Smärtforskning - nyheter om antimateria, opioider och fysioterapi

Smärta-inte längre en osynlig sjukdom

Measuring Peripheral Tissue Activation in Patients with Chronic Pain

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Acute nociceptive pain

- Postoperative pain
- Pain after trauma

Objective findings

Easy to understand

Easy to be understood
Chronic pain

No objective findings

Not easy to understand

Not easy to be understood..
Epidemiology of pain

20 % of the population suffer from some degree of chronic pain (Breivik et al. 2008)

Chronic Pain = a wide spread population disease (WHO 2014)

Most common reason to seek health care (Finnish National Institute for Health and Welfare, (THL,) 2012)

Most common reason for sick leave after psychiatric diagnoses (RFV 2014)

And it costs the society at least $635 billion per year (USA). In Sweden 88 billion SKr/year (SBU 2006)
Living with Chronic Pain:

- Low Quality of life
- Exhausted and depressed
- Increased divorce rate (Andersen TE, 2015)
- Increased mortality (Sjögren P et al 2015)

In spite of these massive effects of chronic pain for the individual and for society, **USUALLY NO SIGNS OF ONGOING PATHOLOGY IN THE PARTS OF THE BODY WHERE IT HURTS!**
PAIN - the invisible disease
CT and MRI usually "normal".
No objective findings.

Common area of pain resulting from whiplash
"Doctor, I have so much pain!"  
"Can you prove that"?  

Drawing by Ragnar Levi/Robert Nyberg
Can we find objective indications of pain generating processes, in the parts of the body where the patient feels the chronic pain?
Kan vi "se" tecken på smärta och specifika smärtmekanismer med PET?

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helkropps PET-CT, PET-centrum, Uppsala
PET scanner – principle:
A positron-emitting radionuclide tracer is connected to a biologically active molecule and administered to a patient.
\[^{11}C\]-N-Methyl-N-propargyl-(S) –amphetamine

**Deprenyl** accumulates in activated astrocytes in CNS as a sign of neuroinflammation -MAO A & B binding

**D-Deprenyl** is a candidate marker for inflammatory processes in peripheral tissues

Exact binding mechanism to inflammatory tissue is not fully described.

Elevated [11C]-D-Deprenyl Uptake in Patients with Chronic Whiplash Associated Disorder Suggests Persistent Musculoskeletal Inflammation.

D-Deprenyl uptake in a representative healthy control (n=14), and a WAD patient (n=22) with chronic pain 3 yrs after injury.

Uptake seen close to the spinous process of vertebra C2, where the pain is located.

PET scan showing a patient with pain in left foot due to ankle sprain.
- CT scan shows no detectable pathology
- The painful sites are the same as sites for increased D-Deprenyl uptake.
- The uptake of D-Deprenyl follows the presence of pain over time.

8 patients PET scanned at 3 different time points
Chronic pain due to Tennis elbow

PET image of NK1 receptor radioligand [11C]GR205171 in subject C (out of ten subjects in total).

Visualizing a SP depending neurogenic inflammation?

http://www.plosone.org/article/info:doi/10.1371/journal.pone.0075859
New perspectives:
Visualization of pain generating processes in the body:

PET adds something to CT/MRI

**For the doctor:** Better understanding of the pain pathophysiology-
An objective diagnostic finding

**For the patient:** A support of the patient’s self report

**For the scientist:** A re-focus upon the peripheral signalling in chronic pain - as a ”driver” of central sensitisation

Taking us closer to ”Precision Medicine”

”Chronic Pain- No longer an invisible disease”

SFAI 2015
Search for D-deprenyl binding sites in inflamed tissue

- Screening 160 G-protein coupled receptors: no hit

- Enzyme Profiling Screen® (n=80): Three hits
  - MAO-B 99% inhibition by DDE
  - MAO-A 55% inhibition by DDE
  - ACE 70% inhibition by DDE
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<th>MAO - A</th>
<th>Protein Localization (score)</th>
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D-Deprenyl binding in PET scans in pain patients

Swedish Protein Atlas 2014
-Doctor, I have so much pain in my right foot..

-Can you prove that?

-YES, I CAN SEE THAT SOMETHING IS WRONG THERE!

Drawing by Ragnar Levi/Robert Nyberg