Central Hypersensitivity in Whiplash

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Peripheral injury in animal models

- Regional sensitization of spinal cord neurones
  - Regional neuronal hyperexcitability
    - Woolf, Nature 1983

- Widespread sensitization of spinal cord and brain
  - Generalized neuronal hyperexcitability
    - Samad et al, Nature 2001

Topics

Central Hypersensitivity:

- Assessment methods
- Evidence
- Clinical relevance
- Incidence
- Prognostic value
- Perspectives
Measurement of pain sensitivity - Psychophysical

**Input**
- Mechanical, thermal, electrical, chemical, etc.

**Response**
- Pain thresholds
  - Detection, tolerance
- Stimulus response
  - VAS, NRS
- Tolerance time
- Area of hyperalgesia

Measurement of pain sensitivity - Electrophysiological

**Input**
- Mechanical, thermal, electrical, chemical, etc.

**Response**
- Lower limb reflex
  - Single stimulus
  - Repeated stimulus
  - Receptive fields
- EEG
  - Latency, amplitude
  - Cortical mapping

Courtesy L. Arendt-Nielsen
Why to measure pain sensitivity?

- Provide patient with a model for pain
- Estimate the prognosis?
- Guide decision-making for interventions?
- Indications for centrally-modulating treatments?

Evidence for central hypersensitivity

Controls Whiplash

Koelbaek et al, Pain 1999
Controls  Whiplash

Koelbaek et al, Pain 1999

Temporal Summation

Courtesy Lars Arendt-Nielsen
Measurements at the Neck

Curatolo et al, Clin J Pain 2001

Measurements at the Leg

Curatolo et al, Clin J Pain 2001
Objective Evidence for Central Hypersensitivity

*Banic et al, Pain 2004*

Result

W: Whiplash - C: Control  
F: Fibromyalgia - C: Control

*Banic et al, Pain 2004*
Pathophysiology: Conclusions

Whipash patients display:
- Enlarged pain areas and facilitated temporal summation:
  - after cutaneous and muscular stimulation
  - at neck and lower limb
- Widespread spinal cord hyperexcitability

The presence of major lesions is not an essential condition for the induction of pain and hypersensitivity

Hypersensitivity may depend on the presence of a peripheral nociceptive input, at least for some conditions
Clinical consequences of central hypersensitivity

• Pain after minimal ongoing nociceptive input and after innocuous stimulation
  ⇒ Amplification of pain
  ⇒ Activity- and load-dependent pain → Disability

• Enlarged pain areas
  ⇒ Tendency to widespread pain
  ⇒ Difficult identification of source of pain → Difficult target of treatment

Is pain sensitivity affected by psychological factors?

• No influence of psychological factors on spinal cord excitability in painfree subjects and whiplash patients

• No influence of depression, anxiety and catastrophizing on pressure, thermal and electrical pain sensitivity in painfree subjects
  Neziri et al, EJP in press

• Modest and inconsistent correlations of psychological factors with pain thresholds in patients

Psychological factors are not the main determinants of sensory hypersensitivity
**Prevalence of widespread hypersensitivity**

![Bar chart showing prevalence of widespread hypersensitivity among females and males.](chart)

Schliessbach et al, unpublished

**Prognostic value of central hypersensitivity**

**Spinal cord hyperexcitability**

- Courtesy L. Arendt-Nielsen

**Sensory hyperexcitability**

- Pressure
- Cold

Groups based on NDI at 6 months:

1. Recovered
2. Mild symptoms
3. Moderate/severe symptoms
4. Healthy controls

Sterling et al, Pain 2010
Spinal cord hyperexcitability

All patient groups had hyperexcitability at 3 weeks

Persisted only for moderate-severe symptoms

Sterling et al, Pain 2010

Sensory hypersensitivity to cold

Only patient with bad outcome had hypersensitivity at 3 weeks

Remained unchanged

Sterling et al, Pain 2010
Implications

• Spinal cord hypersensitivity may reflect the clinical course of pain
  – May be strongly related to an ongoing peripheral nociceptive input

• Generalized sensory hypersensitivity may have a negative prognostic value
  – Induction of plastic changes → Higher likelihood of poor outcome

Take-home messages

Central hypersensitivity:
  – Is likely clinically relevant
  – Can explain part of the discrepancy between lesion and symptoms
  – Is prevalent in chronic pain patients
  – May have negative prognostic value

Central hypersensitivity can be measured individually
  – Main current aim: to better explain patient’s symptoms
  – Possibly also to guide therapeutic decisions
Research Agenda

• Development and validation of diagnostic tools for clinical use

• Investigation of prognostic value

• Linking altered pain modulation with treatments

• Development of specific and clinically applicable therapies for central hypersensitivity