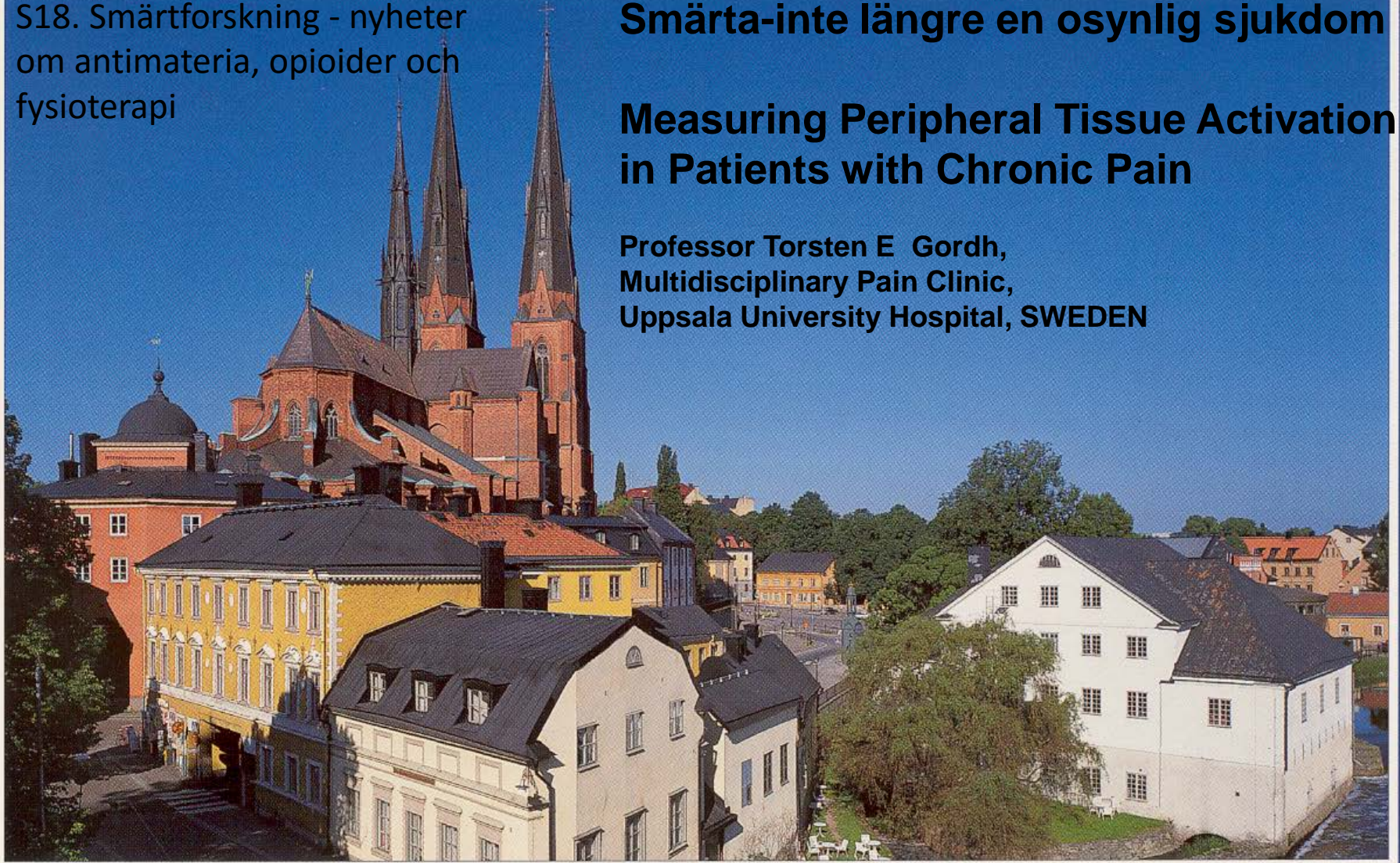


S18. Smärtforskning - nyheter om antimateria, opioider och fysioterapi

Smärta-inte längre en osynlig sjukdom

Measuring Peripheral Tissue Activation in Patients with Chronic Pain

Professor Torsten E Gordh,
Multidisciplinary Pain Clinic,
Uppsala University Hospital, SWEDEN



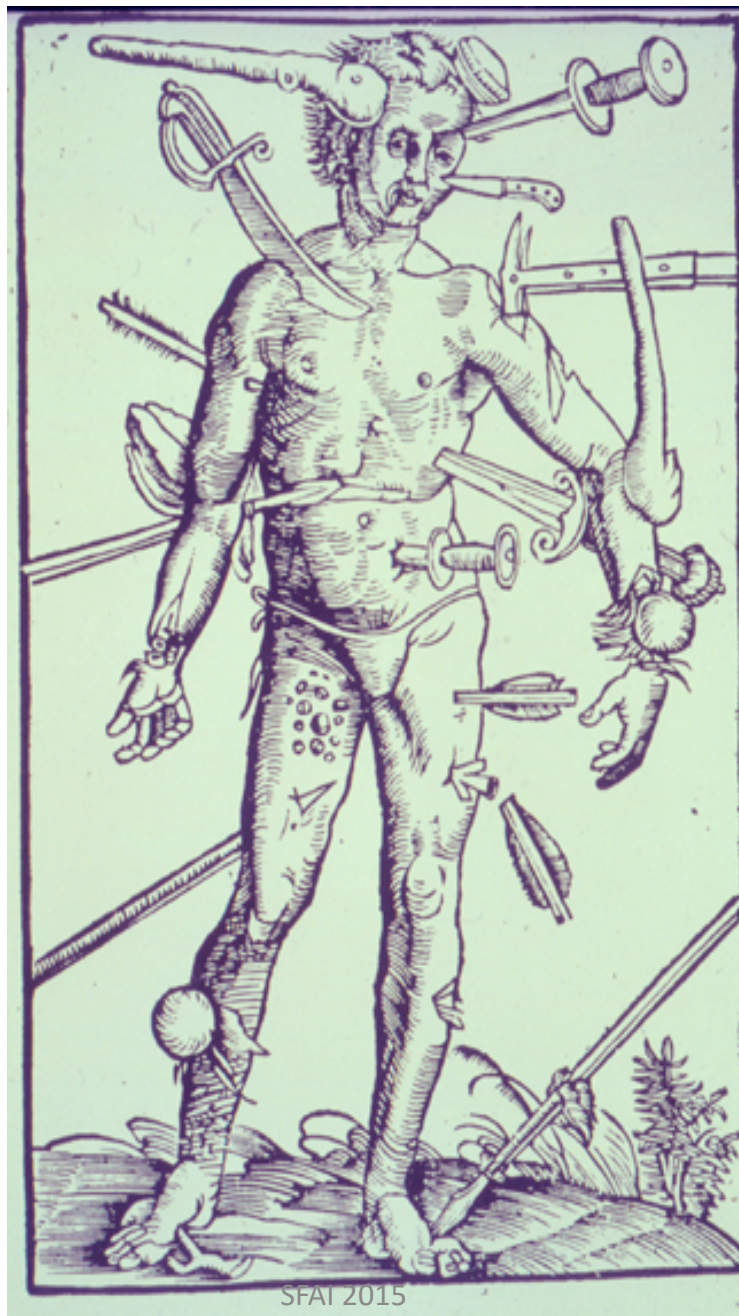
Acute nociceptive pain

- Postoperative pain
- Pain after trauma

Objective findings

Easy to understand

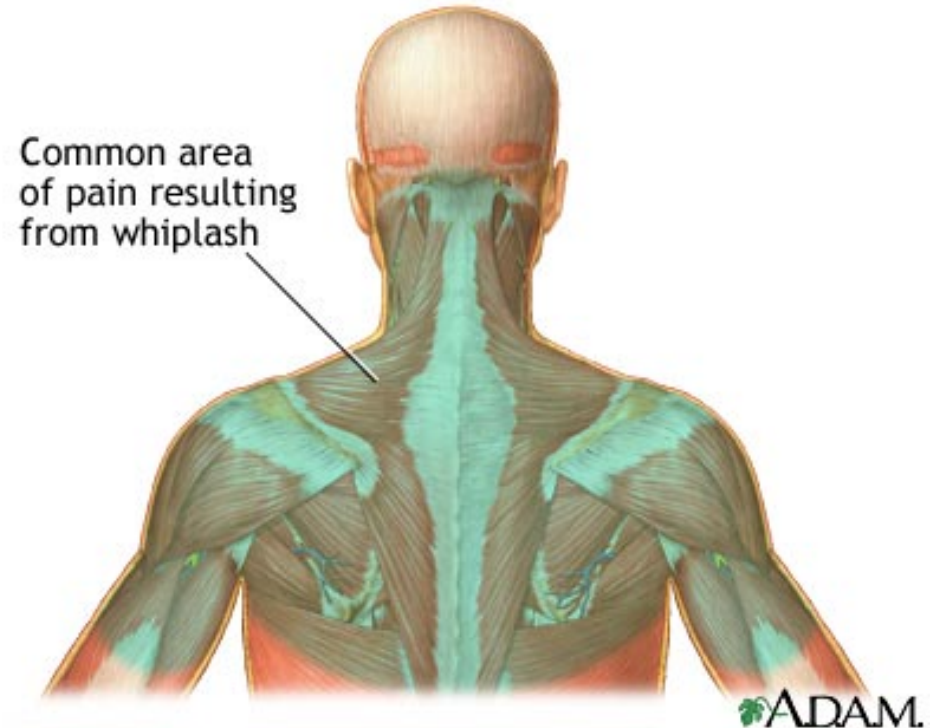
Easy to be understood



Feldtbuch der Wundatzney
von Gersdroff 1517



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 PATHOLGY IN THE PARTS OF THE BODY WHERE IT HURTS!



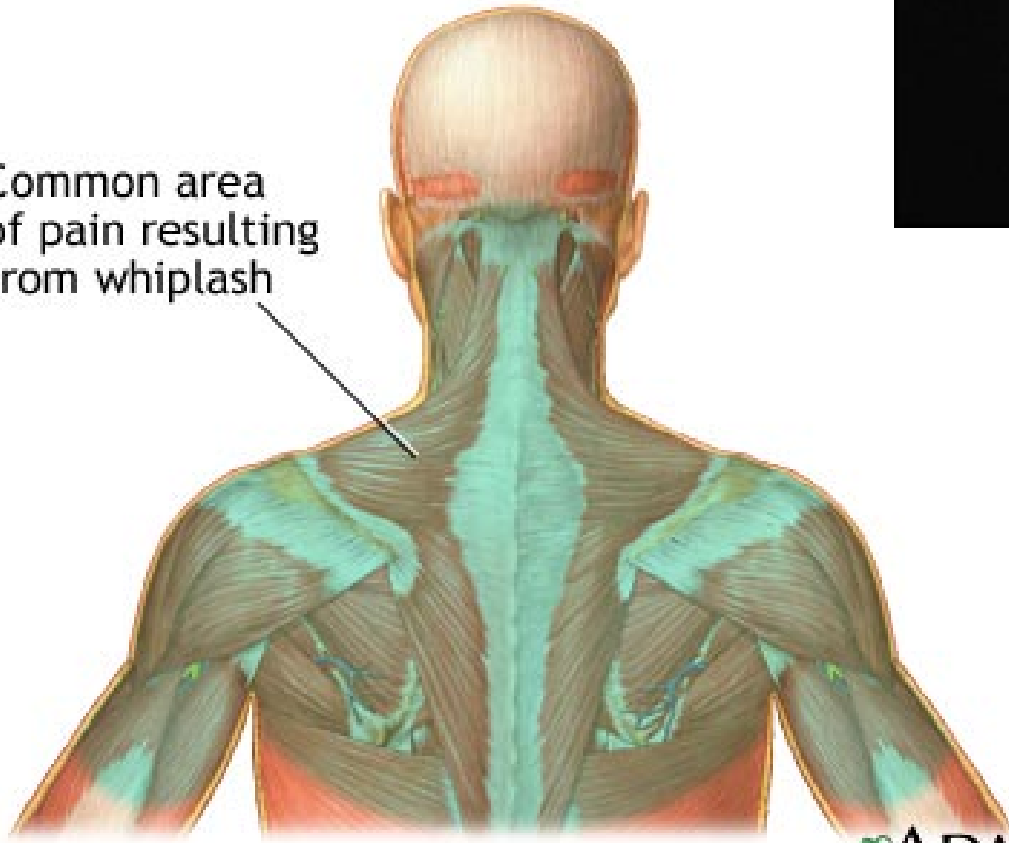
PAIN - the invisible disease

CT and MRI usually "normal".

No objective findings.

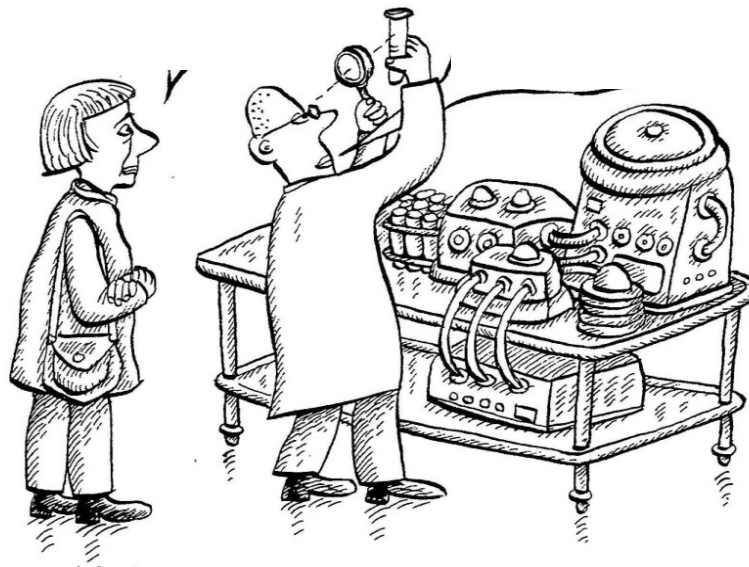


Common area
of pain resulting
from whiplash



ADAM.





-“Doctor, I have so much pain!”

-“Can you prove that”?



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?



Clas Linnman
institutionen för
psykologi

Mats Fredriksson

Jens Sörensen

Torsten Gordh

Mikko Aarnio

Bengt Långström

L Appel

Henry Engler

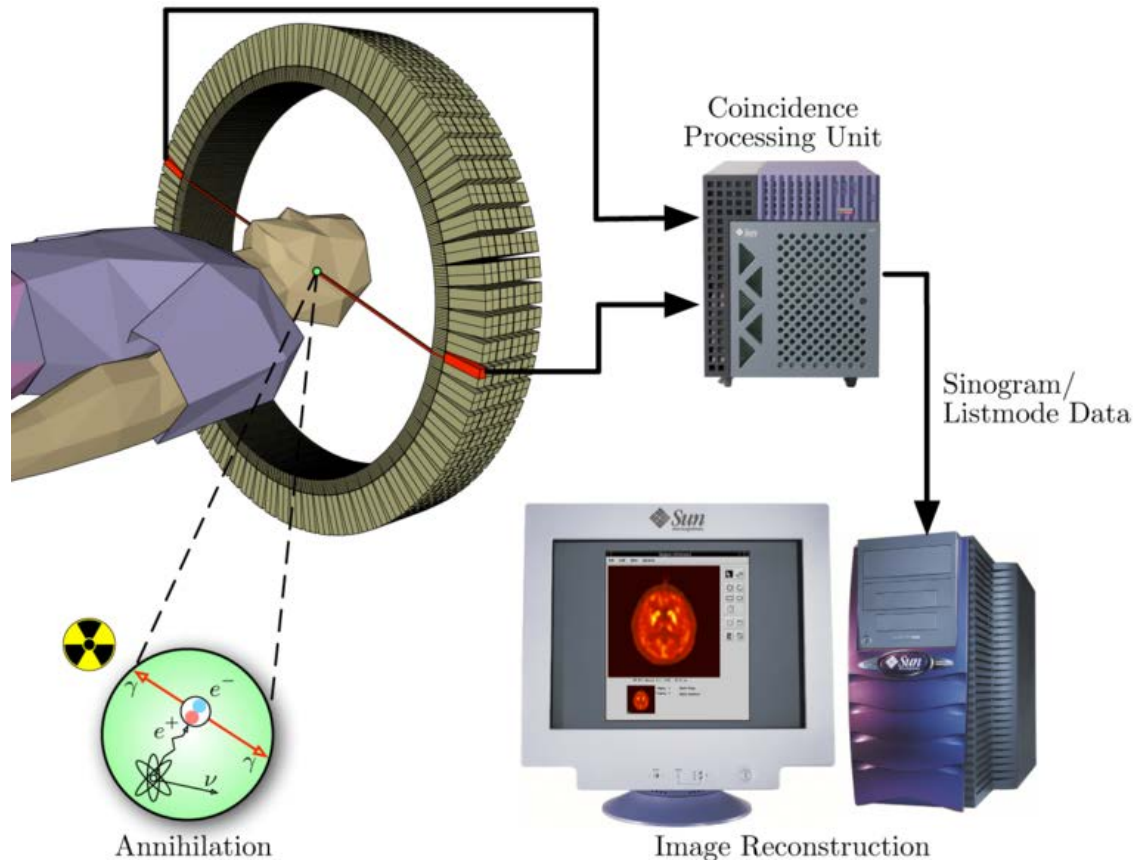
Anne Söderlund

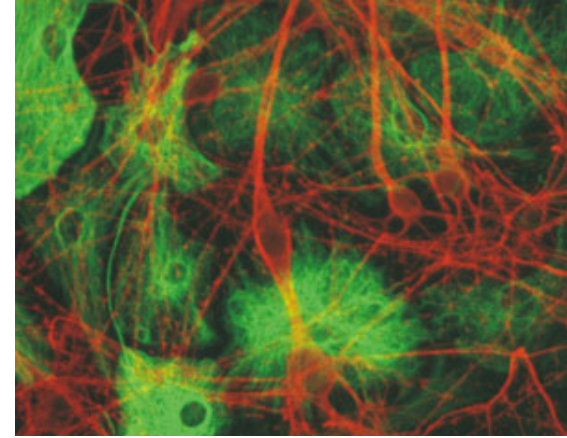
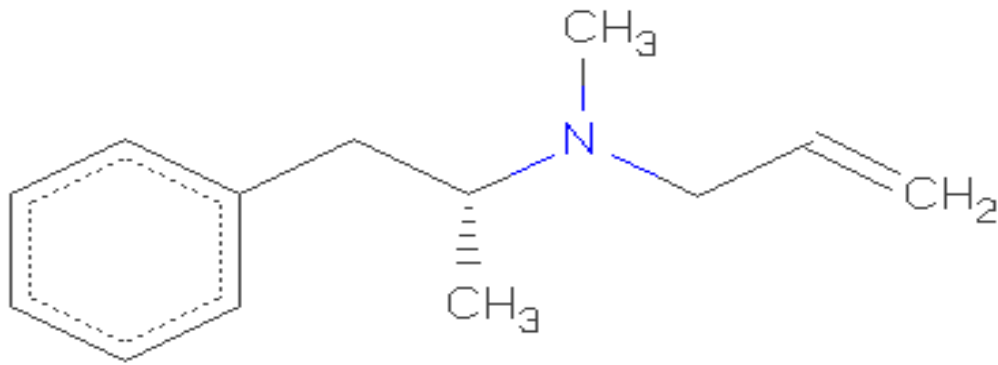
Annika Bring

m. fl

PET scanner – principle:

A positron-emitting radionuclide tracer is connected to a biologically active molecule and administered to a patient





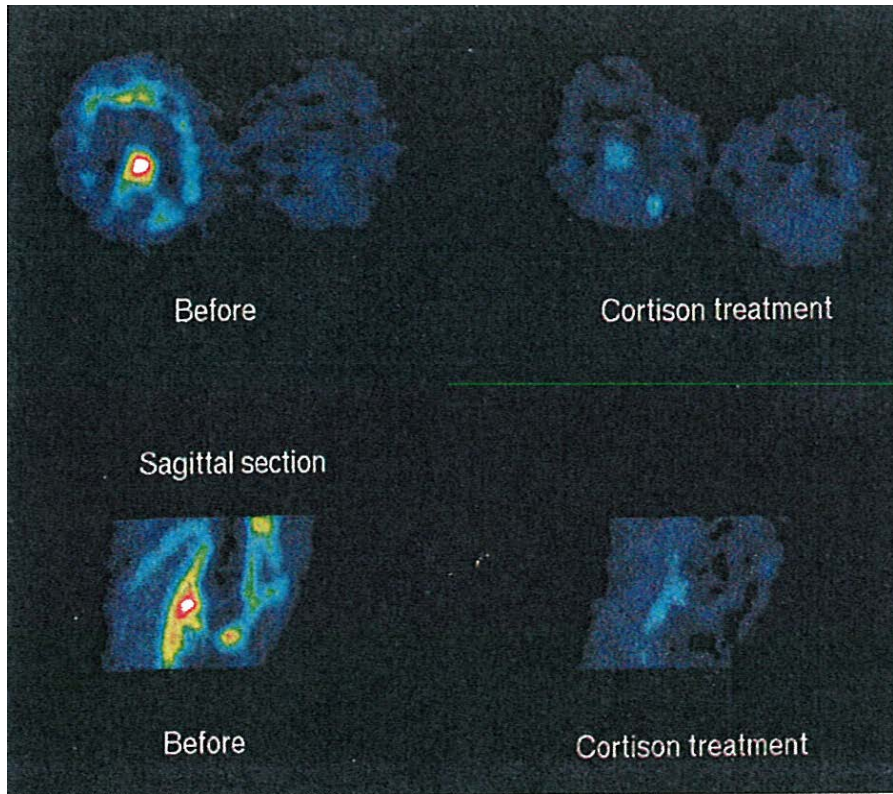
[¹¹C]-N-Methyl-N-propargyl-(S) –amphetamine

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.

D-deprenyl och reumatoid artrit



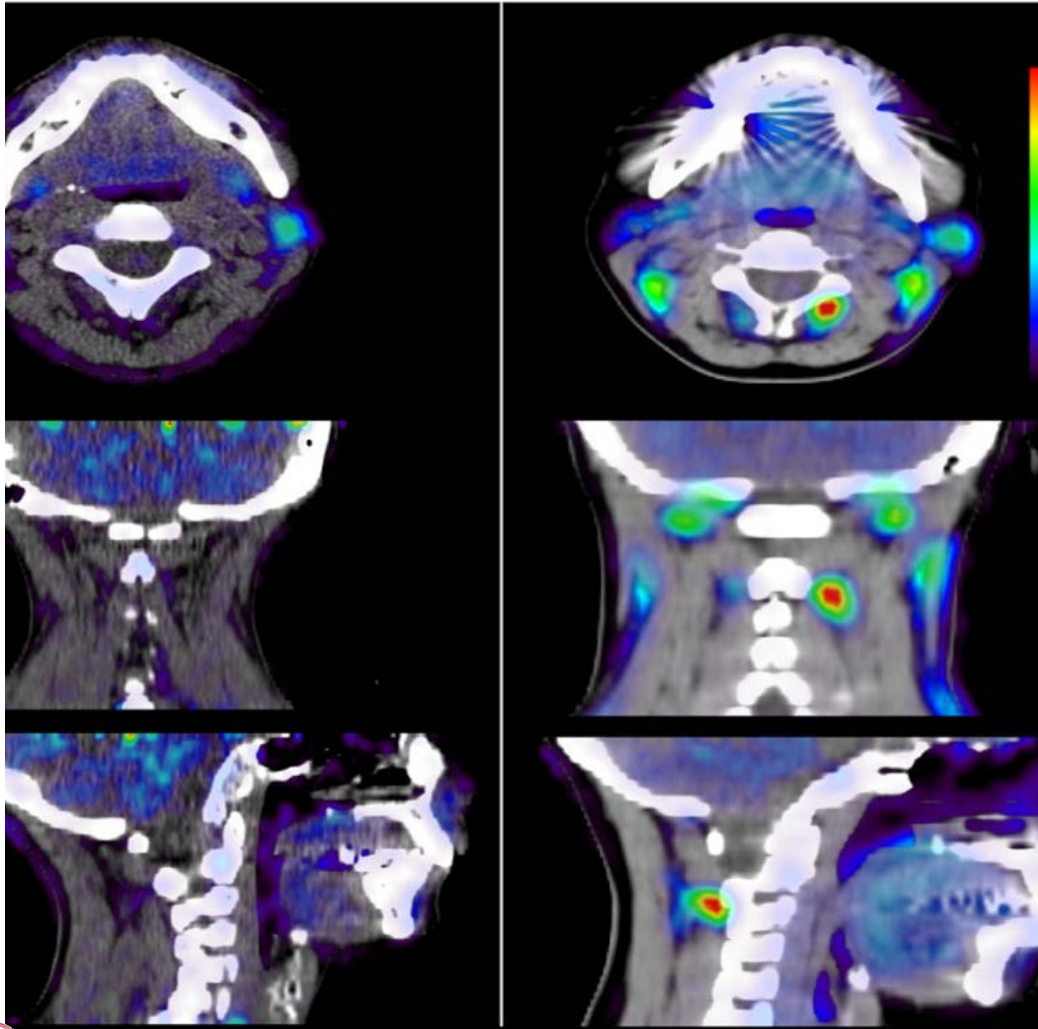
Arbeten av Mats Bergström från cirka 1985

[Positron emission tomography with \$^{11}\text{C}\$ -D-deprenyl in patients with rheumatoid arthritis. Evaluation of knee joint inflammation before and after intra-articular glucocorticoid treatment.](#)

Danfors T, Bergström M, Feltelius N, Ahlström H, Westerberg G, Långström B.
Scand J Rheumatol. 1997

Fig. 1. PET with ^{11}C -D-deprenyl images of RA/patient MW before and after treatment with intraarticular injection of corticosteroids. Upper images cross section images over the knees. Lower images reformatted sagittal midline images of the treated knee.

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.

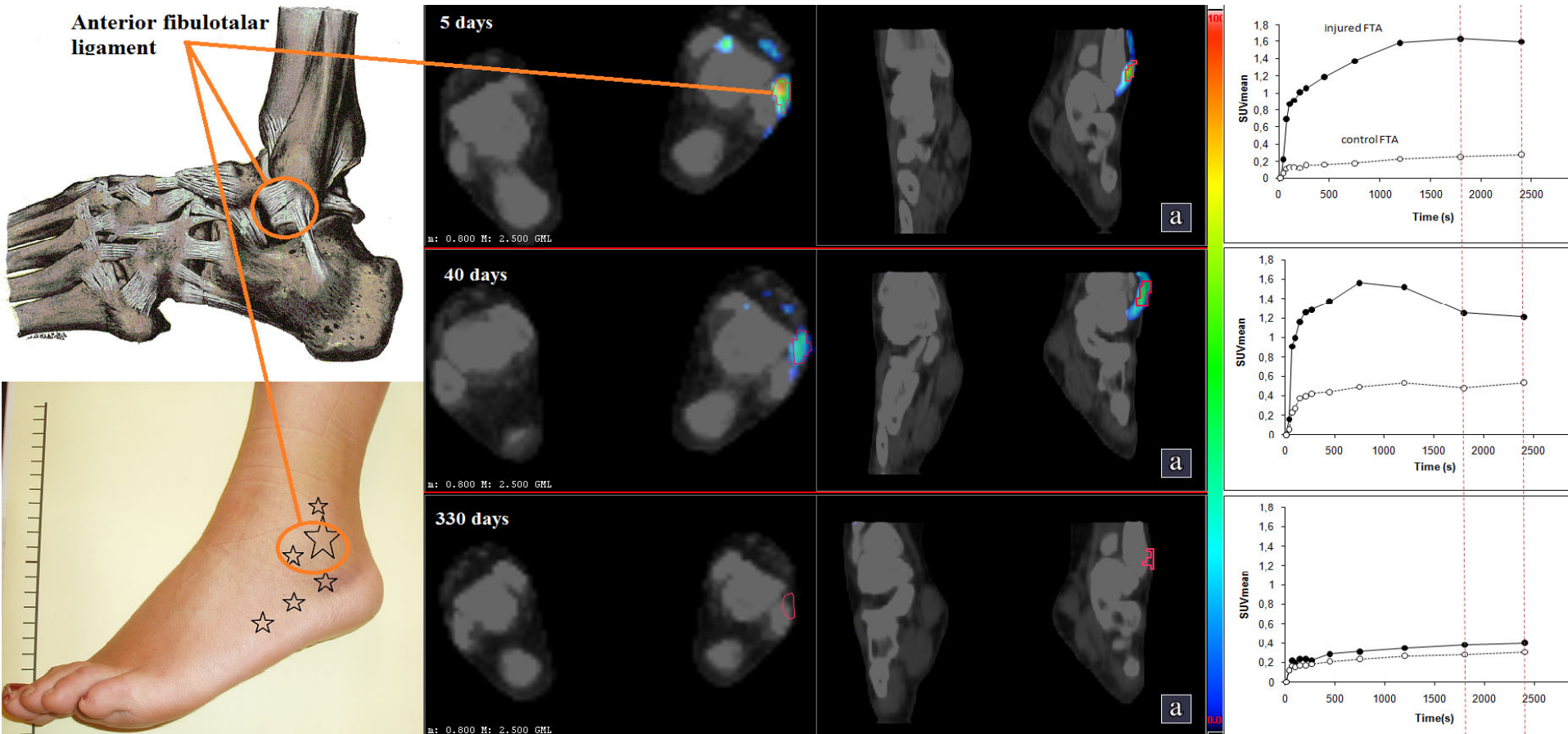
Uptake seen close to the spinous process of vertebra C2, where the pain is located.

Linnman et al. PLoS One 2011



PET scan showing a patient with pain in left foot due to ankle sprain.

- CT scan show 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.



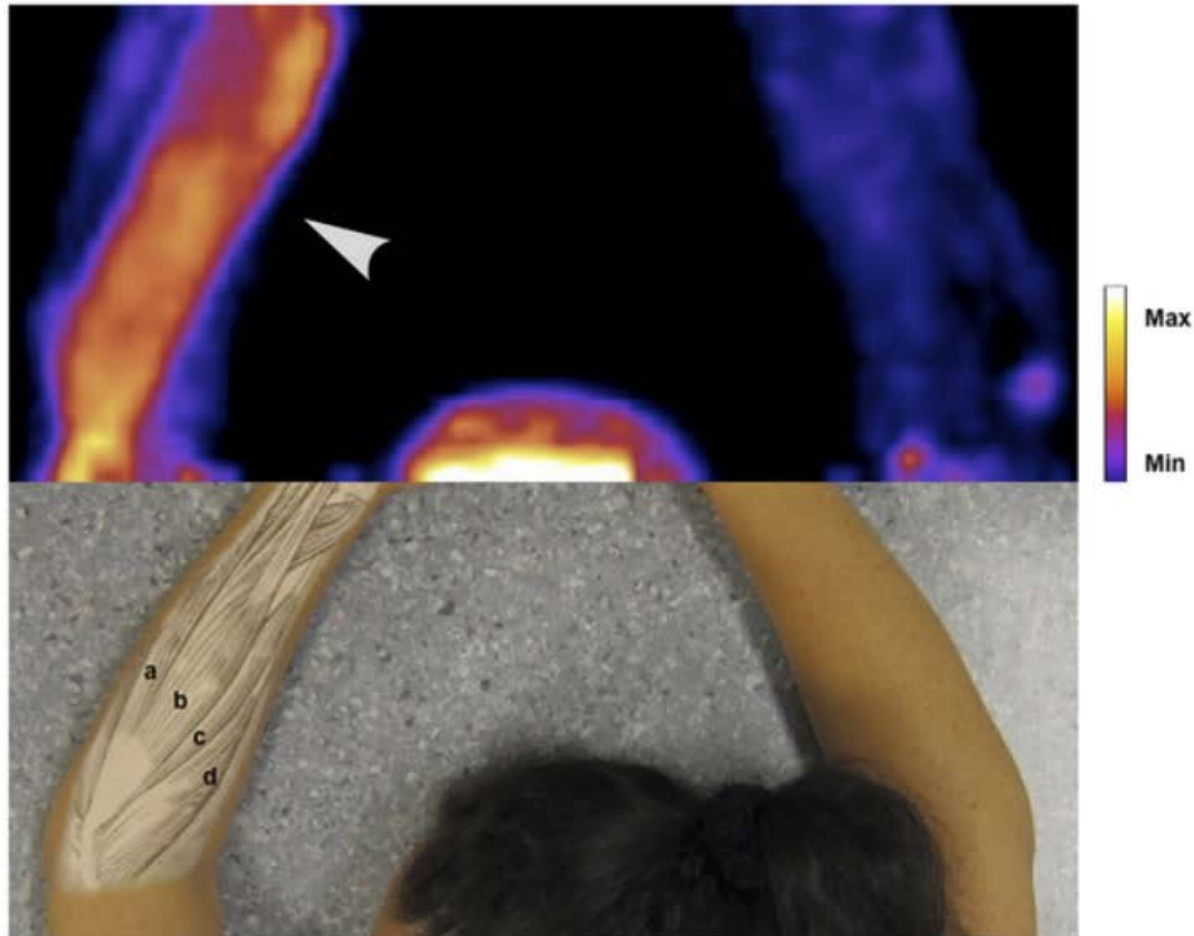
8 patients PET scanned at 3 different time points

SIAI 2015

Gordh T et al. 2015, work in progress

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?

Peterson M, Svärdsudd K, Appel L, Engler H, et al. (2013) PET-Scan Shows Peripherally Increased Neurokinin 1 Receptor Availability in Chronic Tennis Elbow: Visualizing Neurogenic Inflammation?. PLoS ONE 8(10): e75859. doi:10.1371/journal.pone.0075859
<http://www.plosone.org/article/info:doi/10.1371/journal.pone.0075859>



New perspectives:

Visualization of pain generating processes in the body:

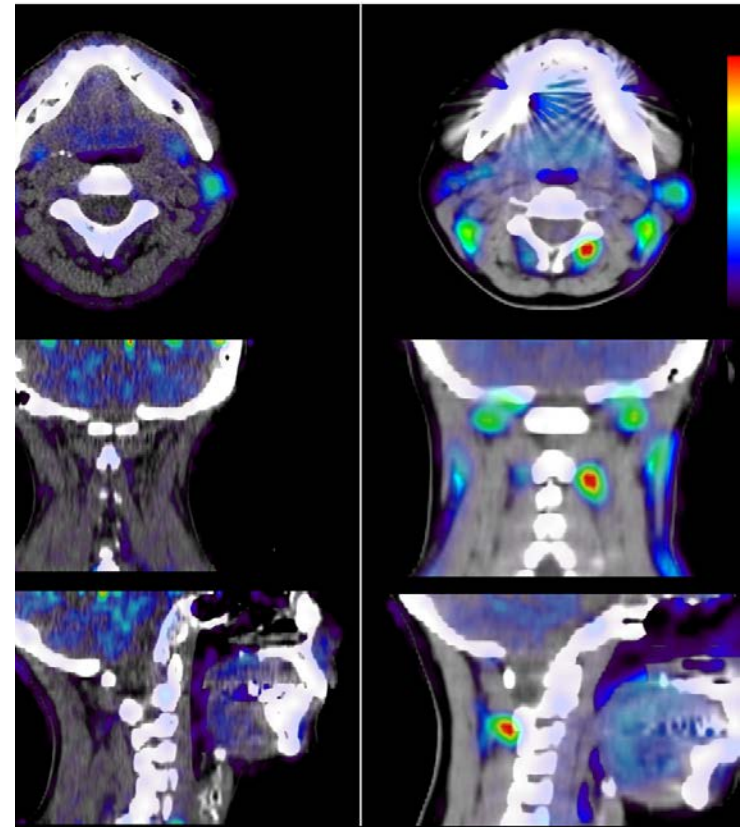
PET adds something to CT/MRI

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"

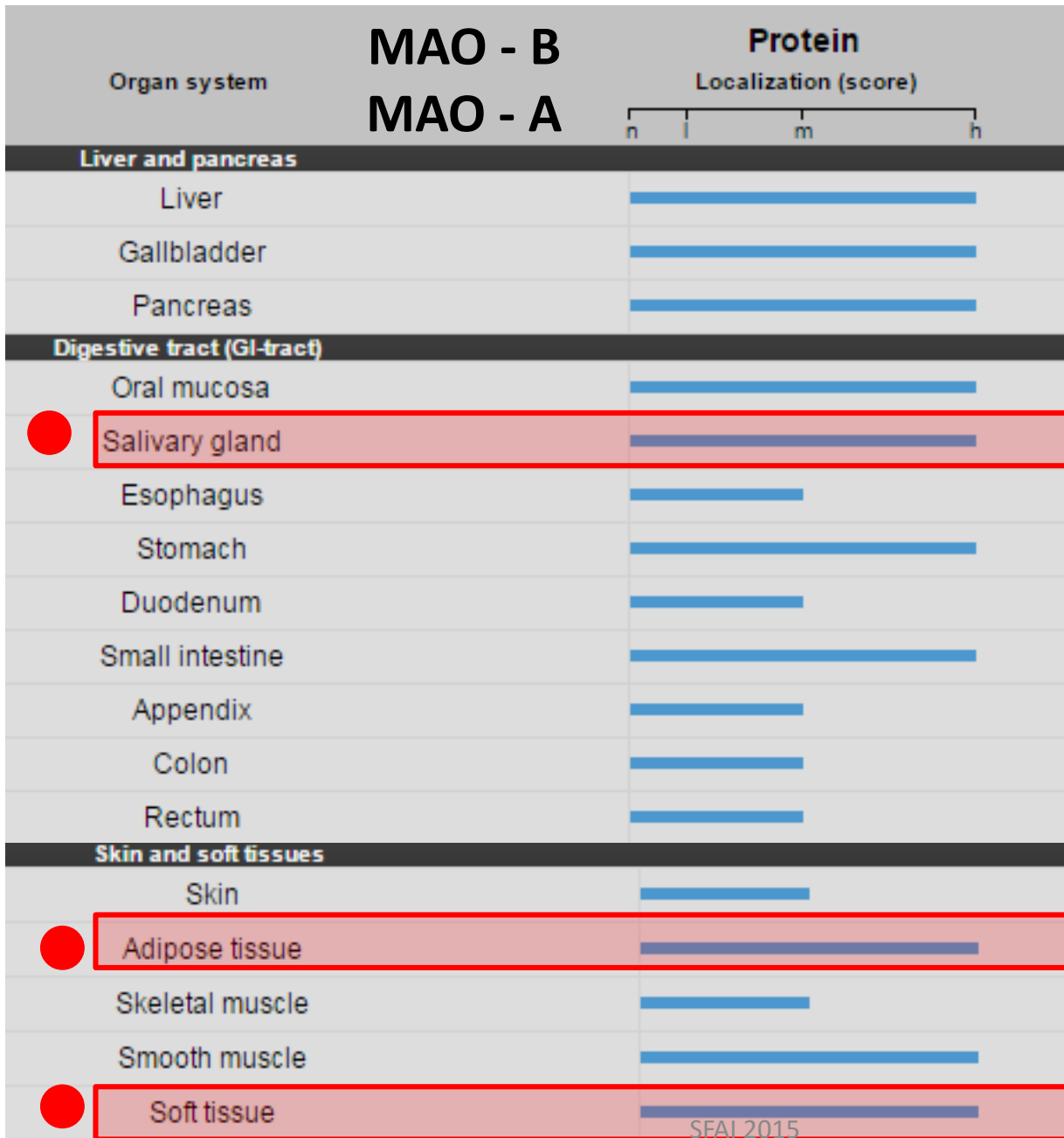


"Chronic Pain- No longer an invisible disease"

Search for D-deprenyl binding sites in inflamed tissue

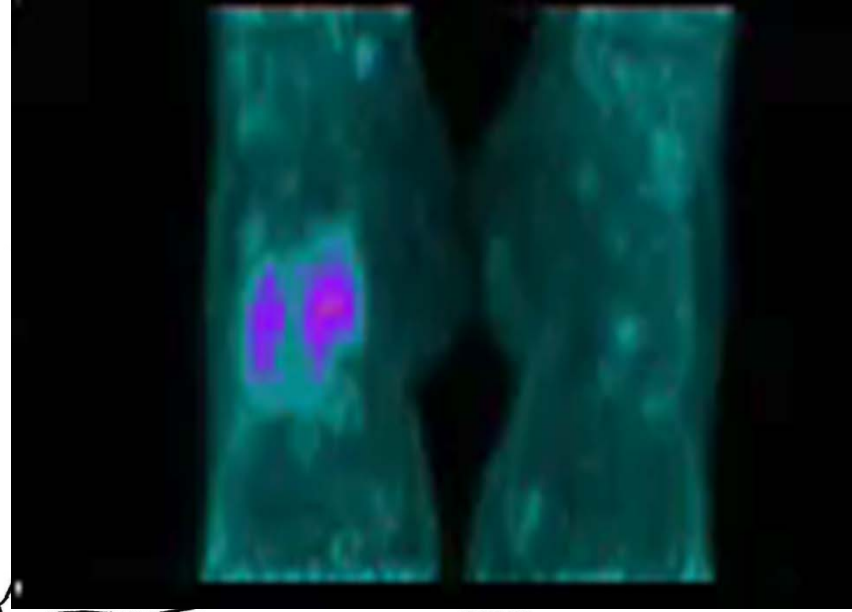
- Screening 160 G-protein coupled receptors : no hit
- Enzyme Profiling Screen[®] (n=80) : Three hits
 - MAO-B **99%** inhibition by DDE
 - MAO-A **55%** inhibition by DDE
 - ACE **70%** inhibition by DDE





● **D-Deprenyl
binding in PET
scans in pain
patients**

Swedish Protein Atlas
2014



Bill Ragsdale / Robert Nyberg

**-Doctor, I have so much pain
in my right foot..**

-Can you prove that?

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





SFAI 2015



UPPSALA
UNIVERSITET



Uppsala Berzelii Technology
Centre for Neurodiagnostics