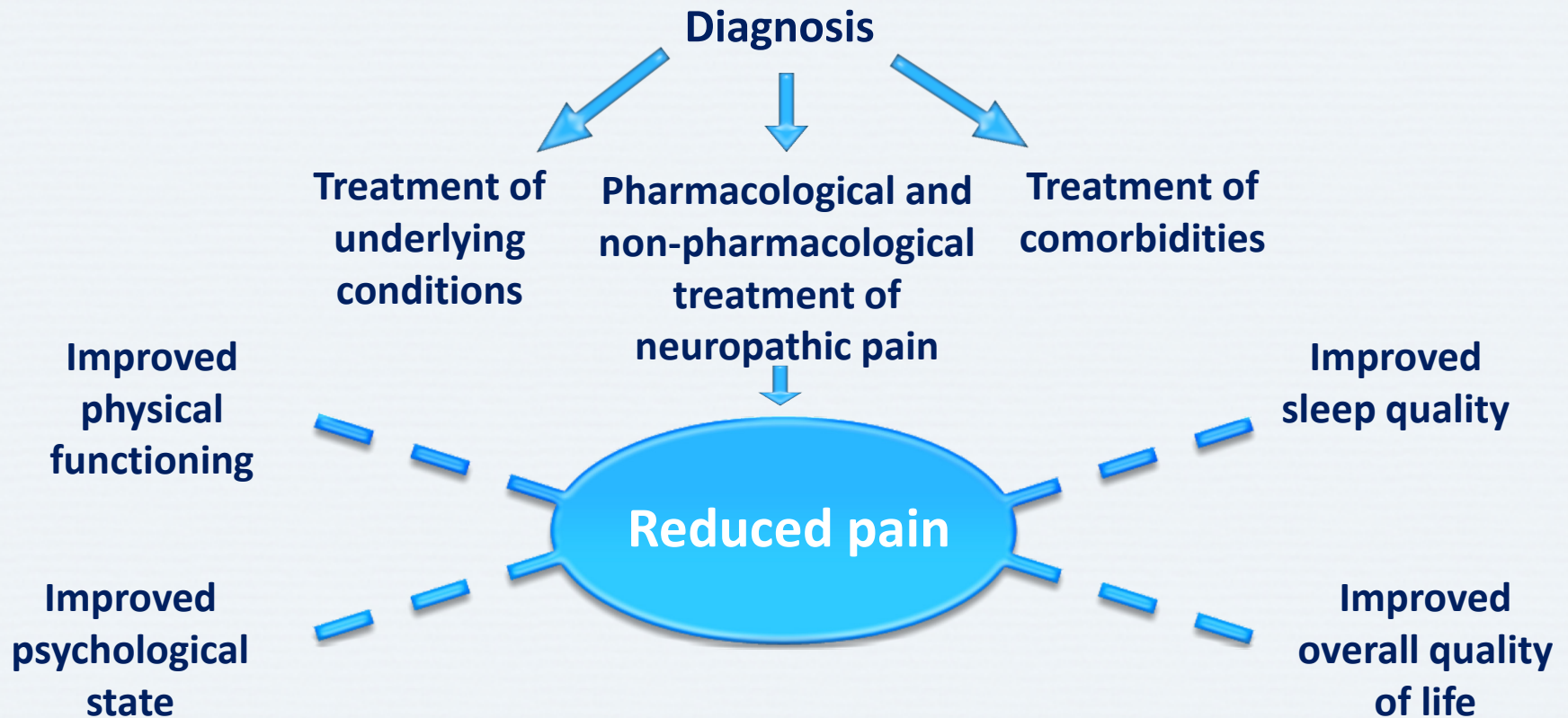

MANAGEMENT

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Goals of Treatment

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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.

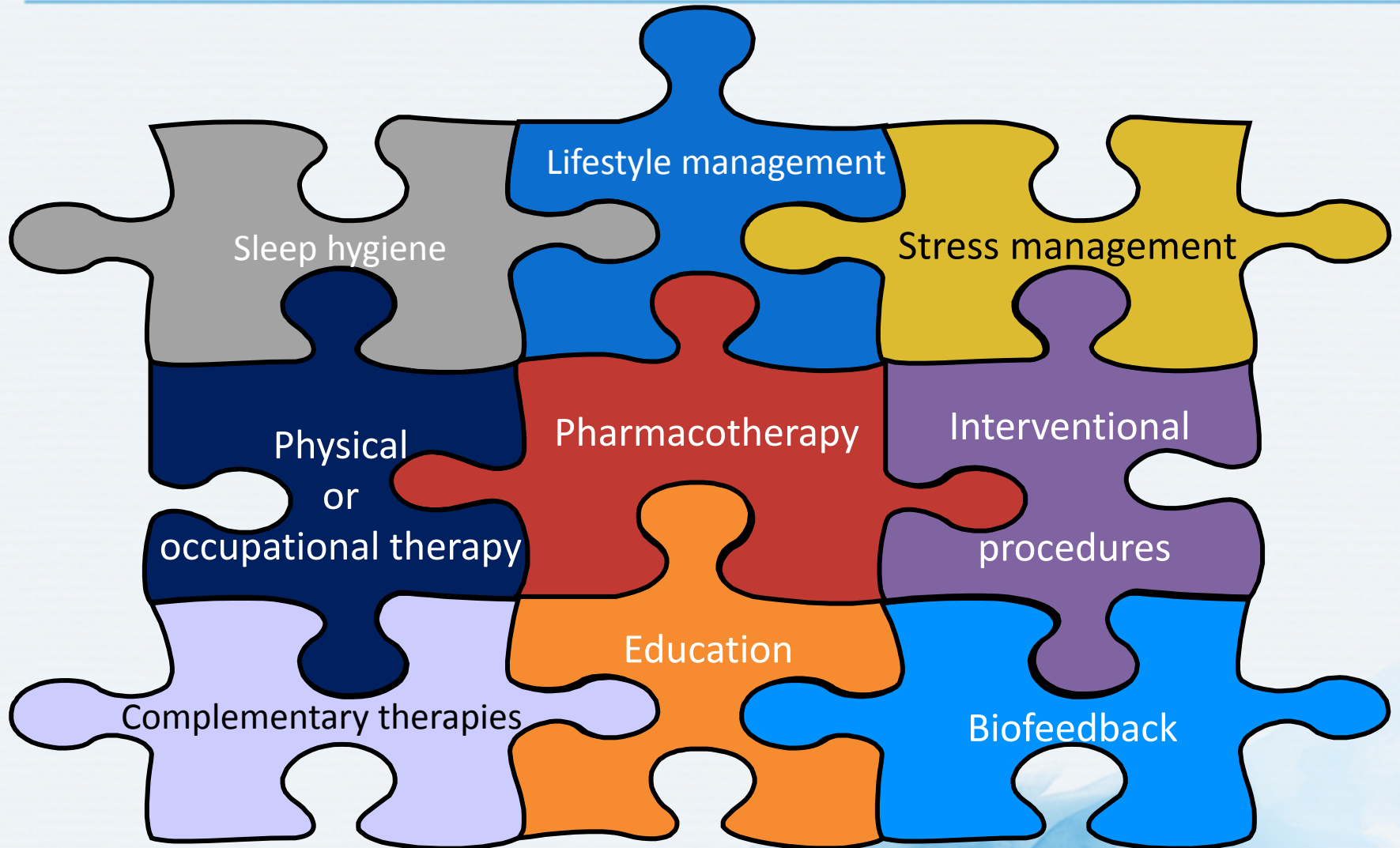
Planning the Management of Painful Diabetic Peripheral Neuropathy: Treatment Goals

Primary	<ul style="list-style-type: none">• >50% pain relief, but be realistic!• Do not let "realistic" lead to a less aggressive pursuit of maximum relief
Secondary	<ul style="list-style-type: none">• Restoration or improvement in functional measures, quality of life, sleep and mood• Treatment should be modifying pain and hopefully improved function will follow• If improved function does not follow, take measures to help patients optimize function in the presence of residual pain

Non-pharmacological Treatment

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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.

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

AAN Guidelines: Non-pharmacologic Treatment of Diabetic Peripheral Neuropathy



Recommended

- Percutaneous electrical nerve stimulation (level B)



Not recommended

- Electromagnetic field treatment (level B)
- Low-intensity laser treatment (level B)
- Reiki therapy (level B)



Insufficient evidence

- Amitriptyline + electrotherapy (level U)

AAN Guidelines: Non-pharmacologic Treatment of Postherpetic Neuralgia



Recommended

- None



Not recommended

- Acupuncture (level B)
- Vitamin E (level B)



Insufficient evidence

- He:Ne laser irradiation
- Cryocautery
- Extract of *Ganoderma lucidum* (lingzhi mushroom)

Latin American Expert Consensus: Non-pharmacological Treatment of Neuropathic Pain



Complementary therapies*

- Acupuncture – provided it is performed by qualified practitioners and with the agreement of the patient
- Thiocctic acid and cytidine/uridine monophosphate



Insufficient evidence

- Herbal therapy**

***Although widely used in practice, little scientific evidence supports its use and the patient must be informed about this. Use or recommendation for use mandates prudence and ethical conduct.**

****These types of treatment are left up to the doctor, who should consider sociocultural aspects of the patient.**

Acevedo et al. J Pain Palliat Care Pharmacother 2009; 23(3):261-81.

South African Guidelines: Non-pharmacologic Treatment of Neuropathic Pain



Recommended

- Psychotherapy, particularly cognitive behavioral therapy
- Transcutaneous electrical nerve stimulation
- Physiotherapy
- Spinal cord stimulation*



Not recommended

- Dorsal root entry zone lesioning (DREZotomy)

*In cases of pain that cannot be managed by pharmacological and companion treatments

Chetty S et al. *S Afr Med J* 2012; 102(5):312-25.

EFNS Guidelines: Non-pharmacologic Treatment of Neuropathic Pain



Recommended

- Electro-acupuncture (level B)
- High-frequency transcutaneous electrical nerve stimulation (level C)
- Repetitive transcranial magnetic stimulation* (level B)



Not recommended

- Peripheral electrical neurostimulation



Insufficient evidence

- Implanted peripheral stimulation

Note: only electrical neurostimulation modalities were reviewed, other non-pharmacological methods were not considered

***Transient efficacy; EFNS = European Federation of Neurological Societies**

Cruccu G et al. *Eur J Neurol* 2007; 14(9):952-70.

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

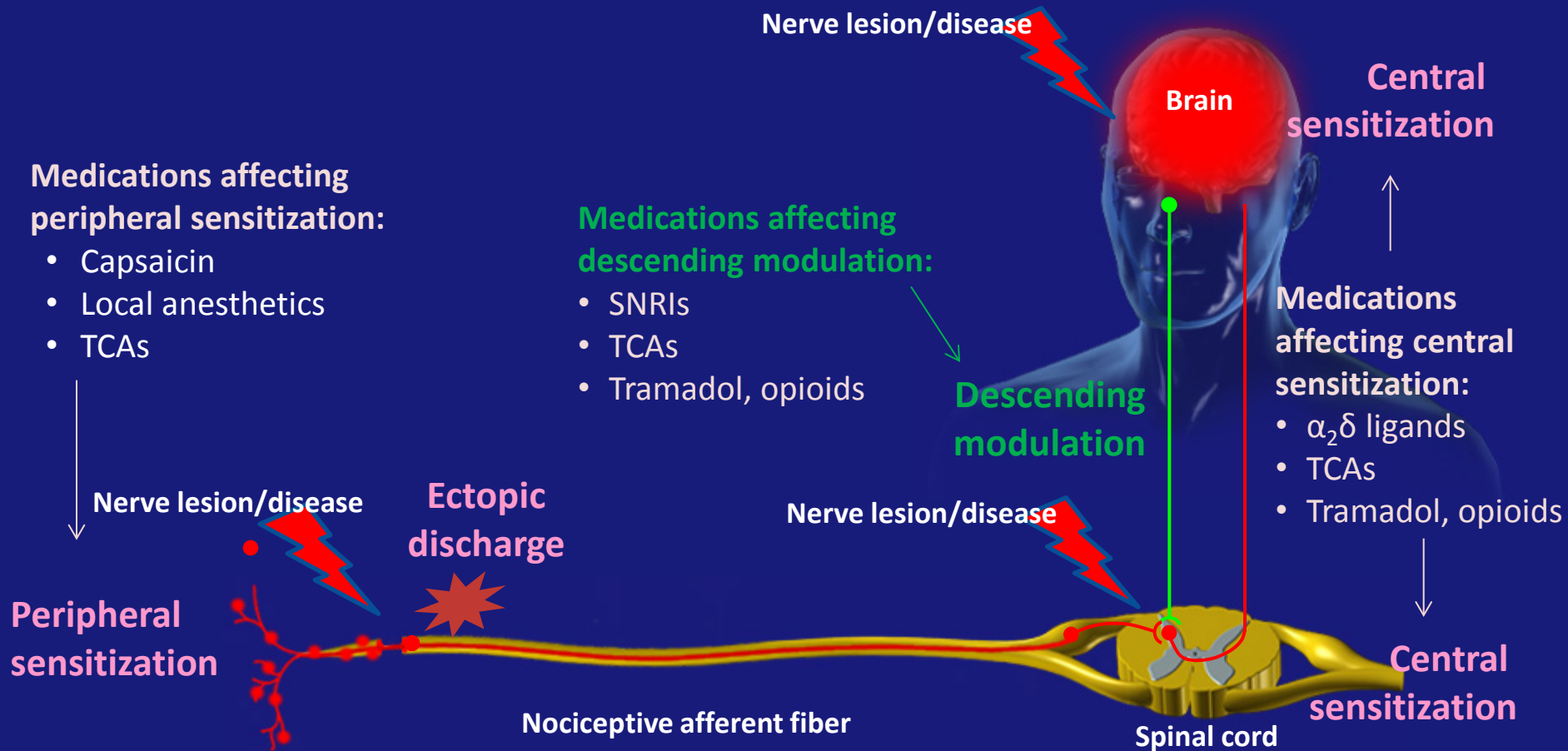
Summary of Non-pharmacologic Treatment Recommendations for Neuropathic Pain

- Transcutaneous electrical nerve stimulation is the only non-pharmacologic treatment modality recommended by the majority of guidelines

Pharmacological Treatment

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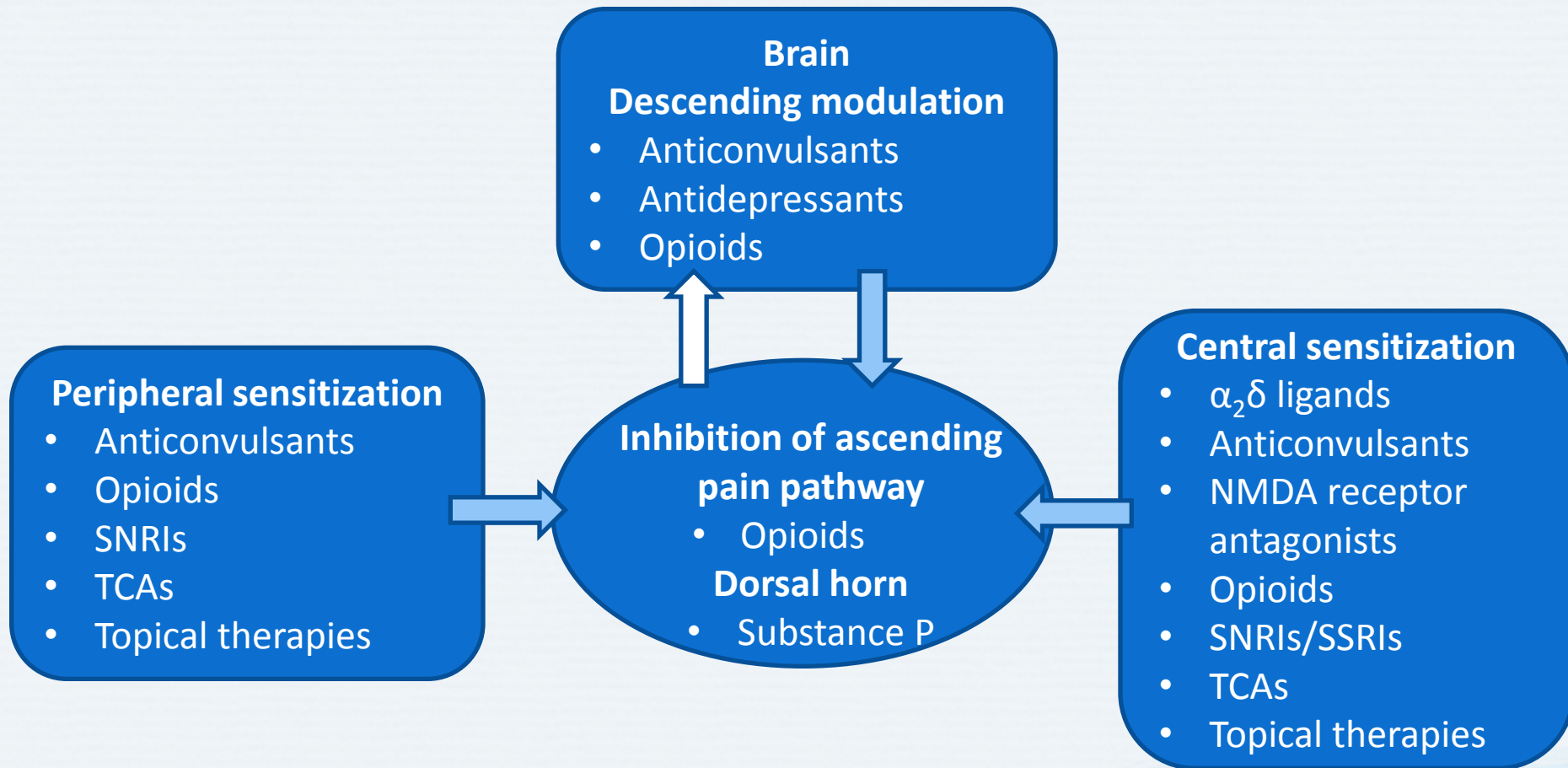
Mechanism-Based Pharmacological Treatment of Neuropathic Pain



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.

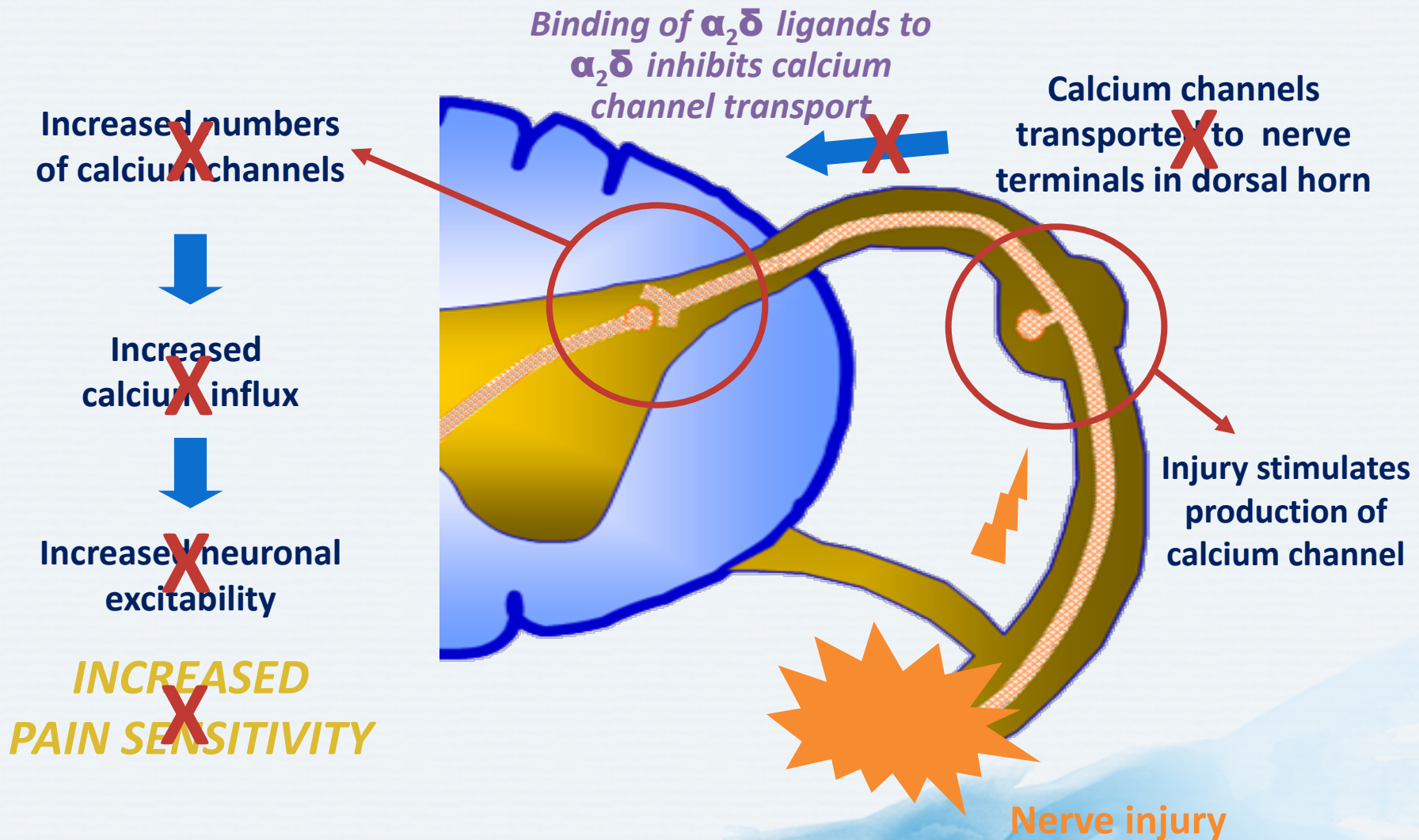
Therapeutic Targets of Neuropathic Pain



NMDA = N-methyl-D-aspartate; SNRI = serotonin-norepinephrine reuptake inhibitor;
SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant

Iyer S. *Expert Opin Pharmacother* 2013; 14(13):1765-75.

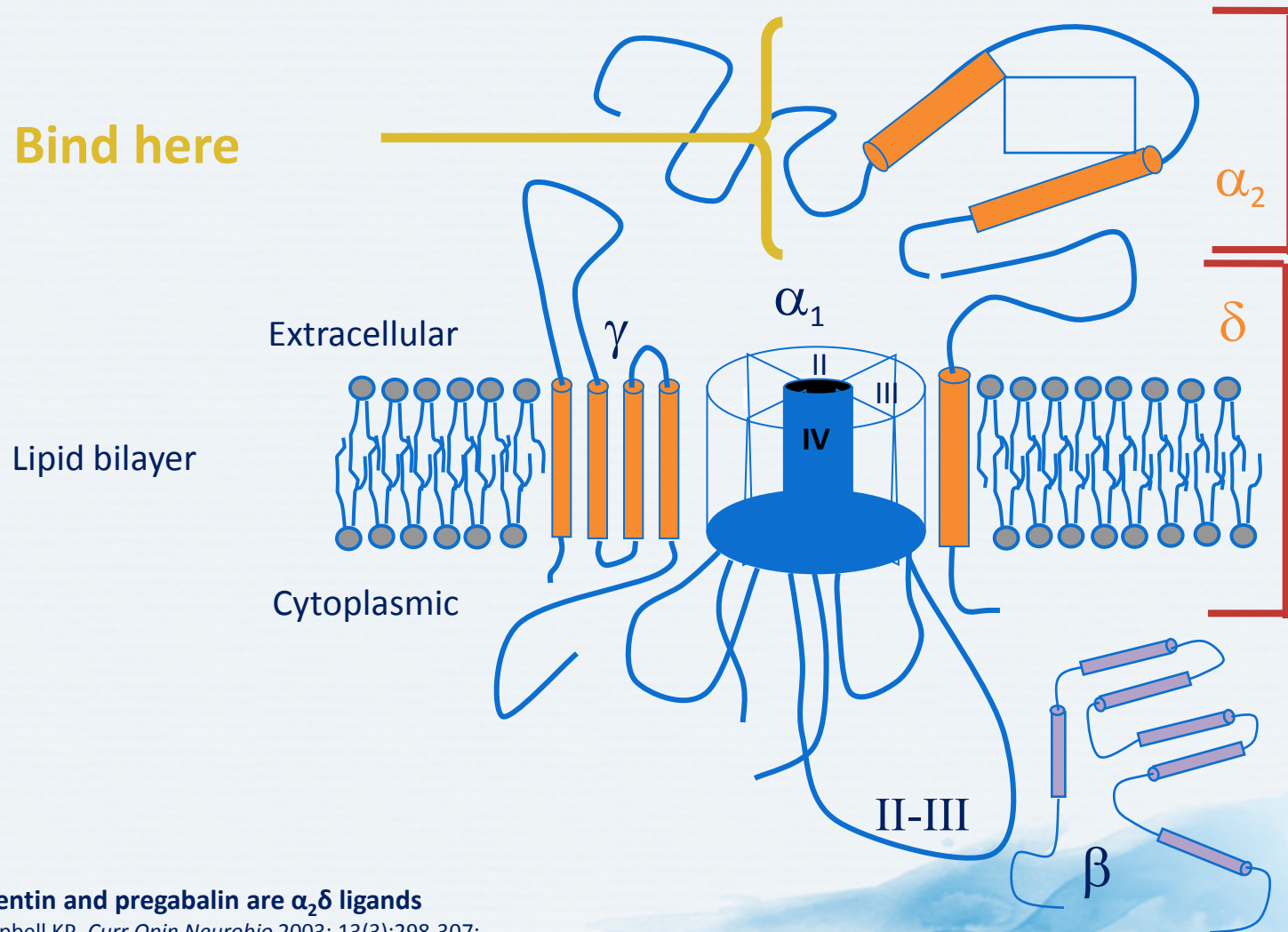
Role of $\alpha_2\delta$ -Linked Calcium Channels in Neuropathic Pain



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

$\alpha_2\delta$ Ligands Bind to $\alpha_2\delta$ Subunit of Voltage-Gated Calcium Channels

Bind here

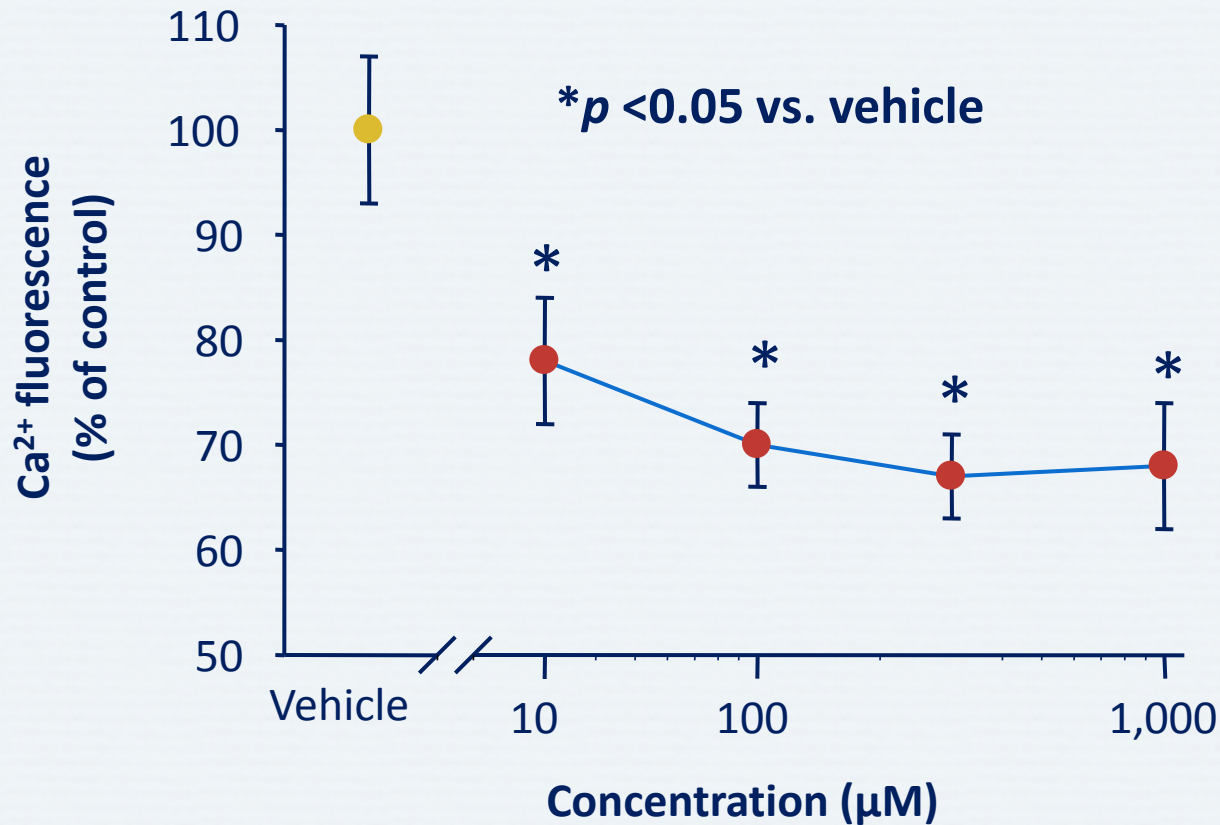


Note: gabapentin and pregabalin are $\alpha_2\delta$ ligands

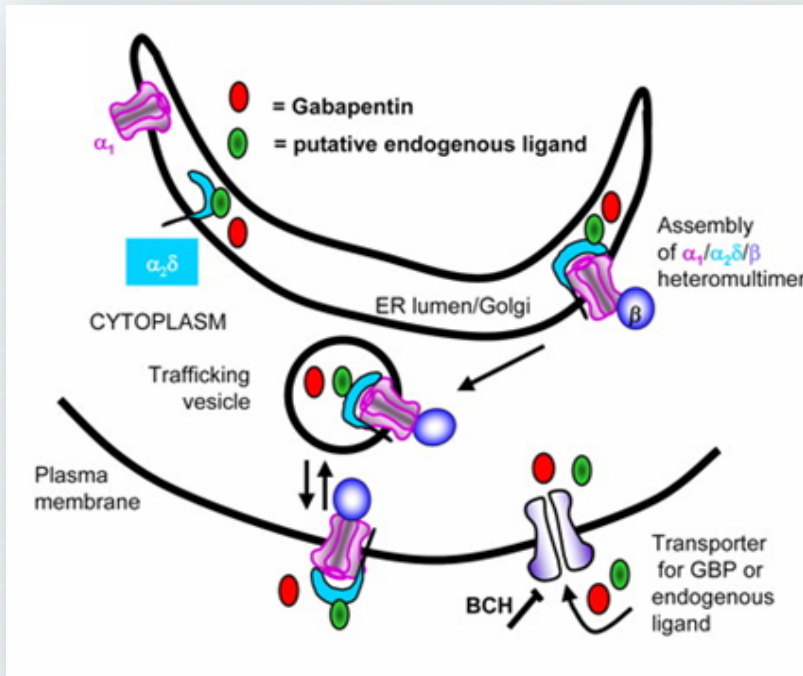
Arikkath J, Campbell KP. *Curr Opin Neurobio* 2003; 13(3):298-307;

Catterall WA. *J Bioenerg Biomembr* 1996; 28(3):219-30; Gee NS et al. *Biol Chem* 1996; 271(10):5768-76..

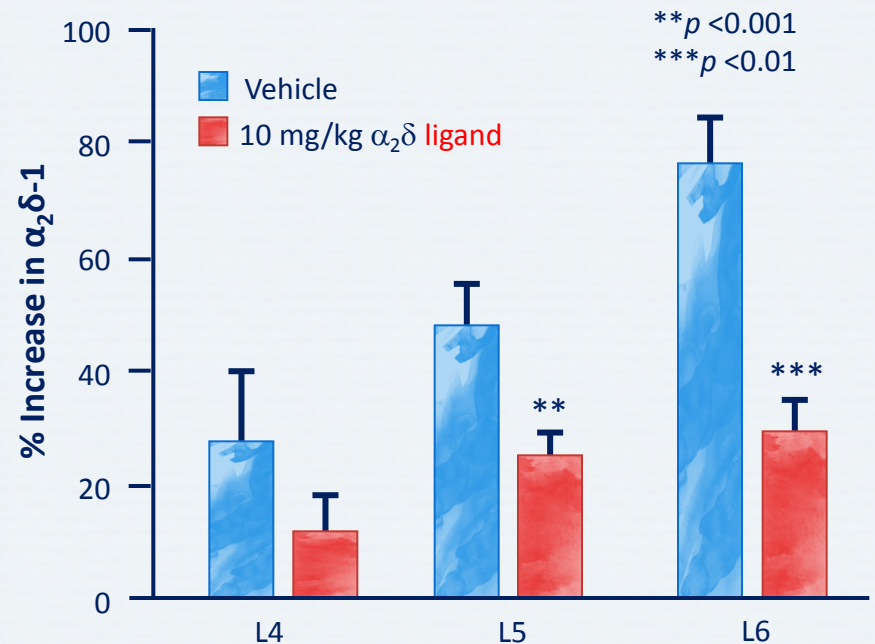
$\alpha_2\delta$ Ligands Reduce Calcium Influx in Depolarized Human Neocortex Synaptosomes



$\alpha_2\delta$ Ligands Modulate Calcium Channel Trafficking



Hendrich et al. 2008



Bauer et al. 2009

- $\alpha_2\delta$ ligands reduce trafficking of voltage-gated calcium channel complexes to cell surface *in vitro*
- $\alpha_2\delta$ ligands prevent nerve-injury induced up-regulation of $\alpha_2\delta$ in the dorsal horn

BCH = 2-(-)-endoamino-bicycloheptene-2-carboxylic acid; ER = endoplasmic reticulum; GBP = gabapentin

Bauer CS et al. *Neurosci* 2009; 29(13):4076-88; Hendrich J et al. *Proc Natl Acad Sci U S A* 2008; 105(9):3628-33.

Adverse Effects of $\alpha_2\delta$ Ligands

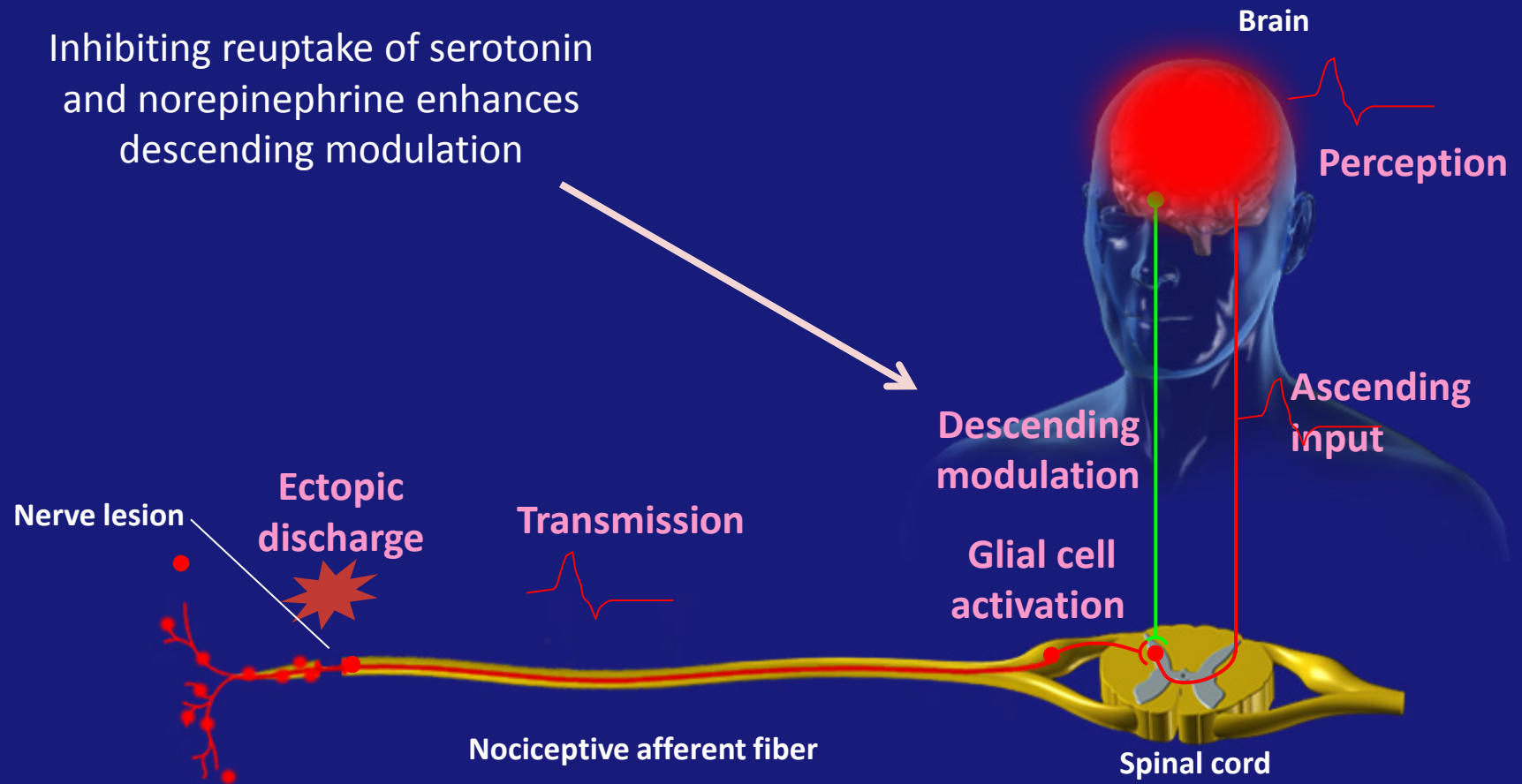
System	Adverse effects
Digestive system	Dry mouth
CNS	Dizziness, somnolence
Other	Asthenia, headache, peripheral edema, weight gain

$\alpha_2\delta$ 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



Suggested Mechanisms of Analgesic Action of Antidepressants

Mechanism of Action	Site of Action	TCA	SNRI
Reuptake inhibition	Serotonin Noradrenaline	+	+
Receptor antagonism	α -adrenergic NMDA	+	- (+) milnacipran
Blocking or activation of ion channels	Sodium channel blocker Calcium channel blocker Potassium channel activator	+	(+) venlafaxine/ - duloxetine ? ?
Increasing receptor function	GABA _B receptor	+ amitriptyline/ desipramine	?
Opioid receptor binding/ opioid-mediated effect	Mu- and delta-opioid receptor	(+)	(+) venlafaxine
Decreasing inflammation	Decrease of PGE2 production decrease of TNF α production		

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

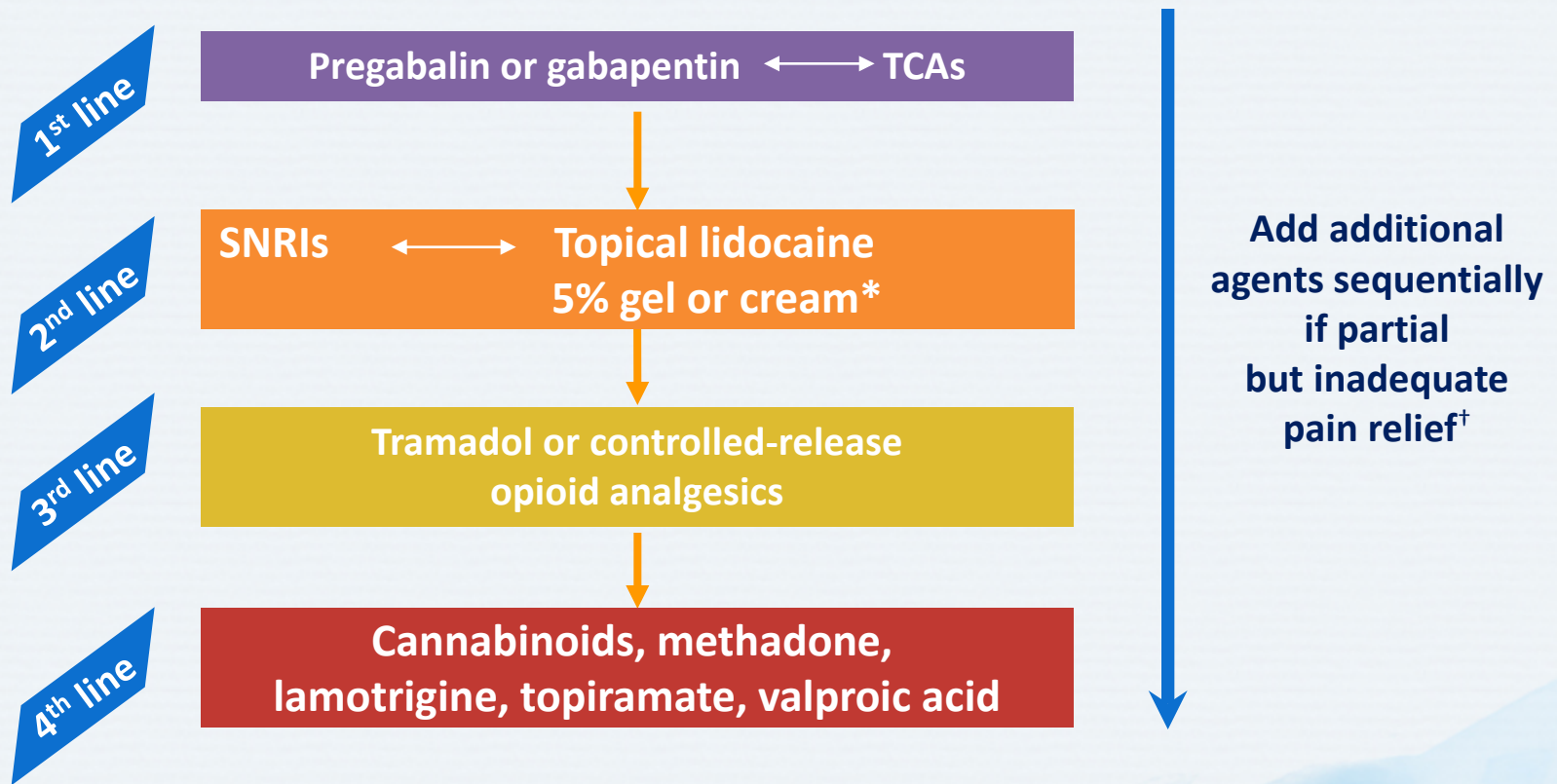
Note: there is insufficient support for the use of nsNSAIDs in neuropathic pain

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.

CPS Recommendations for the Pharmacological Management of Neuropathic Pain

Stepwise Pharmacological Management of Neuropathic Pain



*Useful for focal neuropathy such as post-herpetic neuralgia; [†]Do NOT add SNRIs to TCAs.

CPS = Canadian Pain Society; TCA = tricyclic antidepressant; SNRI = serotonin-norepinephrine reuptake inhibitor

Adapted from: Moulin DE et al. *Pain Res Manag* 2007; 12(1):13-21.

AAN Guidelines: Pharmacological Treatment of Painful Diabetic Peripheral Neuropathy

1st line
(level A)

- Pregabalin

2nd line
(level B)

- Gabapentin
- Duloxetine
- Amitriptyline
- Opioids
- Tramadol

The AAN recognizes that specific care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the circumstances involved.

AAN = American Academy of Neurology

Bril V et al. *Neurology* 2011; 76(20):1758-65.

AAN Guidelines: Pharmacological Treatment of Postherpetic Neurology

1st line
(level A)

- TCAs (amitriptyline,* nortriptyline,** desipramine, maprotiline)
- $\alpha_2\delta$ ligands (gabapentin, pregabalin)
- Opioids
- Topical lidocaine patches
- Preservative-free intrathecal methylprednisolone

***Amitriptyline has significant cardiac effects in the elderly when compared to nortriptyline and desipramine;**

****Limited evidence (level B) to support nortriptyline over amitriptyline**

AAN = American Academy of Neurology

Dubinsky RM *et al. Neurology* 2004; 63(6):959-65.

Latin American Guidelines: Pharmacological Management of Neuropathic Pain

1st line

- $\alpha_2\delta$ ligands (gabapentin, pregabalin)
- TCAs (amitriptyline)

2nd line

- Dual antidepressants (duloxetine)

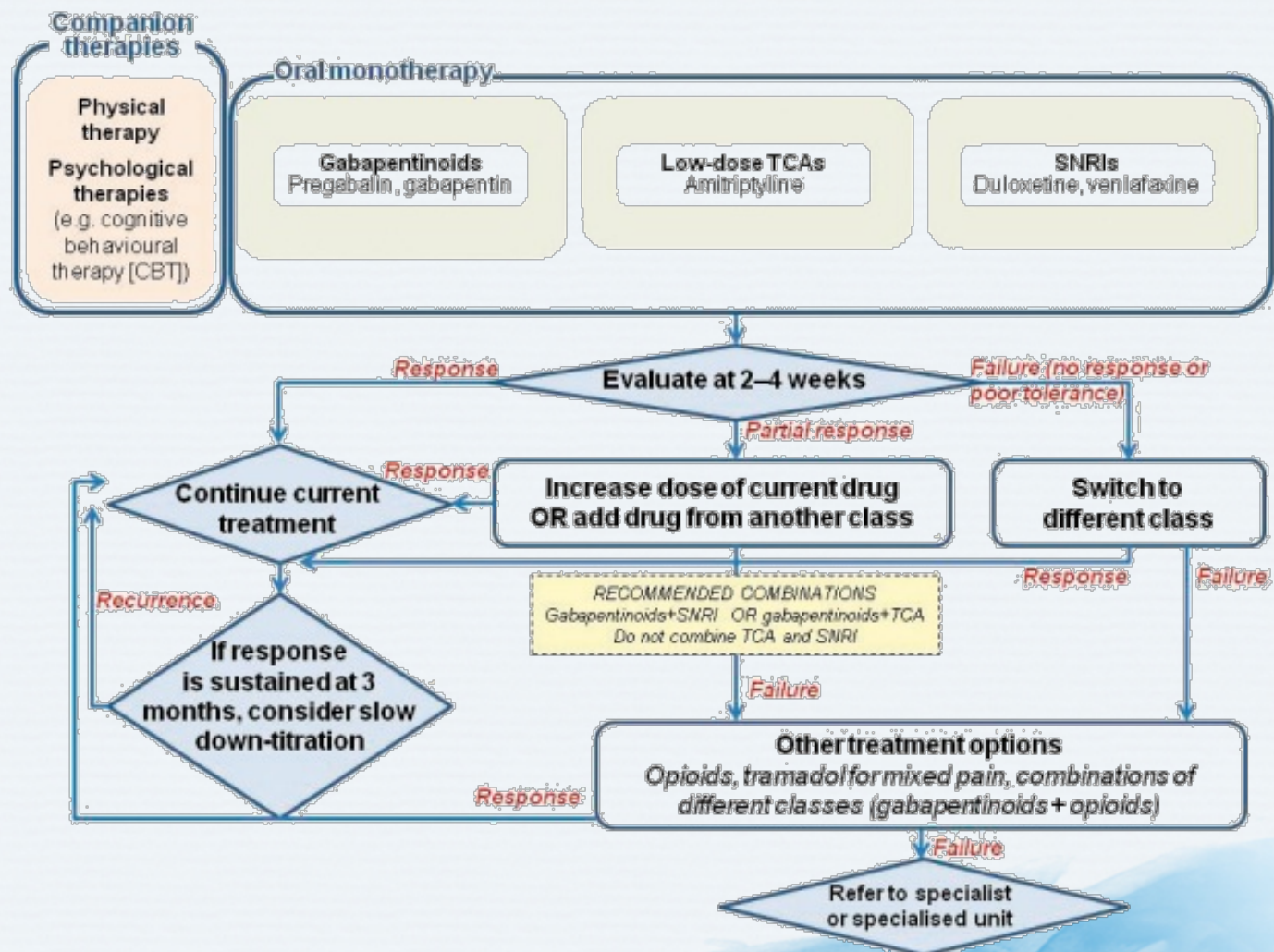
3rd line

- Weak opioids (tramadol)
- Local anesthetics (lidocaine)

4th line

- SNRIs (fluoxetine), sodium channel blockers (carbamazepine), substance P inhibitors (capsaicin), cannabinoids, strong opioids (morphine)

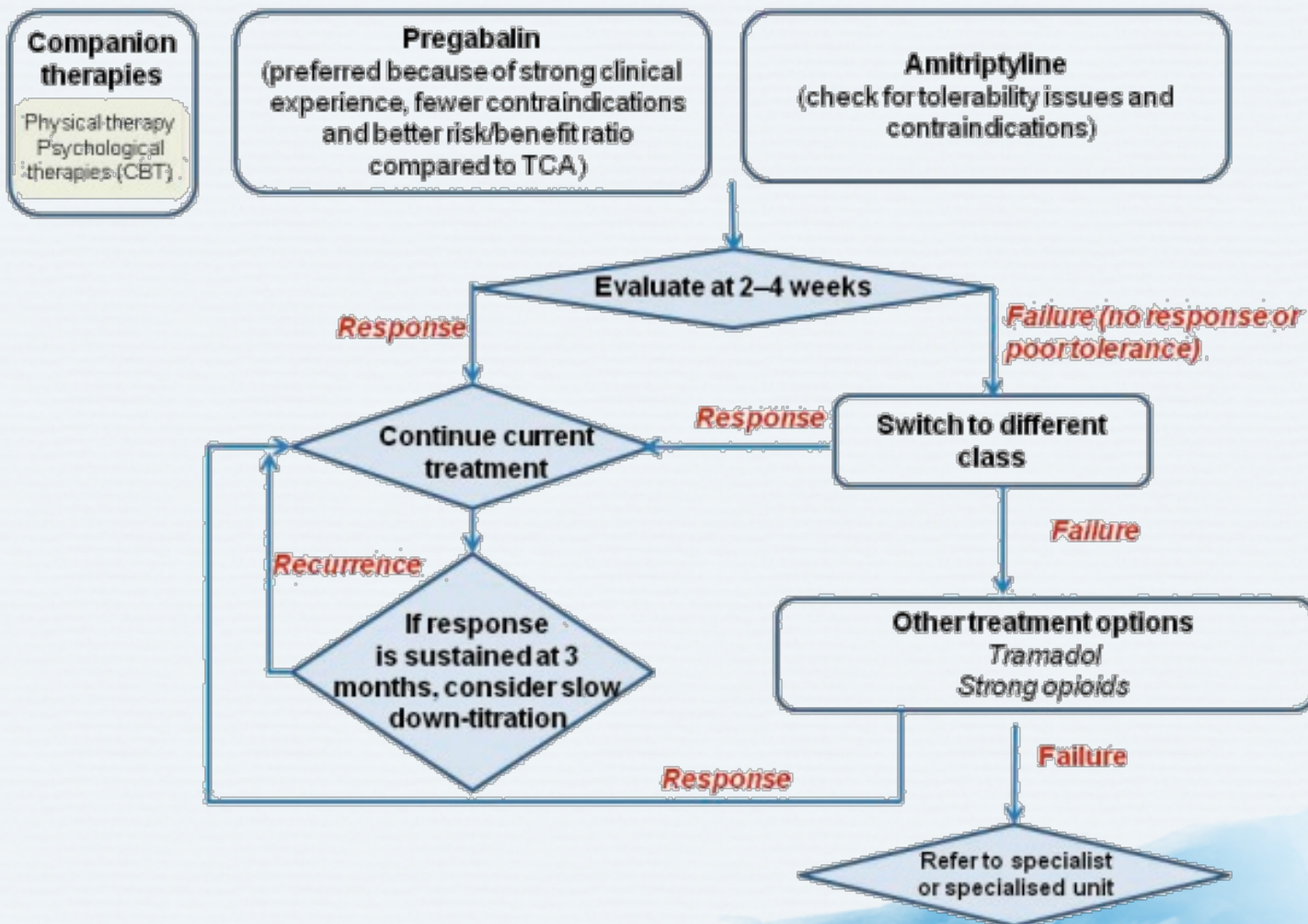
South African Guidelines: Algorithm for the Treatment of Non-localized Peripheral Neuropathic Pain



SNRI = serotonin norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant

Chetty S et al. S Afr Med J 2012; 102(5):312-25.

South African Guidelines: Algorithm for the Treatment of Central Neuropathic Pain



Treatment Recommendations for French-Speaking Maghreb: Peripheral Neuropathic Pain

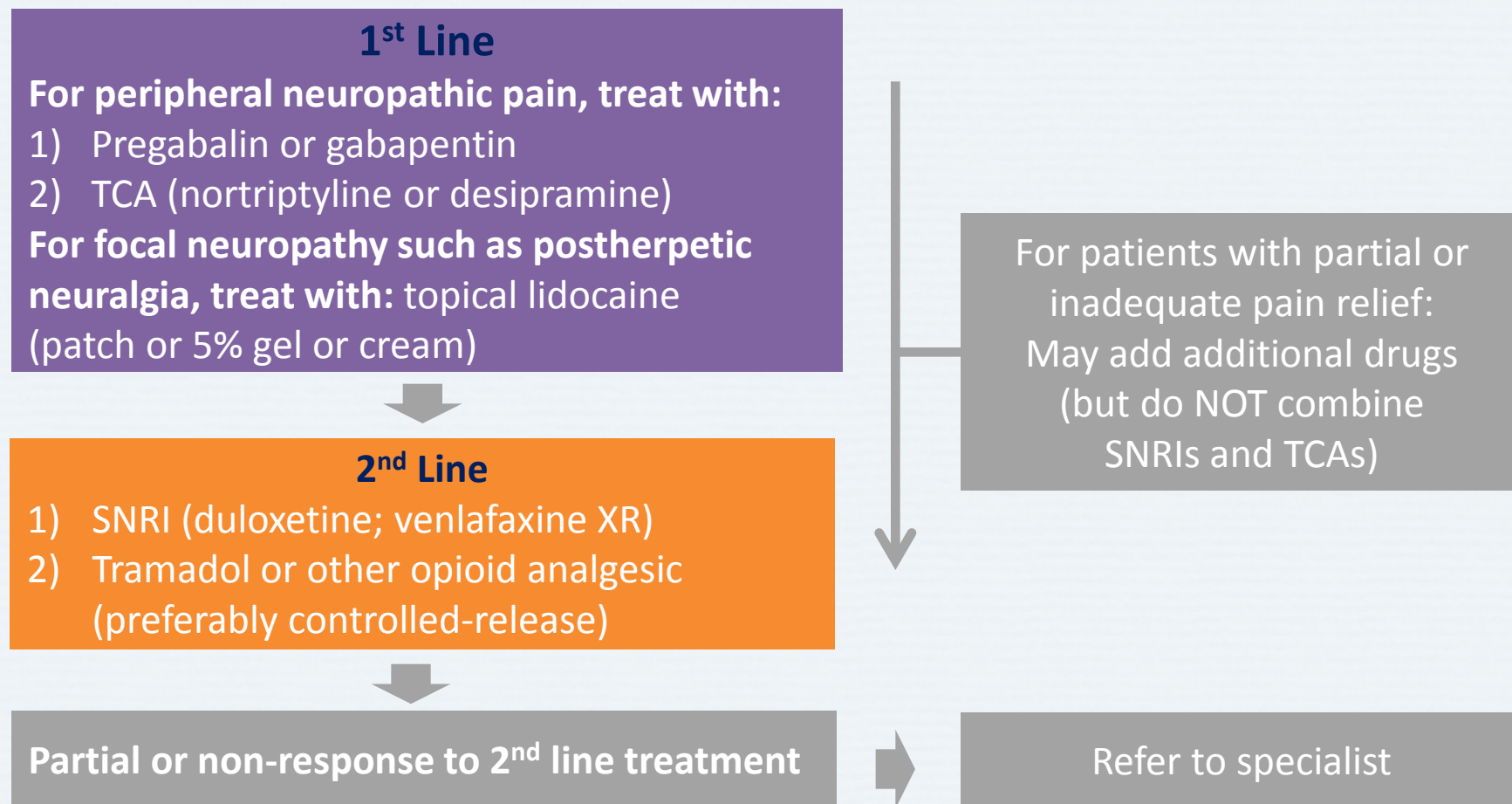
1st line
(level A)

- $\alpha^2\delta$ ligands (gabapentin, pregabalin)
- TCAs
- Topical lidocaine

2nd line
(level B)

- SNRIs (venlafaxine XR or duloxetine)
- Tramadol

Middle East Region Expert Panel Recommendations: Treatment Algorithm for Peripheral Neuropathic Pain



*In patients with focal post-herpetic neuropathy with allodynia,
or any peripheral neuropathic pain associated with a small, localized area of allodynia

NMDA = N-methyl-D-aspartate; SNRI = serotonin-norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant; XR = extended release

Bohlega S et al. J Int Med Res 2010; 38(2):295-317.

Central Neuropathic Pain Treatment Recommendations for the Middle East Region

1st line

- $\alpha_2\delta$ ligands (gabapentin, pregabalin)

Other
treatments

- Opioids*
- SNRIs*
- TCAs

*Benefit appears to be notably less than for peripheral neuropathic pain

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

Bohlega S et al. *J Int Med Res* 2010; 38(2):295-317.

EFNS Guidelines: Pharmacological Treatment of Neuropathic Pain

	DPN	Postherpetic neuralgia	Trigeminal neuralgia	Central pain
1 st line	<ul style="list-style-type: none"> • $\alpha_2\delta$ ligands (gabapentin, pregabalin) • SNRIs (duloxetine, venlafaxine ER) • TCAs 	<ul style="list-style-type: none"> • $\alpha_2\delta$ ligands (gabapentin, pregabalin) • TCAs • Lidocaine plasters 	<ul style="list-style-type: none"> • Gabamazepine • Oxcarbazepine 	<ul style="list-style-type: none"> • $\alpha_2\delta$ ligands (gabapentin, pregabalin) • TCAs
2 nd or 3 rd line	<ul style="list-style-type: none"> • Opioids • Tramadol* 	<ul style="list-style-type: none"> • Capsaicin • Opioids 	<ul style="list-style-type: none"> • Surgery 	<ul style="list-style-type: none"> • Cannabinoids (MS) • Lamotrigine • Opioids • Tramadol (SCI)

Note: recommended treatments may not all be licensed for the indication.

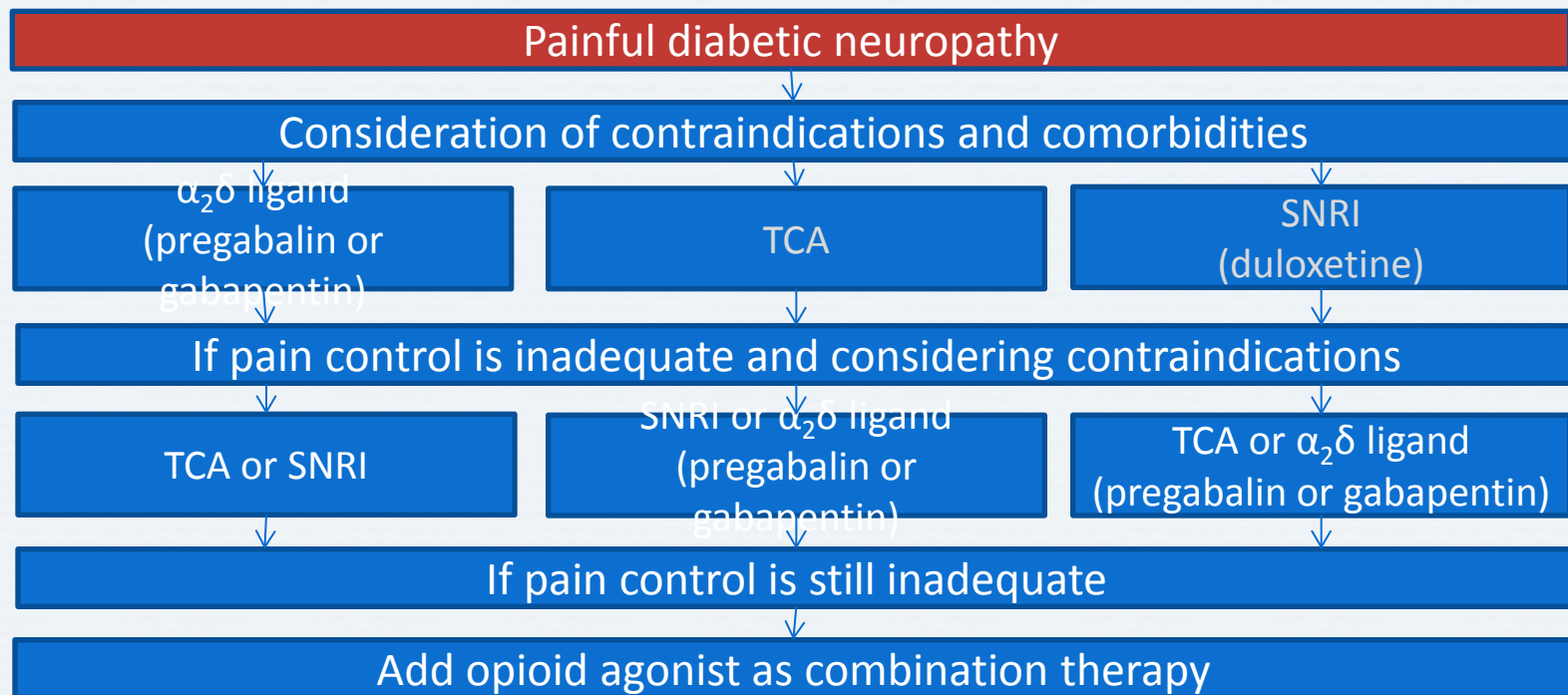
Prescribers should also be aware of contraindications and cautions when using certain agents in certain patients (e.g., elderly).

*Tramadol may be considered first-line in patients with acute exacerbations of pain, especially for the tramadol/acetaminophen combination.

DPN = diabetic peripheral neuropathy; EFNS = European Federation of Neurological Societies; ER = extended release; MS = multiple sclerosis; SCI = spinal cord injury; SNRI = serotonin-norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant

Adapted from: Attal N *et al.* *Eur J Neurol* 2010; 17(9):1113-e88.

Treatment Algorithm for Painful Diabetic Peripheral Neuropathy



Drug Selection According To Clinical Presentation of Neuropathic Pain

Medications		Clinical presentation of neuropathic pain				
		Burning	Lancinating	Hyperalgesia	Allodynia	Paresthesia, dysesthesia
TCA	Amitriptyline	++	+/-	++	++	+
SNRI	Venlafaxine	+	+/-	+	+	+/-
	Duloxetine	++	+/-	++	+	+/-
Na ⁺ channel blockers:	Carbamazepine	+/-	++	+	+	+
	Oxcarbazepine	+/-	++	+	+	+
Ca ²⁺ channel $\alpha_2\delta$ ligands:	Gabapentin	++	+/-	++	++	+
	Pregabalin	++	+/-	++	++	+
Opioids:	Tramadol	+	+/-	+	+	+
	Morphine	+/-	+/-	+/-	+/-	+/-

SNRI = serotonin norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant

Thai Association for the Study of Pain. *Clinical Practice Guidelines for Neuropathic Pain*.

Available at: http://www.pain-tasp.com/download/cpg/CPG_Web5OK.pdf. Accessed: October 10, 2013.

Drug Selection According to Conditions Causing Neuropathic Pain

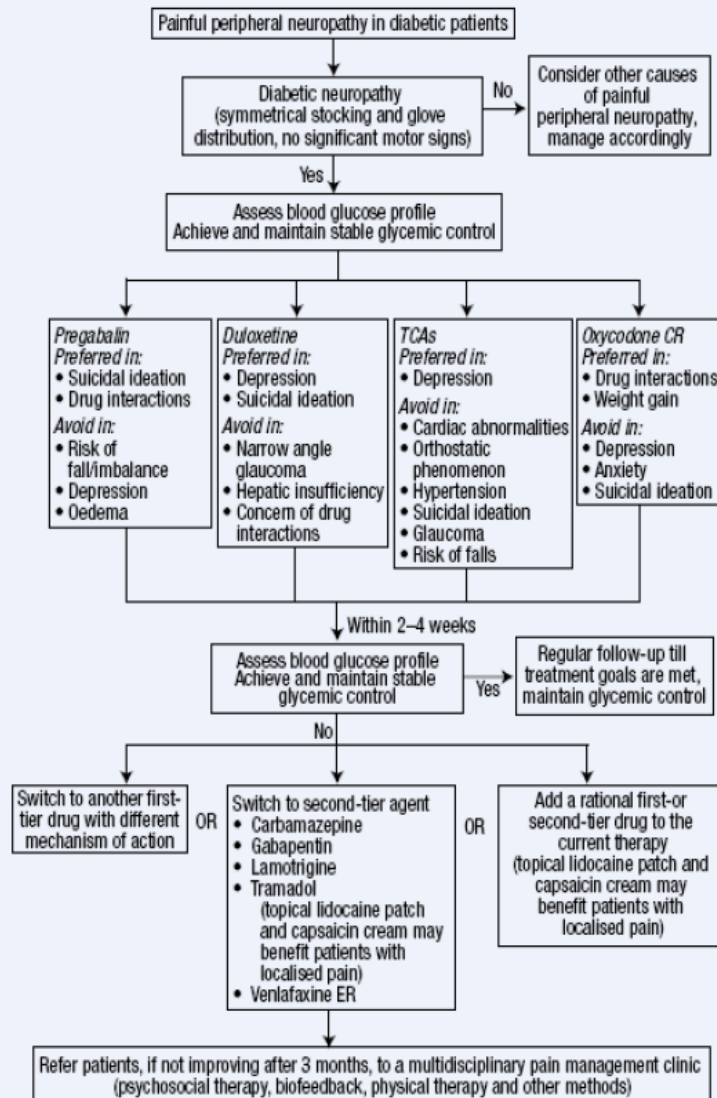
Drug class and drug(s)	Type of neuropathic pain				
	Diabetic peripheral neuropathy	Postherpetic neuralgia	Trigeminal neuralgia	Phantom limb pain	Central pain
TCA Amitriptyline	++	++	+/-	+	++
SNRI Venlafaxine Duloxetine	+ ++	+ +	- -	- -	+/- +/-
Na⁺ channel blocker Carbamazepine Oxcarbazepine	+/- +/-	+/- +/-	++ ++	+ +	+ +
Ca²⁺ channel $\alpha_2\delta$ ligand Gabapentin Pregabalin	++ ++	++ ++	+/- +/-	+ +	+ +
Opioid Tramadol Morphine	+ +/-	+ +/-	- -	+/- +/-	+/- +/-

SNRI = serotonin norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant

Thai Association for the Study of Pain. *Clinical Practice Guidelines for Neuropathic Pain*.

Available at: http://www.pain-tasp.com/download/cpg/CPG_Web5OK.pdf. Accessed: October 10, 2013.

Singapore Pain Management Guidelines for Painful Diabetic Peripheral Neuropathy



ER = extended release;

TCA = tricyclic antidepressant

Yeo A et al. Pain Management Guidelines for General Practitioners 2007.

Pfizer Pte Ltd; Singapore: 2007.

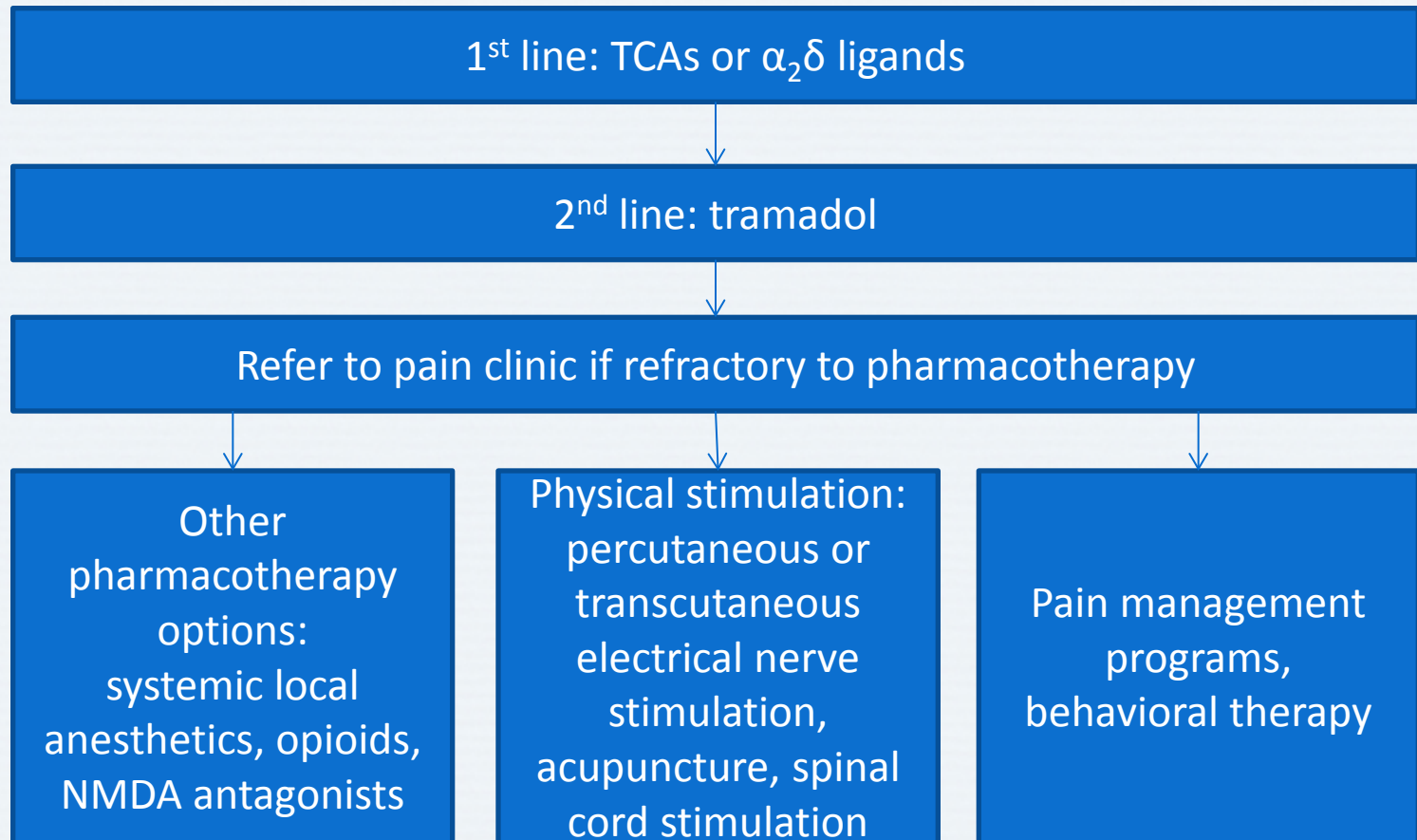
Painful Diabetic Neuropathy Treatment Recommendations: Philippines

<i>Agent type</i>	<i>Reason for recommendation</i>	<i>Agents</i>
First tier	≥2 randomized controlled trials on painful diabetic neuropathy, functional outcomes	Pregabalin, gabapentin, duloxetine
Second tier	1 randomized controlled trial on painful diabetic neuropathy; ≥1 randomized controlled trials on other painful neuropathies	Venlafaxine XR, oxycodone CR, tramadol, amitriptyline
Topical	Mechanism of action	Lidocaine
Other	Insufficient evidence for any recommendation	Alpha-lipoic acid, vitamin B complex, SSRIs, capsaicin

CR = controlled release; SSRI = selective serotonin reuptake inhibitor; XR = extended release

Rosales RL et al. In: *Compendium of Philippine Medicine 2009*. PPD Healthcare Publishing; Manila, Philippines: 2009.

Hong Kong Multidisciplinary Panel on Neuropathic Pain: Treatment Recommendations for Painful Diabetic Peripheral Neuropathy



NMDA = N-methyl-D-aspartate; TCA = tricyclic antidepressants

The Multidisciplinary Panel on Neuropathic Pain. *Handbook of Neuropathic Pain Management Guidelines*. UBM Medica; Hong Kong: 2009.

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

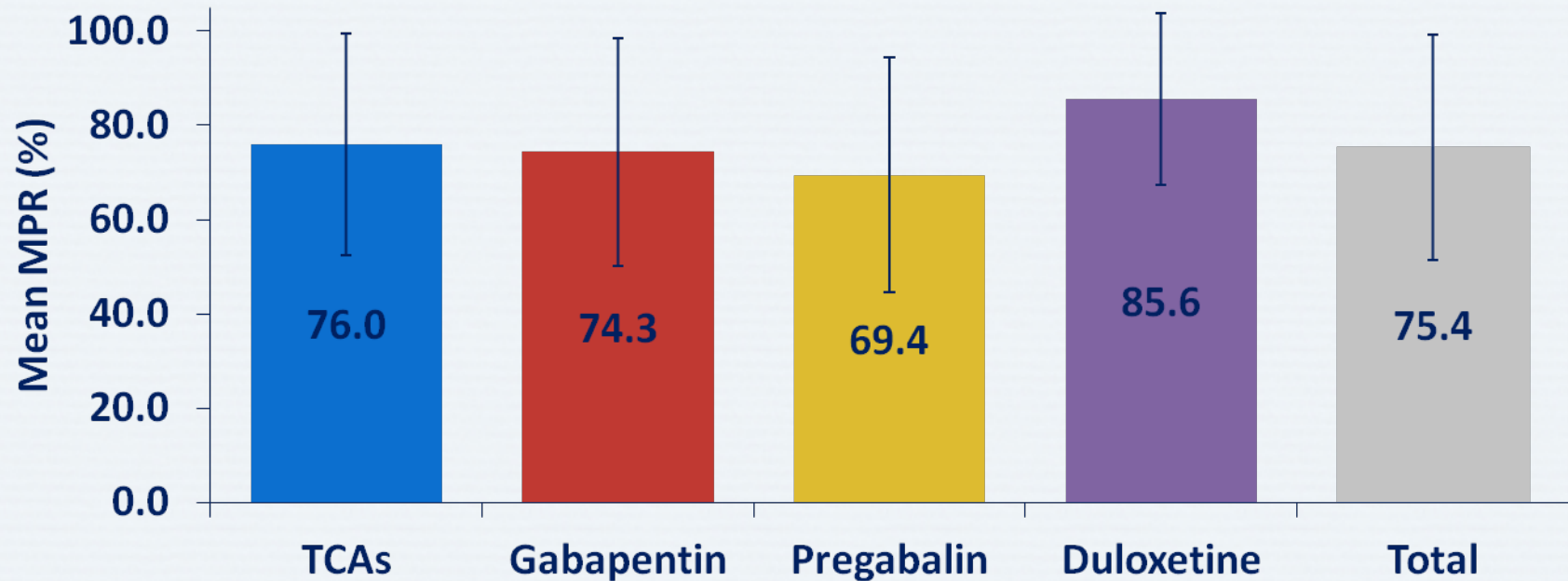


- Patients with mixed pain may benefit from combination therapy

Adherence



Adherence to Neuropathic Pain Medications in Suboptimal Patients with Painful Diabetic Peripheral Neuropathy



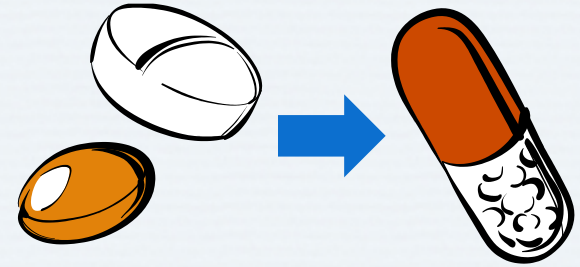
Non-adherence to neuropathic pain medication (i.e., MPR <80%) was significantly associated with non-adherence to oral antihyperglycemic therapies.

Strategies to Improve Adherence

- **S**implify regimen
- **I**mpart knowledge
- **M**odify patient beliefs and human behavior
- **P**rovide communication and trust
- **L**eave the bias
- **E**valuate adherence

Simplifying Medication Regimen

- If possible, adjust regimen to minimize:
 - Number of pills taken
 - Number of doses per day
 - Special requirements (e.g, bedtime dosing, avoiding taking medication with food, etc.)



- Recommend all medications be taken at the same time of day (if possible)
- Link taking medication to daily activities, such as brushing teeth or eating
- Encourage use of adherence aids such as medication organizers and alarms

Imparting Knowledge

- Provide clear, concise instructions (written and verbal) for each prescription
- Be sure to provide information at a level the patient can understand
- Involve family members if possible
- Provide handouts and/or reliable websites for patients to access information on their condition
- Provide concrete advice on how to cope with medication costs

Modifying Patient Beliefs and Behaviors: Motivational Interviewing Technique

Techniques

- Express empathy
- Develop discrepancy
- Roll with resistance
- Support self efficacy

Examples

- “It’s normal to worry about medication side effects”
- “You obviously care about your health; how do you think not taking your pills is affecting it?”
- “I understand that you have a lot of other things besides taking pills to worry about”
- “It sounds like you have made impressive efforts to work your new medication into your daily routine”

Providing Communication and Trust: Communication Tips

- Be an active listener
 - Focus on the patient
 - Nod and smile to show you understand
- Make eye contact



- Be aware of your own body language
 - Face the patient
 - Keep arms uncrossed
 - Remove hands from pockets
- Recognize and interpret non-verbal cues

Leaving the Bias



Evaluating Adherence: 4-Step Strategy for Detecting Non-adherence

1

Ask an open-ended question about taking medicine



2

Normalize and universalize non-adherence to reverse the judgmental environment



3

Make the role of accurate information about adherence in medical decision-making explicit



4

Don't ask about "forgetting" or "missed" doses until the first 3 steps have set the stage

Summary

A decorative blue watercolor splash is located in the bottom right corner of the slide, blending into the light blue background.

Management: Summary

- Realistic treatment goals should be set in conjunction with the patient
- Most treatment guidelines consider TCAs and $\alpha_2\delta$ ligands as first-line therapy for most types of neuropathic pain
 - Topical lidocaine should also be considered for focal neuropathy
 - Guideline recommendations differ regarding use of SNRIs, opioids and tramadol in various types of neuropathic pain
- Non-pharmacologic treatments should be considered as complementary treatment to pharmacological therapy whenever appropriate
 - Transcutaneous electrical nerve stimulation is the only non-pharmacologic treatment modality recommended by the majority of guidelines

TCA = tricyclic antidepressant; SNRI = serotonin norepinephrine reuptake inhibitor

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