Mechanisms of Tension-type headache

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Genetics

• First degree relatives of probands have a 3 fold increased risk of chronic tension-type headache (Østergaard et al. 1997)

• Mode of inheritance is probably multifactorial (Russell et al. 1998)

• Genetic factors probably play a role in CTTH
Psychiatric comorbidity and headache status

<table>
<thead>
<tr>
<th></th>
<th>Migraine unadjusted</th>
<th>Migraine adjust. for TTH</th>
<th>TTH unadjusted</th>
<th>TTH adjust. for migraine</th>
</tr>
</thead>
<tbody>
<tr>
<td>p value</td>
<td>p value</td>
<td>p value</td>
<td>p value</td>
<td>p value</td>
</tr>
<tr>
<td>Mental health</td>
<td>0.002</td>
<td>0.04</td>
<td>&lt; 0.0001</td>
<td>0.0003</td>
</tr>
<tr>
<td>Physical health</td>
<td>0.0005</td>
<td>0.06</td>
<td>&lt; 0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Depression</td>
<td>0.02</td>
<td>0.31</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Eysenck</td>
<td>0.03</td>
<td>0.43</td>
<td>&lt; 0.0001</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>
Tenderness

• Increased tenderness of pericranial myofascial tissues (Langemark and Olesen 1987)

• Tenderness is correlated to both intensity and frequency of headache (Jensen et al. 1993)

• Tenderness is increased during headache (Jensen et al. 1993)

• Increased tenderness both in muscles and tendons (Bendtsen et al. 1996)
Technique of palpation

1. Bimanual when possible
2. Use 2. And 3. Fingertips
3. Use small rotating movements for 5 seconds at each spot
4. Evaluate the entire muscle and its insertions
5. Evaluate as a minimum the temporal, masseter and neck muscles
6. Coronoid process, lateral pterygoid sternocleidomastoid and frontal muscles also important
Recording the response to palpation

0. No visible reaction and denial of tenderness
1. No visible reaction, but verbal report of discomfort or mild pain
2. Facial expression of discomfort
3. Verbal report of painful tenderness
4. Marked grimacing or withdrawal and verbal report of marked tenderness and pain (taught bands etc. not useful)
Supra-threshold pain sensitivity

P<0.05

CTTH

Controls

Pain ratings VAS

Temporal muscle

Trapezius muscle

Ant. tibial muscle

Temporal skin

Trapezius skin

Ant. tibial skin

Ashina et al. Cephalalgia 2006
Value of palpation to patient management

1. Helps patients believe there is no tumor
2. Demonstrates source of pain
3. Supports relaxation and biofeedback
4. Supports reduction of stress (tension in muscles indicates tension in mind)
BASIC NEUROSCIENCE

CONTINUOUS PAINFUL INPUT

MUSCLE

C-fiber

CENTRAL SENSITIZATION

NO

SP, CGRP, VIP, NPY, EAA

CGRP, SP, PGE2, 5-HT, Bradykinin

↓↓↓

BASIC NEUROSCIENCE
Plasma CGRP

CGRP (pmol/l)

Cranial circulation

Peripheral circulation

Ashina et al. Neurology 2000
GTN INDUCED Tension-type Headache

Sensitization of sensory afferents or dilatation

Sensitization of trigeminal nucleus or spinal dorsal horn

Ashina et al. Brain 2000
HEADACHE INTENSITY

Visual Analogue Scale (%)

0 15 30 60 90 120 Min

0 -5 -10 -15 -20 -25 -30 -35

L-NMMA

Placebo

Ashina et al. Lancet 1999
MUSCLE HARDNESS

Change in hardness (%)

Min
0 60 120

L-NMMA
Placebo

Ashina et al, Brain 1999

*
TENSION-TYPE HEADACHE

Blood Flow, PGE2, ATP, Glutamate, Bradykinin

MICRODIALYSIS

C-fiber

CENTRAL SENSITIZATION

TENDERNESS

MUSCLE
<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Ex 1</th>
<th>Ex 2</th>
<th>Pex 1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients</strong></td>
<td>P = 0.03</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*MUSCLE BLOOD FLOW*

Ashina et al, *Brain* 2002
INTERSTITIAL LACTATE

$P = 0.38$

Ashina et al, Brain 2002
Voxel-based morphometry in CTTH

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

<table>
<thead>
<tr>
<th>Prognostic factors for TTH</th>
<th>Multivariate OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per 10 years increase)</td>
<td>1.4 (0.9-2.1)</td>
</tr>
<tr>
<td>Not being married</td>
<td>3.8 (1.5-9.8)</td>
</tr>
<tr>
<td>Poor self-rated health</td>
<td>1.6 (0.6-4.0)</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.8 (0.7-4.4)</td>
</tr>
<tr>
<td>No physical activity</td>
<td>1.9 (0.6-5.6)</td>
</tr>
<tr>
<td>Sleeping problems</td>
<td>2.7 (1.1-6.4)</td>
</tr>
<tr>
<td>Chronic tension-type headache</td>
<td>6.1 (1.7-22.3)</td>
</tr>
<tr>
<td>Active migraine</td>
<td>5.3 (1.9-14.5)</td>
</tr>
<tr>
<td></td>
<td>Migraine</td>
</tr>
<tr>
<td>------------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>Epidemiol</td>
<td>15%, M/F = 1/3</td>
</tr>
<tr>
<td>Genetics (RR)</td>
<td>MO 1.9; MA 3.8</td>
</tr>
<tr>
<td></td>
<td>Multifactorial</td>
</tr>
<tr>
<td>Triggers</td>
<td>Stress, Food, Wine, NTG</td>
</tr>
<tr>
<td>Biological M</td>
<td>↑ CGRP</td>
</tr>
<tr>
<td>Characteristic</td>
<td>All or none</td>
</tr>
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</table>
# Treatment response

<table>
<thead>
<tr>
<th></th>
<th>Migraine</th>
<th>TTH</th>
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</thead>
<tbody>
<tr>
<td><strong>Acute</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non specific</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Triptans</td>
<td>+++</td>
<td>(+)</td>
</tr>
<tr>
<td><strong>Prophylactics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Betablockers</td>
<td>+++</td>
<td>?</td>
</tr>
<tr>
<td>Valproate</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>Topiramate</td>
<td>+++</td>
<td>?</td>
</tr>
<tr>
<td>TCA</td>
<td>(+)</td>
<td>+++</td>
</tr>
</tbody>
</table>
Conversion of episodic to chronic headache

Jensen et al., 1998
Conclusions

• TTH is the most prevalent and least studied headache disorder
• Tension and ischemia is not the only mechanism
• Tenderness of myofascial tissues is important in most but not all cases
• Co-morbidity with anxiety and less with depression
• Genetic background to CTTH
• No drug registered for prophylaxis of CTTH