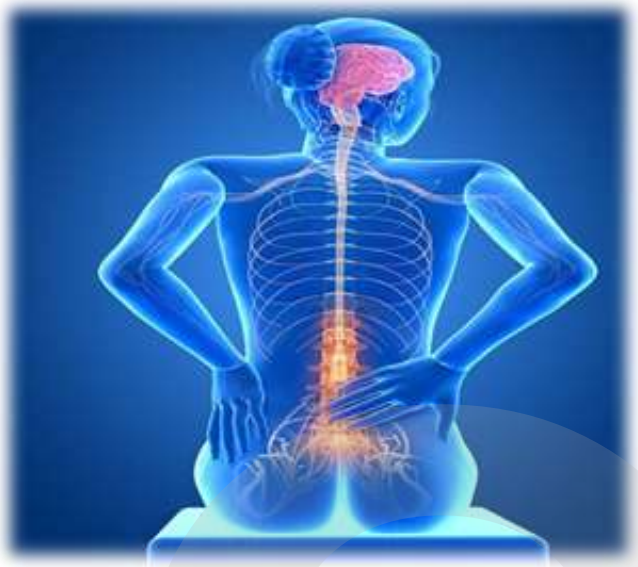


The Role of Central Sensitization in Chronic Pain

Musculoskeletal Update for Primary Care

DHARMA COLGAN, PHD, C-IAYT

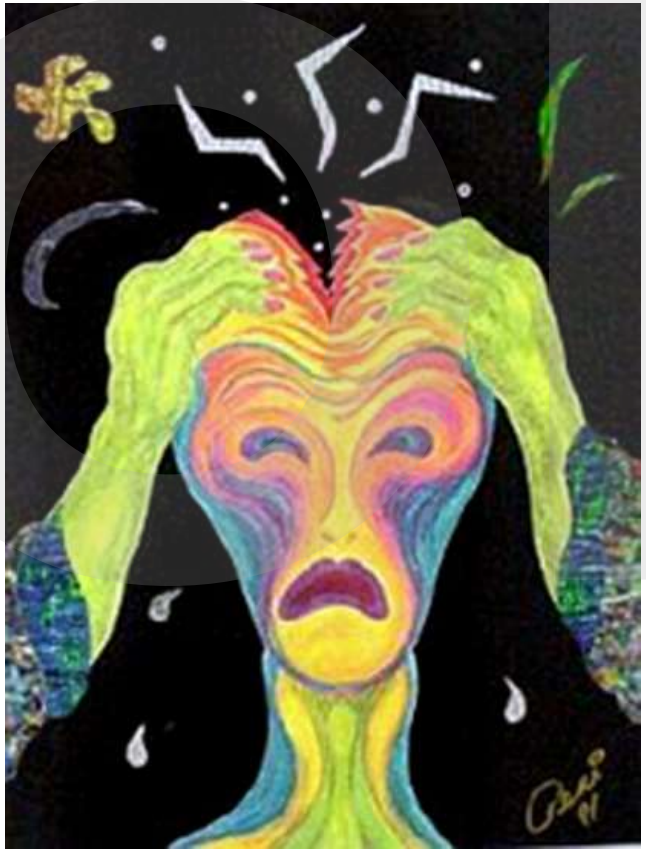
DEPARTMENT OF NEUROLOGY

OREGON CENTER FOR COMPLEMENTARY AND ALTERNATIVE MEDICINE IN NEUROLOGICAL DISORDERS

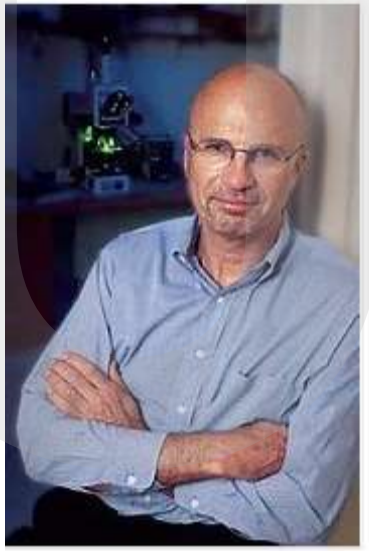
OREGON HEALTH & SCIENCE UNIVERSITY

No disclosure. No conflicts of interest.

Central Sensitization



"CNS can change, distort or amplify pain, increasing its degree, duration, and spatial extent in a manner that no longer directly reflects the specific qualities of peripheral noxious stimuli, but rather the particular functional states of circuits in the CNS."[1]



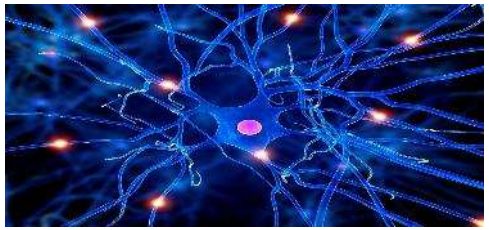
Objectives

1. **Define** central sensitization (CS) and **Discuss** underlying candidate mechanisms
2. **Identify** clinical indicators of CS
3. **Recognize** chronic pain conditions in which CS is present
4. **Highlight** biopsychosocial contributors
5. **Review** an algorithm to identity patients with CS-related symptoms in primary care settings
6. **Review treatment** guidelines

Pain

- Nociceptive Pain
  - Somatic Pain
  - Visceral Pain

- Neuropathic Pain
  - Peripheral & Central Neuropathic Pain



Pain

Nociceptive Pain

Somatic Pain
Visceral Pain

Pain sensation that is in proportion to the amount of tissue damage

Neuropathic Pain

Peripheral & Central Neuropathic Pain

Pain arising as a direct consequence of a lesion or disease affecting the somatosensory system

Central nervous system sensitization

Amplification of neural signaling within the CNS that elicits pain hypersensitivity

The lack of a definitive clinical test for persistent pain does not mean that the condition has no biological basis. – Mark R. Hutchinson, 2018

Does it matter?

Clinical Importance

1. **Patients with predominant CS report** [2,3]
   - Greater severity, chronicity and disability
   - Lower quality of life
2. **Predict poor prognosis** [4-6]
3. **Mediate treatment outcome** [6-8]

Taken together, accumulating evidence supports the clinical importance of CS in people with chronic musculoskeletal pain.

Definitions of Central Sensitization (CS)

1983

Woolf[9]

- An amplification of neural signaling within the CNS that elicits pain hypersensitivity

2011

International Association for the Study of Pain (IASP)[10]

- Increased responsiveness of nociceptive neurons in the CNS to normal or subthreshold afferent input

2016

Akinci[11]

Exaggerated response (hypersensitivity) of central pain-signaling pathways mainly caused by:

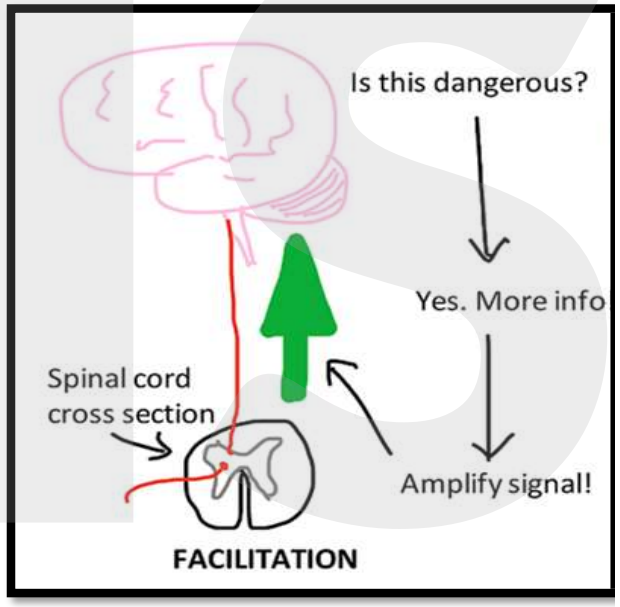
- Increased membrane excitability and synaptic transmission of dorsal horn neurons
- Reduced inhibition of descending pathways
- Altered sensory processing in the brain

2017

G.M. Schafer[12]

- Comprising a multitude of different mechanisms taking place in the dorsal horn of the spinal cord, ascending and descending pathways in the dorsal column, the brainstem and pain centers in the forebrain, all leading ultimately to amplification of innocuous and painful stimuli and to the extension of receptive fields

Top-Down Candidate Mechanisms

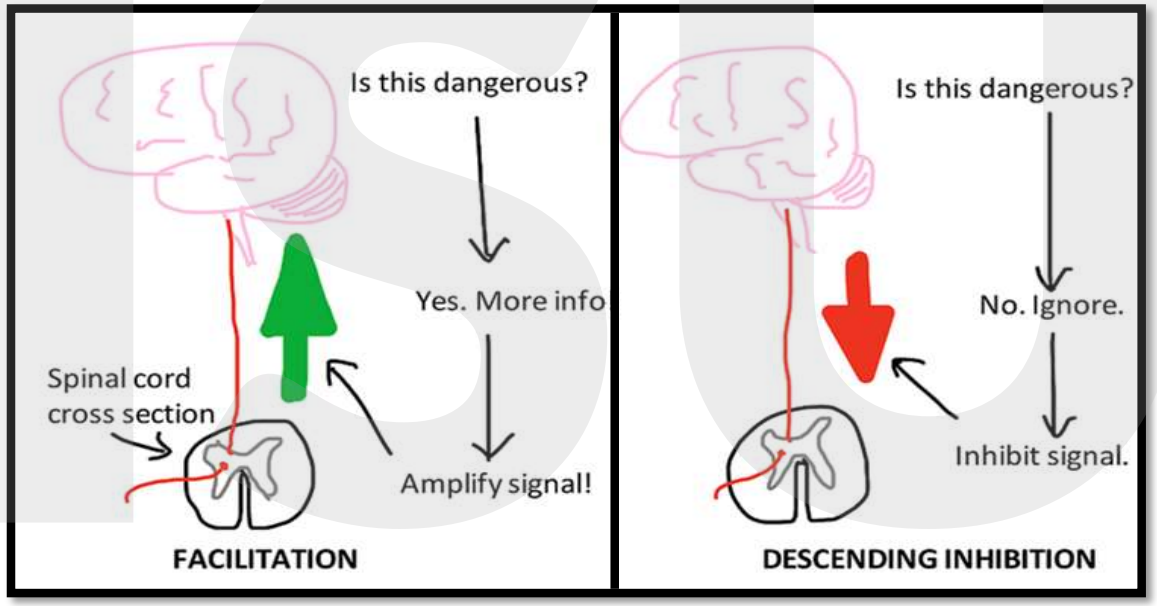


Accelerator

Brakes

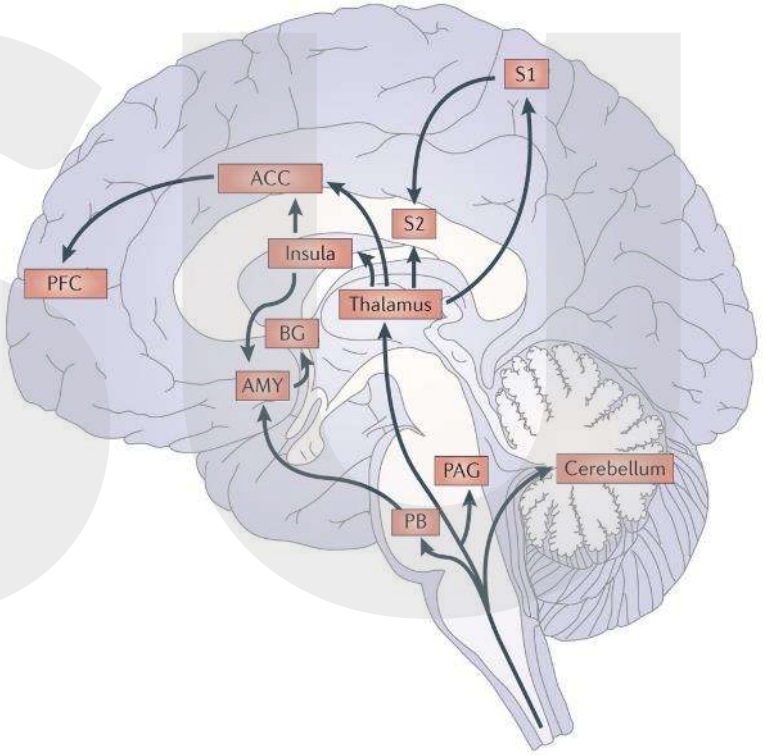
Top-Down Candidate Mechanisms

- Increased membrane excitability and synaptic efficacy of dorsal horn neurons[13]
  - Reduced threshold for neuron activation
  - Increased receptive field
  - Increased response to painful stimuli
- Reduced inhibition of descending pathways[14]



Top-Down Candidate Mechanisms

Altered sensory processing in the brain

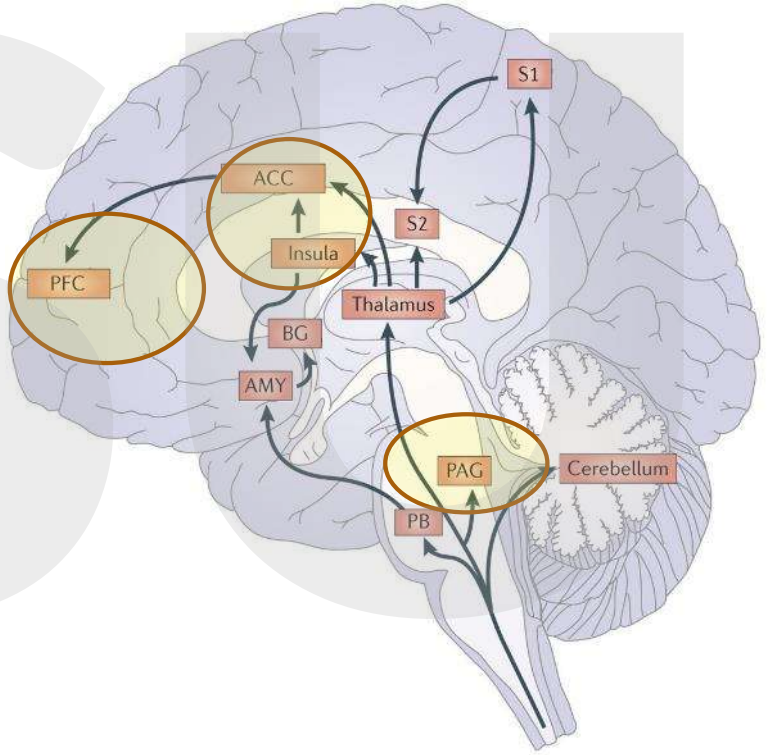


Nature Reviews | Neuroscience

Top-Down Candidate Mechanisms

Structural Changes [16]

- **Decrease in gray matter volume**:
  - Affective pain processing (cingulate, insular)
  - Stress (parahippocampal gyrus)
  - Cognitive-affective regulation that influences descending inhibitory control of pain (pre-frontal cortex)
- **Functional changes**
  - Increased connectivity within pain processing areas
  - Decreased connectivity to pain inhibition brain areas.



Nature Reviews | Neuroscience

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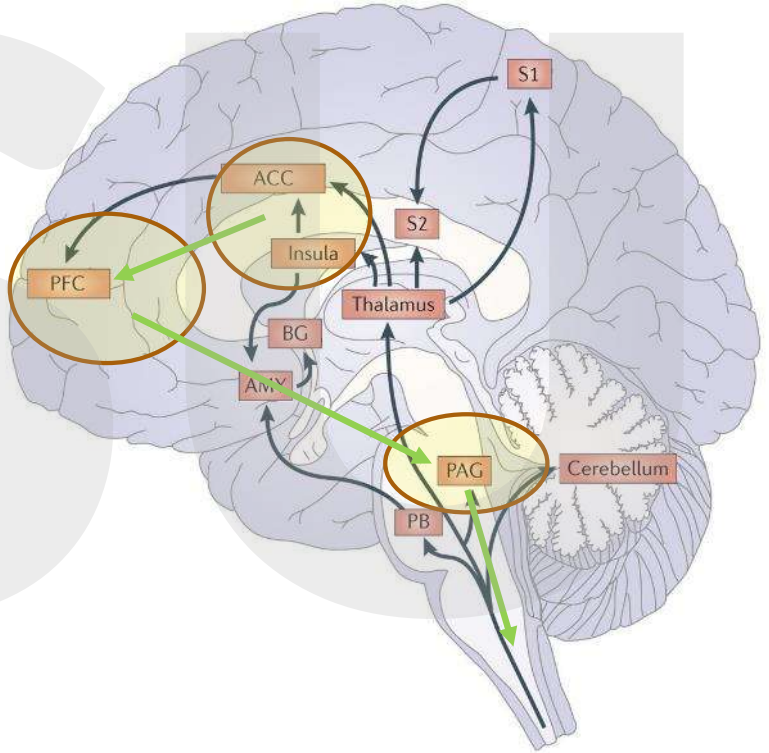


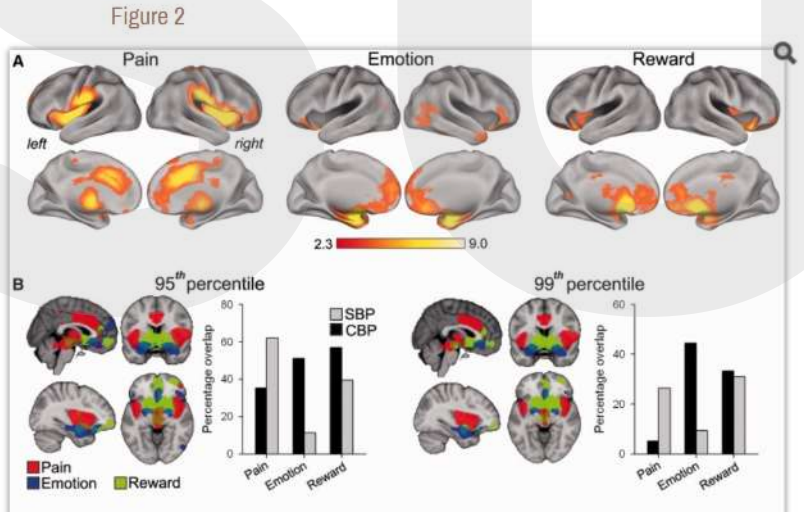
Nature Reviews | Neuroscience

The brain is getting better at pain.

Accelerator is too active and the brakes are no longer functioning properly.

Congruent with Brain Images of cLBP

Systematic review of cross-sectional and longitudinal brain imaging studies suggest the chronification of back pain is correlated with a shift away from ***acute pain circuits*** to the engagement of ***emotion circuits*.** [17]



Bottom-Up Candidate Mechanisms

- Amplified stress response that triggers the release of pro-inflammatory cytokines and activation of spinal cord gila. [18-20]

Progression from acute pain to CS

Progression from acute pain to CS pain

neurobiological and
biopsychosocial influences
may alter tissue sensitivity

TIME

Progression from acute pain to CS pain

neurobiological and biopsychosocial influences may alter tissue sensitivity

amplification of neural signaling

TIME

Progression from acute pain to CS pain [21]

neurobiological and biopsychosocial influences may alter tissue sensitivity

amplification of neural signaling

PAIN MEMORY

TIME

2. Clinical indicators of CS[22]

Tactile allodynia

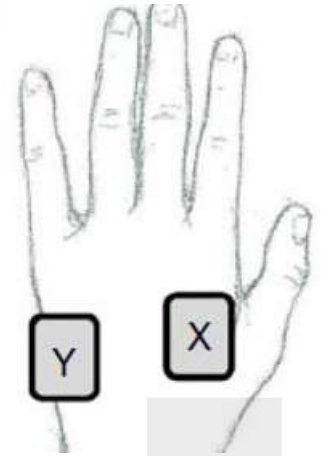
- pain caused by a stimulus that does not normally elicit pain

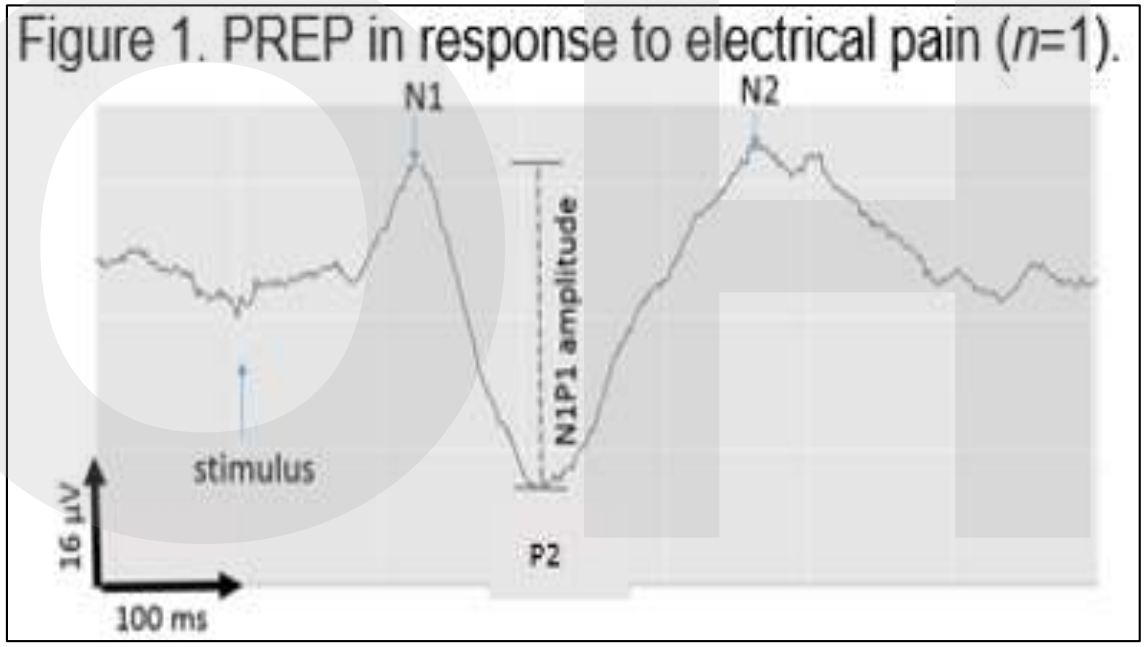
Pressure hyperalgesia

- increased sensitivity to pain

- **Widespread pain** (secondary hyperalgesia)
  - pain in remote areas, beyond the previously injured tissue
- **Prolong pain** once stimuli is removed
- **Absence of adaptive central pain-inhibiting mechanisms**
  - pain habituation

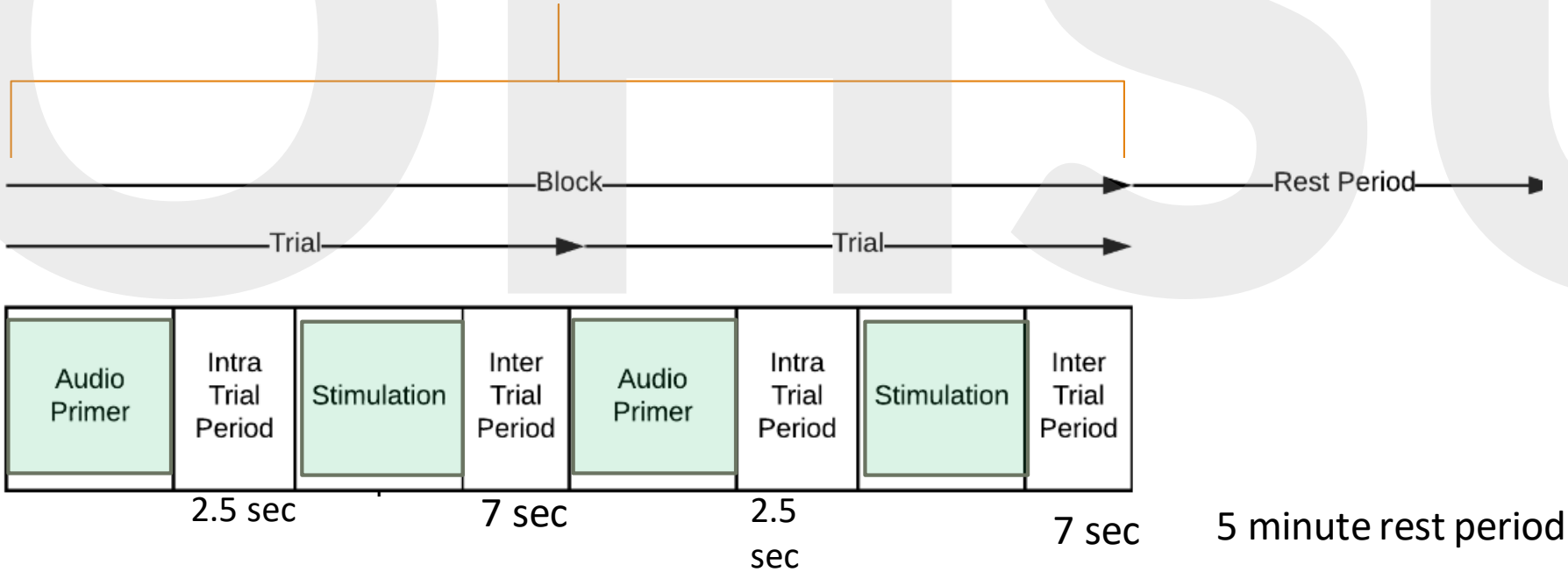
2. Clinical indicators of CS





Electrical Pain Paradigm

20 trials = I block



5 minute rest period

Figure created by Tab Memmott

2. Clinical indicators of CS

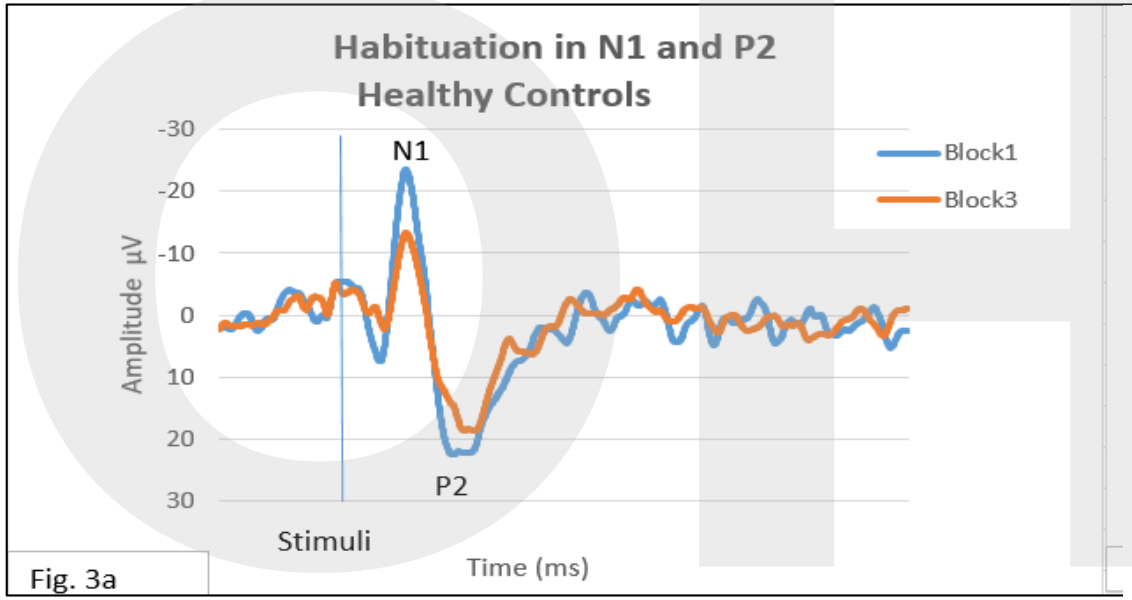


Fig. 3a

2. Non-pain indicators of CS[23-25]

Characteristics of CS

- Trauma history
- Post-traumatic stress
- Increased responsiveness to a variety of stimuli
  - Bright lights, touch, noise, pesticides, medication, temperature, stress, emotions

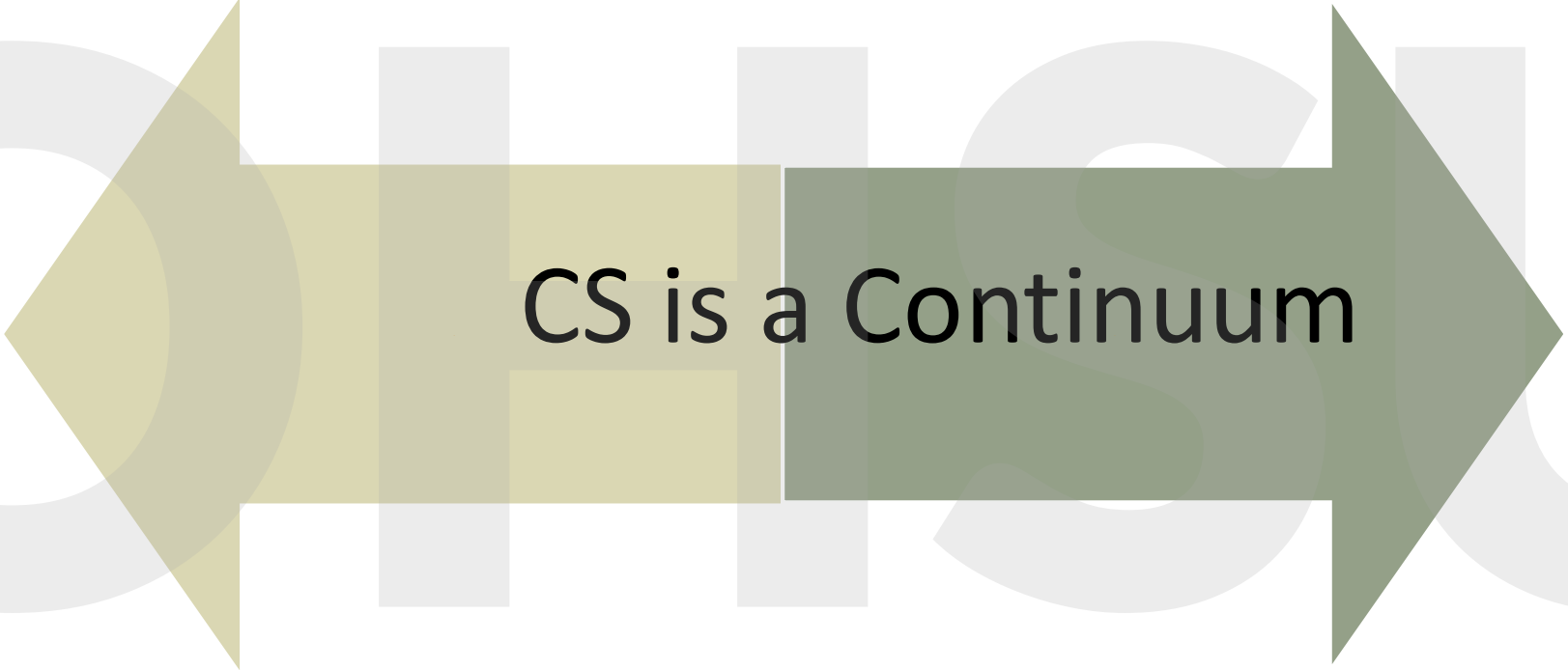
May be related to CS

- Fatigue
- Sleep disturbance
- Poor Concentration
- Tingling
- Numbness

General intolerance to a variety of physical and emotional stressors.

3. Pains Conditions in which CS is present

3. Pains Conditions in which CS is present



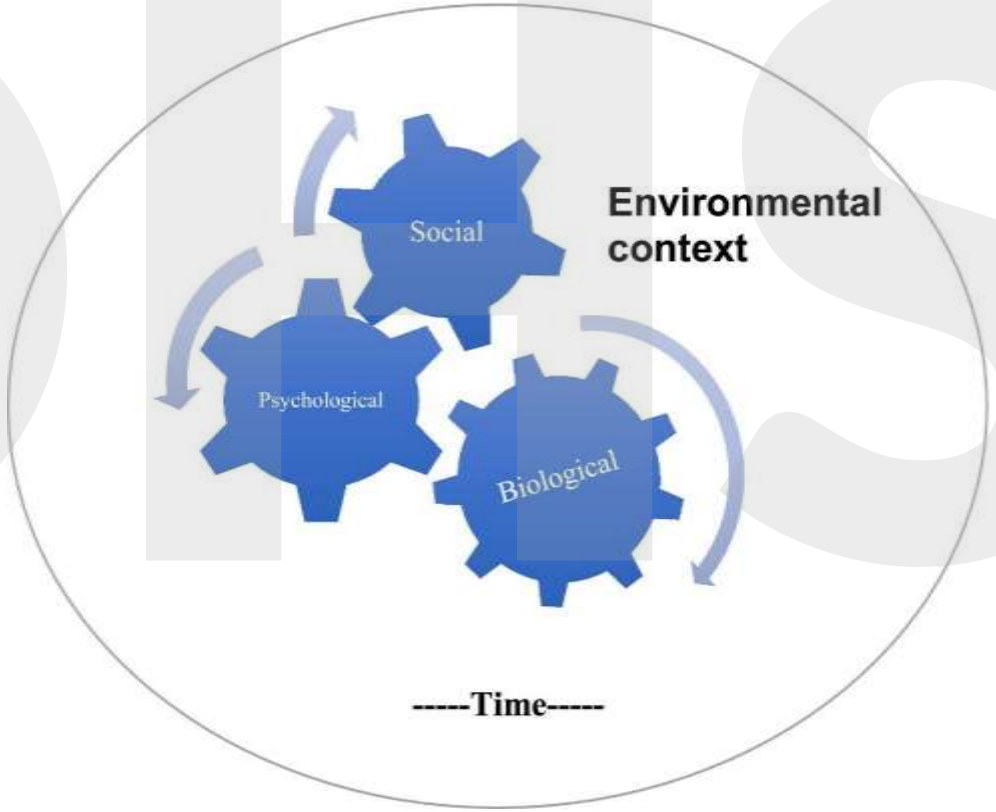
Acute
More tissue pain
Less brain pain

Chronic
Less tissue pain
More brain pain

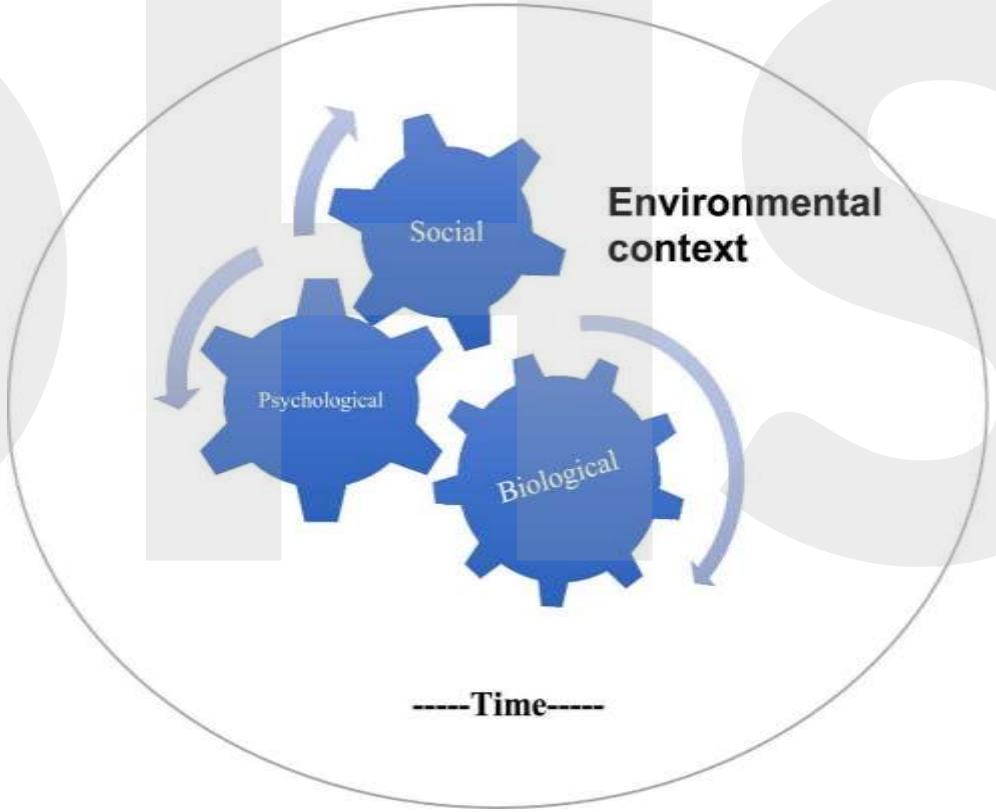
Medical Diagnosis [1, 26]	CS is predominant characteristic	CS is present in a subgroup
Chronic whiplash disorders	X	
Fibromyalgia	X	
Chronic fatigue	X	
Irritable Bowl syndrome	X	

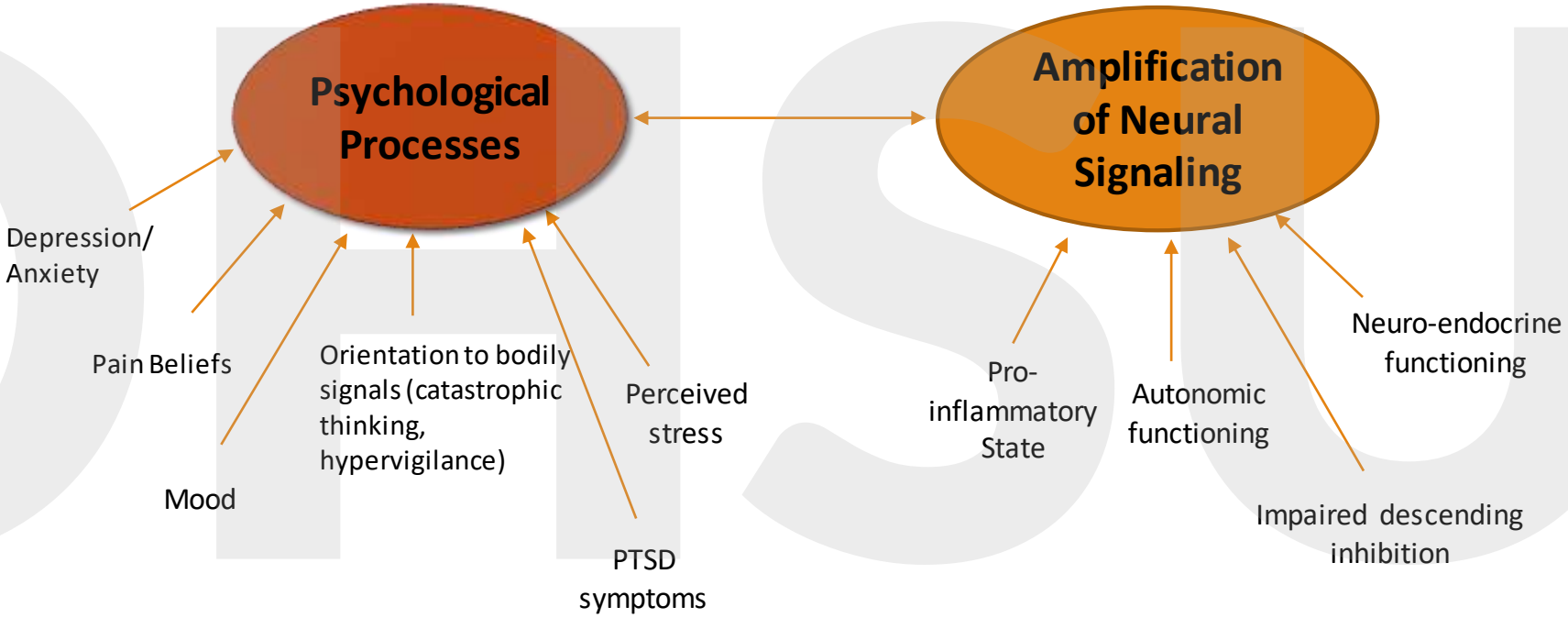
Medical Diagnosis [25-34]	CS is predominant characteristic	CS is present in a subgroup
Chronic whiplash disorders	X	
Fibromyalgia	X	
Chronic fatigue	X	
Irritable Bowl syndrome	X	
Chronic low back pain		X
(Sub) acute whiplash disorders		X

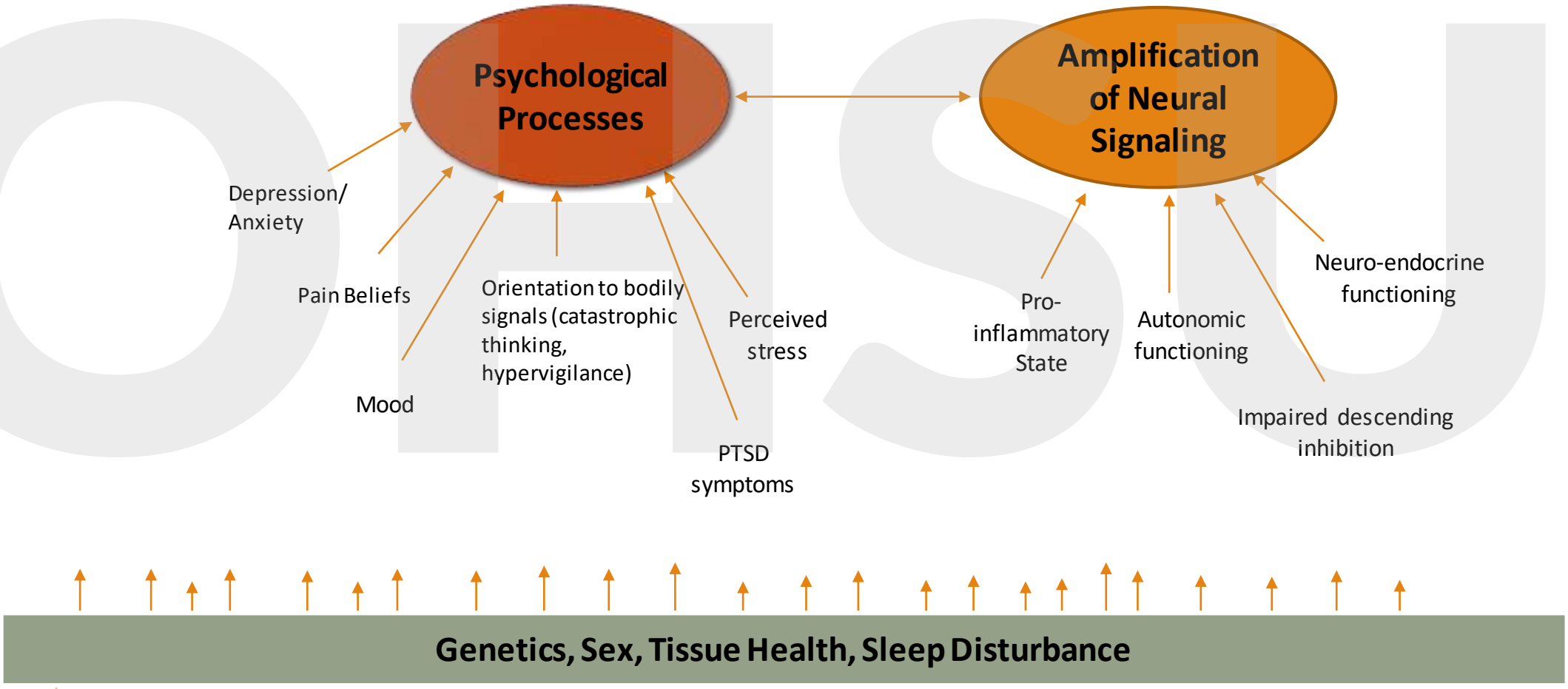
4. Biopsychosocial Contributors [35-37]



4. Biopsychosocial **Contributors** [35-37]




Psychological Processes
Amplification of Neural Signaling
Depression/ Anxiety
Pain Beliefs
Mood
Orientation to bodily signals (catastrophic thinking, hypervigilance)
Perceived stress
PTSD symptoms
Pro-inflammatory State
Autonomic functioning
Neuro-endocrine functioning
Impaired descending inhibition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Neuro-endocrine functioning
Impaired descending inhibition
Genetics, Sex, Tissue Health, Sleep Disturbance

Environmental Contributors

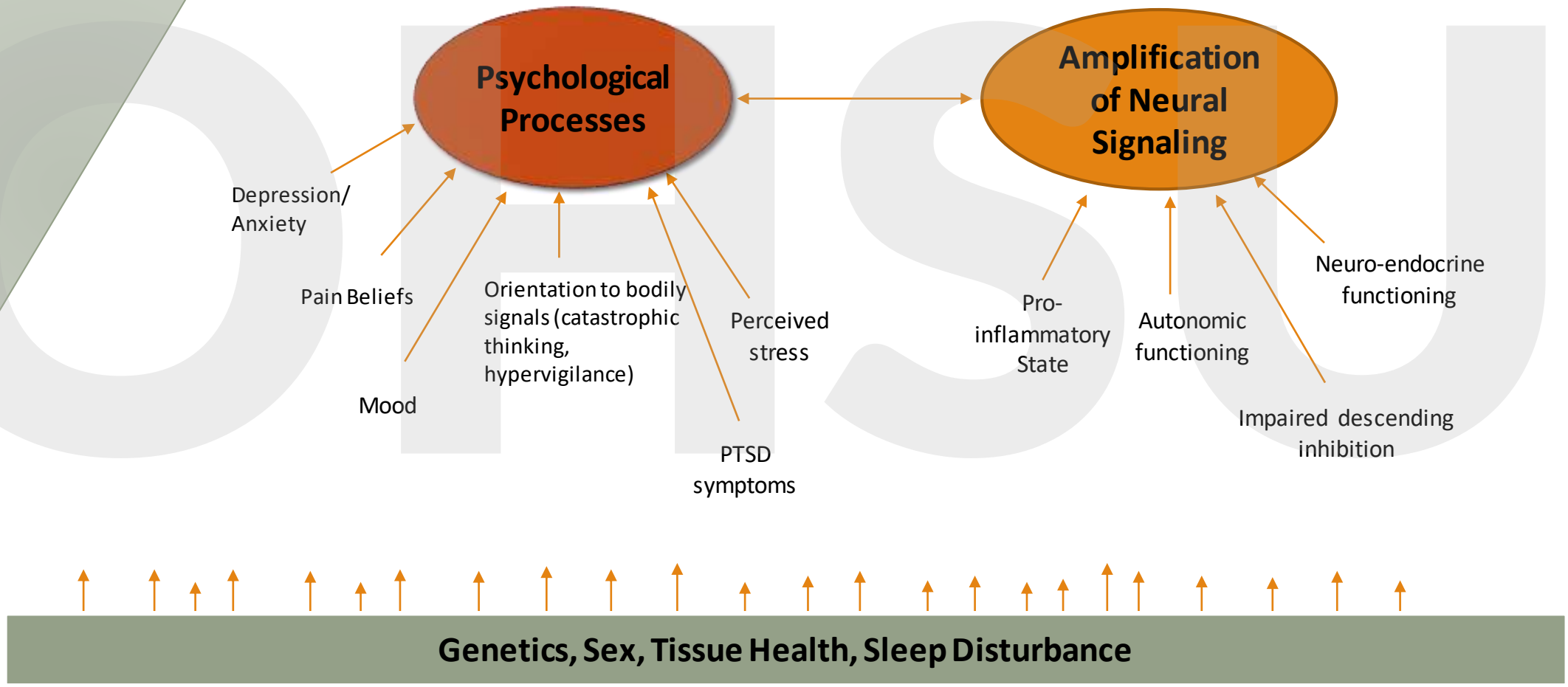
Socioeconomic status

Social Support

Trauma

Social Learning

Ethnic Discrimination



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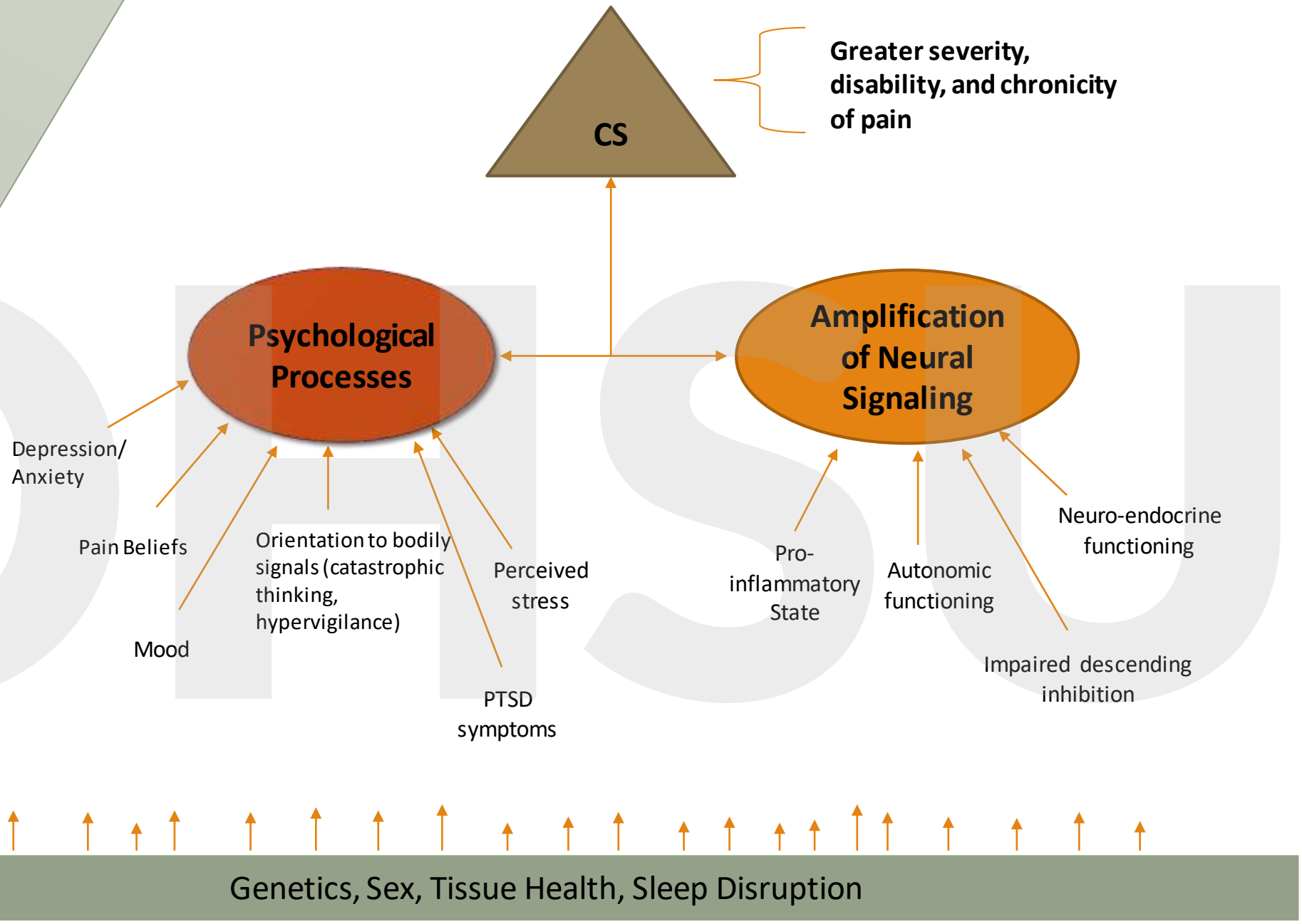


Interoceptive Awareness [38-40]

- How the CNS attends to, appraises, and responds to bodily sensations.
- Provides a moment-by-moment mapping of the body's internal landscape across conscious and unconscious levels.
- Interplay between perception of bodily states and cognitive-affective appraisal of these bodily states, informing response selection to maintain homeostasis.
- Anatomically, these processes take place in the insula.

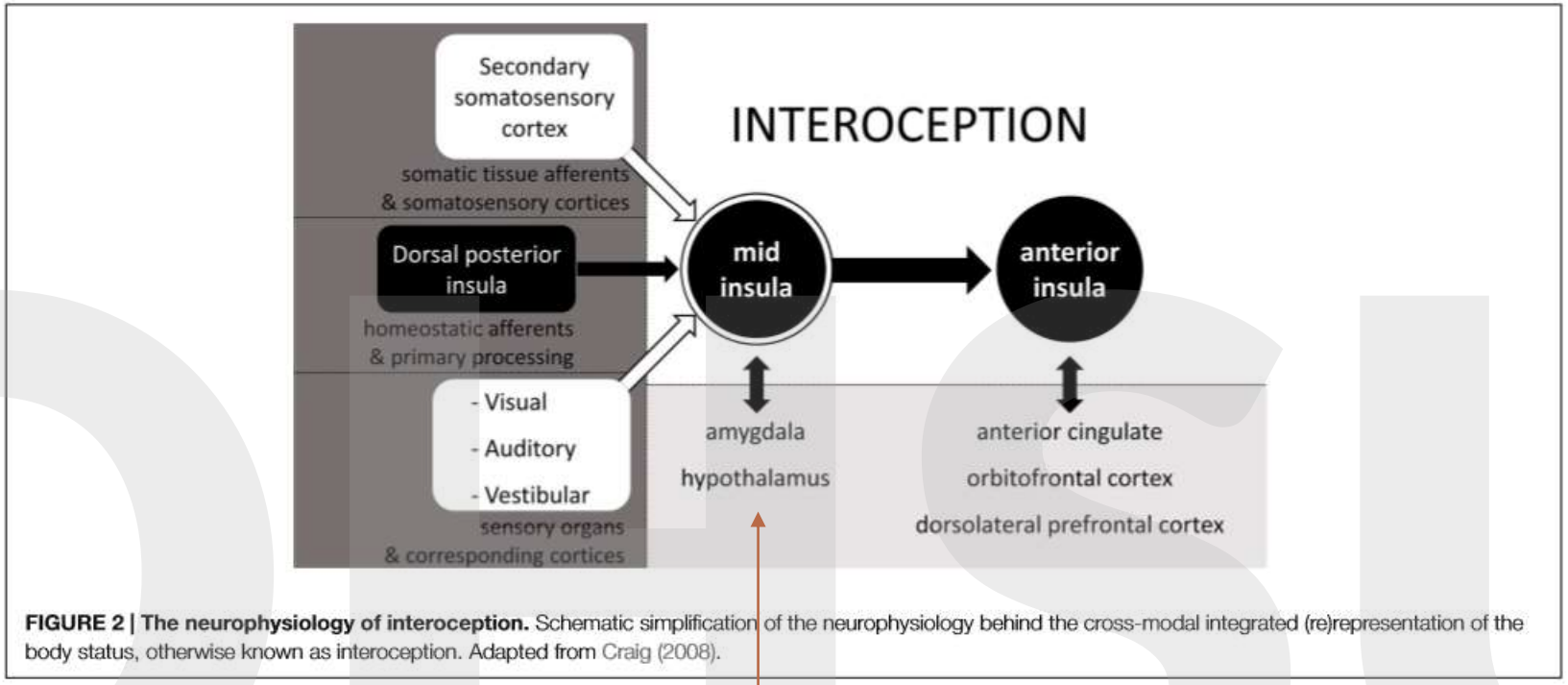


FIGURE 2 | The neurophysiology of interoception. Schematic simplification of the neurophysiology behind the cross-modal integrated (re)representation of the body status, otherwise known as interoception. Adapted from Craig (2008).

Salience, emotional memories, and ANS status

Ceunen, E., Vlaeyen, J. W., & Van Diest, I. (2016). On the origin of interoception. *Frontiers in psychology*, *7*, 743.

Interoceptive Awareness

- **Maladaptive**
  - Hypervigilance and catastrophizing activate the sympathetic nervous system, resulting in hypersensitivity in peripheral tissues
- **Adaptive**
  - Mindful awareness of bodily sensations without cognitive-affective reactivity
  - View bodily sensation as informative for decision-making, engendering regulation of stress and pain processing.

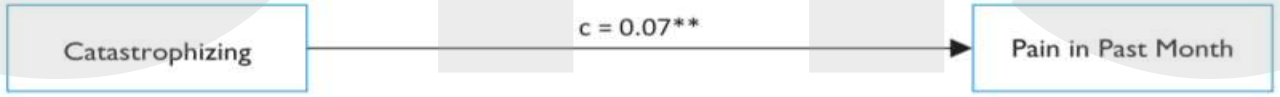


Figure 3. The mediating effect of pain sensitization (as measured by P40 cuff inflation pressure and cuff aftersensations) in the relationship between catastrophizing and pain in the past month controlling for opioid use and depression. *$P < 0.05$; **$P < 0.01$.

Those with high body awareness and very low PC had the highest probability of being in the complete habituation group.

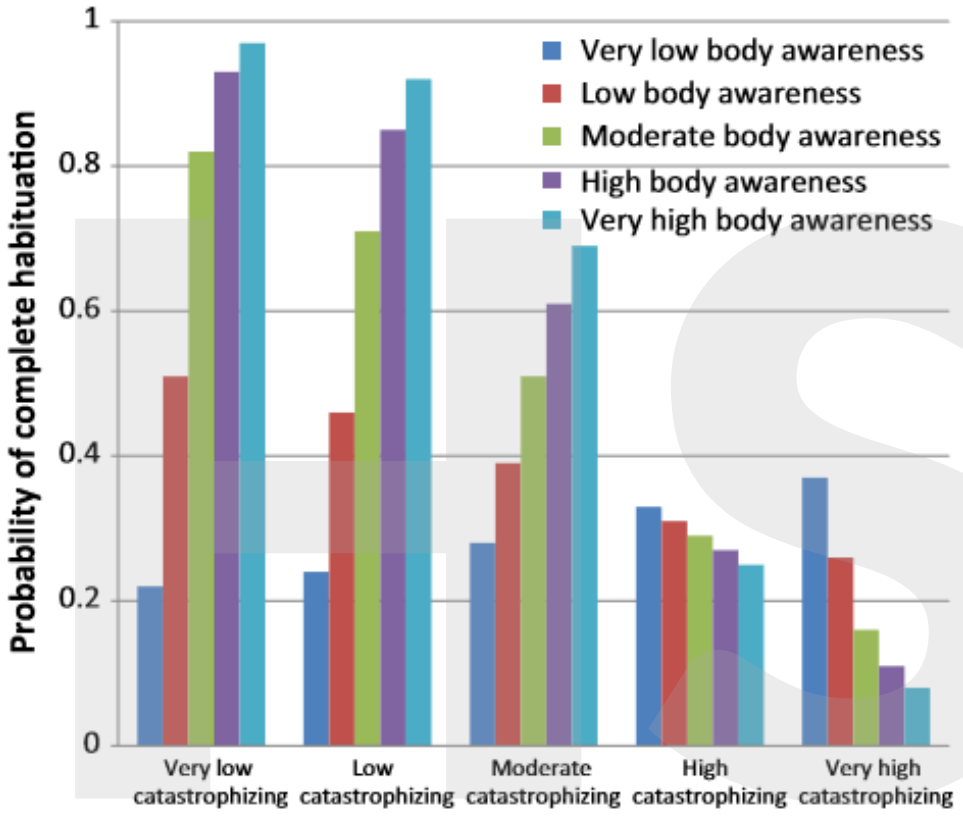
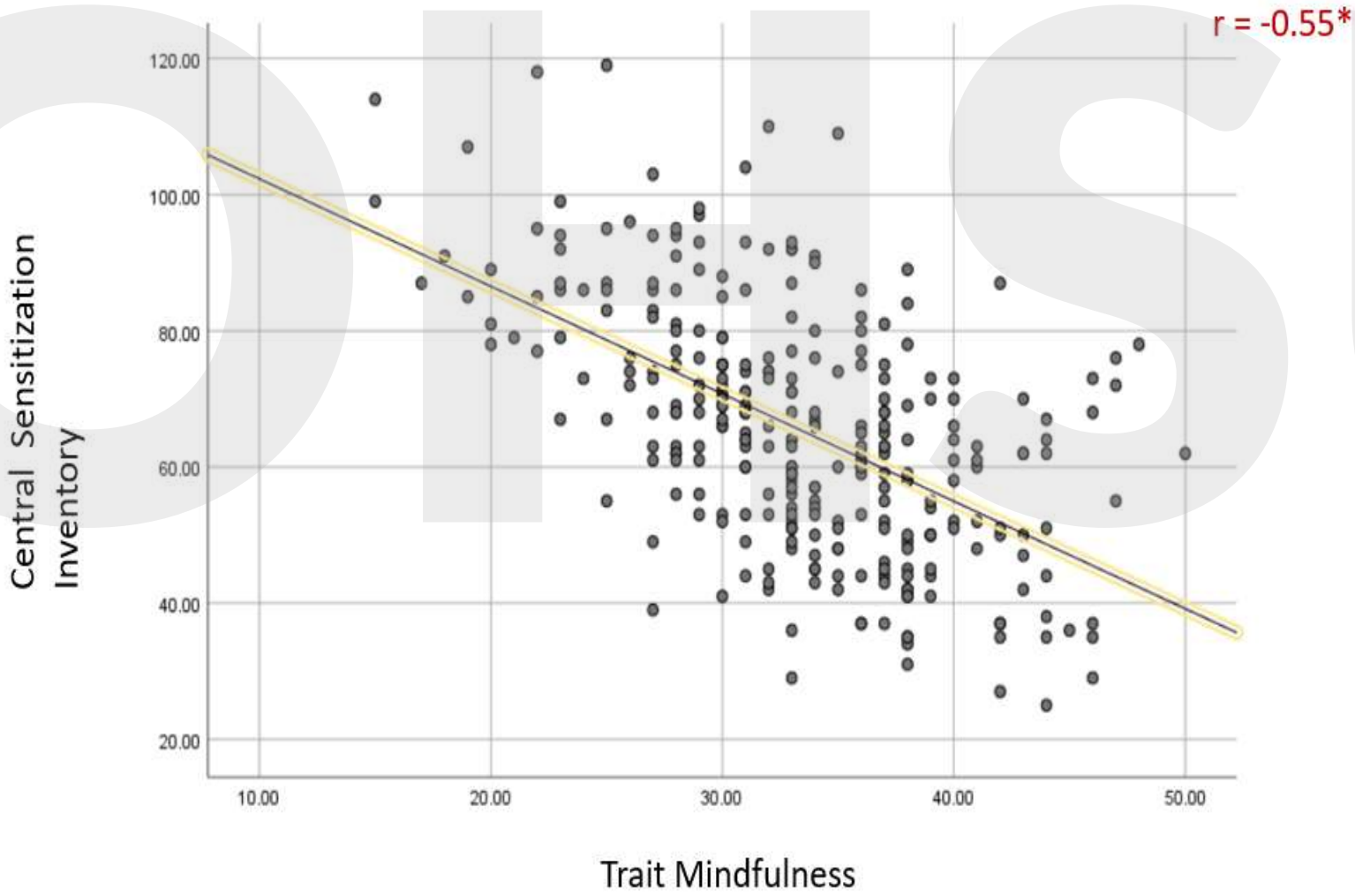


Fig. 2 Probability levels of being in complete habituation group according to interaction between body awareness and pain catastrophizing

Those with high body awareness and high levels of PC and had the lowest probability of being in the complete habituation group.

Ginzburg, K., Tsur, N., Karmin, C., Speizman, T., Tourgeman, R., & Defrin, R. (2015). Body awareness and pain habituation: the role of orientation towards somatic signals. *Journal of behavioral medicine*, *38*(6), 876-885.

Preliminary Data
(*n*=300 of chronic pain patients)



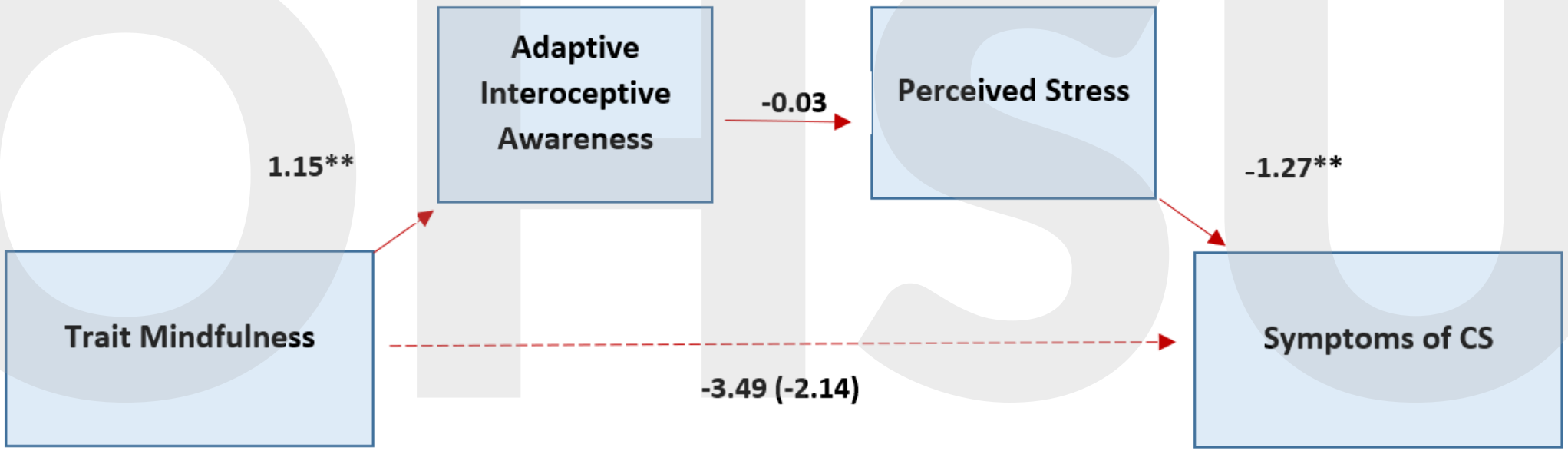
p < .001

Colgan, 2020

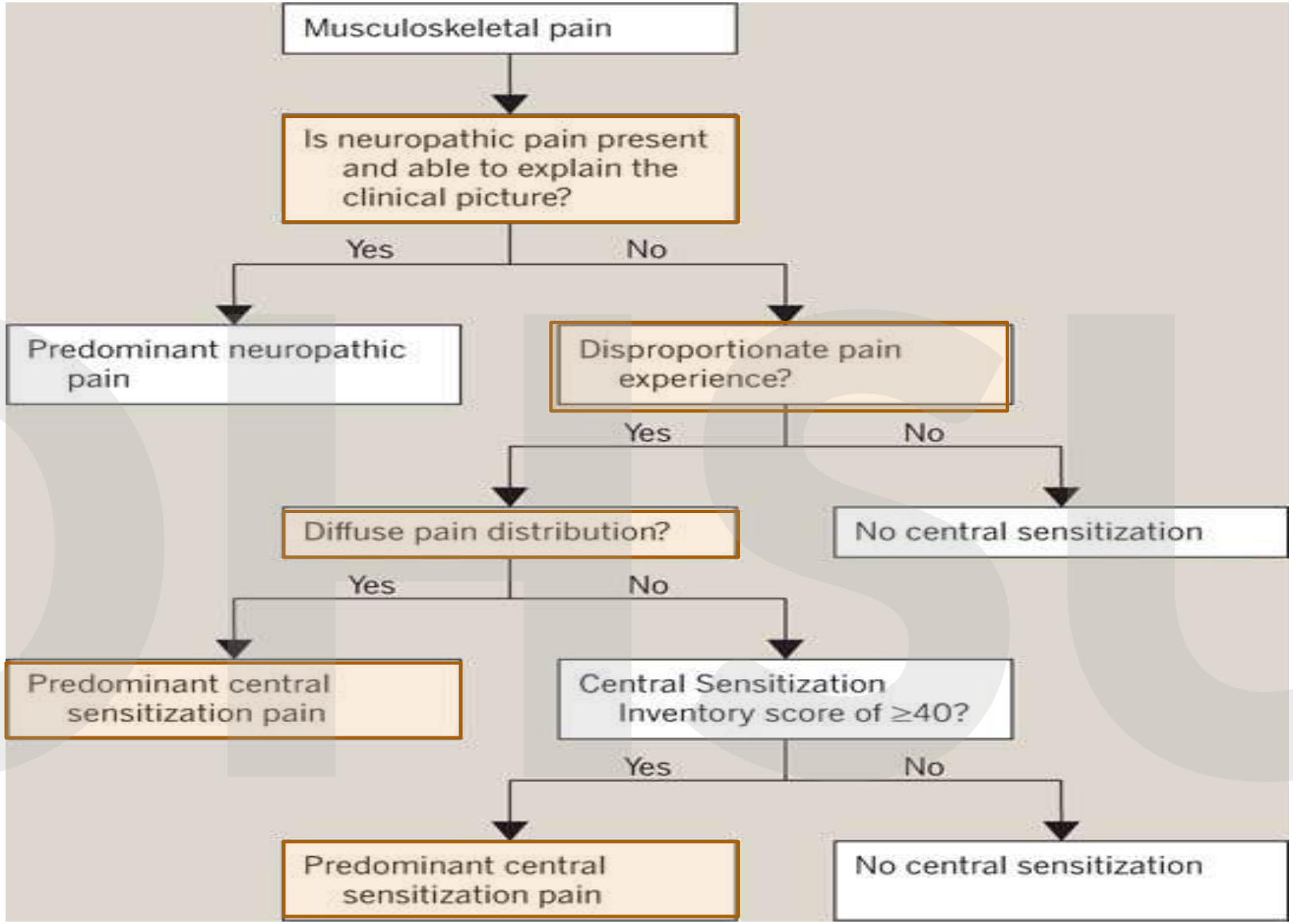
Colgan, 2020

Figure 2.

Path Analysis with Unstandardized Beta Coefficients.



5. Algorithm to identity patients with CS-related symptoms



Nijs, J., Goubert, D., & Ickmans, K. (2016). Recognition and treatment of central sensitization in chronic pain patients: not limited to specialized care. *Journal of Orthopaedic & Sports Physical Therapy*, *46*(12), 1024-1028.

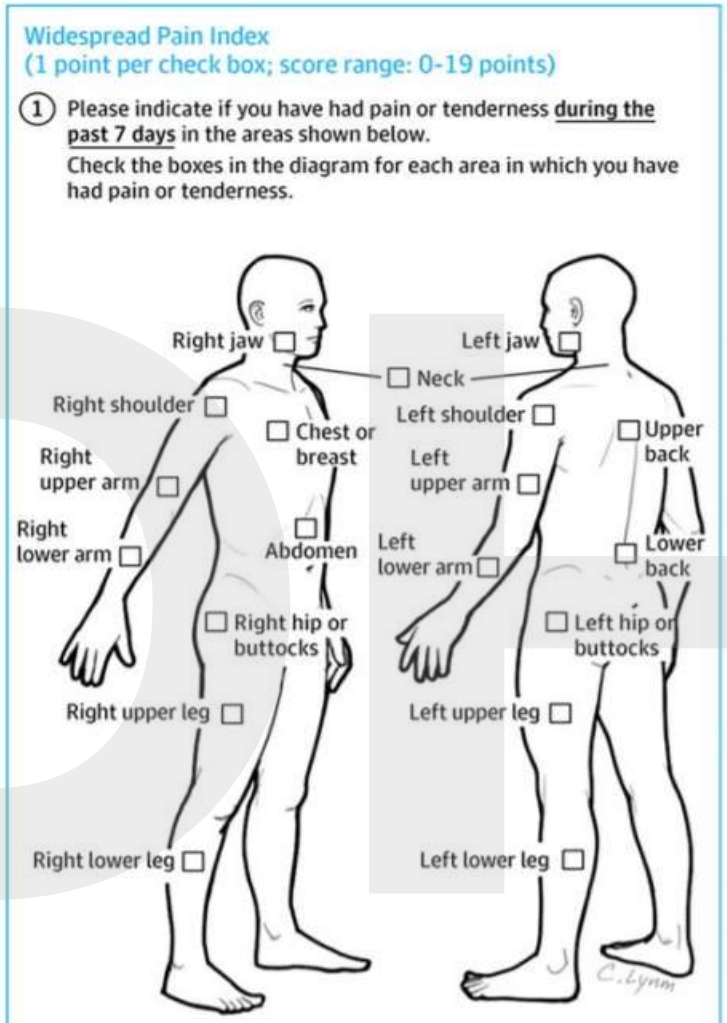


FIGURE 2 The 2011 Survey Criteria for Fibromyalgia (Wolfe et al., 2011) using the Michigan Body Map (Brummett, Bakshi et al., 2016)

CENTRAL SENSITIZATION INVENTORY: PART A

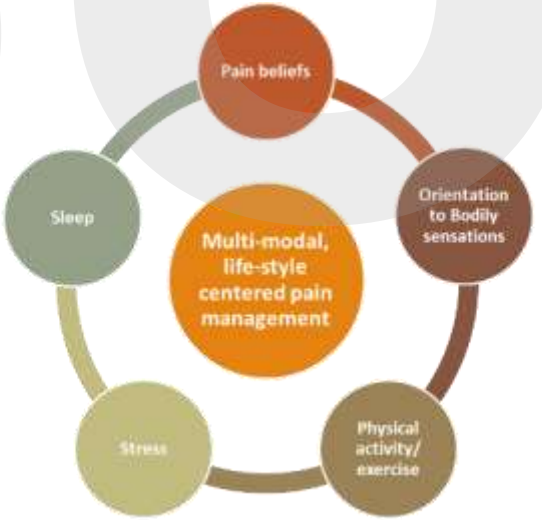
Name: _____ Date: _____

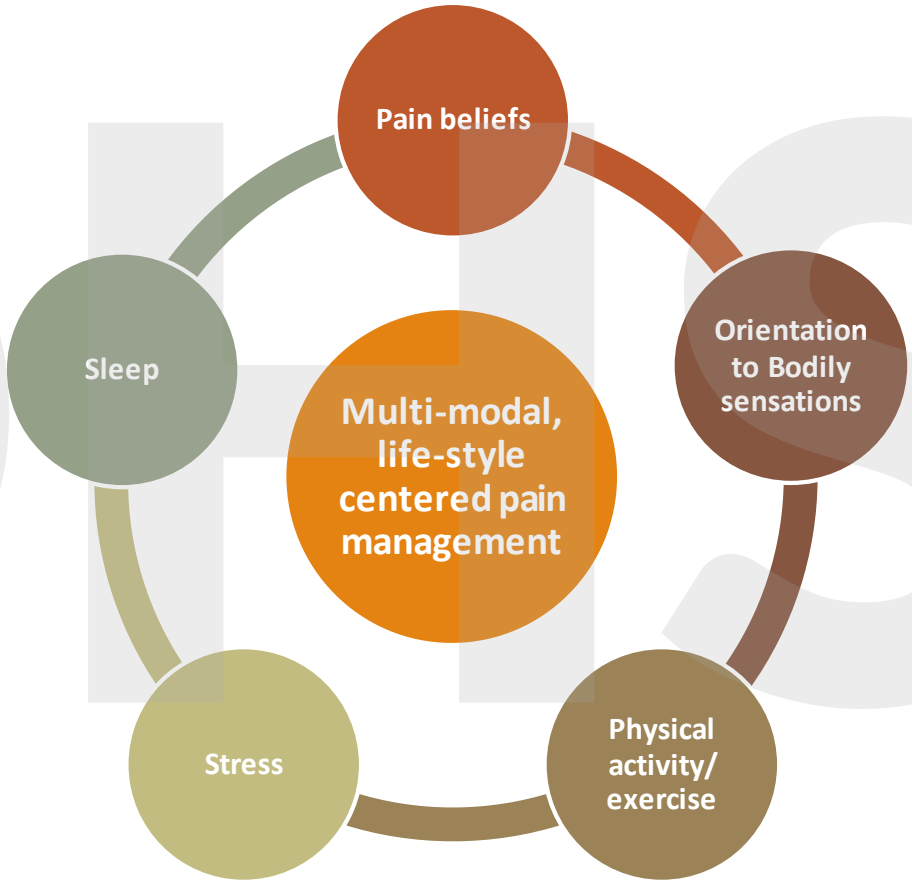
Please circle the best response to the right of each statement.

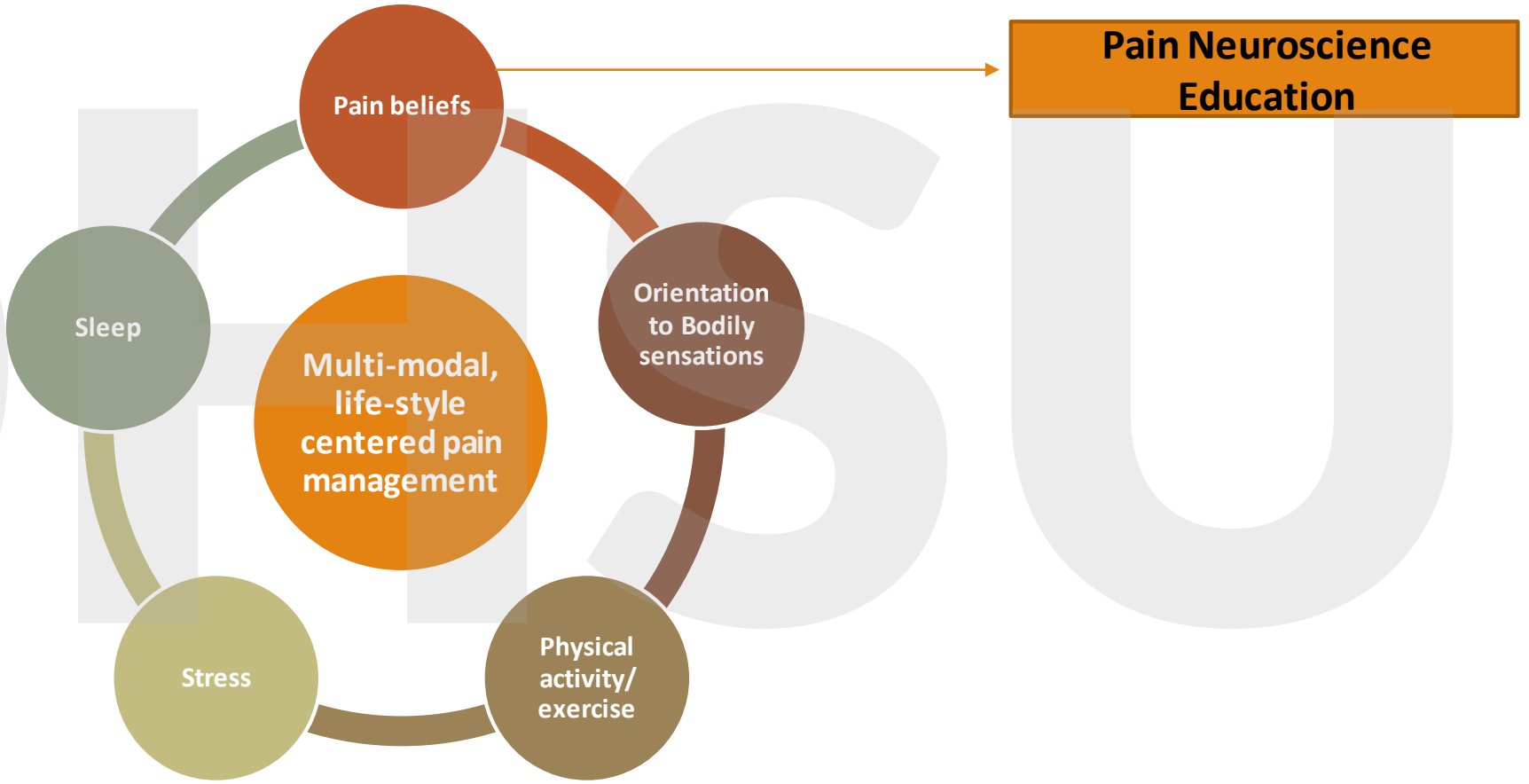
1	I feel tired and unrefreshed when I wake from sleeping.	Never	Rarely	Sometimes	Often	Always
2	My muscles feel stiff and achy.	Never	Rarely	Sometimes	Often	Always
3	I have anxiety attacks.	Never	Rarely	Sometimes	Often	Always
4	I grind or clench my teeth.	Never	Rarely	Sometimes	Often	Always
5	I have problems with diarrhea and/or constipation.	Never	Rarely	Sometimes	Often	Always
6	I need help in performing my daily activities.	Never	Rarely	Sometimes	Often	Always
7	I am sensitive to bright lights.	Never	Rarely	Sometimes	Often	Always
8	I get tired very easily when I am physically active.	Never	Rarely	Sometimes	Often	Always
9	I feel pain all over my body.	Never	Rarely	Sometimes	Often	Always
10	I have headaches.	Never	Rarely	Sometimes	Often	Always
11	I feel discomfort in my bladder and/or burning when I urinate.	Never	Rarely	Sometimes	Often	Always

6. Nonpharmacological Treatment Guidelines

- **Treat the biopsychosocial individual suffering from chronic pain.**[45]
- Multimodal treatment approach that targets sustaining factors.
- Systematic reviews suggest combining evidenced-based physical and psychological therapies may be more effective in reducing MSK than stand-alone interventions.[46-48]




Pain beliefs
Orientation to Bodily sensations
Physical activity/ exercise
Stress
Sleep
Multi-modal, life-style centered pain management


Pain beliefs
Pain Neuroscience Education
Sleep
Orientation to Bodily sensations
Multi-modal, life-style centered pain management
Stress
Physical activity/ exercise

Pain Neuroscience Education

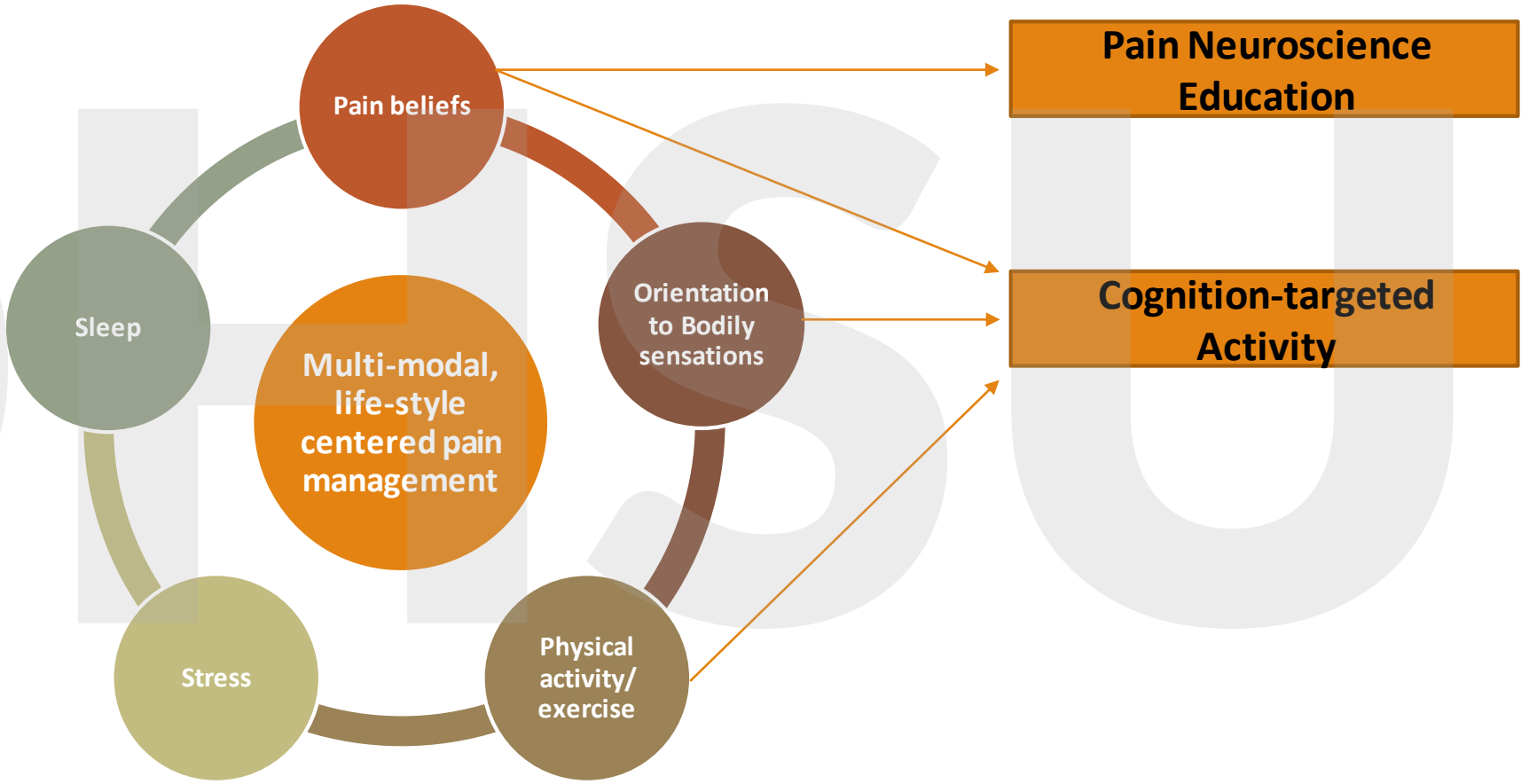
- **Adjunct to treatment**
- PNE focuses on scientific concepts that underlie the experience of pain, including neurophysiological, neurobiological, sociological, and physical components
- **Aims** [49]
  - 1) Decrease the threatening nature of pain
    increased patient understanding that the source of pain is the brain's appraisal of threat in response to bodily sensation, not tissue damage.

  2) Increase patients' awareness of the interaction between psychology and physiology
    providing information about the powerful influence of psychological processes that can *'turn up'* or *'turn down'* the pain experience.

  3) Underscores the adaptability, and therefore, trainability of the pain processing in CNS.

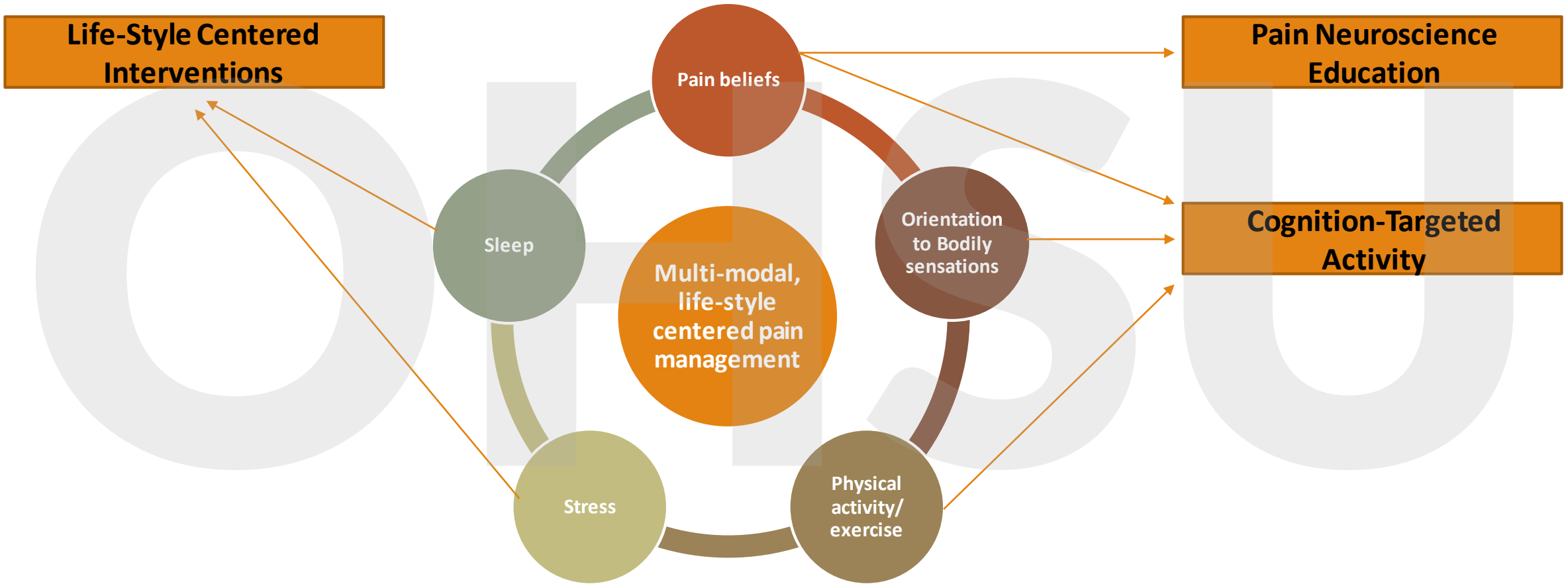
Pain Neuroscience Education

Combining PNE with a movement-based intervention has been associated with significant reductions in kinesiophobia, catastrophic thinking, pain-related disability, and healthcare utilization in individuals with chronic musculoskeletal pain.[50-52]


Pain beliefs
Sleep
Orientation to Bodily sensations
Multi-modal, life-style centered pain management
Stress
Physical activity/ exercise
Pain Neuroscience Education
Cognition-targeted Activity

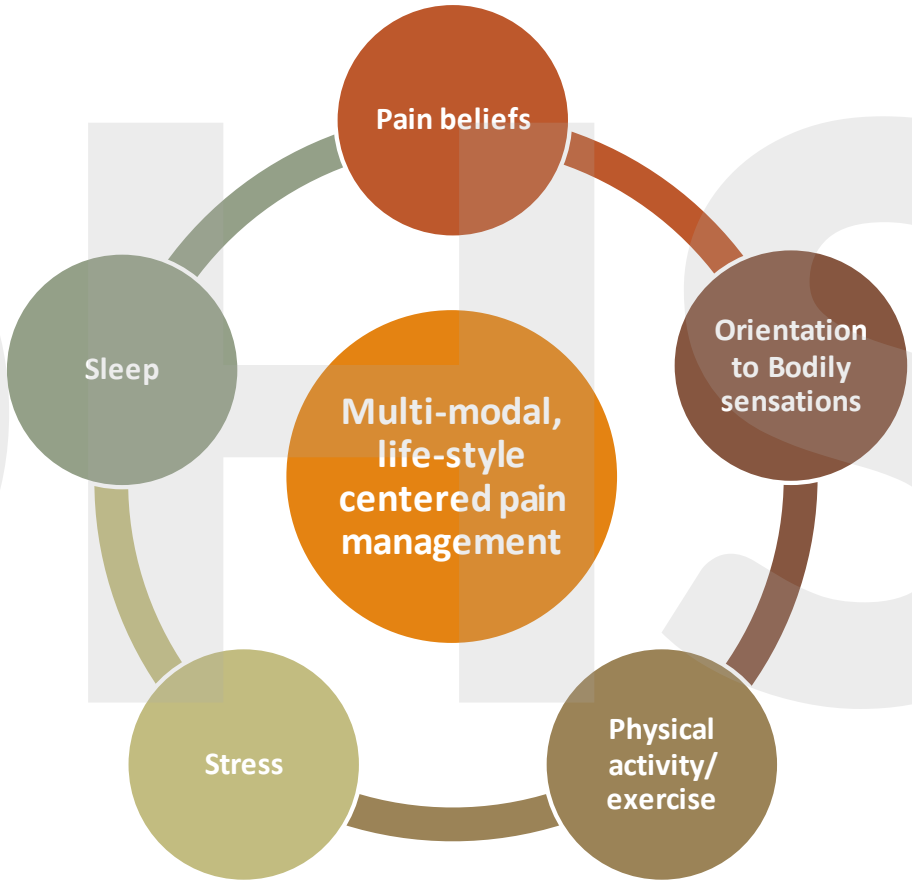
Pain Neuroscience Education + **Cognition-Targeted Activity**

- Graded activity/graded exercise therapy
- Graded exposure [53,54]


Life-Style Centered Interventions
Pain beliefs
Sleep
Multi-modal, life-style centered pain management
Orientation to Bodily sensations
Stress
Physical activity/ exercise
Pain Neuroscience Education
Cognition-Targeted Activity

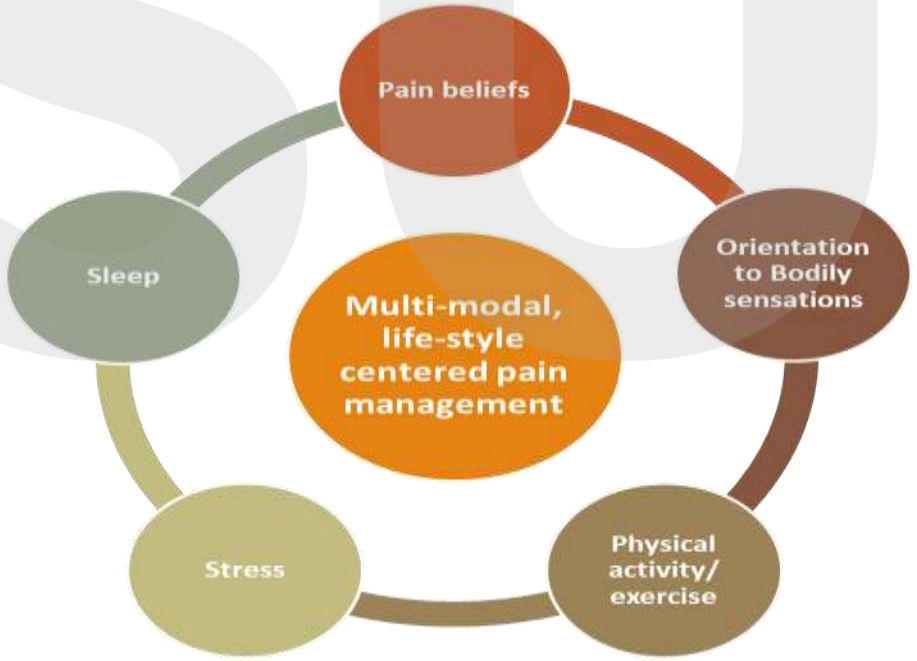
Pain Neuroscience Education + **Cognition-Targeted Activity** + **Lifestyle-Centered Interventions**

- CBT Insomnia[55, 56]
- Mindfulness-Based Stress Reduction[57-59]


Pain beliefs
Orientation to Bodily sensations
Physical activity/ exercise
Stress
Sleep
Multi-modal, life-style centered pain management

In Summary

- Accumulating evidence supports the clinical importance of CS in people with chronic pain.
- CS is thought to be driven by top-down cognitive processes and bottom-up physiological processes.
- Mediate treatment outcomes.
- Identify and Treat the biopsychosocial contributors to CS.



Thank you.

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