Pain neuroscience & chronic musculoskeletal pain: 
Recent developments

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Content overview: 4 questions

1. Why do some musculoskeletal pain patients develop central sensitization while others don’t?

2. For treatment purposes, does it matter whether a musculoskeletal pain patient has central sensitization or not?

3. How do we recognize central sensitization in patients with musculoskeletal pain?

4. How do we treat central sensitization in patients with musculoskeletal pain?
Long-term potentiation
Central Nervous System Mechanisms of Pain Modulation
Cognitive emotional sensitization

catastrophizing
kinesiophobia
somatization
stress
depression
Q1: Why do some musculoskeletal pain patients develop central sensitization while others don’t?

The role of psychological trauma

- Chronic non-specific low back pain (n=149)
  - Trauma exposure
    - Generalized hyperalgesia
  - No trauma exposure
    - Local hyperalgesia

Tesarz et al. Pain 2015
The role of physical trauma
chronic non-specific neck pain

whiplash

no whiplash exposure

generalized hyperalgesia

local hyperalgesia

Malflief et al. Pain Physician 2015
Van Oosterwijck et al. Eur J Pain 2013
Stone et al. Man Ther 2013

Dysfunctional endogenous analgesia in response to exercise
Cognitive-emotional factors, including maladaptive pain cognitions

Central sensitisation (ie, hypersensitivity of the nervous system)
Whiplash-associated disorders

Impaired cervical neuromuscular control

Post-traumatic stress
Dysfunctional stress response systems

Nijs & Ickmans The Lancet 2014;384(9938):109-111.
Stress & central sensitization

Stress → glutamate ↑ → CNS excitability ↑

GABA ↓ → serotonin ↓ → ↓ inhibition
Stress & central sensitization

- Glutamate $\uparrow$
- CNS excitability $\uparrow$
- GABA $\downarrow$
- Serotonin $\downarrow$
- Inhibition $\downarrow$

Chronic stress affects the brain

- Chronic stress
- Hippocampal atrophy
- Amygdala hypertrophy
- Prefrontal cortex atrophy
- Inhibition $\uparrow$
Brain changes in chronic pain

- hippocampal atrophy
- amygdala hypertrophy
- prefrontal cortex atrophy

~ structural brain abnormalities in chronic low back pain:
- gray matter↓ DLPFC
- gray matter↑ amygdala

Kregel et al. *Sem Arthr Rheum* 2015

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Treating the brain in chronic pain?

**CBT**: low level evidence
functional + structural prefrontal improvements
~ treatment related improvements

**Multidisciplinary treatment**: low level evidence
decreased amygdala connectivity + PFC gray matter↑

**Exercise therapy**: preliminary evidence
functional connectivity improvements

Kregel et al. submitted.
Stress & sleep interconnected

stress $\uparrow$  sleep $\downarrow$

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Sleep deprivation triggers brain inflammation


Q2: For treatment purposes, does it matter whether a musculoskeletal pain patient has central sensitization or not?

Central sensitization predicts pain following surgery

Shoulder impingement syndrome
Total knee replacement
Thoracotomy

Baert et al. Osteoarthritis Cartilige 2016
Yarnistky et al. Pain 2008
Auto targeted neurostimulation for chronic low back pain
A fourfold-blind RCT


Central sensitization mediates treatment effect in chronic low back pain

placebo group slightly better

Time x Group x Central Sensitization interaction:
- walking ability
- disability

Central sensitization of clinical importance in chronic low back pain (n=38)

Central sensitization ~ pain catastrophizing
~ less stairs / minute
~ more pain
~ poorer functioning
~ maladaptive pain perceptions
~ fear of movement

Huysmans et al. submitted

Q2: For treatment purposes, it does matter whether a musculoskeletal pain patient has central sensitization.
Q3: How do we recognize central sensitization in patients with musculoskeletal pain?

Applying modern pain neuroscience in clinical practice: Criteria for the classification of central sensitization pain

Pain Physician 2014

Low back pain: Pain Physician 2015

Post-cancer pain: Acta Oncologica 2016
Low Back Pain

Disproportionate low back pain experience?

YES

Diffuse pain distribution?

YES

Central Sensitization Inventory ≥ 40?

YES

Central Sensitization Low Back Pain

NO

no Central Sensitization

NO

no Central Sensitization

NO

Central Sensitization Low Back Pain

DIFFUSE PAIN DISTRIBUTION

NO

no Central Sensitization

CENTRAL SENSITIZATION INVENTORY ≥ 40?

yes

CENTRAL SENSITIZATION LOW BACK PAIN

NO

no Central Sensitization

nociceptive pain

neuropathic pain

central sensitization
Q4: How do we treat central sensitization in patients with musculoskeletal pain?
Pain neuroscience education activates endogenous analgesia

Adapting manual therapy to central sensitization

Hands-on treatment:
• Following pain neuroscience education
• Explain brain effects
• Do not ↑ pain anticipation
• Do not rely on pain self-report


Lluch et al. Manual Therapy 2015
Exercise is (pain)medicine!

Pharmacological pain treatment targets one of the following:
- neurotransmitter
- receptor
- ion channel
- cell type

Exercise therapy effects all in one!

Exercise therapy $\rightarrow$ central sensitization↓

RCT examining Modern Neuroscience Approach to chronic spinal pain

3 sessions pain neuroscience education
15 sessions cognition-targeted exercise therapy
= 12 wks treatment

vs. evidence-based exercise therapy

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 Preliminary findings RCT (n=98)  
Malfliet, Kregel, et al.

pain catastrophizing ↓  
fear ↓  
ilness perceptions ↑  

~ pain↓ + daily functioning↑  

central sensitization↓  

Take home messages

Central sensitization = inhibition↓ + facilitation↑ + pain matrix↑  

Not synonym for chronic pain  

Treatment should account for central sensitization:  
- Pain neuroscience education  
- Exercise therapy  
- Stress management  
- Sleep interventions
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