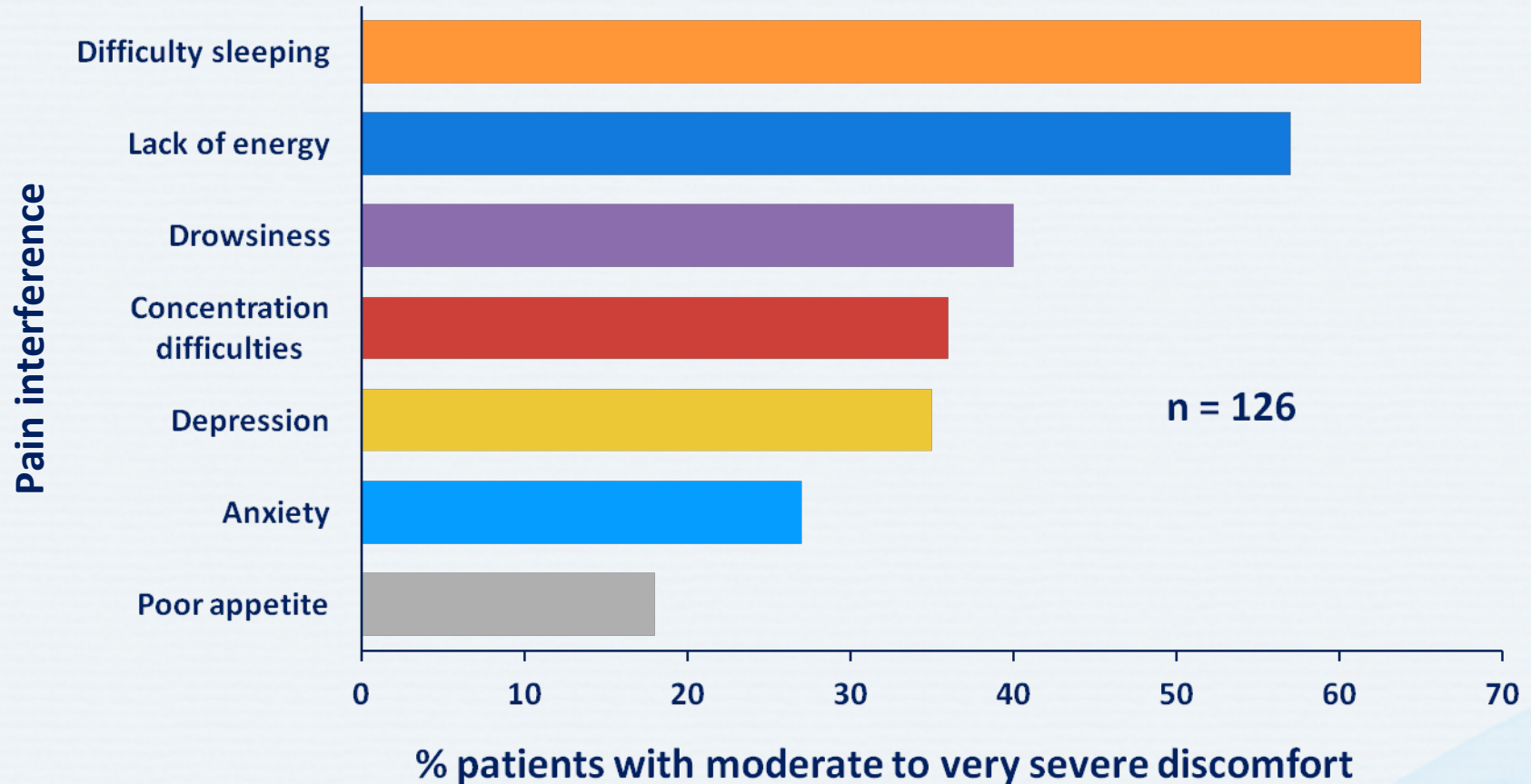
Chronic Neuropathic Pain Has a Significant Impact on Daily Functioning



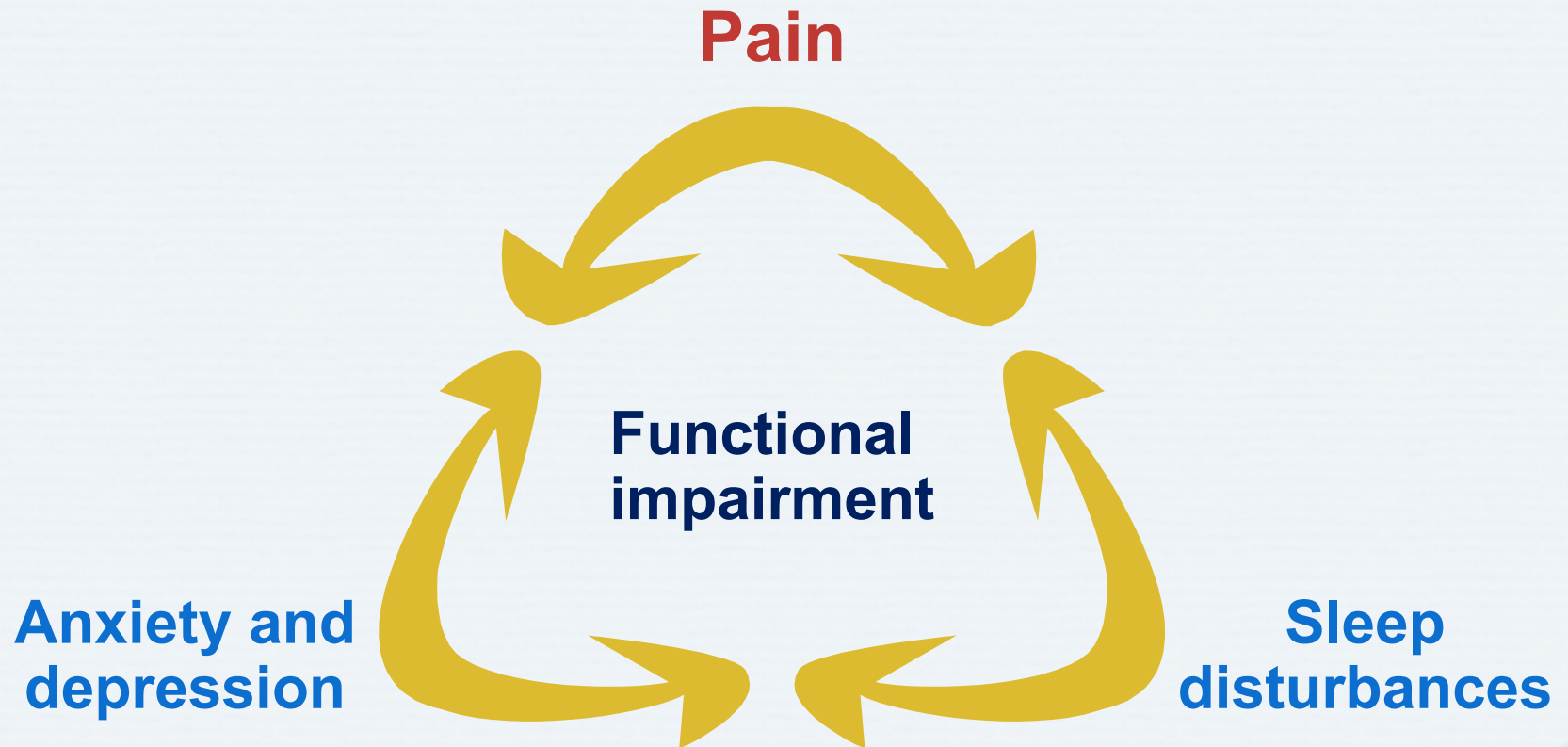
BPI = Brief Pain Inventory, which scores extent pain interferes with activities in last 24 hours from 0 (does not interfere) to 10 (completely interferes)

Adapted from: Smith BH *et al. Clin J Pain* 2007; 23(2):143-9.

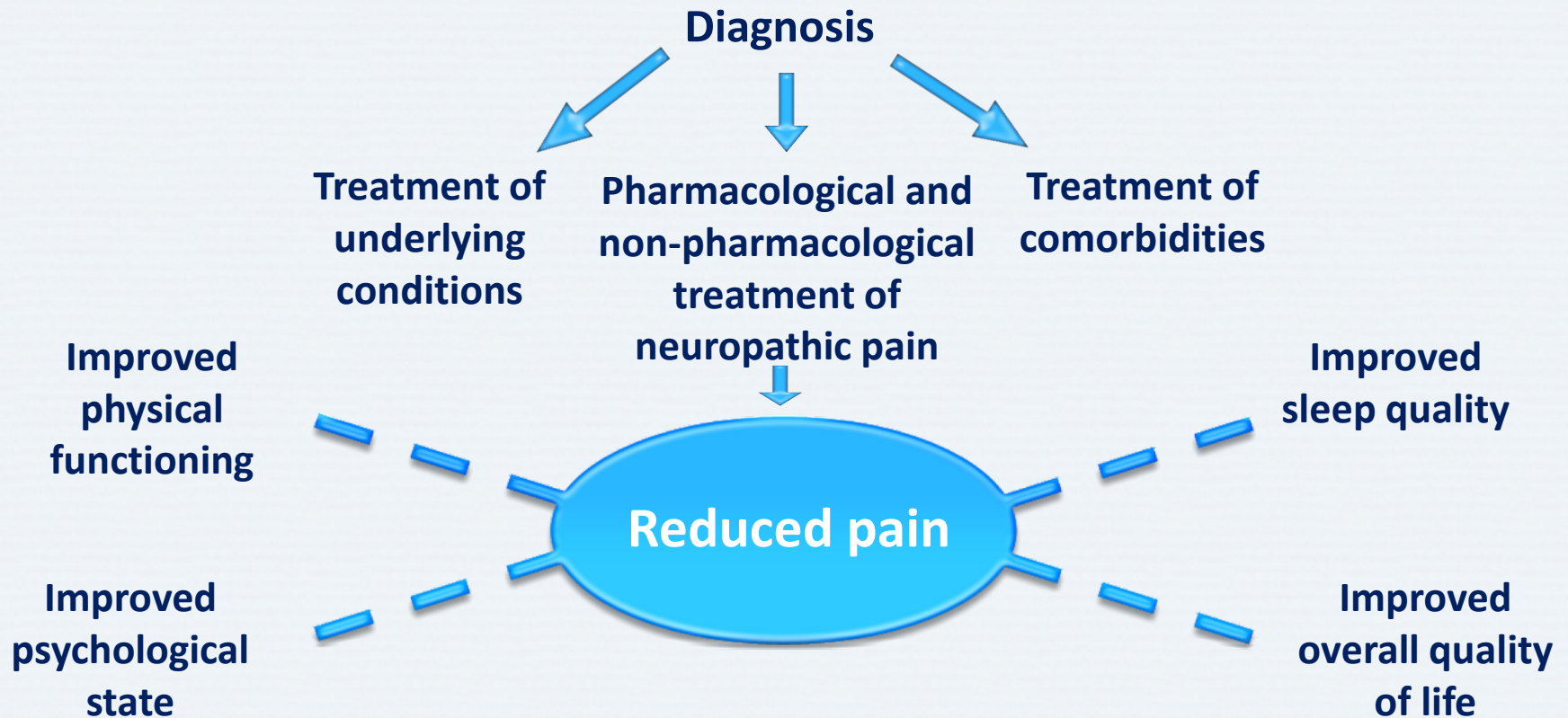
Patients with Peripheral Neuropathic Pain Experience Significant Comorbid Symptoms



Neuropathic Pain Is Associated with Sleep Disturbance, Anxiety and Depression



Management of Neuropathic Pain



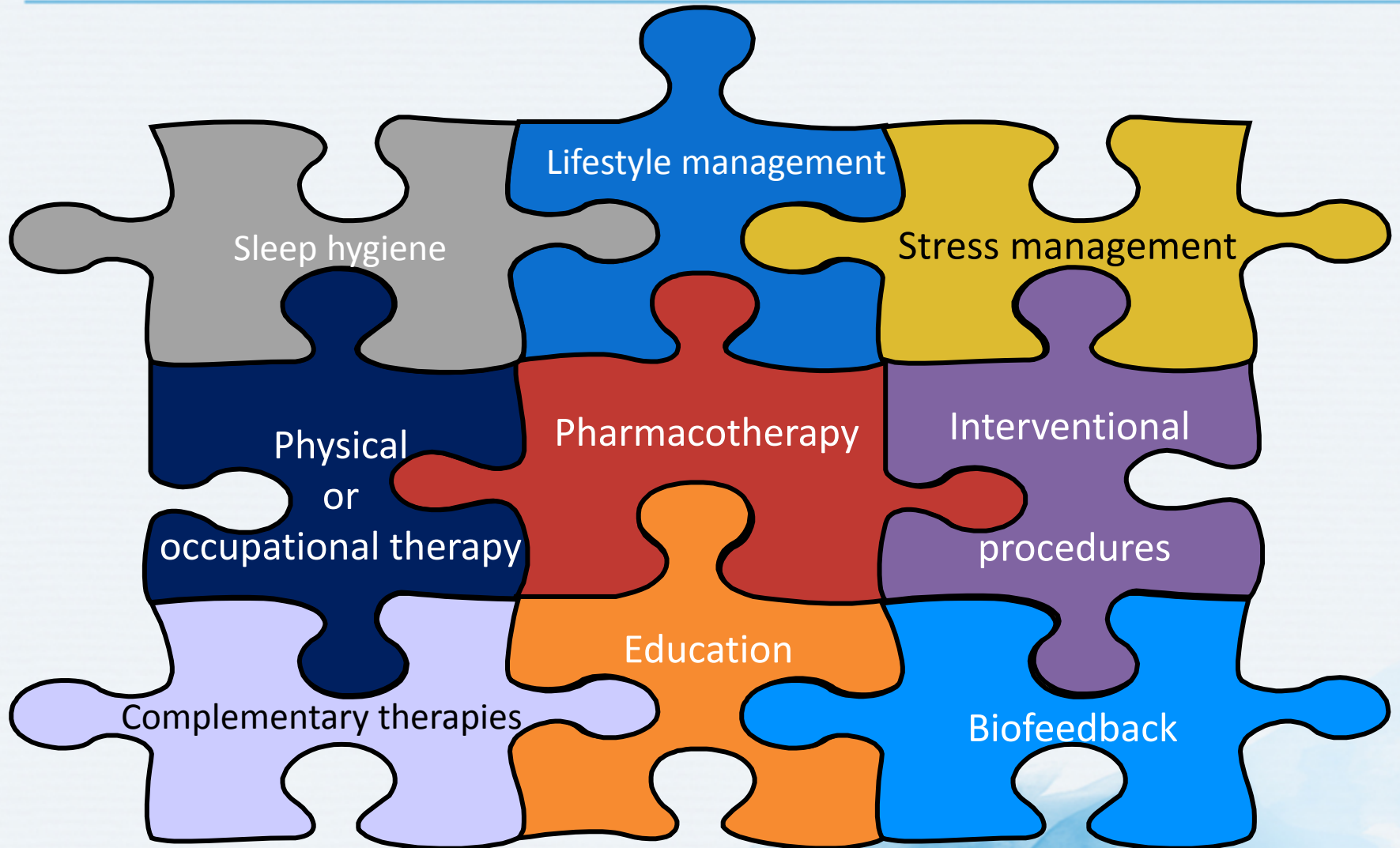
The *earlier* a diagnosis is made, the more opportunities there are to *improve patient outcomes*

Goals in the Treatment of Neuropathic Pain



***Note: pain reduction of 30–50% can be expected with maximal doses in most patients**
Argoff CE et al. *Mayo Clin Proc* 2006; 81(Suppl 4):S12-25; Lindsay TJ et al. *Am Fam Physician* 2010; 82(2):151-8.

Multimodal Treatment of Neuropathic Pain



Various Non-pharmacological Treatments Are Available for Neuropathic Pain¹⁻⁶

Physiotherapy¹



Psychotherapy/CBT^{6,7}



Multimodal pain management programs^{5,6}

Alternative therapies and spiritual healing¹⁻⁴



Patient education¹



Various non-pharmacological treatment modalities are mentioned in guidelines, but **no modality is universally recommended**¹⁻⁵

CBT = cognitive behavioral therapy

1. Chetty S et al. *S Afr Med J* 2012; 102(5):312-25; 2. Bril V et al. *Neurology* 2011; 76(20):1758-65; 3. Cruccu G et al. *Eur J Neurol* 2007; 14(9):952-70; 4. Pittler MH, Ernst E. *Clin J Pain* 2008; 24(8):731-35; 5. Dubinsky RM et al. *Neurology* 2004; 63(6):959-65; 6. Freynhagen R, Bennett MI. *BMJ* 2009; 339:b3002; 7. Morley S. *Pain* 2011;152(3 Suppl):S99-106.

Discussion Question

**WHAT NON-PHARMACOLOGICAL
APPROACHES TO NEUROPATHIC PAIN
MANAGEMENT HAVE YOU FOUND HELPFUL
FOR YOUR PATIENTS?**

Evidence for Non-pharmacological Therapies in Neuropathic Pain

- Studied therapies include:
- Limited evidence for most modalities

The effectiveness of B vitamins in reducing chronic neuropathic pain has not been established

- Magnets
- Dietary supplements
- Imagery
- Spiritual healing
- Cannabis extract
- Carnitine
- Electrostimulation
- Magnets

IASP NeuPSIG Recommendations: Interventional Management of Neuropathic Pain



Weakly Recommended

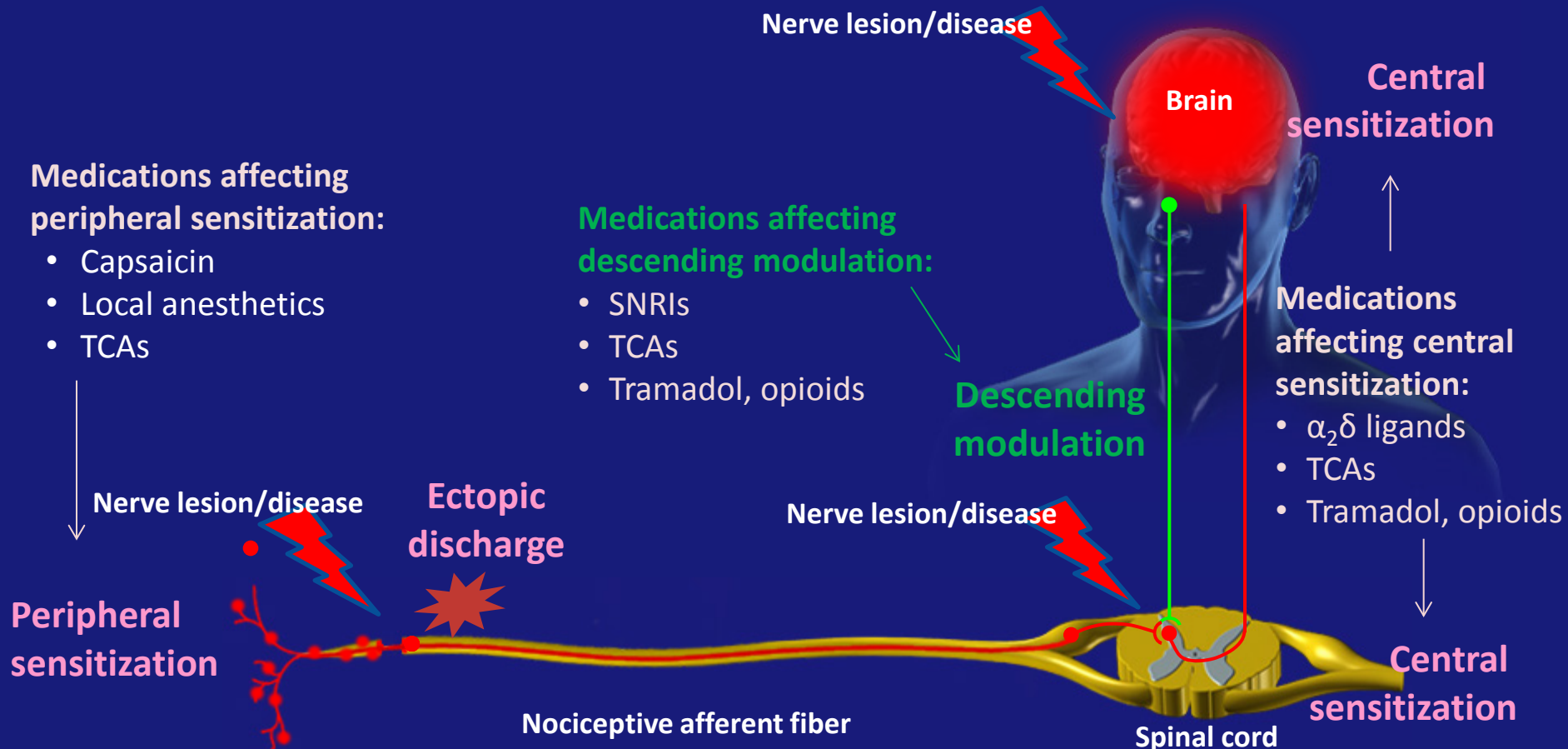
- Epidural or paravertebral nerve block(s) for herpes zoster
- Epidural steroid injection(s) for radiculopathy
- Spinal cord stimulation for failed back surgery syndrome with radiculopathy and complex regional pain syndrome 1



Not recommended

- Sympathetic nerve blocks for postherpetic neuralgia
- Radiofrequency lesioning for lumbar radiculopathy

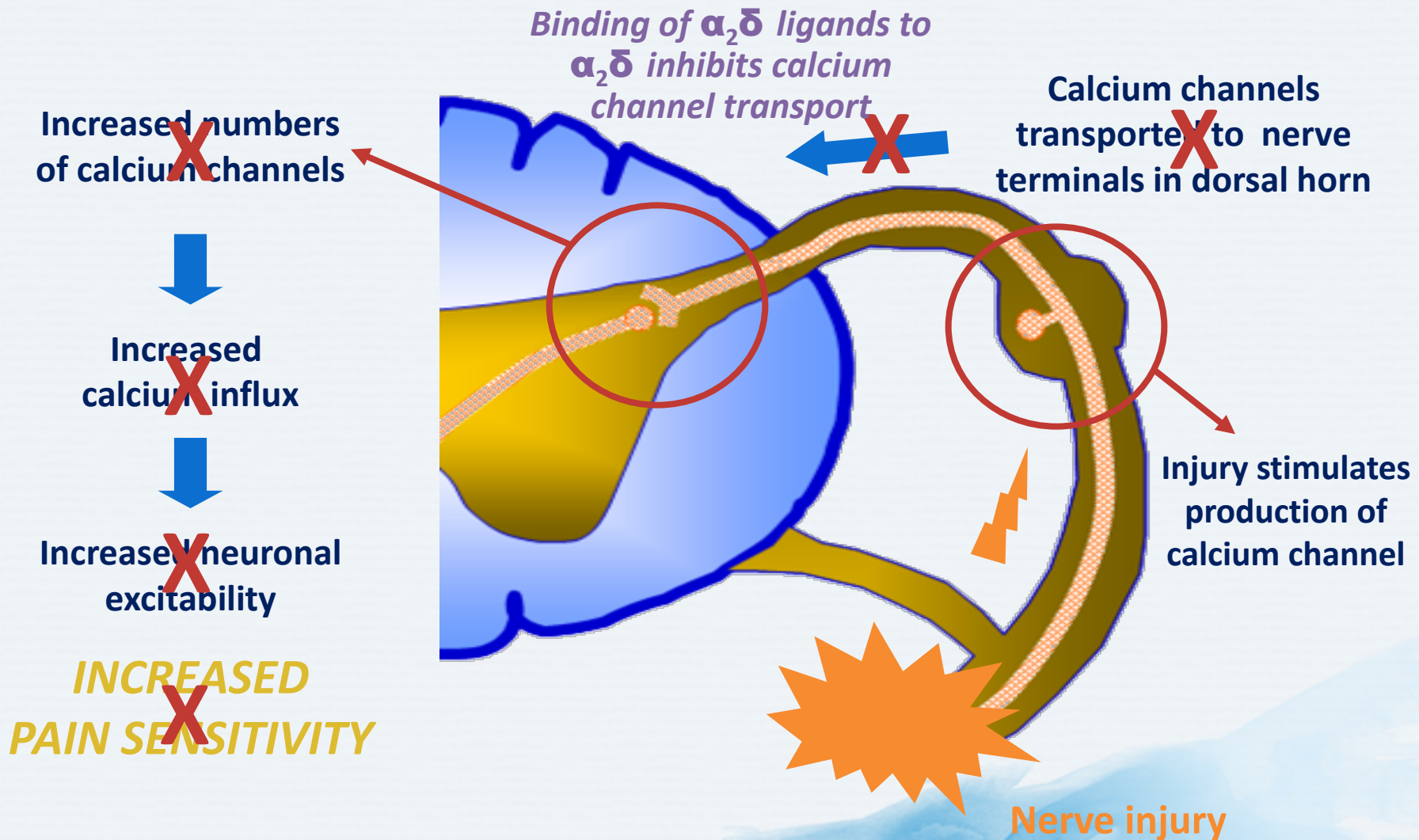
Mechanism-Based Pharmacological Treatment of Neuropathic Pain



SNRI = serotonin-norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant

Adapted from: Attal N *et al.* *Eur J Neurol* 2010; 17(9):1113-e88; Beydoun A, Backonja MM. *J Pain Symptom Manage* 2003; 25(5 Suppl):S18-30; Jarvis MF, Boyce-Rustay JM. *Curr Pharm Des* 2009; 15(15):1711-6; Gilron I *et al.* *CMAJ* 2006; 175(3):265-75; Moisset X, Bouhassira D. *NeuroImage* 2007; 37(Suppl 1):S80-8; Morlion B. *Curr Med Res Opin* 2011; 27(1):11-33; Scholz J, Woolf CJ. *Nat Neurosci* 2002; 5(Suppl):1062-7.

Role of $\alpha_2\delta$ -Linked Calcium Channels in Neuropathic Pain



Note: gabapentin and pregabalin are $\alpha_2\delta$ ligands
Bauer CS et al. *J Neurosci* 2009; 29(13):4076-88.

Adverse Effects of $\alpha_2\delta$ Ligands

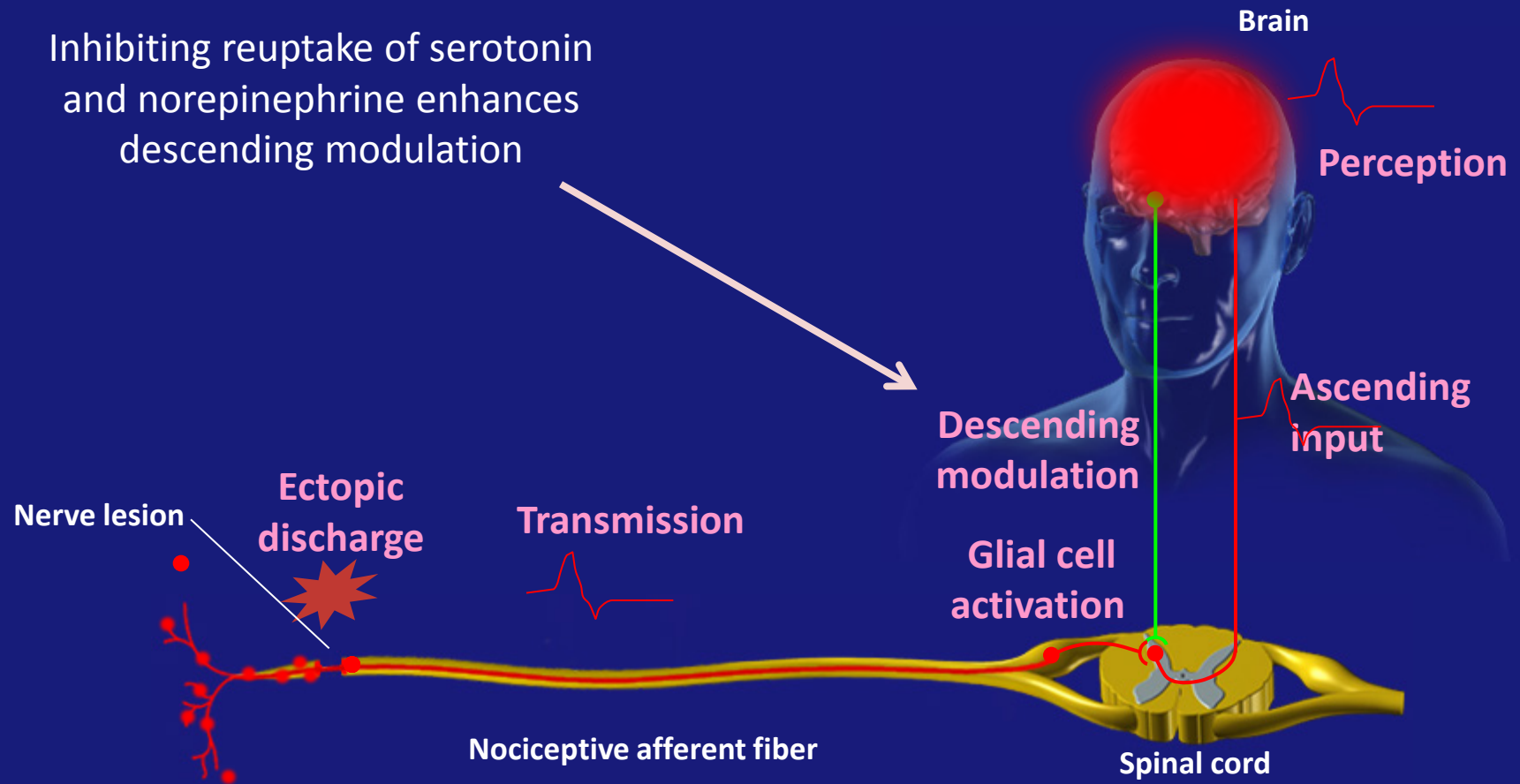
System	Adverse effects
Digestive system	Dry mouth
CNS	Dizziness, somnolence
Other	Asthenia, headache, peripheral edema, weight gain

$\alpha_2\delta$ ligands include gabapentin and pregabalin

CNS = central nervous system

Attal N, Finnerup NB. *Pain Clinical Updates* 2010; 18(9):1-8.

How Antidepressants Modulate Pain



Adverse Effects of Antidepressants

System	TCAs	SNRIs
Digestive system	Constipation, dry mouth, urinary retention	Constipation, diarrhea, dry mouth, nausea, reduced appetite
CNS	Cognitive disorders, dizziness, drowsiness, sedation	Dizziness, somnolence
Cardiovascular	Orthostatic hypotension, palpitations	Hypertension
Other	Blurred vision, falls, gait disturbance, sweating	Elevated liver enzymes, elevated plasma glucose, sweating

Pharmacological Management of Neuropathic Pain

STEP 1

Initiate treatment with one or more **first-line** treatments:

- $\alpha_2\delta$ ligands (gabapentin, pregabalin)
- SNRIs (duloxetine, venlafaxine)
- TCAs* (nortriptyline, desipramine)
- Topical lidocaine (for localized peripheral pain)

STEP 2

- If there is partial pain relief, add another first-line medication
- If there is no or inadequate pain relief, switch to another first-line medication

STEP 3

If first-line medications alone and in combination fail, consider **second-line** medications (opioids, tramadol) or **third-line** medications (bupropion, citalopram, paroxetine, carbamazepine, lamotrigine, oxcarbazepine, topiramate, valproic acid, topical capsaicin, dextromethorphan, memantine, mexiletine) or referral to pain specialist

*Use tertiary amine TCAs such as amitriptyline only if secondary amine TCAs are unavailable

Note: there is insufficient support for the use of nsNSAIDs in neuropathic pain

nsNSAID = non-specific non-steroidal anti-inflammatory drug; SNRI = serotonin-norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant

Dworkin RH et al. *Mayo Clin Proc* 2010 ; 85(3 Suppl):S3-14; Freynhagen R, Bennett MI. *BMJ* 2009; 339:b3002.

Prescribing Recommendations for First-Line Medications

Medication	Starting dose	Titration	Max. dosage	Trial duration
$\alpha_2\delta$ ligands				
Gabapentin	100–300 mg at bedtime or tid	↑ by 100–300 mg tid every 1–7 days	3600 mg/day	3–8 weeks + 2 weeks at max. dose
Pregabalin	50 mg tid or 75 mg bid	↑ to 300 mg/day after 3–7 days, then by 150 mg/day every 3–7 days	600 mg/day	4 weeks
SNRIs				
Duloxetine	30 mg qd	↑ to 60 mg qd after 1 week	60 mg bid	4 weeks
Venlafaxine	37.5 mg qd	↑ by 75 mg each week	225 mg/day	4–6 weeks
TCAs (desipramine, nortriptyline)	25 mg at bedtime	↑ by 25 mg/day every 3–7 days	150 mg/day	6–8 weeks, with ≥2 weeks at max. tolerated dosage
Topical lidocaine	Max. 3 5% patches/day for 12 h max.	None needed	Max. 3 patches/day for 12–18 h max.	3 weeks

SNRI = serotonin-norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant

Dworkin RH et al. *Mayo Clin Proc* 2010; 85(3 Suppl):S3-14.

But... Patients with Chronic Pain of Just One Type of Pain Pathophysiology May be Rare

- Patients may have different pathophysiologic mechanisms contributing to their pain
 - e.g., complex regional pain syndrome has multiple potential mechanisms, including nerve injury and inflammation – “mixed pain state”



- Therapies that will work better for a particular patient are likely to depend on the mechanisms contributing to the patient's pain



- Patients with mixed pain may benefit from combination therapy

Discussion Question



WHAT TREATMENT APPROACH WOULD YOU TAKE WITH A PATIENT SUFFERING FROM MIXED PAIN DUE TO COMPLEX REGIONAL PAIN SYNDROME?

Complex Regional Pain Syndrome

- *What is it?*
 - Exaggerated response to trauma, characterized by intense prolonged pain, delayed recovery of function, vasomotor disturbances and trophic changes
 - Causes are unclear, but may include exaggerated local inflammatory response, nerve injury and involvement of the central and peripheral nervous systems
- *How common is it?*
 - Thought to occur in 1 in 2000 cases of limb trauma
- *How should it be treated?*
 - Physiotherapy is the mainstay of treatment
 - Combination of pharmacological agents may be necessary

Key Messages

- Neuropathic pain is pain caused by a lesion or disease of the somatosensory nervous system
- Up to 10% of the population may suffer from neuropathic pain, which is associated with significant patient-reported burden
- Neuropathic pain can be distinguished from nociceptive pain through common verbal descriptors and simple bedside tests
 - Several easy screening tests are also available
- Non-pharmacological therapies, including patient education, are important components of neuropathic pain management
- When it comes to pharmacotherapy, most treatment guidelines consider antidepressants and $\alpha 2\delta$ ligands as first-line therapy for most types of neuropathic pain