

PAIN AND YOUR BRAIN

Mental Health & Peripheral Neuropathy

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Disclosures

- I have no financial disclosures or conflicts of interest with the material in this presentation
- My opinions are my own and do not reflect the interests of the Army, DOD, or US Govt.

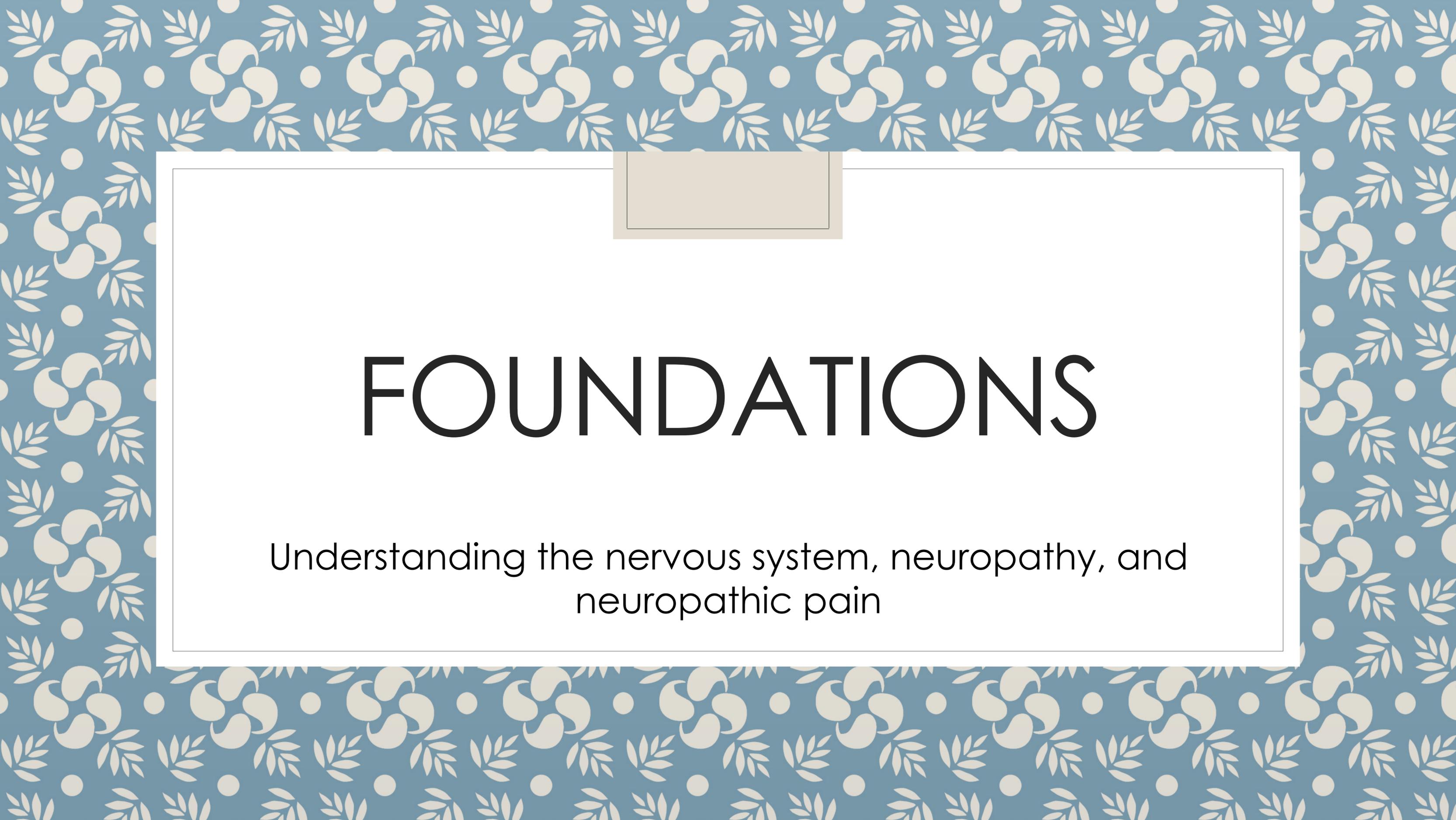
Objectives

By the end of this presentation, learners will be able to:

1. Develop a basic understanding of the ascending & descending pathways of the somatosensory nervous system
2. Appreciate basic mechanisms involved in the chronification of pain including central and peripheral sensitization
3. Recognize the relationships between physical and psychiatric symptoms in chronic illness
4. Apply the biopsychosocial model in the treatment of peripheral neuropathy
5. Practice self-management of peripheral neuropathy symptoms

Outline

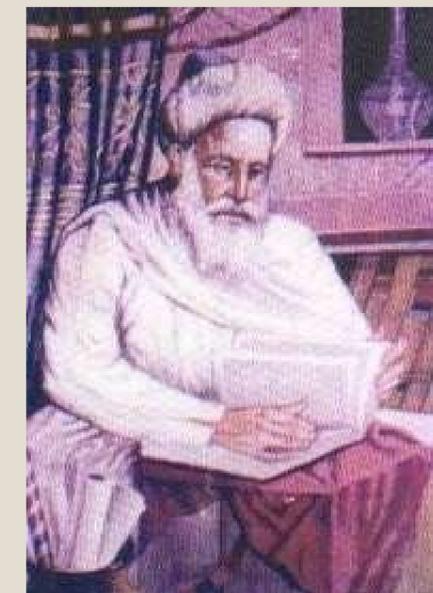
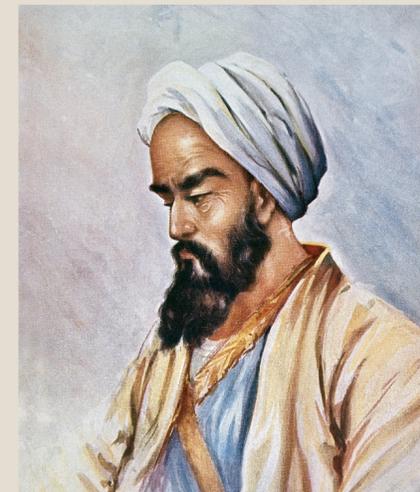
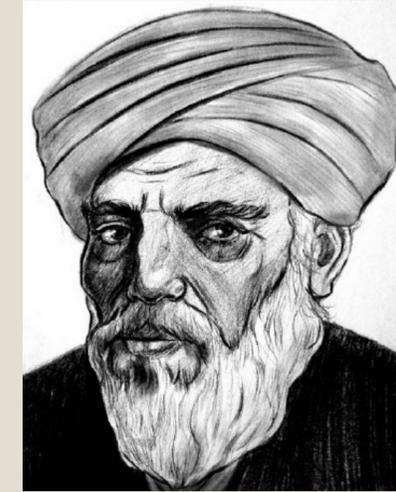
- History, definitions and core concepts
 - Organization of nervous system
 - Classification and pathophysiology of neuropathies
 - Ascending & descending somatosensory pathways
- Central & Peripheral Sensitization, Gate control theory
- Psychiatric comorbidities and effect on treatment outcomes
- Treatment & self-management



FOUNDATIONS

Understanding the nervous system, neuropathy, and
neuropathic pain

History of Neuropathy

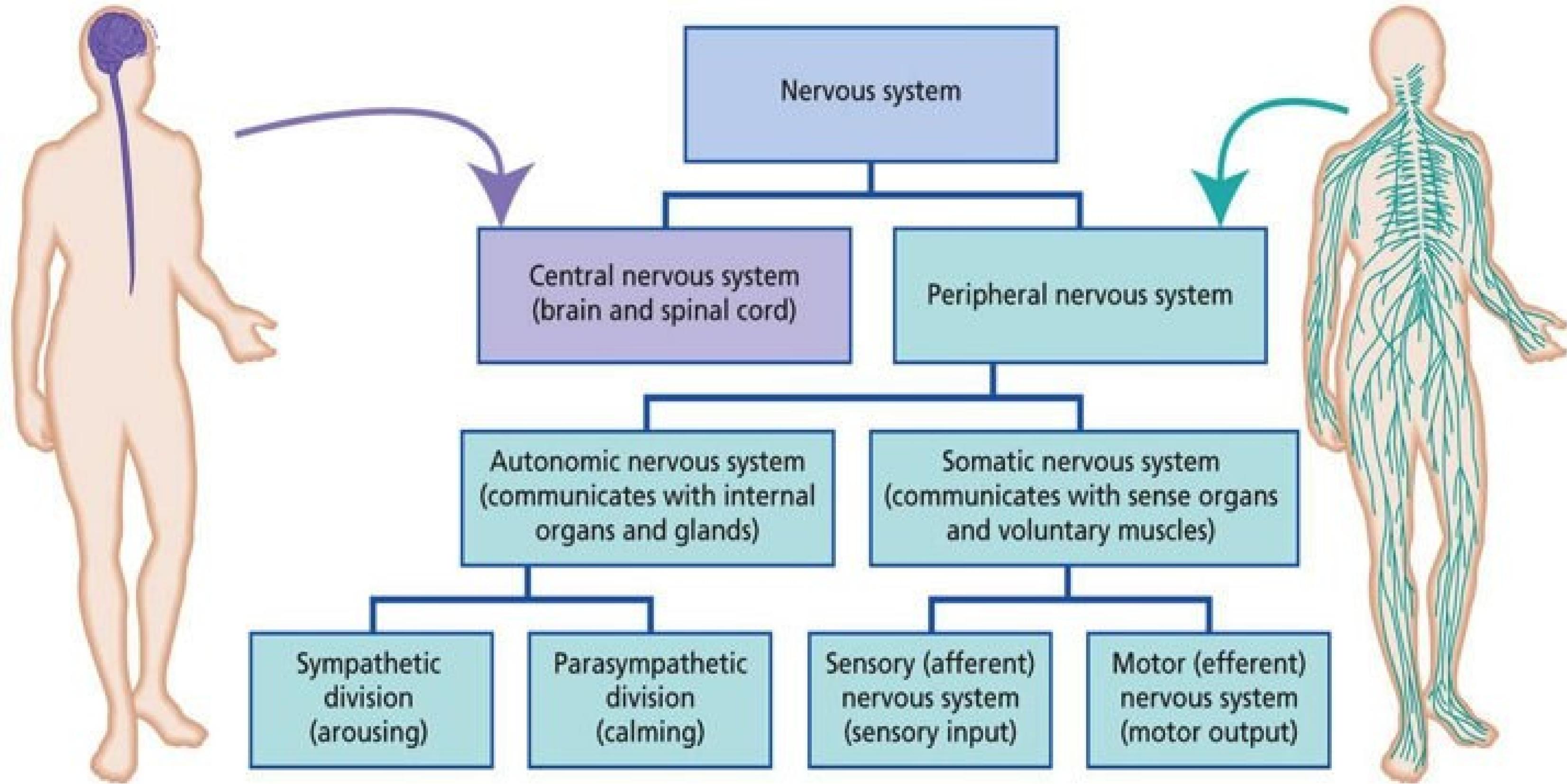


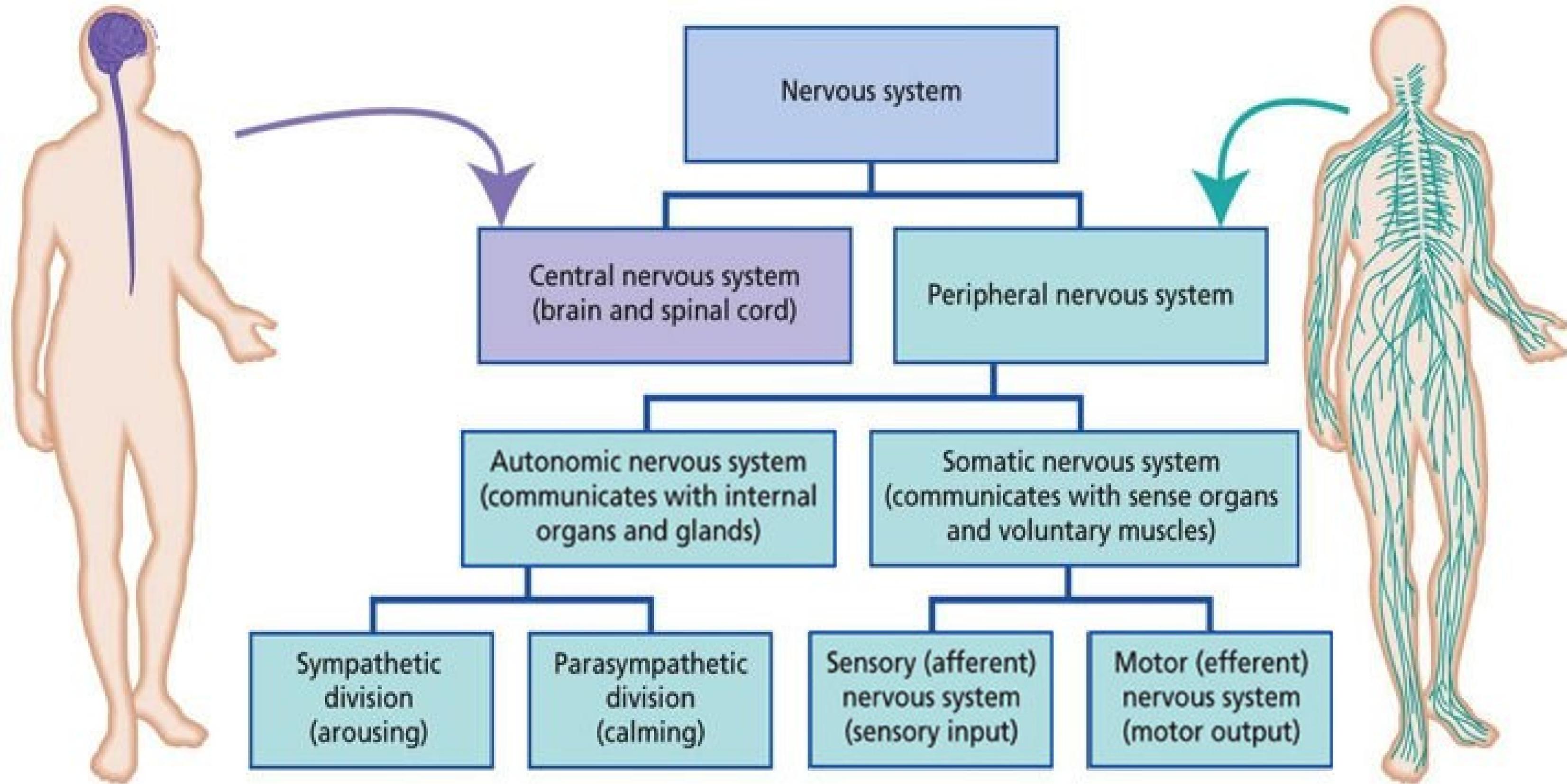
- First conceptualized by Persian physicians during Islamic Golden Age
 - "Vaja al asab"
 - Numbness, tingling, needle-like; connections with stroke
 - Nerve injuries viewed as more painful than others
- Further built upon in 18th & 19th centuries
 - *Injuries of Nerves & Their Consequences* (1872)
 - Neuralgia, "causalgia" aka CRPS
- Term "neuropathy" coined in 1924 (Gr *neuro* + *pathy* = nerve suffering)
- "Modern age" of neuropathy beginning with gabapentin RCTs in 1998
- Affects ~30 million Americans (~10%)

Definitions



- Neuropathy = a disturbance of function or pathological change in a nerve/nerves
 - One nerve → *mononeuropathy*
 - Several nerves → *mononeuropathy multiplex*
 - Diffuse & bilateral → *polyneuropathy*





Autonomic nervous system
(communicates with internal
organs and glands)

Autonomic

- Variable
- Heart rate, blood pressure, digestion, sweating, sexual fxn

Sensory (afferent)
nervous system
(sensory input)

Sensory

- Variable
- Vibration, touch, proprioception; temperature & **pain**

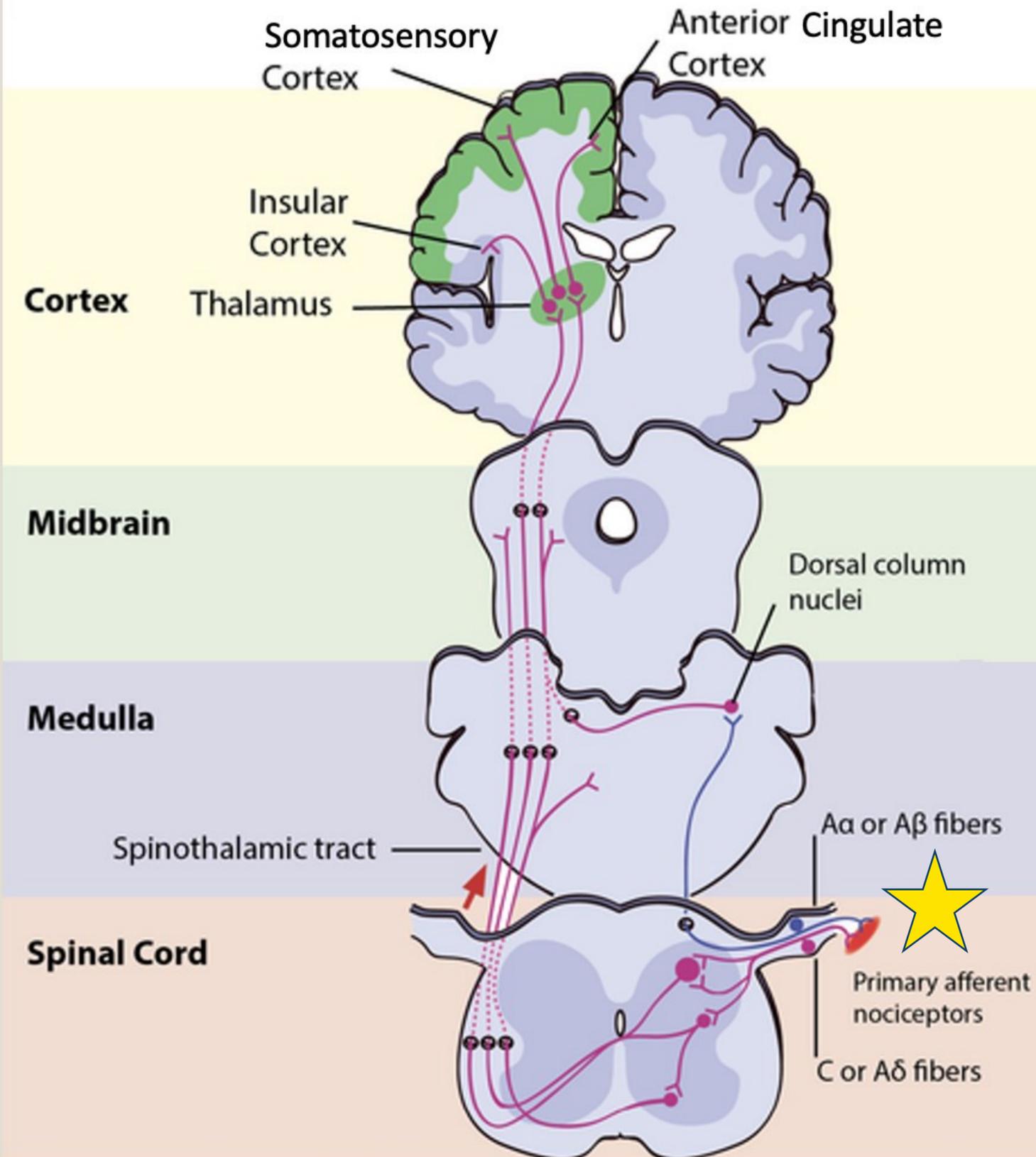
Motor (efferent)
nervous system
(motor output)

Motor

- Muscle weakness

Physical Symptoms of Neuropathy

Pain processing



Ascending SS Pathway

- A δ + C fibers \rightarrow spinothalamic tract
 - Pain & temperature
 - SLOOOOW
- A α + A β fibers \rightarrow dorsal column
 - Touch, vibration, proprioception
 - FAST!
- Gate control theory*
- Conscious awareness: memory & learning, behavior modification

Somatosensory Pathway

Sensory / Discriminative

- *Where does it hurt?*
- Lateral thalamus
- Somatosensory cortex

Affective / Motivational

- *How much does it hurt?*
- Medial thalamus
- Anterior cingulate cortex, insular cortex, prefrontal cortex, amygdala

Descending Pathways

- Serotonin and norepinephrine released from midbrain



- Decreased attention

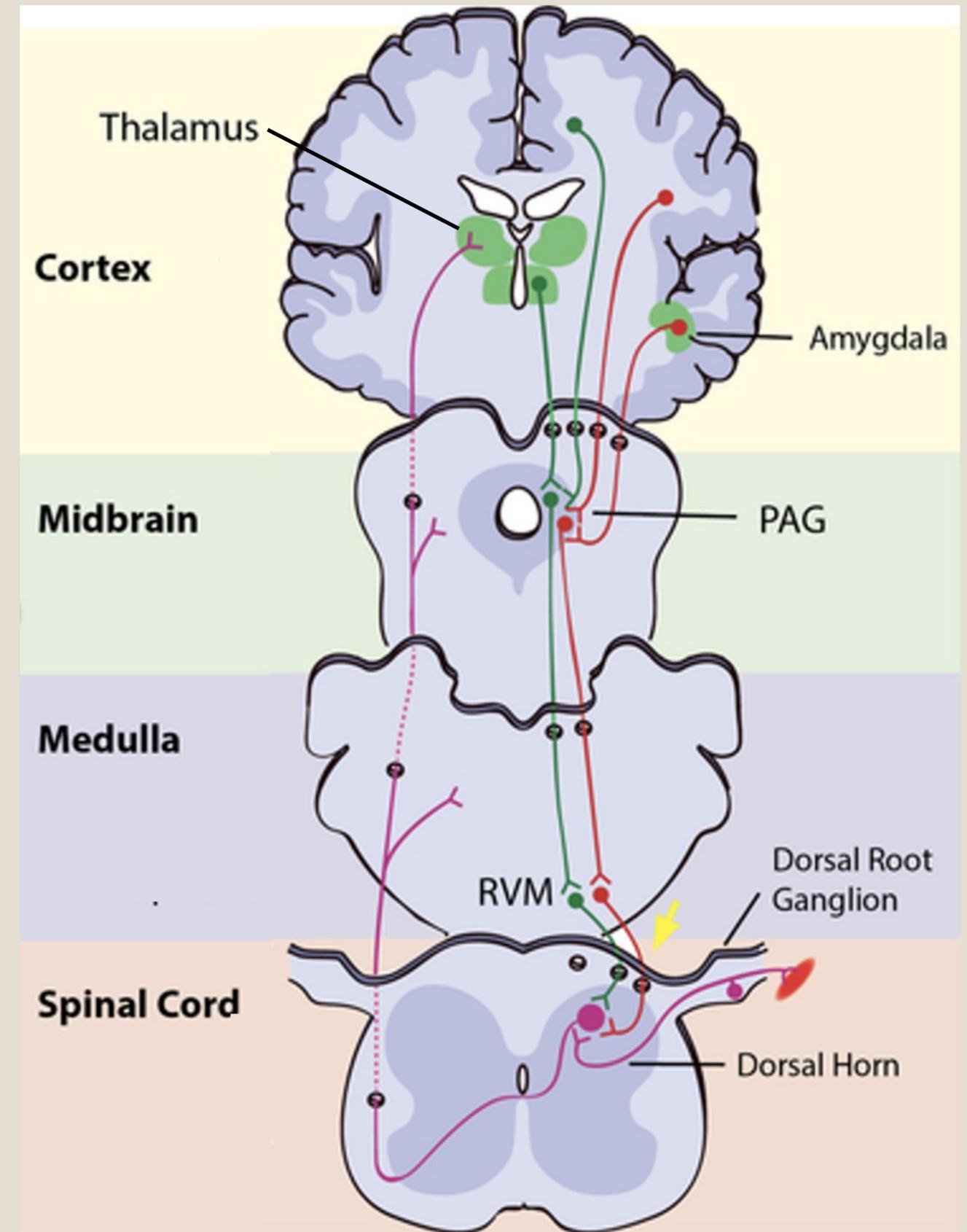


- Positive emotional state

- Release of endogenous opioids within spinal cord



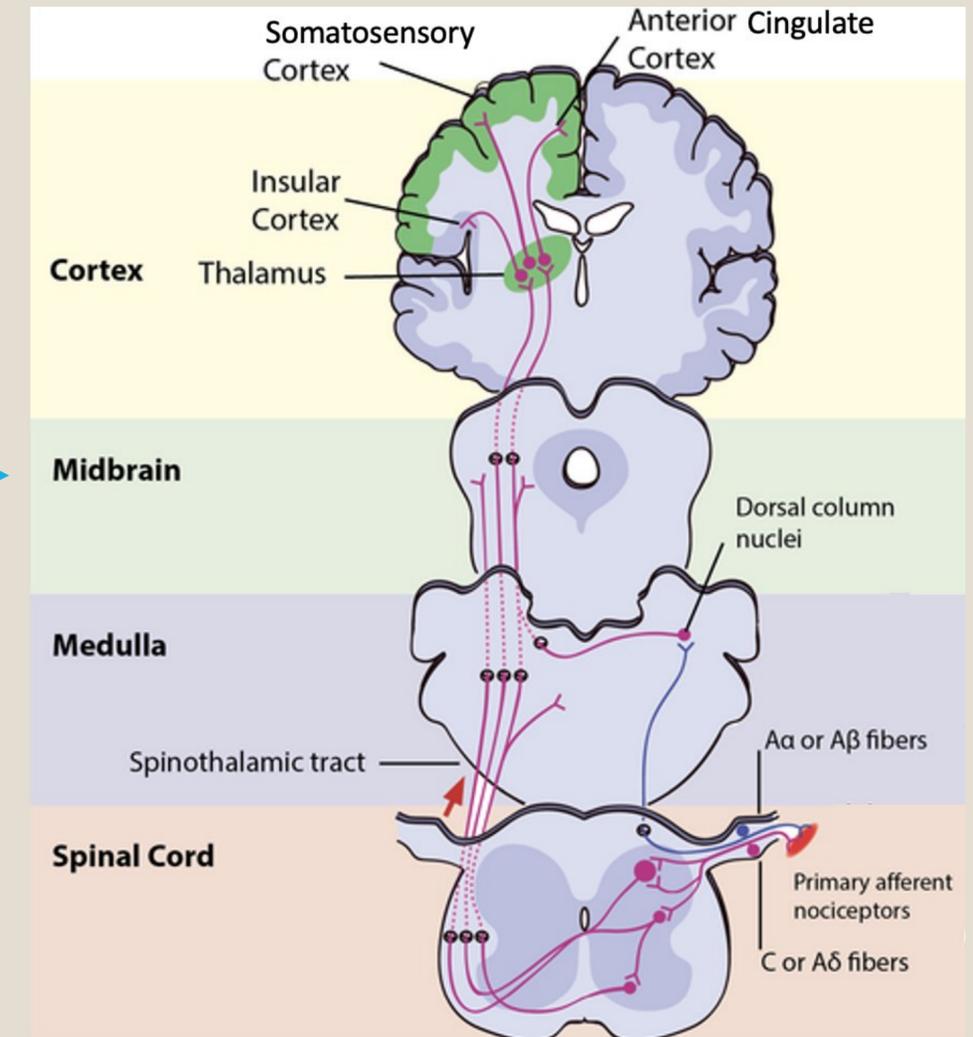
Decreased pain



More Definitions



- Pain = an unpleasant **sensory** and **emotional** experience associated with, or resembling that associated with, actual or potential tissue damage
- Neuropathic Pain = pain caused by a lesion or disease of the somatosensory nervous system →
 - Central neuropathic pain (if in CNS)
 - Peripheral neuropathic pain (if in PNS)



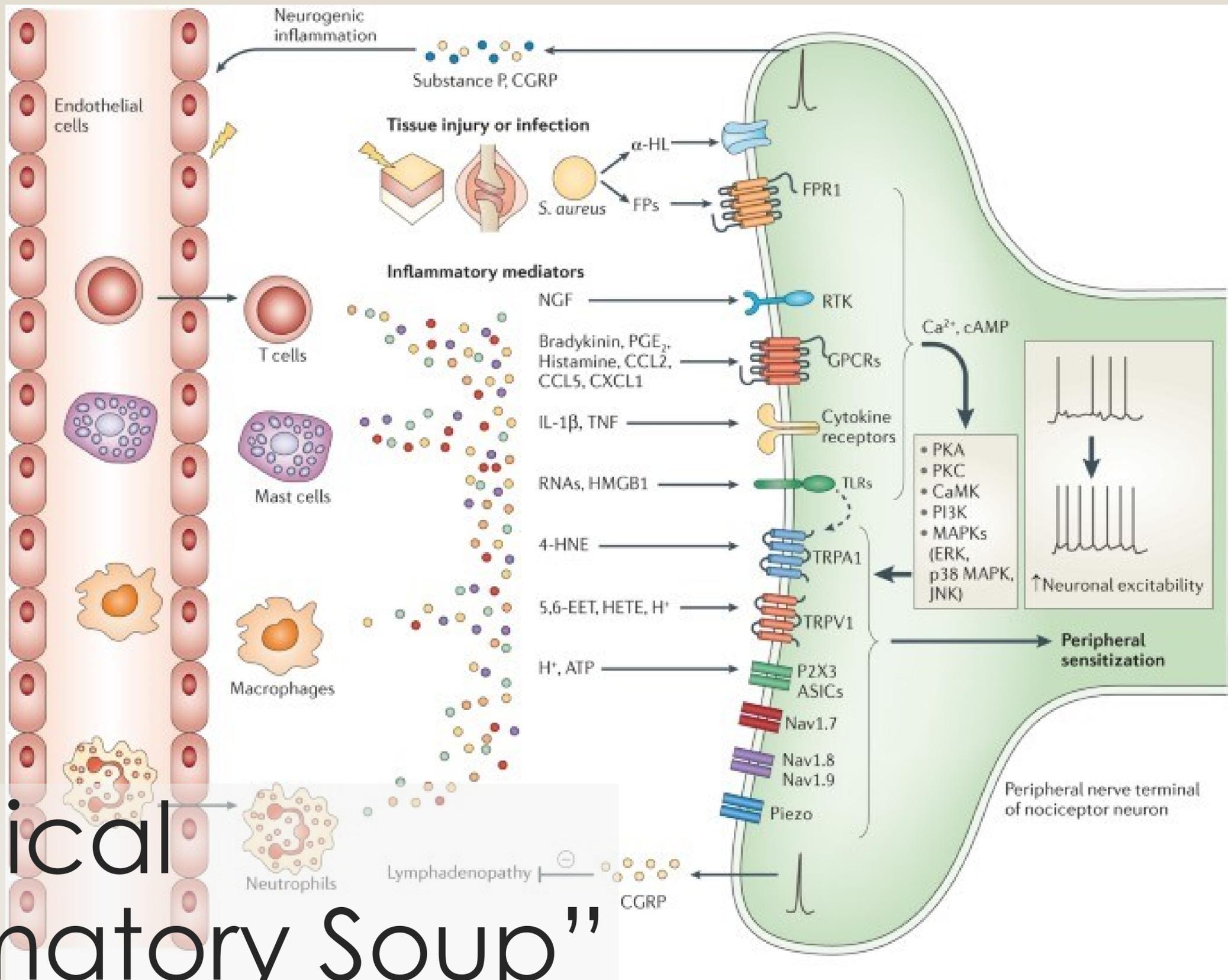
Causes of Peripheral Neuropathy

Inherited

- Charcot-Marie-Tooth & subtypes
- Many others involving various genetic mutations

Acquired

- **Injury/trauma**
- **Diabetes mellitus**
- Nerve-specific autoimmune (GBS, CIDP)
- Other autoimmune (SLE, RA, Sjogren's)
- Decreased blood supply (vascular disease)
- Drugs – HIV, chemotherapy
- Toxins e.g. agent orange, alcohol abuse
- Vitamin deficiency
- Infections (e.g. shingles, leprosy, lyme)

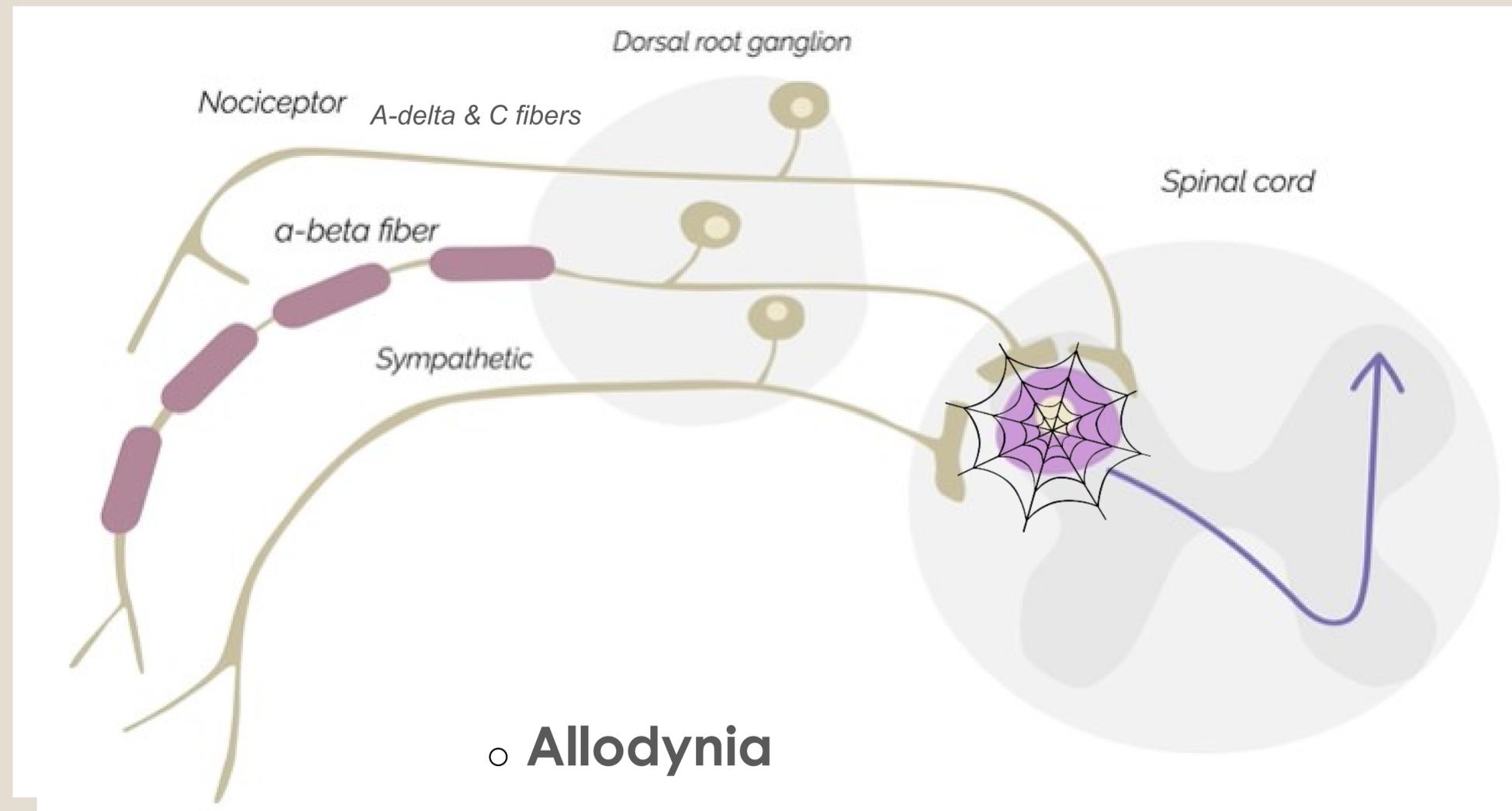


“Chemical Inflammatory Soup”

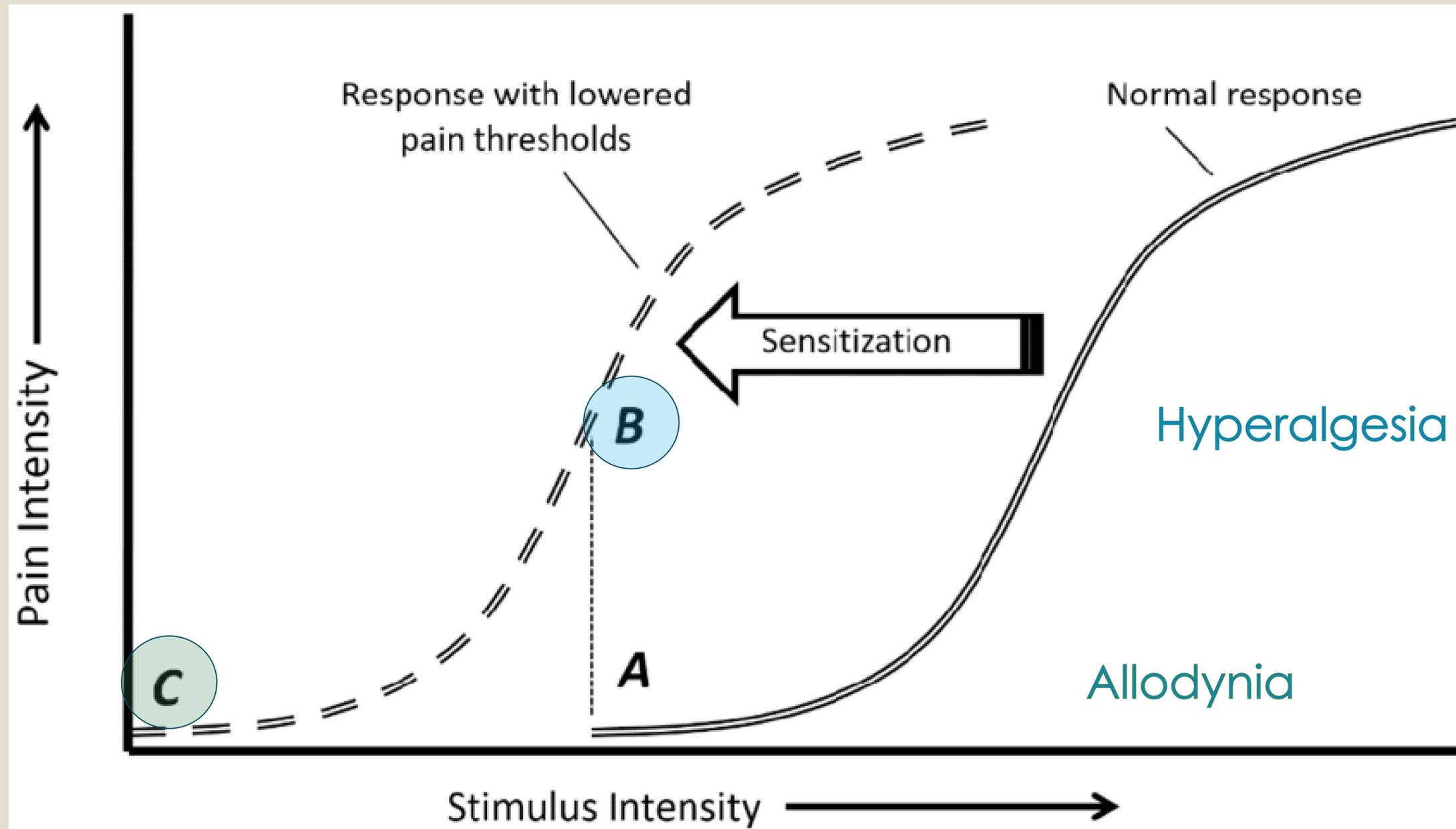
Central Sensitization



Central Sensitization



Central & Peripheral Sensitization



Central Sensitization

Noxious stimulus → signal → brain → PAIN!



- Chronic stress
 - Increased sympathetic nervous system activation
 - Increased activation of HPA axis (stress & cortisol)
- Can occur in many organ systems

Central Sensitization Inventory

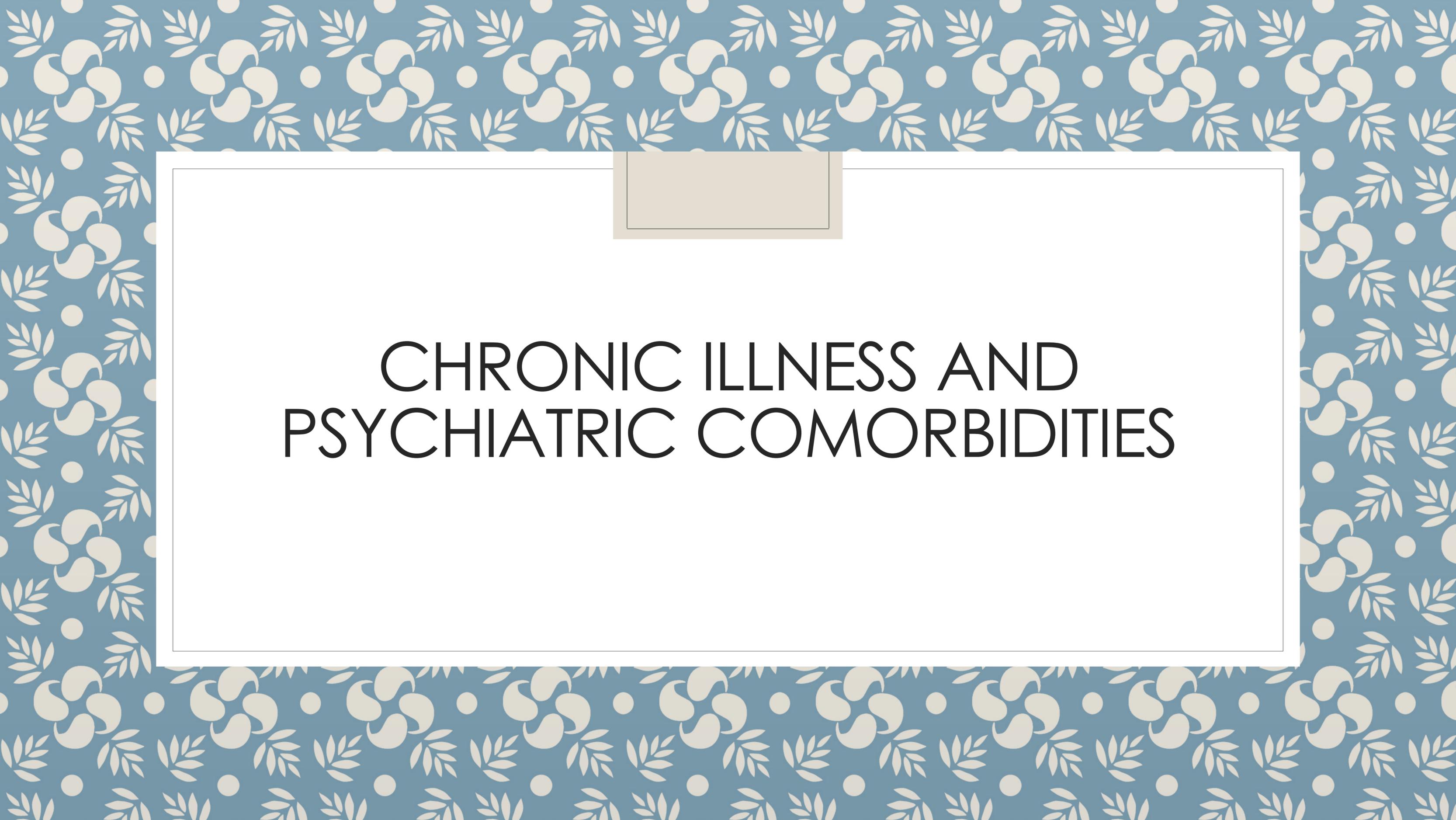
- Restless leg syndrome
- Chronic fatigue syndrome
- Fibromyalgia
- Temporomandibular disorder
- Migraine
- Irritable bowel syndrome
- Multiple chemical sensitivities
- Neck injury (including whiplash)
- Anxiety or panic attacks
- Depression

1. I feel tired and unrefreshed when I wake from sleeping.	14. I have skin problems such as dryness, itchiness, or rashes.
2. My muscles feel stiff and achy.	15. Stress makes my physical symptoms get worse.
3. I have anxiety attacks.	16. I feel sad or depressed.
4. I grind or clench my teeth.	17. I have low energy.
5. I have problems with diarrhea and/or constipation.	18. I have muscle tension in my neck and shoulders.
6. I need help in performing my daily activities.	19. I have pain in my jaw.
7. I am sensitive to bright lights.	20. Certain smells, such as perfumes, make me feel dizzy and nauseated.
8. I get tired very easily when I am physically active.	21. I have to urinate frequently.
9. I feel pain all over my body.	22. My legs feel uncomfortable and restless when I am trying to go to sleep at night.
10. I have headaches.	23. I have difficulty remembering things.
11. I feel discomfort in my bladder and/or burning when I urinate.	24. I suffered trauma as a child.
12. I do not sleep well.	25. I have pain in my pelvic area.
13. I have difficulty concentrating.	

Never | Rarely | Sometimes | Often | Always

Mild: 30 to 39
Moderate: 40 to 49

Severe: 50 to 59
Extreme: 60 to 100



CHRONIC ILLNESS AND PSYCHIATRIC COMORBIDITIES

Psych comorbidities

- Anxiety
- Depression
- Sleep
- Catastrophizing

Bidirectional relationship

Chronic Pain

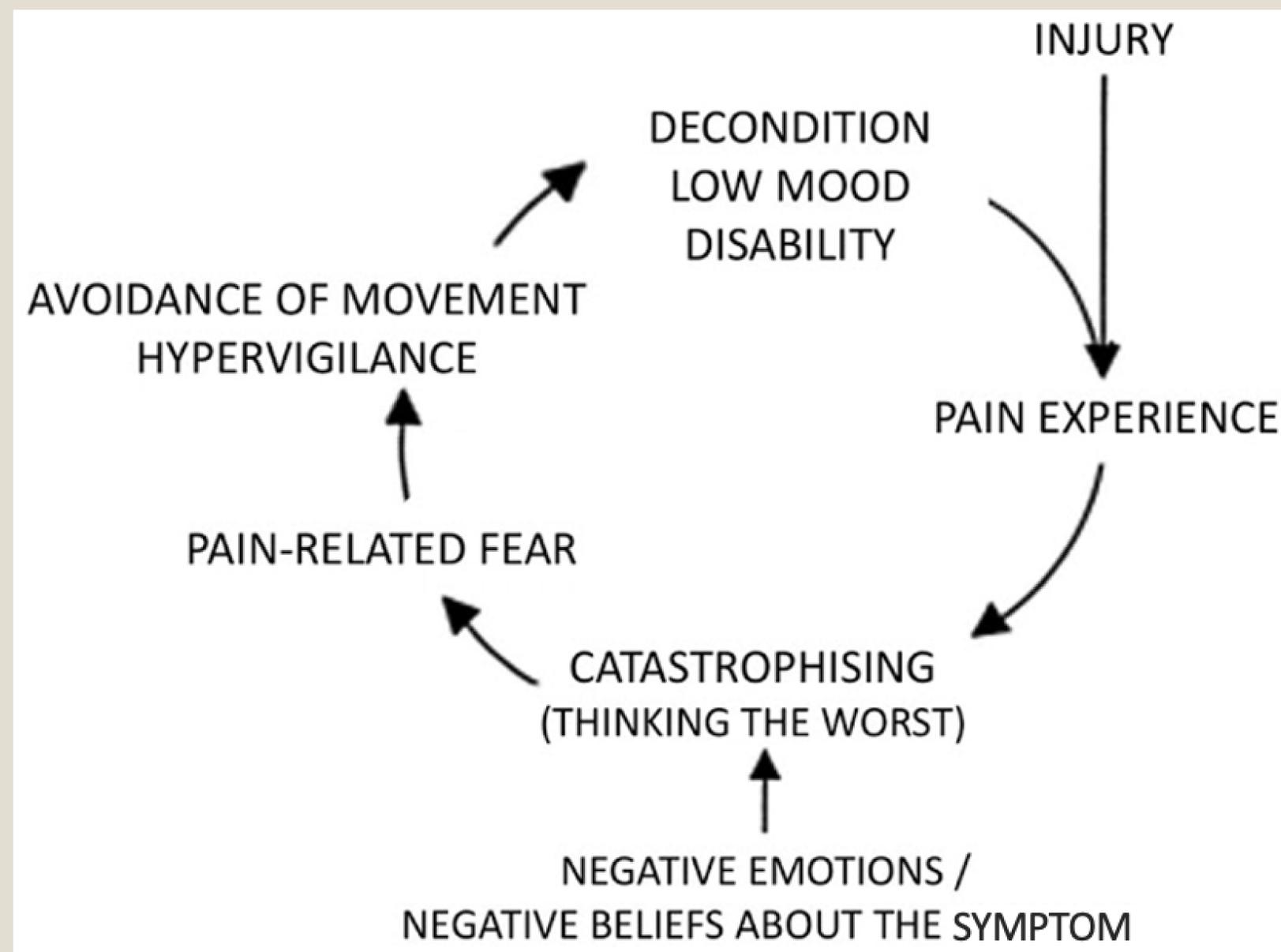
- Including PN

Emotional Aspects of Neuropathic Pain (2017)

- Compared to chronic pain w/o neuropathy, pts with neuropathic pain experience:
 - Worse health-related QOL
 - Greater psychological distress
 - Increased interference with sleep
 - Greater disability
- Affective disturbances are common
 - Depression, lack of joy, social withdrawal
 - Anxiety, stress → **fear & avoidance cycle**
 - Insomnia

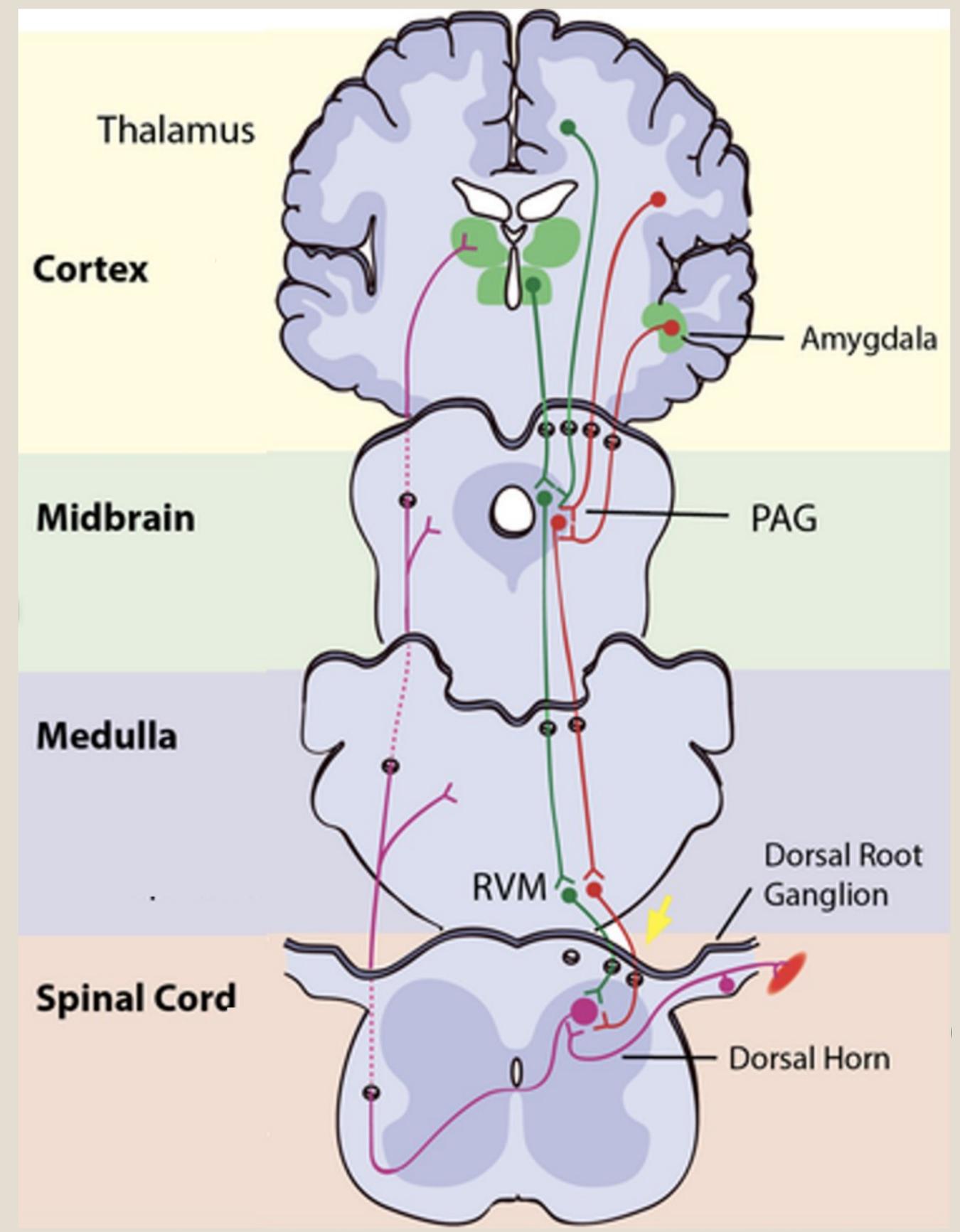
Fear-Avoidance Cycle

- Feed-forward loop
- Individuals with higher self-rated pain tend to experience **more** tension/anxiety



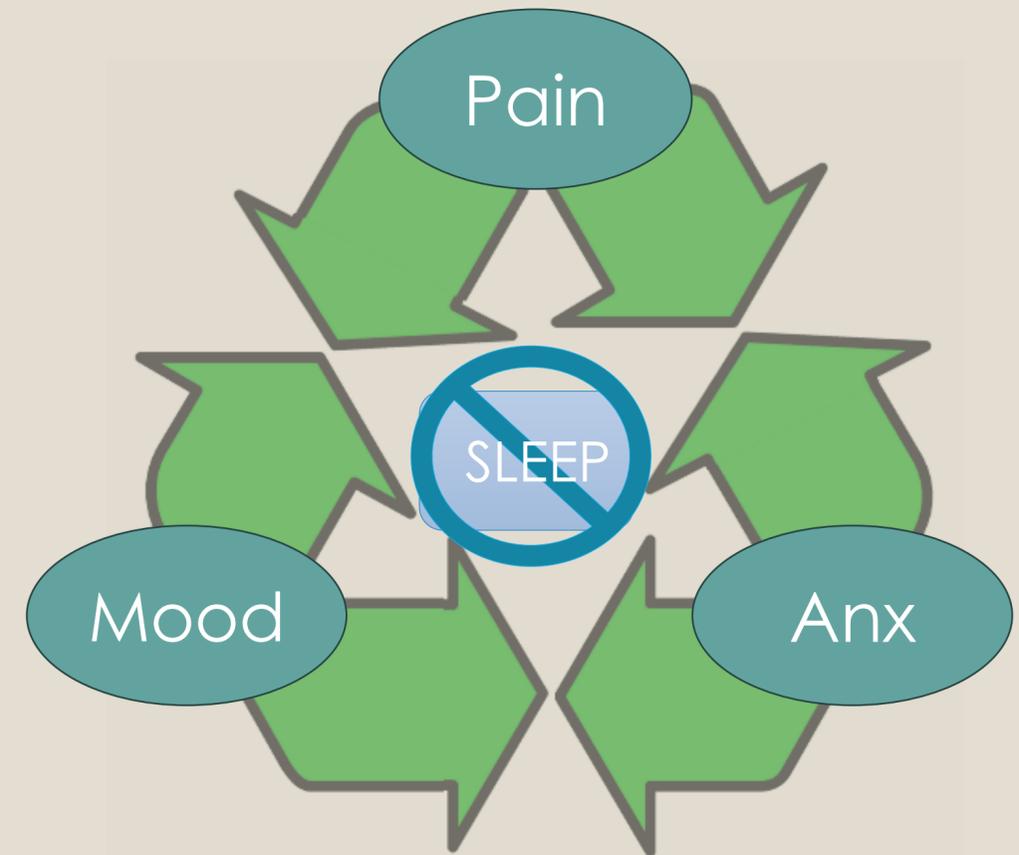
Emotional Aspects of Neuropathic Pain (2017)

- Depression is predictive of pain, even more so when pain is neuropathic
- Antidepressants (TCA & SNRI) able to help two-fold:
 1. Pain itself (via descending pain pathway)
 2. Mood disturbances exacerbating the pain



Emotional Aspects of Neuropathic Pain (2017)

- Insomnia – trouble falling & staying asleep
 - Sleep deprivation has bidirectional relationships with:
 - Pain threshold
 - Mood disturbances
 - Anxiety
- Simultaneous treatment of comorbidities is best



Bottom Line

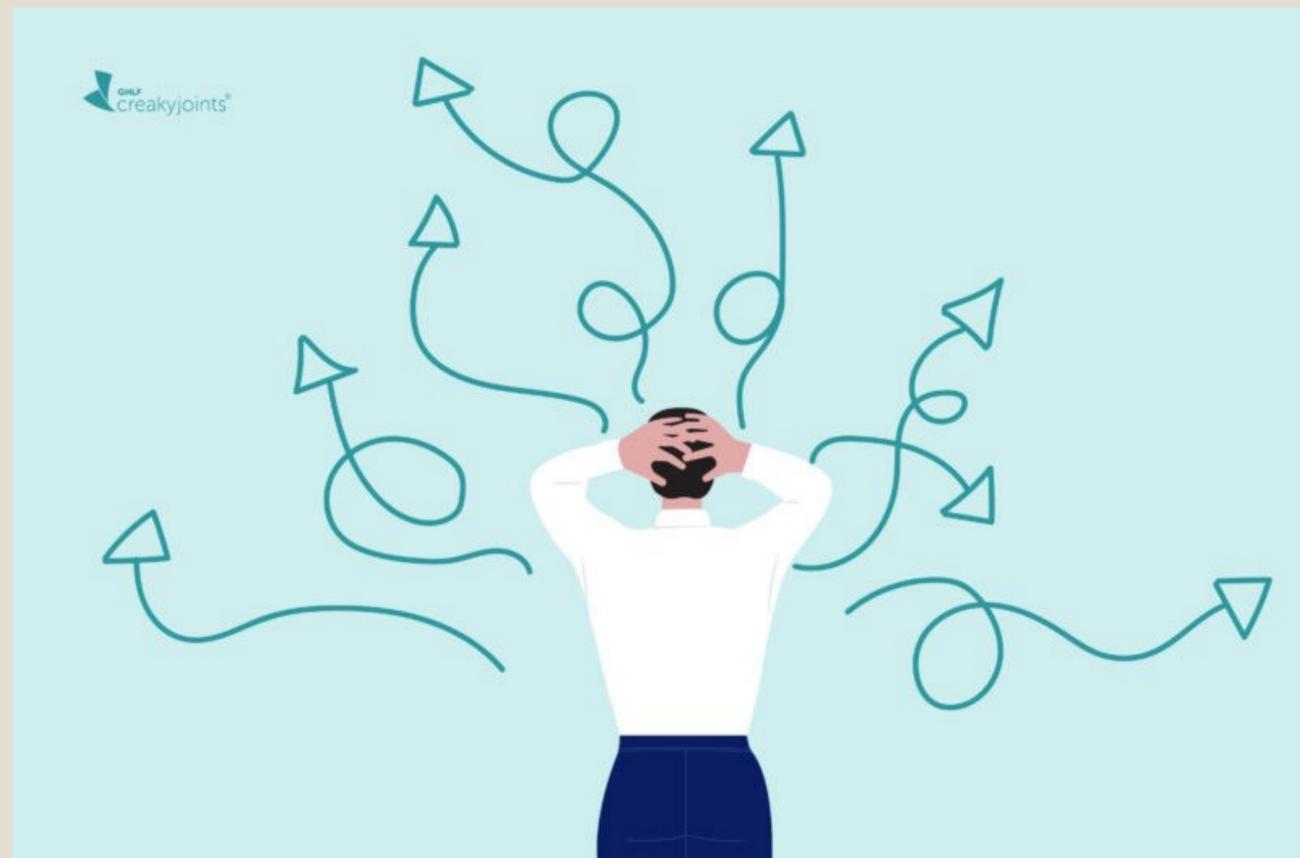
When psychological factors are not addressed:

Patients receive suboptimal care

AND

Have suboptimal treatment outcomes

Catastrophic Thinking

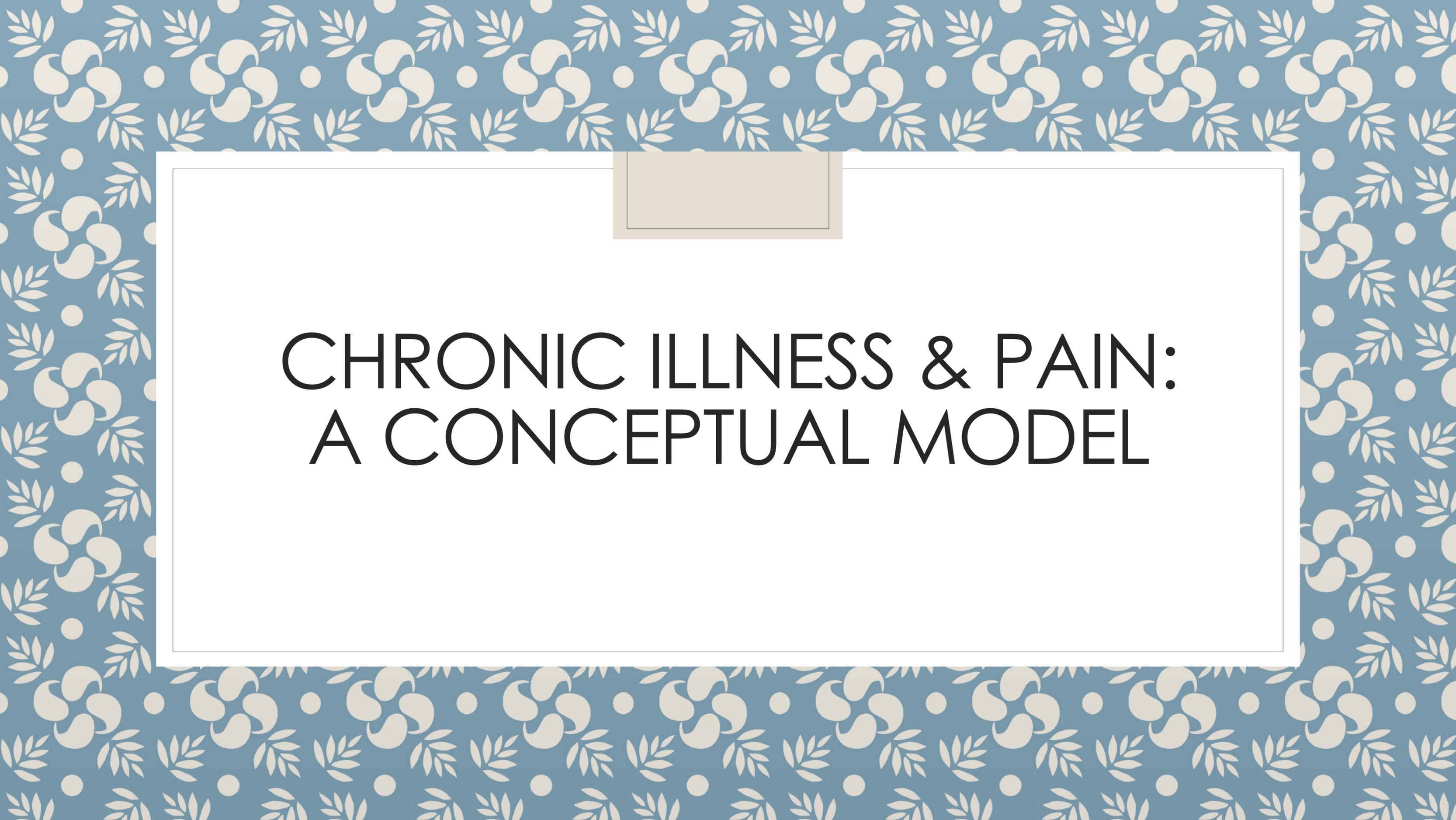


<https://creakyjoints.org/living-with-arthritis/mental-health/10-ways-to-curb-catastrophizing/>

- Imagining the worst possible outcome of an action or event
- An exaggerated negative mental state experienced during actual or *anticipated* pain
 - → panic
- Cognitive distortion ← modifiable!

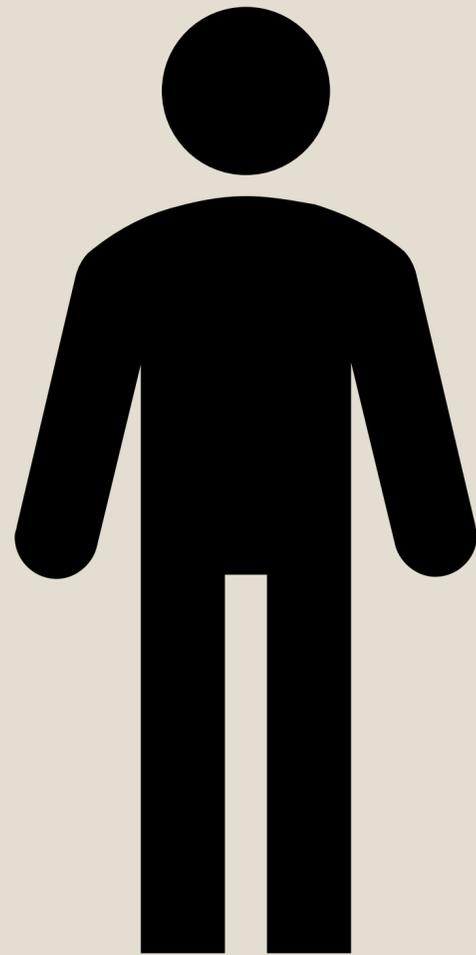
	Not at all	To a slight degree	To a moderate degree	To a great degree	All the time
I worry all the time about whether the pain will end	0	1	2	3	4
I feel I can't go on	0	1	2	3	4
It's terrible and I think it's never going to get any better	0	1	2	3	4
It's awful and I feel that it overwhelms me	0	1	2	3	4
I feel I can't stand it anymore	0	1	2	3	4
I become afraid that the pain will get worse	0	1	2	3	4
I keep thinking of other painful events	0	1	2	3	4
I anxiously want the pain to go away	0	1	2	3	4
I can't seem to keep it out of my mind	0	1	2	3	4
I keep thinking about how much it hurts	0	1	2	3	4
I keep thinking about how badly I want the pain to stop	0	1	2	3	4
There's nothing I can do to reduce the intensity of the pain	0	1	2	3	4
I wonder whether something serious may happen	0	1	2	3	4

- **Pain catastrophizing** is associated with:
 - Greater pain
 - Cortical changes that reinforce pain (and negative affective states)
 - Poor response to medical treatments



CHRONIC ILLNESS & PAIN: A CONCEPTUAL MODEL

Mind-Body ~~Dualism~~



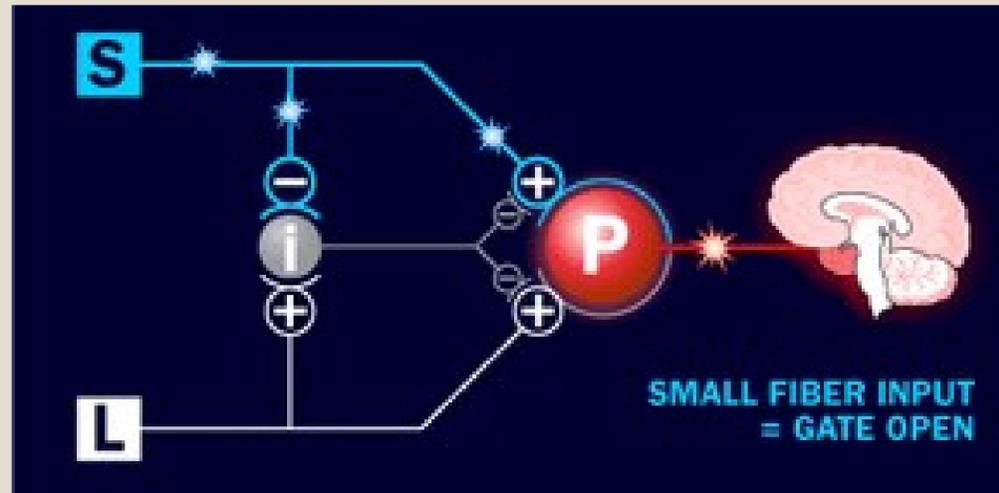
OR



- Reductionist biomedical model
 - That which could not be explained conveniently "psychiatric" in origin
- Gate control theory, neuromatrix theory, descending modulation of neuropathy sx demonstrated this is **not** true

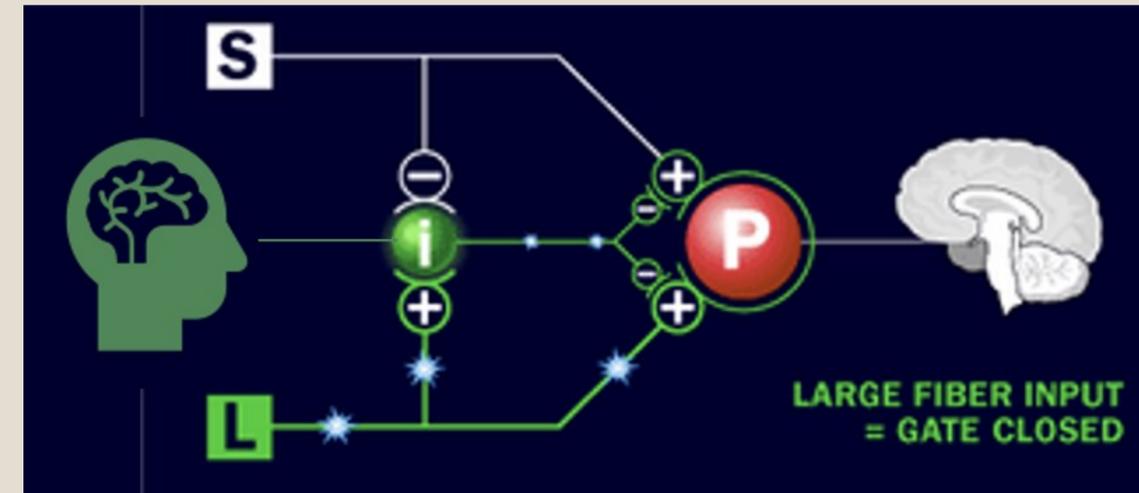
"Of course it is all happening inside your head... but why on earth should that mean that it is not real?"

-J.K. Rowling



Open the Gate – Increase Pain

1. Stress and Tension
 - Anxiety/worry, anger, depression
 - Bodily tension
2. Mental Factors
 - Attention
 - Boredom
3. Lack of Activity
 - Sedentary lifestyle

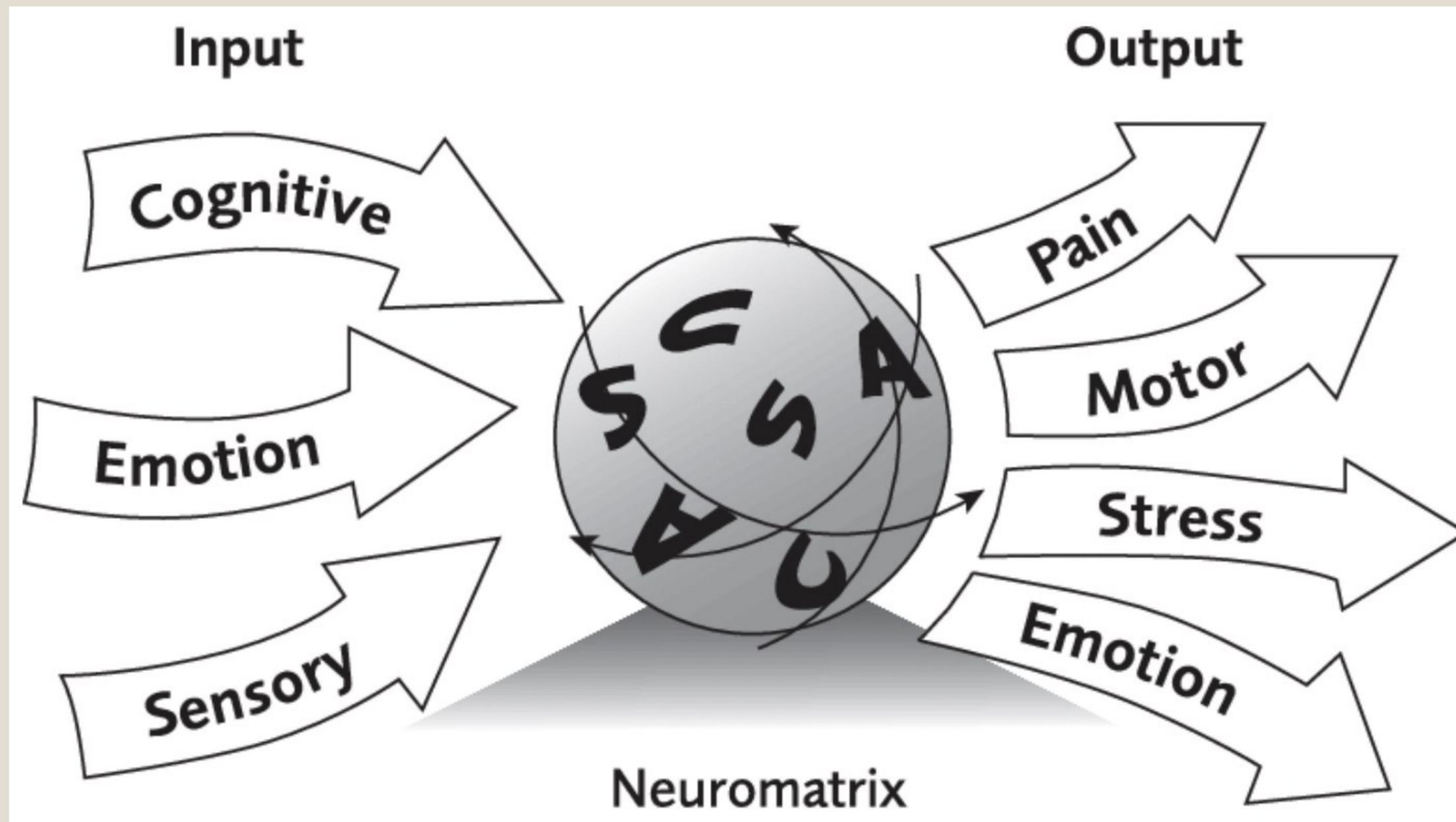


Close the Gate – Decrease Pain

1. Relaxation and Contentment
 - Happiness & optimism
 - Self-regulation to decrease stress
2. Mental Factors
 - Active participation in life
 - Distraction with other things
3. Activity – regular exercise
4. Other Physical Factors
 - Medications
 - Counter-stimulation (e.g. heat, massage, TENS, acupuncture).

Gate Control Theory

Neuromatrix Theory

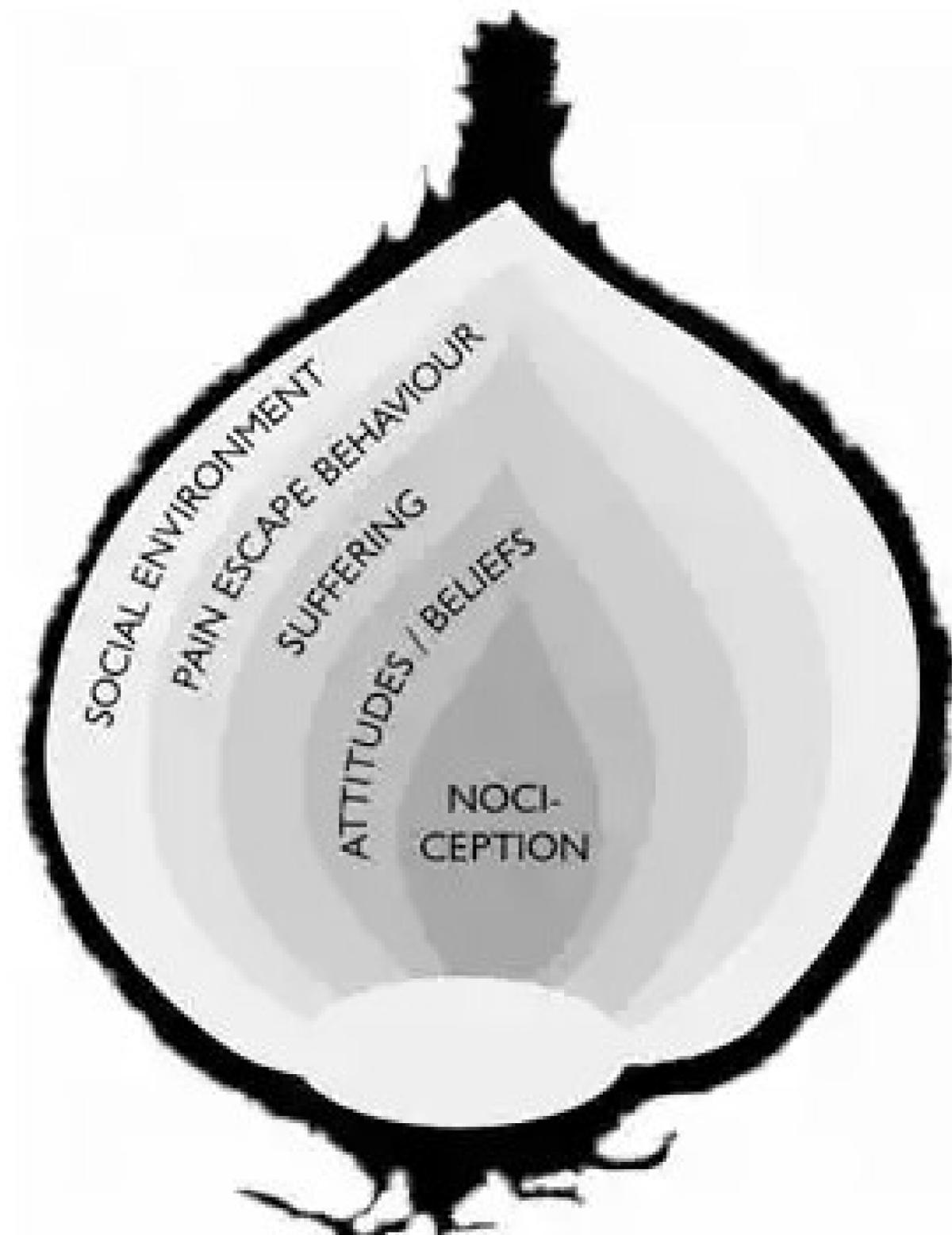


**ENGEL'S
CONCEPTUAL MODEL OF ILLNESS**



**LOESER'S
CONCEPTUAL MODEL OF PAIN**





Managing Chronic Neuropathic Pain: Recent Advances & New Challenges (2022)

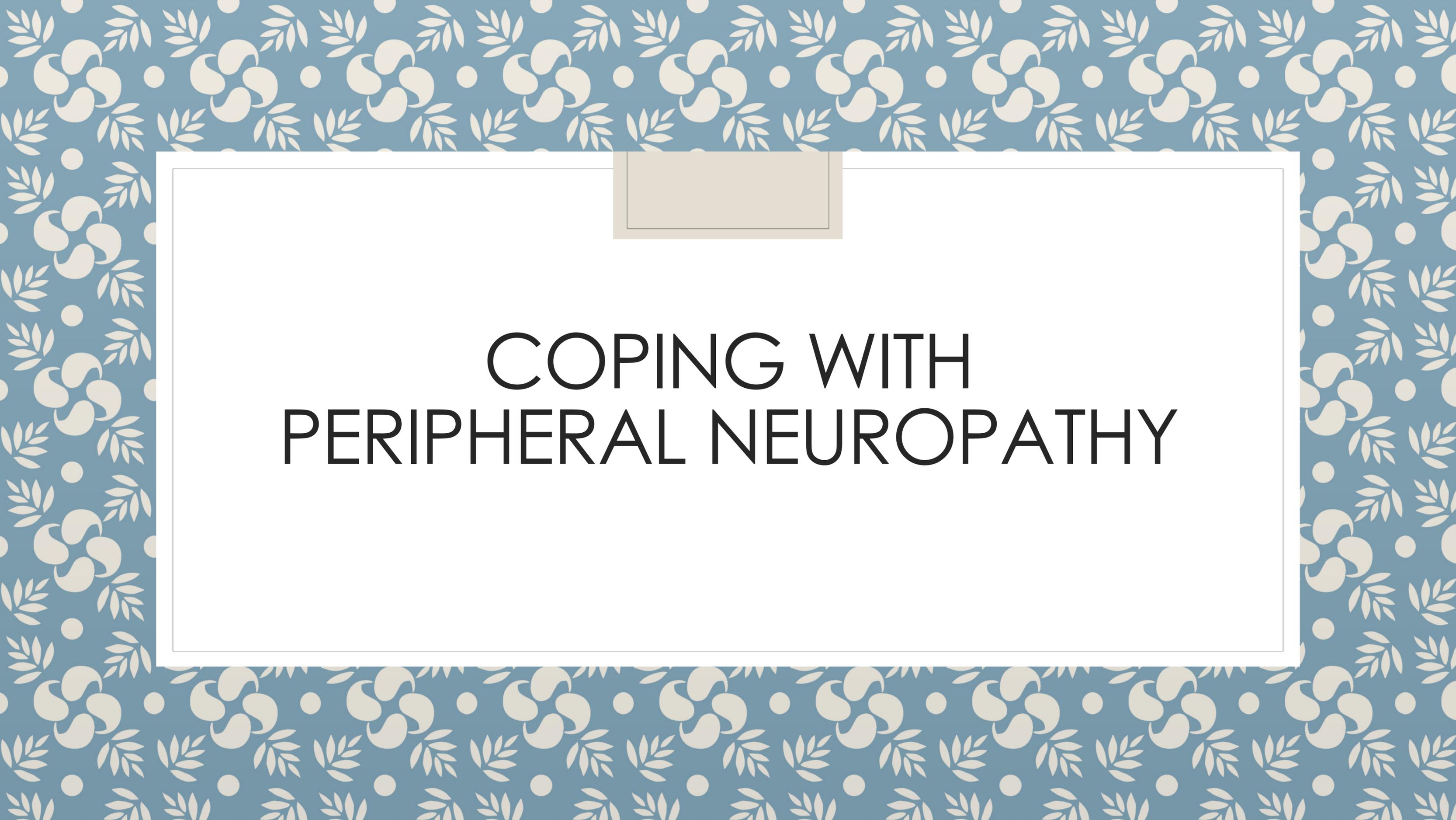
- Qutenza
- Mirogabalin
- Ipidacrine
- Bumetanide
- Minocycline
- Agmatine sulfate
- IVIG
- Topical CBD oil
- Dextromethorphan post-ketamine
- Cetuximab
- Nano curcumin
- PF-06372865
- Topical Fisionerv
- Lacosamide
- Intrathecal baclofen
- Sodium nitrite SR
- Alpha-lipoic acid
- Lidocaine infusion
- 1-4 chlorokynurenine
- Topical turpentine oil
- Dronabinol
- Neublazin
- Botulinum toxin A
- Cebranopadol
- BG00010 (neurotrophic factor)
- Sativex
- Topical ketamine
- Neurostimulation & neuromodulation
- Epidural motor cortex stimulation
- SCS
- DBS
- Peripheral n. stimulation
- TENS
- Electroceuticals
- rTMS
- tDCS
- Remote electrical neuromodulation
- Immersive virtual reality
- BreEStim
- Scrambler therapy
- Optogenetics
- Photon stimulation (pulsed infrared light)
- Vibration stimulation
- Molecular modalities
- Stem cell transplant
- Oxygen & ozone therapy
- Aptiva

Treatment of Chronic Pain

- As with other chronic illnesses, it is managed, not cured
- Multi-disciplinary approach targeting all areas of the onion
 - Holistic
 - Self-management
 - Goal is improved functionality

Before you heal someone, ask him if he's willing to give up the things that made him sick.





COPING WITH PERIPHERAL NEUROPATHY

Dealing with any Diagnosis

May be more or less challenging based on:

1. Degree of predictability
 - Relapsing-remitting, waxing-waning, or chronic progressive?
 - Feelings of insecurity, impending doom
2. Degree of disability
 - How much does it interfere with your life?
3. Stigma
 - Of an “invisible illness”
4. Degree of monitoring required
 - Often intense at onset, then less frequent
 - Fatigue (patient, family, care team)
5. Certainty of prognosis
 - 25% of PN pts may never find underlying cause

Response to Illness

1. Crisis

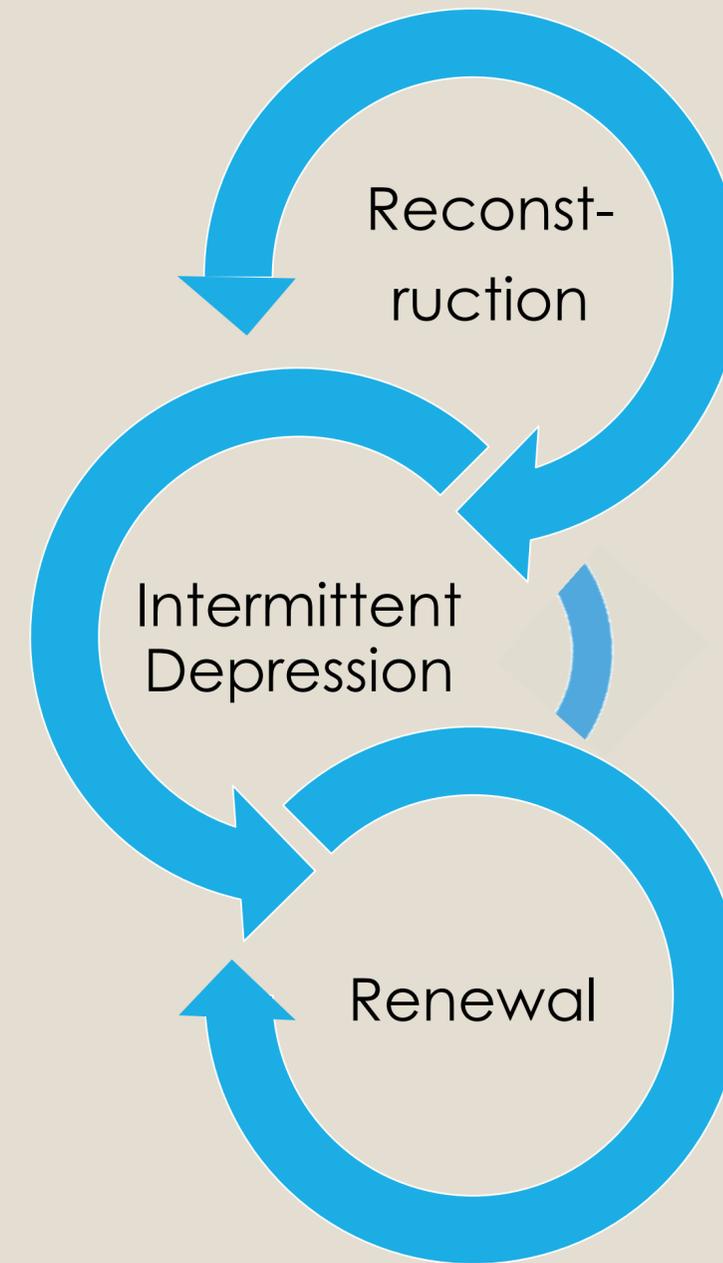
- Acute response
- Most do well here

2. Isolation

- Less attention, feel forgotten by others
- You reaching out to others

3. Anger

- At God? Yourself?
- Perceived anger from others (family, friends, medical team)
- Suicidality common



Existential Struggles

Why me?

- Find your own answer
- Make peace with it, and move on to another question

What now?

- Find meaningful things on which to focus your attention that are not the suffering

“He who has a why to live can bear almost any how.”

-Friedrich Nietzsche

MAN'S SEARCH FOR MEANING VIKTOR E. FRANKL

WITH A NEW FOREWORD BY
HAROLD S. KUSHNER



- 1 Things I can no longer do
e.g. running
- 2 Things I couldn't do before, but can now
e.g. time for hobbies
- 3 Things I do the same as before
e.g. watching a movie
- 4 Things I can still do, but differently
e.g. go to the mall, but need a wheelchair
- 5 Things I can do differently, just not yet
e.g. go to a game

Navigating Changing Roles

- Ask yourself – exactly what was it about your previous life/activities that was most enjoyable? How can you maintain that?
 - Try something new
- Stop beating yourself up
- Set small, SMART goals*
 - Short, medium, and long-term
- If you're feeling overwhelmed, be direct
- Don't just do something, stand there

SMART Goals



Specific

The goal is concrete and tangible - everyone knows what it looks like.



Measurable

The goal has an objective measure of success that everyone can understand.



Attainable

The goal is challenging, but should be achievable with the resources available.



Relevant

The goal meaningfully contributes to larger objectives that align with your values



Timely

This goal has a deadline or, better yet, a timeline of progress milestones.

Common, but not normal

- While depression and anxiety are common responses to having a chronic painful illness, that doesn't mean you have to 'just deal with it'
- Distress is distress, and distress is treatable!
- Recognize the symptoms, ask for help, don't be embarrassed
- Improved outcomes when mental illnesses are treated



SLEEP HYGIENE

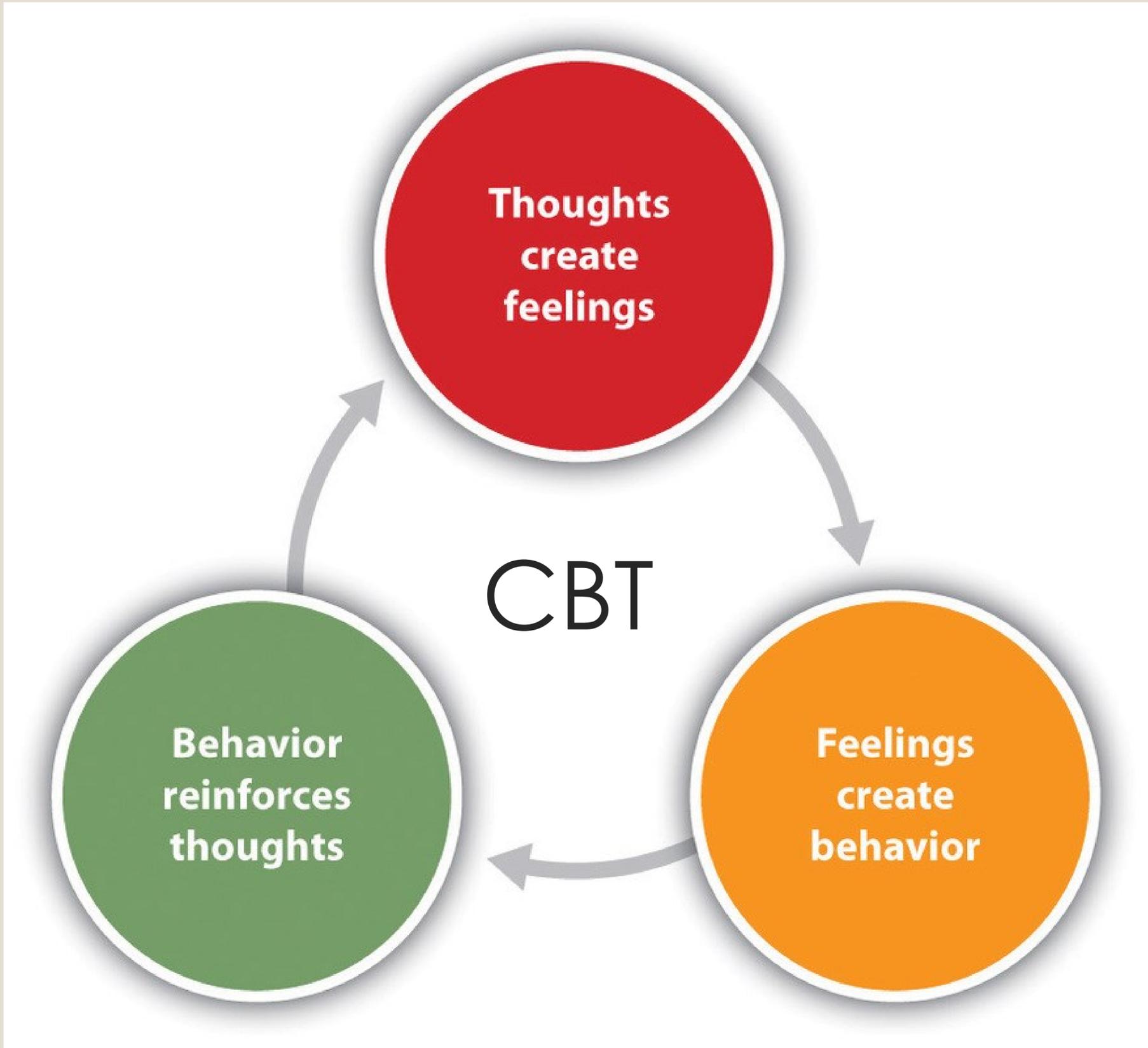


Relationships

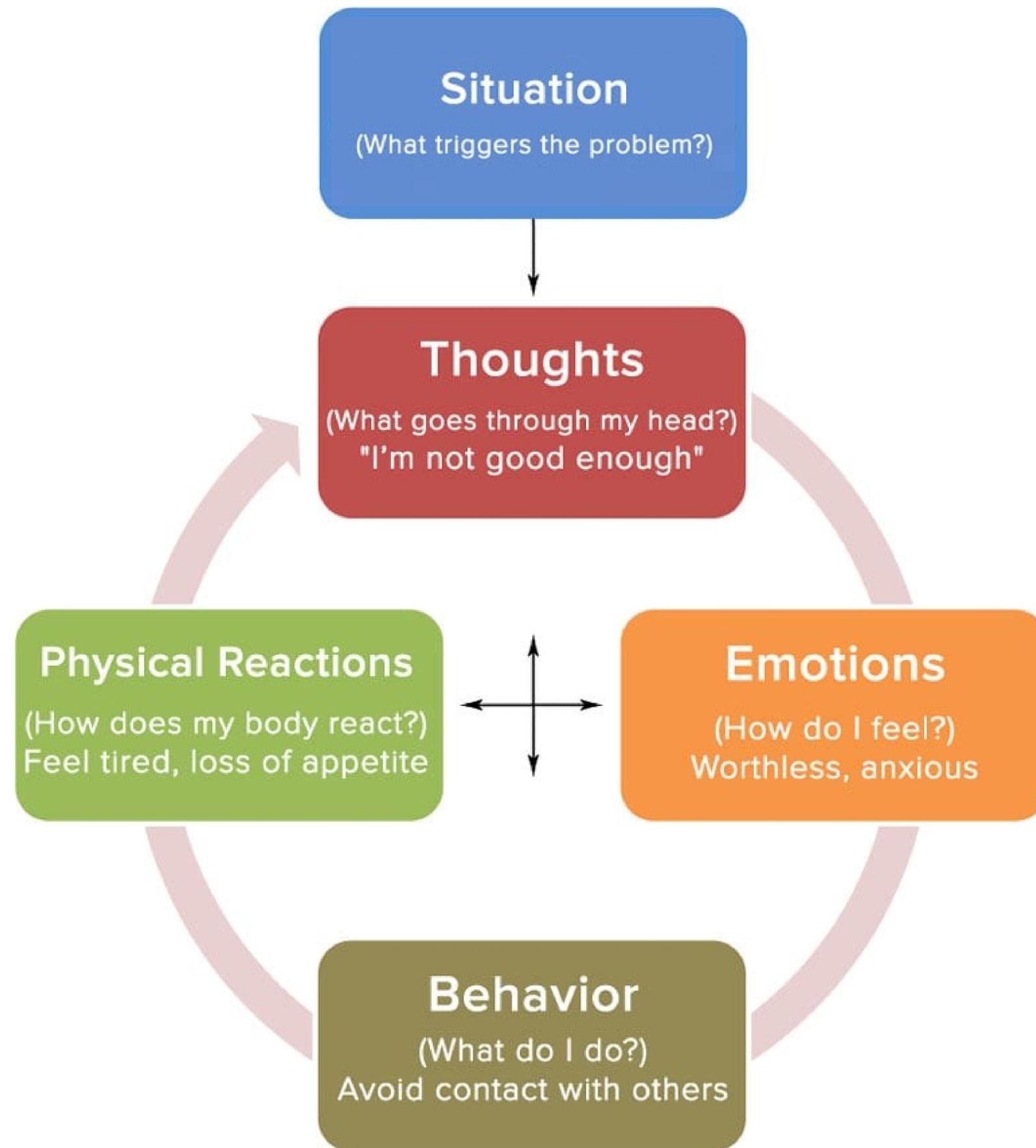
- Chronic illness is not only an individual issue, but an interpersonal one
- Fear of losing friends, being dumped by loved ones
- Good social supports make a big difference in how the ill person copes
- Stay connected!

Avoid Self-Fulfilling Prophecies

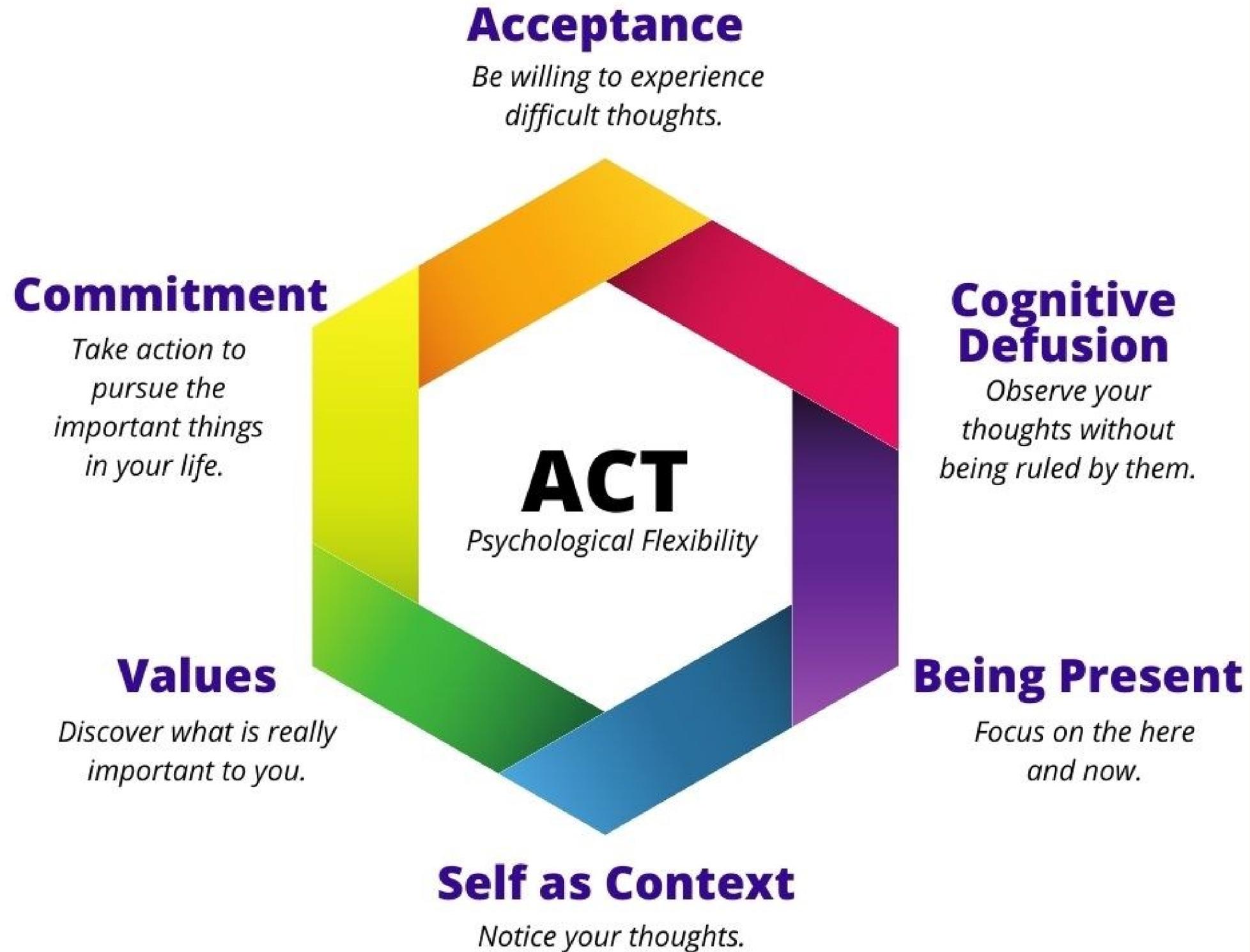
- The way we view ourselves is often what we project to others – when we perceive that they also identify with this view, it further reinforces our view of ourselves



CBT



ACT



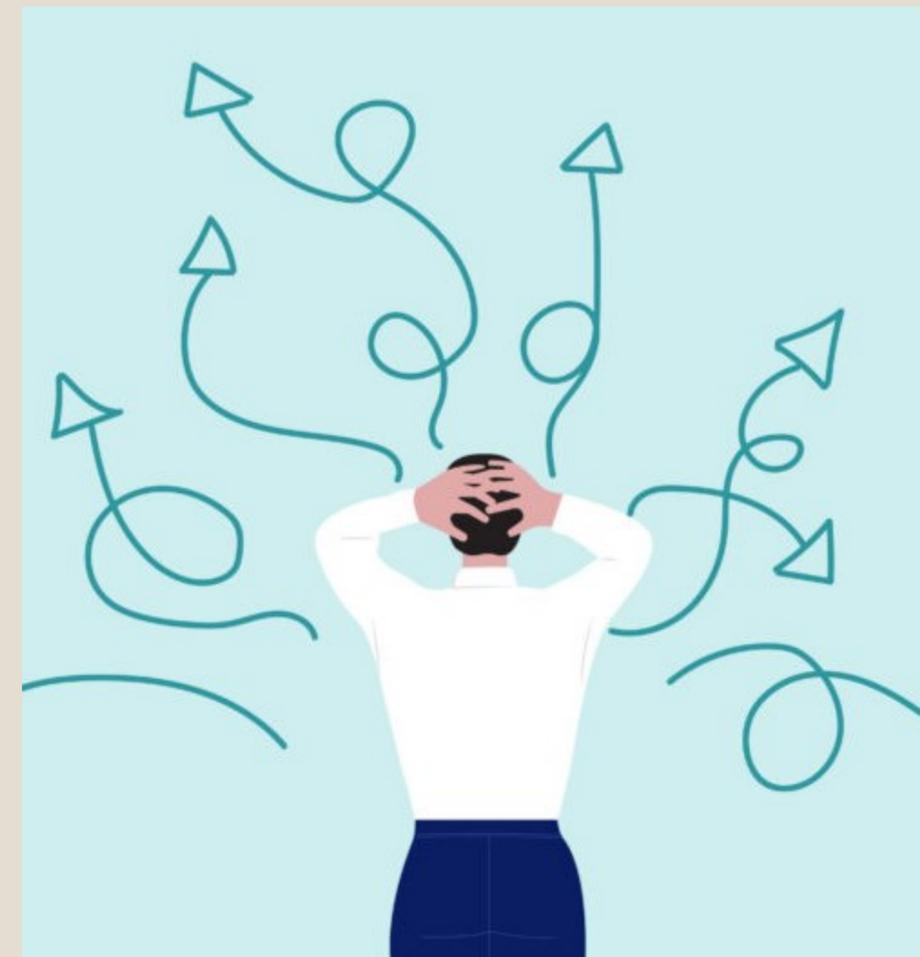
Practical Strategies



- Sleep, activity, nutrition
 - Ensure adequate vitamin intake
 - Fruits and vegetables, omega-3 fats
 - Supplements?
- Relaxation / stress reduction
 - Diaphragmatic breathing (Ujjayi)
 - Parasympathetic vs. sympathetic activation
 - Visualization / guided imagery
 - Progressive muscle relaxation
- Live in the moment – “*the here and now*”
 - Mindfulness meditation
 - Acceptance & Commitment
- Traditional East Asian Medicine
 - Acupuncture/Acupressure
 - Yoga

De-Catastrophizing Techniques

- Think about *why* you're having the thoughts
- Play it out
- Remember that thoughts are not facts
- Use *realistic* thought challenging
- Try the "chances are" method
- Talk to the catastrophizing part of your brain
- Give yourself space
- Preempt catastrophizing with wiggle room
- Practice "acceptance-commitment" therapy
- Ground yourself



<https://creakyjoints.org/living-with-arthritis/mental-health/10-ways-to-curb-catastrophizing/>

Resources for You



- <https://www.foundationforpn.org/>



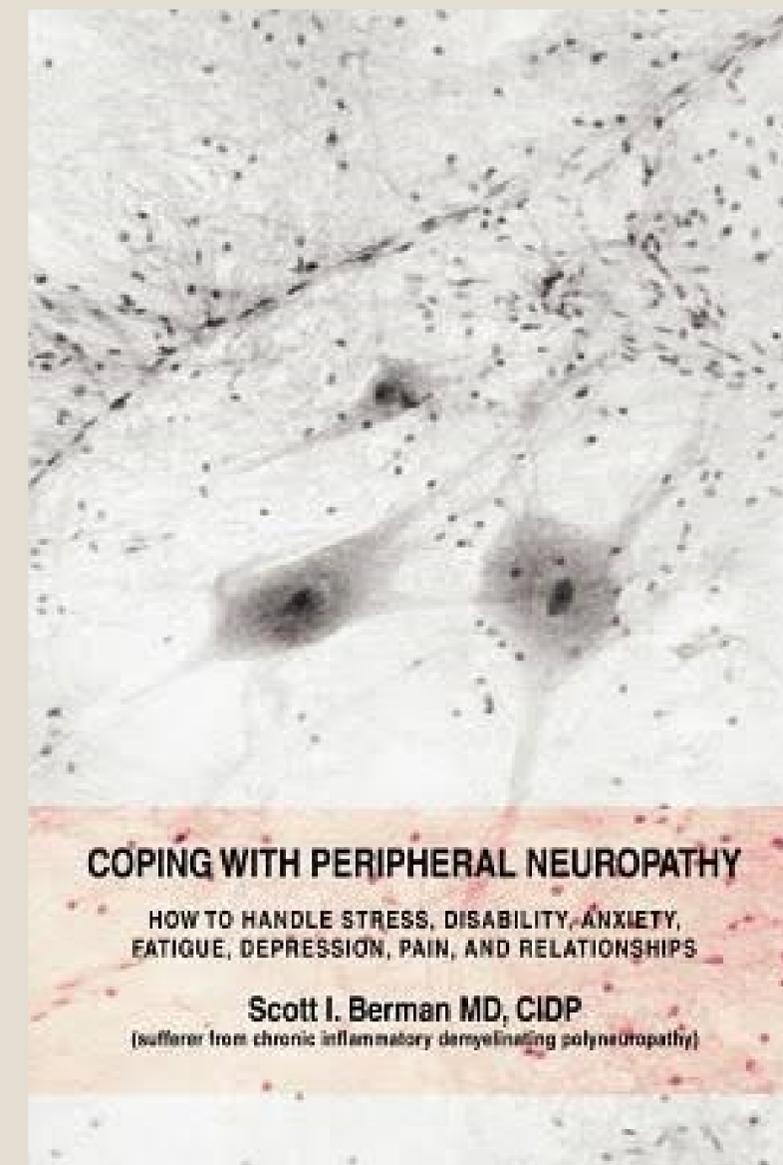
- <https://neuropathyjournal.org/>



- <https://pnsnetwork.org/>



- <http://www.neuropathyaction.org/>



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Questions?

