FACULTY OF HEALTH SCIENCES
UNIVERSITY OF COPENHAGEN

GLOBAL EXCELLENCE IN HEALTH

Danish Headache Center

Tension-type headache
Pathophysiology

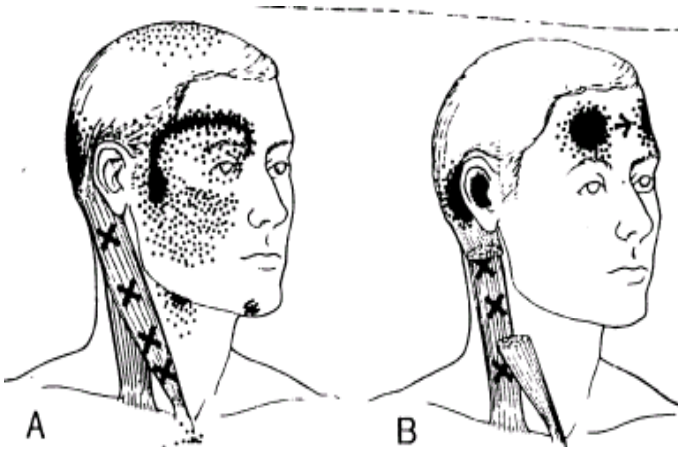
Lars Bendtsen
Associate professor, MD, PhD, Dr Med Sci
Danish Headache Center, Department of Neurology
Glostrup Hospital, University of Copenhagen, Denmark
European Headache School, Belgrade, May, 2012

Pathophysiology of Tension-Type Headache

- Peripheral mechanisms
  - Muscular factors
- Central mechanisms
  - Altered central nociception

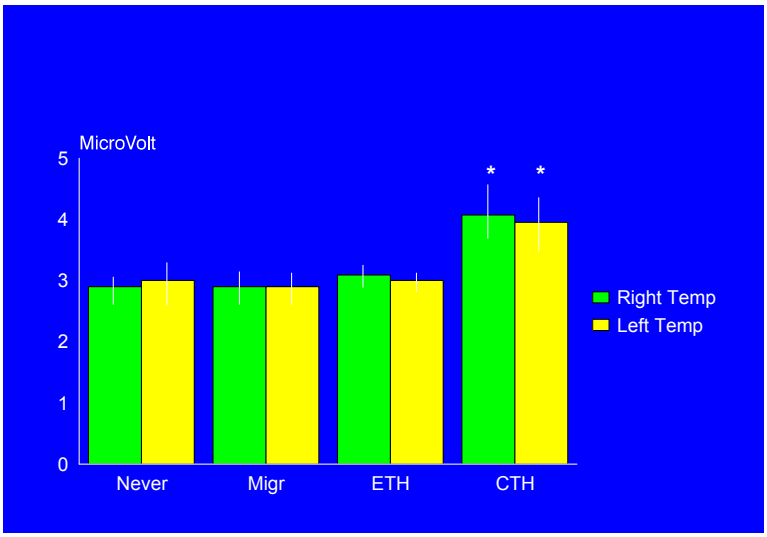
Bendtsen and Fernández-de-las-Peñas, Cur. Pain Head. Rep. 2011

Episodic Tension-Type Headache
Referred pain from myofascial tissues



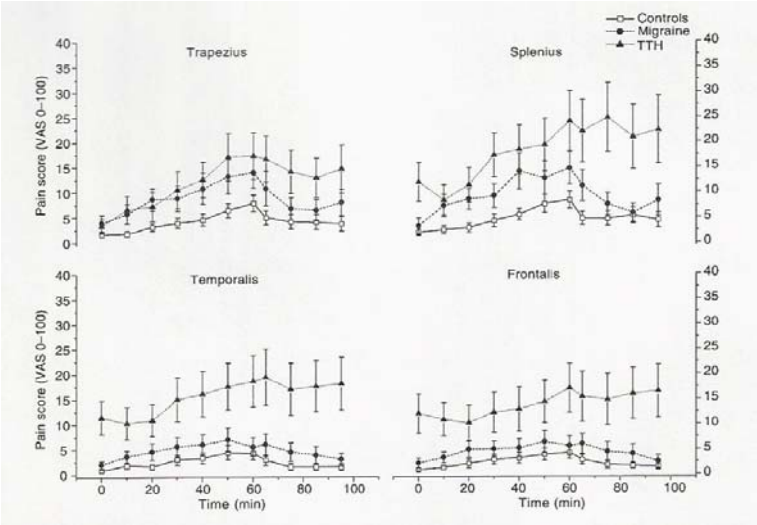
Travell and Simons, The Trigger Point Manual 1983

Muscle activity



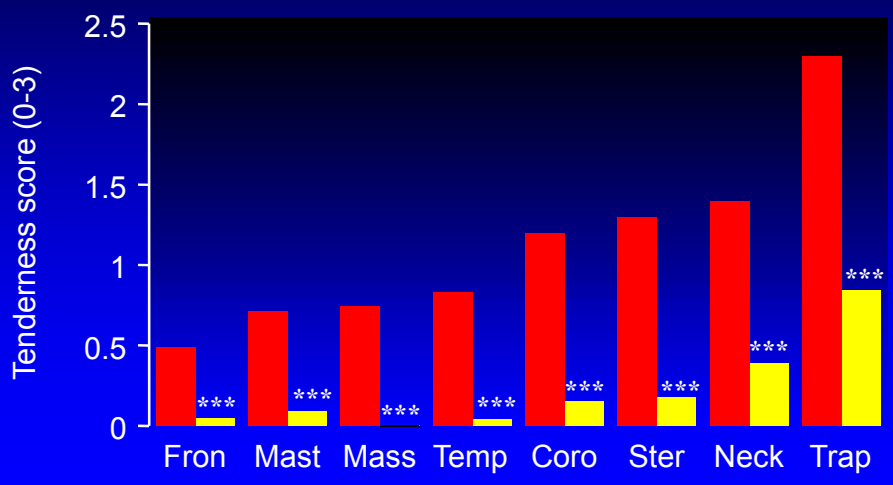
Jensen et al., Electroenceph. clin. Neurophysiol. 1994

Stress-induced pain and muscle activity in patients with migraine and tension-type headache



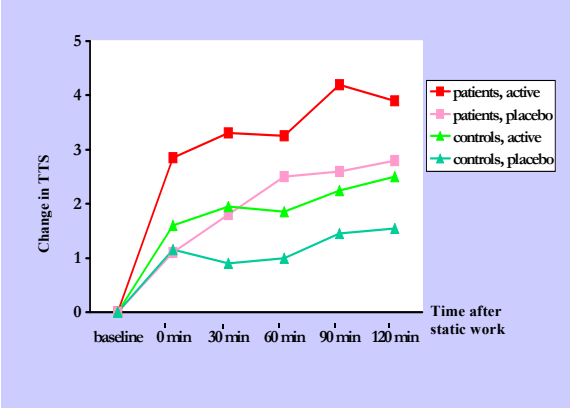
Leistad et al., Cephalalgia 2006

Local tenderness scores



Bendtsen et al., Arch Neurol 1996

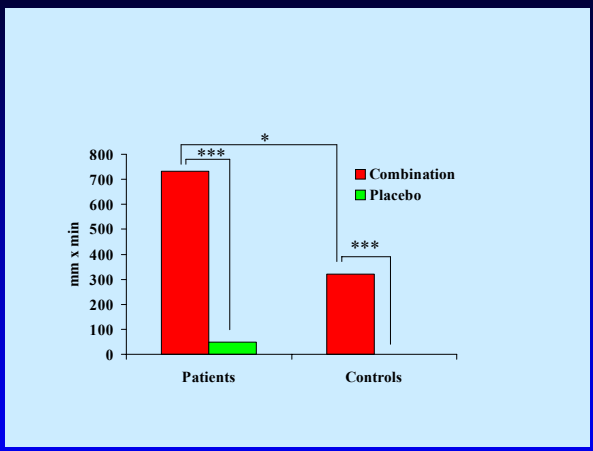
Tenderness induced by static exercise



Patients with frequent ETTH developed significantly more shoulder and neck tenderness in response to static exercise than healthy controls (P=0.04).

Christensen et al., Cephalalgia 2005

Pain induced by infusion of endogenous substances

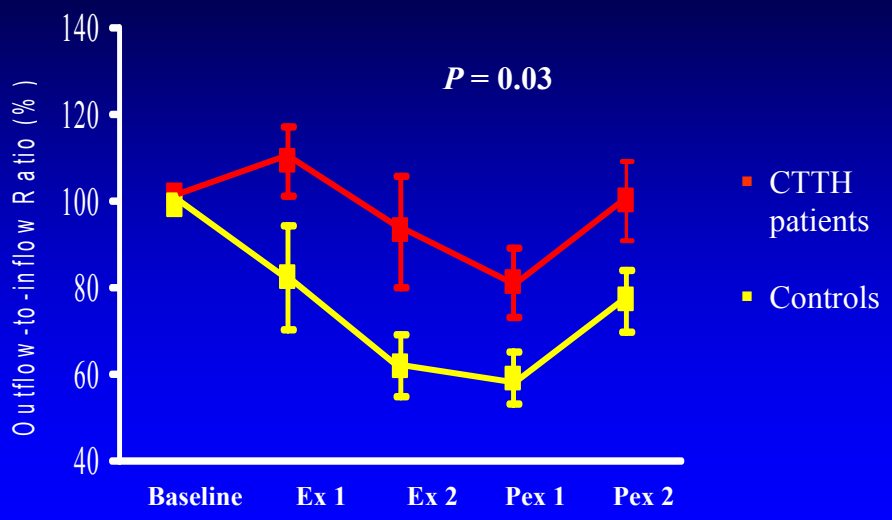


Patients with frequent ETTH experienced significantly more pain in response to infusion of endogenous substances in trapezius muscle than healthy controls (P≤0.05).

Mork et al., Cephalalgia 2004

Microdialysis

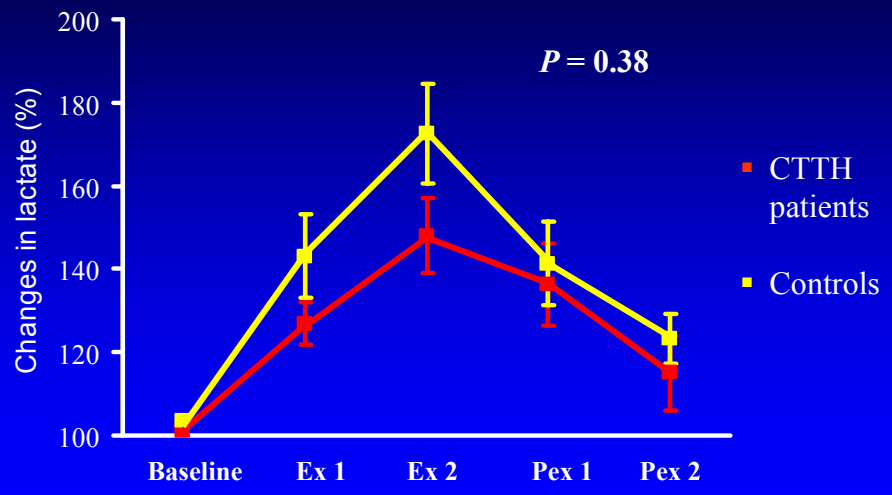
Muscle blood flow during exercise



Ashina et al., Brain 2002

Microdialysis

No in vivo signs of muscle ischemia or inflammation

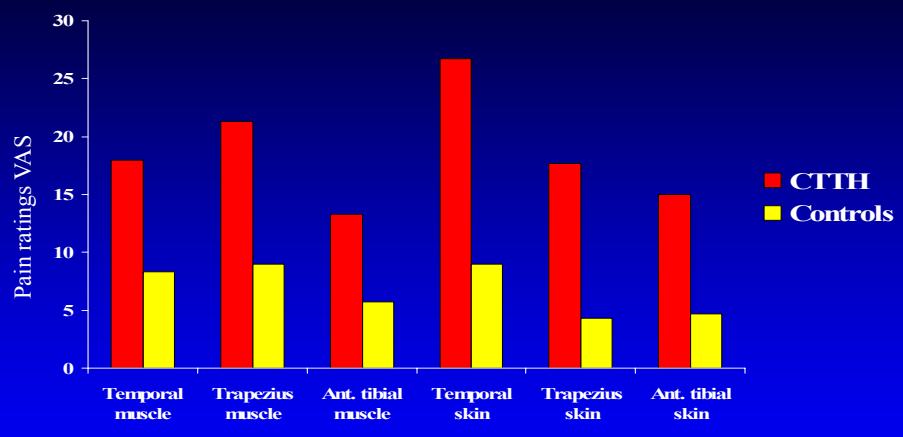


Ashina et al., Brain 2002, Cephalalgia 2003

Peripheral factors

- Summary
  - Tenderness and hardness is increased
  - Degree of tenderness is significantly related to headache frequency, intensity and treatment outcome
  - Increased tenderness in response to static exercise
  - Experimental tenderness precedes headache
  - Decreased blood flow during exercise
- Conclusion
  - Muscular factors are probably of primary importance

Suprathreshold pain sensitivity in chronic TTH



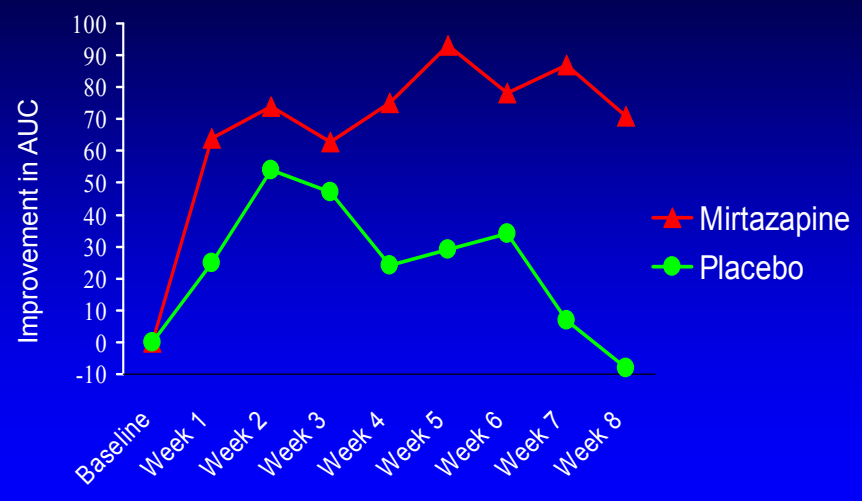
Patients have considerably increased pain sensitivity both in skin and muscle and both in cephalic and extracephalic regions ($P<0.05$).

Ashina et al., Cephalalgia 2006

Central factors in chronic TTH

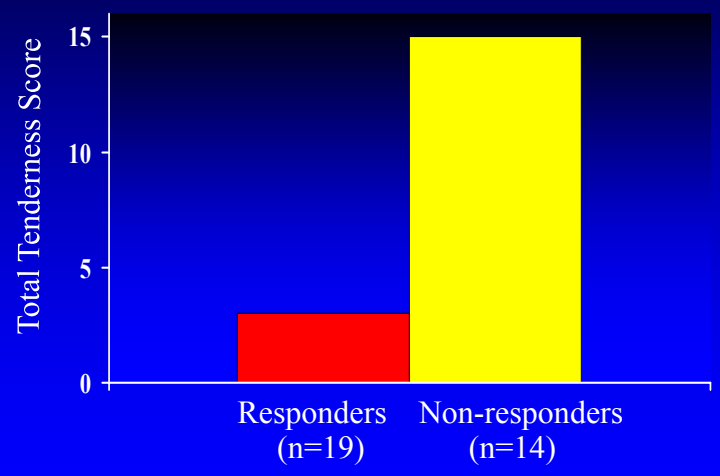
- The hyperalgesia is generalized (found in all tissues examined) and of comparable degree in all examined locations
- Increased central pain sensitivity in chronic, but not in infrequent episodic, TTH
- Decreased antinociceptive activity in chronic TTH (*Sandrini et al. 2006)*

Mirtazapine in chronic tension-type headache



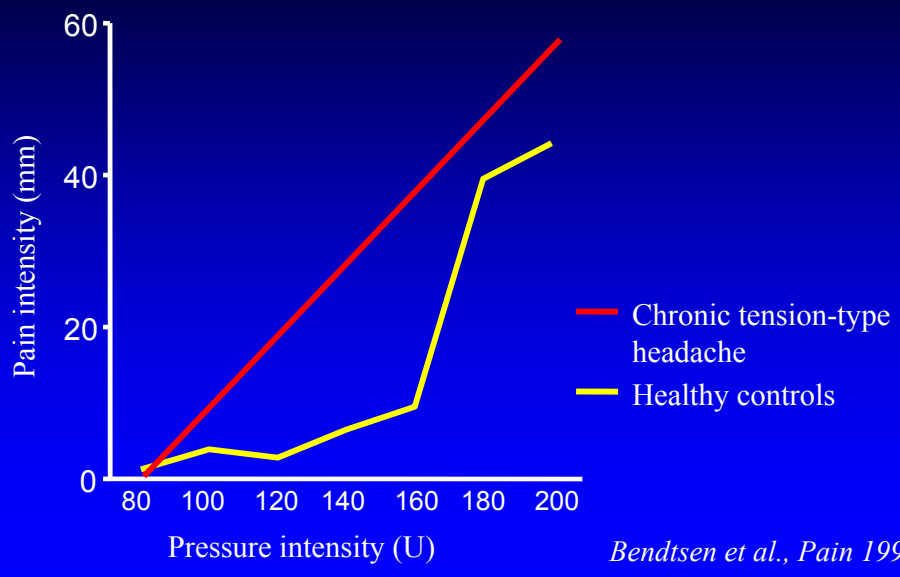
Bendtsen and Jensen, Neurology 2004

Tenderness in responders and non-responders to amitriptyline



Bendtsen and Jensen, Cephalalgia 2000

Stimulus-response function, trapezius muscle



Bendtsen et al., Pain 1996

Chronic tension-type headache

Continuous painful input from pericranial myofascial tissues

induce ↓ and maintain

central sensitization such that normally innocuous stimuli become painful

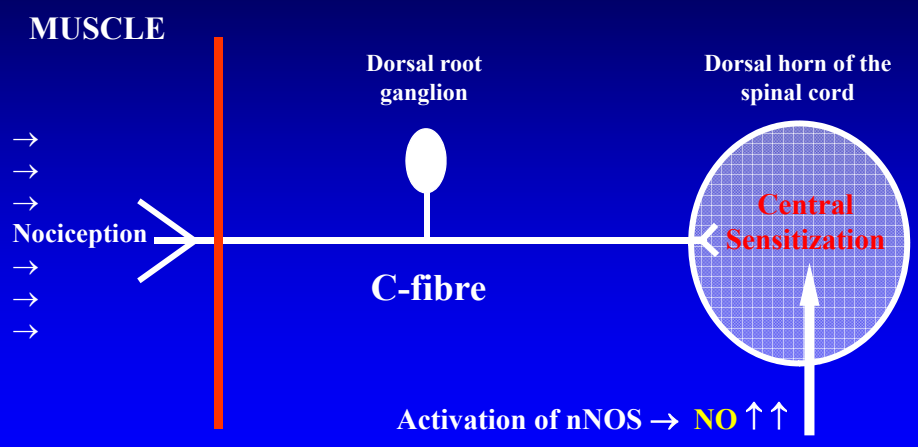
Conversion from episodic to chronic tension-type headache

Bendtsen, Cephalalgia 2000

Central sensitization in chronic TTH

- How to test this hypothesis?

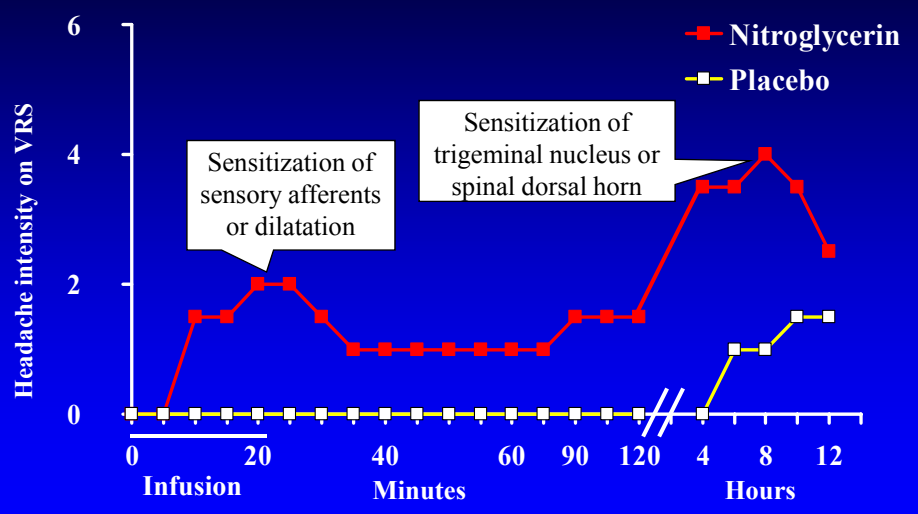
Nitric oxide and nociception



Increased platelet NOS in CTTH *(Sarchielli 2002)*

Ashina 1999

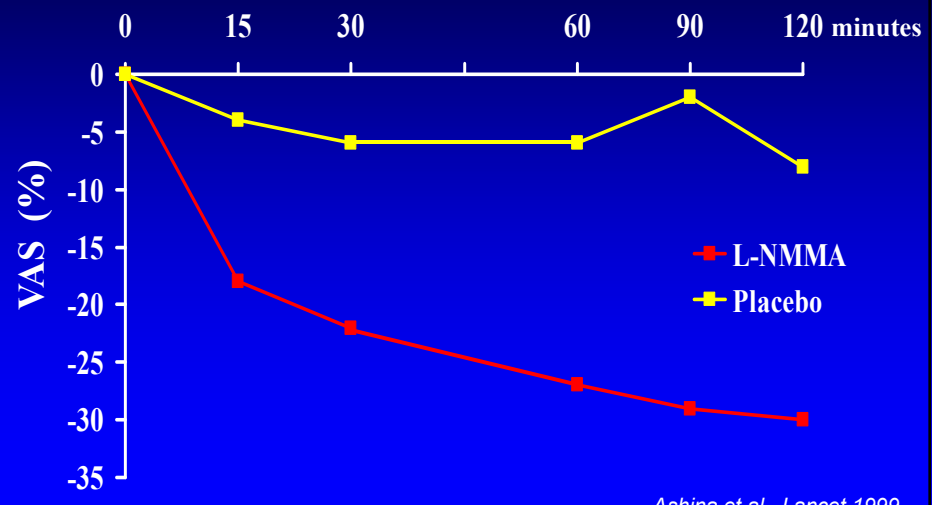
Nitric oxide induced headache in CTTH



Ashina et al., Brain 2000

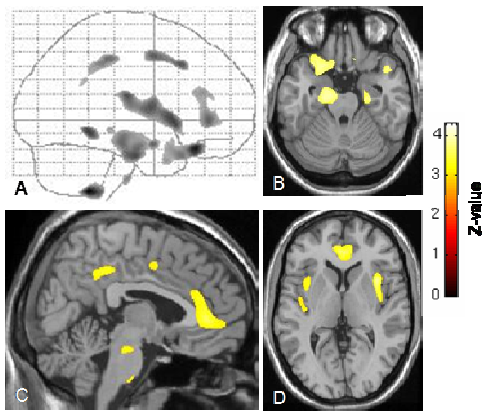
Treatment with a NOS inhibitor in CTTH

Headache intensity over time



Ashina et al., Lancet 1999

Voxel-based morphometry in chronic tension-type headache



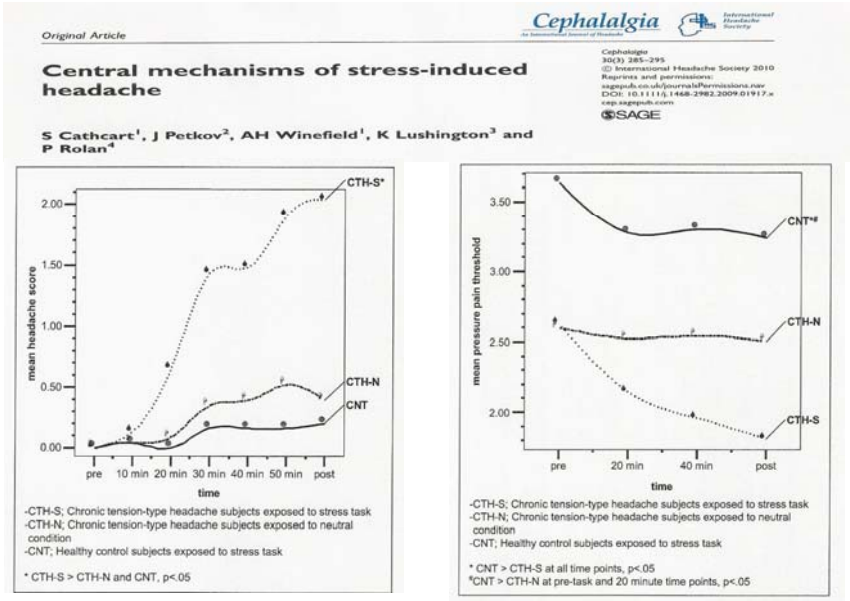
MOH vs. controls: no change
Migraine vs controls: no change
MOH vs. migraine: no change

Chronic TTH vs. controls:
Decrease in grey matter in the ant. & post. cingulate cortex, insulae, brainstem, precuneus and parahippocampus

Decrease in grey matter positively correlated to headache duration in years

Most likely a consequence of central sensitization

Schmidt-Wilcke et al., Neurology 2005



Original Article

Cephalalgia

Cephalalgia
30(3) 285–295
© International Headache Society 2010
Reprints and permissions:
sagepub.co.uk/journalsPermissions.nav
DOI: 10.1111/j.1468-2982.2009.01917.x
cep.sagepub.com
SAGE

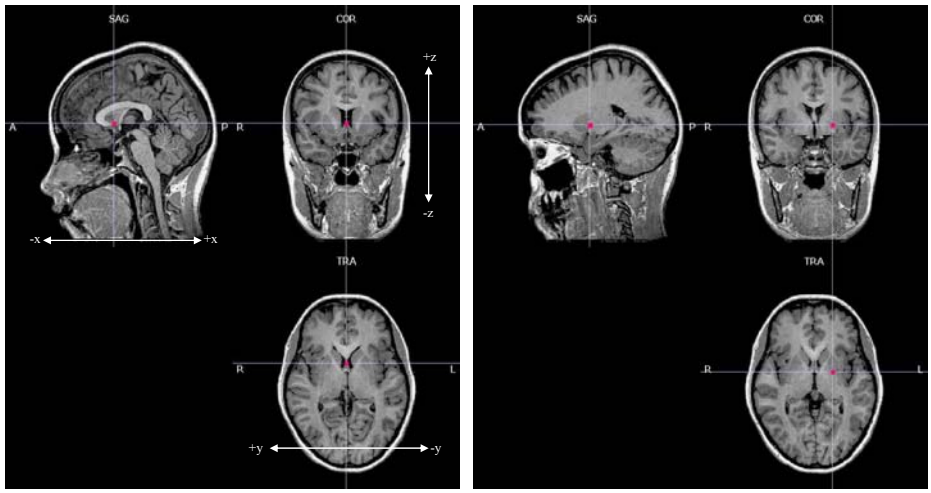
Central mechanisms of stress-induced headache

S Cathcart[1], J Petkov[2], AH Winefield[1], K Lushington[3] and P Rolan[4]

Cathcart et al., Cephalalgia 2010

CTTH at baseline P200 5th train

Controls at baseline P200 5th train



Buchgreitz et al., Brain, 2008

Brain Advance Access published August 30, 2008

doi:10.1093/brain/awn199 Brain (2008) Page 1 of 7

Abnormal pain processing in chronic tension-type headache: a high-density EEG brain mapping study

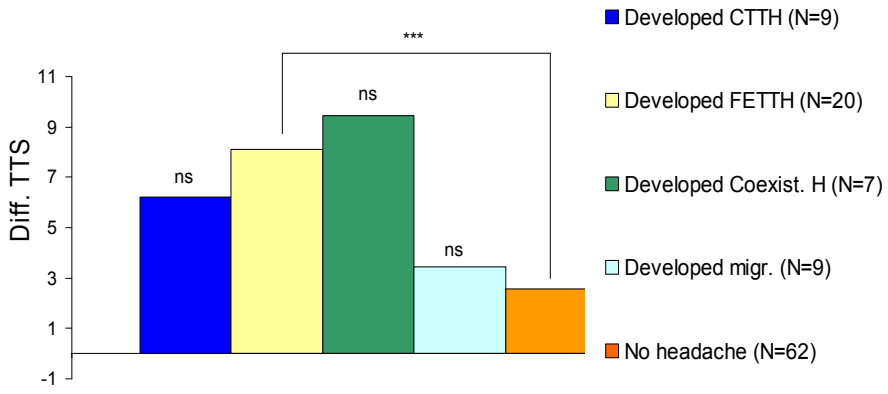
L. Buchgreitz,[1] L.L. Egsgaard,[2] R. Jensen,[1] L. Arendt-Nielsen[2] and L. Bendtsen[1]

Conclusions

- Lack of reduction in brain activity during tonic muscle pain in patients with chronic TTH may be explained by impaired inhibition of the nociceptive input
- Supraspinal response to muscle pain is abnormal in chronic TTH

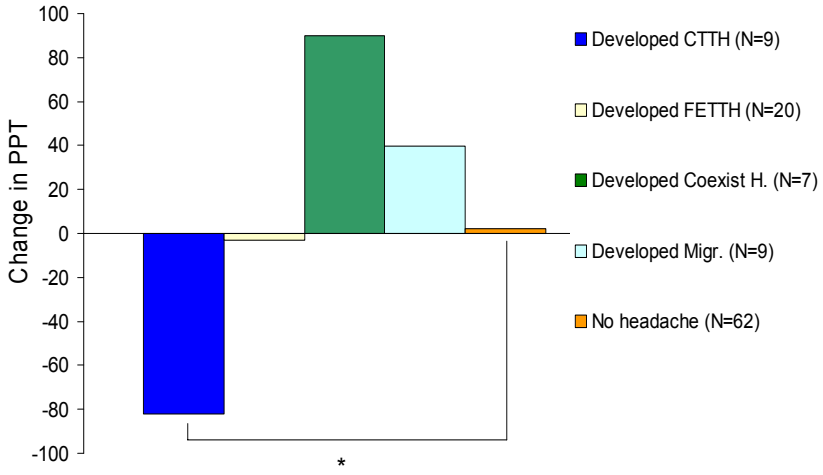
Buchgreitz et al., Brain, 2008

Change in Total Tenderness Score from 1989 to 2001



Buchgreitz et al., Pain 2008

Change in Pressure Pain Threshold from 1989 to 2001



Buchgreitz et al., Pain 2008

Tenderness and pain sensitivity in relation to development of TTH

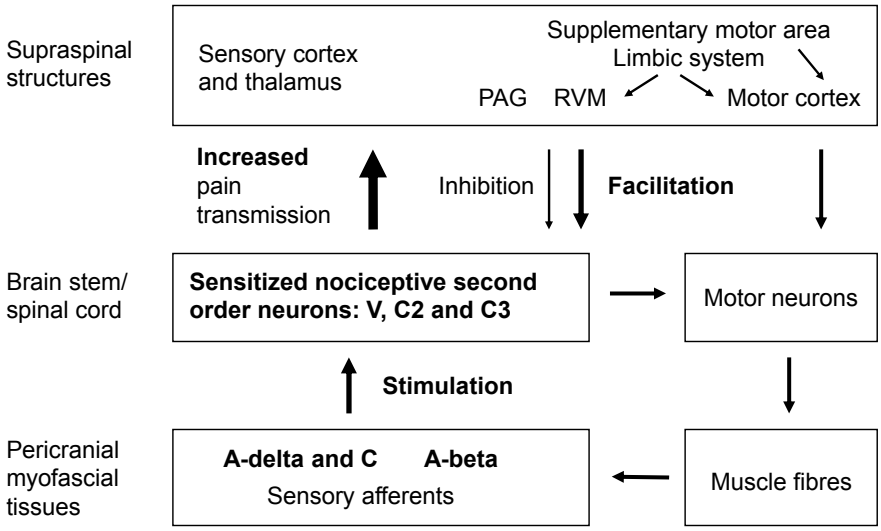
- Subjects who developed episodic TTH had increased tenderness but normal pain sensitivity at follow-up
- Subjects who developed chronic TTH had normal pain sensitivity at baseline but developed increased central pain sensitivity at follow-up
- Conclusions
  - Increased central pain sensitivity is not a risk factor but a consequence of frequent headache
  - Central sensitization plays an important role for the chronification of TTH

Buchgreitz et al., Pain 2008

Central factors in chronic TTH
Summary

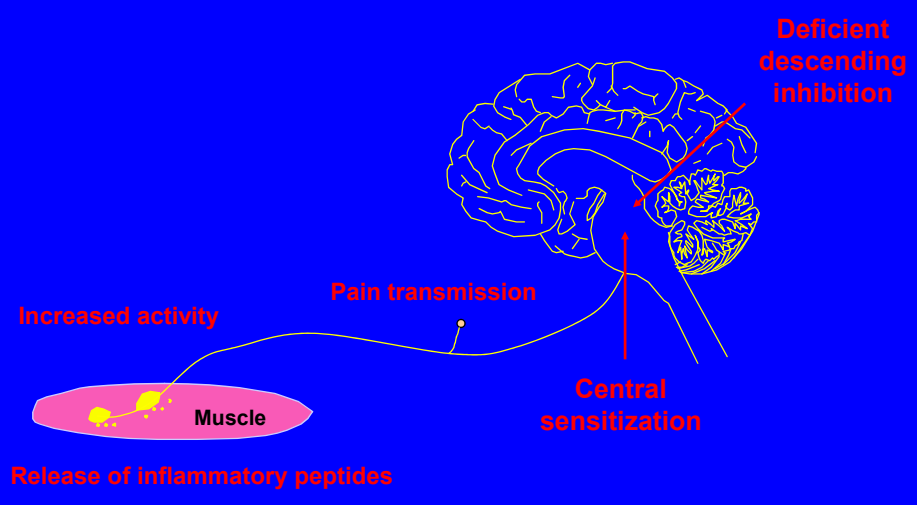
- The central nervous system is sensitized in chronic, but not in episodic, tension-type headache
- Central sensitization may be induced by prolonged painful input from pericranial myofascial tissues
- Descending pain inhibition may be deficient

ABERRANT PAIN PROCESSING

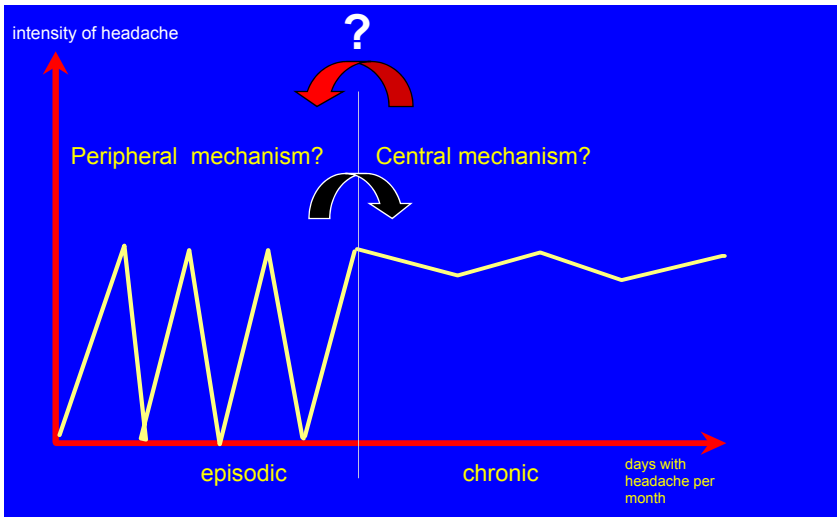


Bendtsen, Cephalalgia 2000

Chronic tension-type headache
Peripheral and central mechanisms



Conversion of episodic to chronic headache



Jensen et al., 1998

Future perspectives

- Identify source of peripheral nociception to prevent development of central sensitization and thereby conversion of episodic to chronic TTH
- Reduce established central sensitization
- Animal model (*Ellrich et al. 2005, 2006*)
- Muscular factors
  - Abnormal activation or release of chemical mediators
- Central factors
  - Neuroimaging
  - Reduction of central sensitization, e.g., by nitric oxide inhibitors or NMDA-antagonists