Idiopathic Intracranial Hypertension
Rigmor Højland Jensen, The 5th Iranian International Headache and Pain Conference October 11-13th 2017

Disclosure: Lectures for Pfizer, Berlin-Chemie, Allergan, Merck Conducting trials for ATI, Medotech, Electrocore, and Linde Gas ltd. Director in LTB, and Trustee in IHS
Background and signs of IIH

- Blurred vision
- Obesity
- Visual loss
- Papilledema
- Headache
Historical incidence data

The incidence is predicted to rise in line with the global obesity epidemic.


WHO Global obesity epidemic

2010

- UK 24.1% of population obese
- USA 29.8% of population obese

2014

- UK 26.9% of population obese
- USA 32.6% of population obese

Table 1: Worldwide published incidence rates of idiopathic intracranial hypertension

<table>
<thead>
<tr>
<th>Study Location</th>
<th>Duration of Study (years)</th>
<th>Patients (n)</th>
<th>Female:Male ratio</th>
<th>Obesity (% of patients)</th>
<th>Incidence per 100,000 people per year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rochester, MN, USA</td>
<td>15</td>
<td>9</td>
<td>8:1</td>
<td>70%</td>
<td>1.00</td>
</tr>
<tr>
<td>Benghazi, Libya</td>
<td>7</td>
<td>81</td>
<td>15:1</td>
<td>71%</td>
<td>2.23</td>
</tr>
<tr>
<td>Louisiana, USA</td>
<td>1</td>
<td>78</td>
<td>4:5:1</td>
<td>69%</td>
<td>1.10</td>
</tr>
<tr>
<td>Iowa, USA</td>
<td>1</td>
<td>27</td>
<td>8:1</td>
<td>67%</td>
<td>0.90</td>
</tr>
<tr>
<td>Parma, Italy</td>
<td>10</td>
<td>10</td>
<td>4:1</td>
<td>70%</td>
<td>0.28</td>
</tr>
<tr>
<td>Belfast, Northern Ireland</td>
<td>5</td>
<td>42</td>
<td>6:1</td>
<td>-</td>
<td>0.51</td>
</tr>
<tr>
<td>Spain</td>
<td>10</td>
<td>28</td>
<td>8:7:1</td>
<td>100%</td>
<td>3.20</td>
</tr>
<tr>
<td>Israel</td>
<td>2</td>
<td>91</td>
<td>14:1</td>
<td>50%</td>
<td>0.94</td>
</tr>
<tr>
<td>Oman</td>
<td>11</td>
<td>40</td>
<td>3:1</td>
<td>60%</td>
<td>2.18</td>
</tr>
<tr>
<td>Israel</td>
<td>2</td>
<td>428</td>
<td>18:5:1</td>
<td>59%</td>
<td>2.02</td>
</tr>
<tr>
<td>Sheffield, UK</td>
<td>2</td>
<td>16</td>
<td>15:1</td>
<td>-</td>
<td>1.56</td>
</tr>
</tbody>
</table>

*Body mass index greater than 26 kg/m². †Obesity defined as more than 20% heavier than ideal weight. ‡Obesity not defined. §Body mass index greater than 30 kg/m². ‖Clinical observation and body mass index higher than 30 kg/m².

Markey, Jensen & Sinclair  Lancet Neurology 2016
Serous meningitis

Pseudotumour cerebri

Benign intracranial hypertension

Primary

Idiopathic Intracranial Hypertension

Secondary

Secondary raised ICP

Diagnosis - Secondary Pseudotumour cerebri

- Venous Sinus Thrombosis
- Anaemia
- Obstructive Sleep Apnoea
- Drug-related
- CSF Hyperproteinaemia / Hypercellularity e.g. spinal cord tumour / meningitis / Guillain Barré syndrome
- Renal Failure
- Endocrine diseases e.g. Addison’s / Cushing’s / Hypothyroidism / Turner’s syndrome
Diagnosis - Drugs reported to be associated with pseudotumour cerebri

Careful history to exclude drug causes

<table>
<thead>
<tr>
<th>*Tetracyclines / minocycline/ doxycycline</th>
<th>*Corticosteroids (and withdrawal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>*Nitrofurantion</td>
<td>Beclomethasome</td>
</tr>
<tr>
<td>*Sulphonamides e.g. trimethoprim</td>
<td>Cimetidine</td>
</tr>
<tr>
<td>Nalidixic acid</td>
<td>*Lithium</td>
</tr>
<tr>
<td>*Vitamin A excess and retinoids</td>
<td>Tamoxifen</td>
</tr>
<tr>
<td>Depo Provera</td>
<td>*Ciclosporin</td>
</tr>
<tr>
<td>Combined Oral Contraceptive Pill</td>
<td>NSAIDs</td>
</tr>
</tbody>
</table>
Diagnostic error in IIH

- 40% of patients labelled with IIH referred to a neuro-ophthalmology clinic don’t have IIH!
- Error is due to inaccurate identification of papilloedema or ICP(lp) in headache patients
  - 79% had a unnecessary LP
  - 96% received acetazolamide unnecessarily
  - 3% has shunt surgery

- Obesity is common in young women with primary headaches - cannot presume IIH

Fisayo et AL  Neurology 2016
Recommendations for IIH:

- ICP ≥25 cmCSF
  - Caution - snap shot reading
  - ICP varies diurnally and with positioning

- If clinical findings are out of keeping with the pressure..........................
  - The pressure should be questioned and in some cases the LP repeated.
Diagnosis - is it papilloedema?

**Papilledema**

- Mild papilloedema with elvation of nasal disc margin (arrow).

**Pseudopapilloedema**

- Indistinct nasal disc margin and absent physiological cup (arrow).

**Severe papilloedema**

- Severe papilloedema with cotton wool spots, nerve fiber layer haemorrhage (arrows).

- Surface and buried optic nerve head drusen. Note the absence of the physiological cup and anomalous vascular branching (arrow).

*Mollan S & Sinclair A  Practical Neurology 2014*
MR findings

25 IIH-patients and 25 controls
Most sensitive findings:
Empty sella and nerve sheath distension = most reliable signs.
Posterior globe flattening: specific but not sensitive. No changes in lateral ventricles (+VBM) and no relation to clinical presentations.

Jan Hoffmann et al Cephalalgia 2013
Background

- Headache is present in >90% of patients at diagnosis.
- Headache often persists even after the intracranial pressure has normalized.
- Mechanisms of chronification are unknown.
- Patients often report difficulties in cognitive functioning.
- Poor compliance to treatment and long-term follow-up.
- Very sparsely studied.
IIH symptoms in 165 patients

Wall et al. JAMA Neurol. 2014;71(6):693-701
How does the IIH-Headache present?

Migraine

Tension-Type Headache

Low pressure headache
Overdrainage?

Medication Overuse Headache

Low Pressure Headache
Post lumbar puncture

Depression? Anxiety? Other comorbidities?
Field testing of the IHCD-3 Beta criteria for IIH-headache

<table>
<thead>
<tr>
<th>Headache aggravated by:</th>
<th>Patients with IIH n (%)</th>
<th>sensitivity, %</th>
<th>Controls n (%)</th>
<th>specificity, %</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>• bending forwards</td>
<td>22 (50)</td>
<td>50</td>
<td>15 (44)</td>
<td>56</td>
<td>0.61</td>
</tr>
<tr>
<td>• coughing or straining</td>
<td>31 (71)</td>
<td>71</td>
<td>12 (35)</td>
<td>65</td>
<td><strong>0.002</strong></td>
</tr>
<tr>
<td>• routine physical activity</td>
<td>28 (64)</td>
<td>64</td>
<td>25 (74)</td>
<td>26</td>
<td>0.35</td>
</tr>
<tr>
<td>• morning hours</td>
<td>9 (20)</td>
<td>20</td>
<td>10 (29)</td>
<td>71</td>
<td>0.36</td>
</tr>
<tr>
<td>Relief after CSF withdrawal</td>
<td>23 (72)</td>
<td>72</td>
<td>7 (24)</td>
<td>76</td>
<td><strong>&lt;0.001</strong></td>
</tr>
<tr>
<td>Retrobulbar pain</td>
<td>28 (64)</td>
<td>64</td>
<td>14 (41)</td>
<td>59</td>
<td>0.05</td>
</tr>
<tr>
<td>Pulsatile tinnitus</td>
<td>28 (64)</td>
<td>64</td>
<td>9 (27)</td>
<td>73</td>
<td><strong>0.002</strong></td>
</tr>
<tr>
<td>Blurred vision</td>
<td>29 (66)</td>
<td>65</td>
<td>18 (53)</td>
<td>47</td>
<td>0.25</td>
</tr>
<tr>
<td>Transient visual obscurations</td>
<td>28 (64)</td>
<td>64</td>
<td>12 (35)</td>
<td>65</td>
<td><strong>0.01</strong></td>
</tr>
<tr>
<td>Double vision</td>
<td>20 (20)</td>
<td>46</td>
<td>8 (24)</td>
<td>76</td>
<td><strong>0.04</strong></td>
</tr>
</tbody>
</table>

Yri et al Cephalalgia 2015
New proposed criteria

Any headache fulfilling criterion C

Idiopathic intracranial hypertension (IIH) has been diagnosed according to the Friedman and Jacobsen Criteria, with CSF pressure >250mm CSF (measured by lumbar puncture performed in the lateral decubitus position, without sedative medications, or by epidural or intraventricular monitoring)

At least three of the following:

1. A new kind of headache or exacerbation of pre-existing headache has developed in temporal relation to intracranial hypertension
2. One or both of the following:
   A. Headache is relieved after withdrawal of CSF to reduce pressure to 120–170mm CSF
   B. Headache is aggravated by coughing or straining
3. Headache with at least two of the following:
   A. Daily occurrence
   B. Focal location
   C. Retrobulbar pain
4. Headache accompanied by at least one of the following:
   A. Pulsatile tinnitus
   B. Papilledema

Not better accounted for by another ICHD-3-beta diagnosis

Yri et al Cephalalgia 2015
Summary: Headache in IIH was

- Present in up to 93% at diagnosis
- Daily occurring in 82%
- Focal in 84%
- Pulsating in 77%
- Strictly unilateral in 30%

- IIH-headache very different from M and TTH, more intense, more chronic and refractory to triptans and/or analgesics.
- Aggravation by physical activity and straining, relief after lbp and the pulsating tinnitus are cardinal symptoms

Yri et al Cephalalgia 2015
The course of headache in idiopathic intracranial hypertension: a 12-month prospective follow-up study

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Keywords: clinical course, follow-up studies, headache, idiopathic intracranial hypertension

Received 18 March 2014
Accepted 26 May 2014

The course of headache in idiopathic intracranial hypertension: a 12-month prospective follow-up study

Background and purpose: Our aim was to prospectively describe the course of headache during the first year of idiopathic intracranial hypertension (IIH).

Methods: Patients with newly diagnosed IIH were consecutively included from December 2010 to June 2013. Treatment according to standard guidelines was initiated. Headache history was obtained by headache diaries and standardized interviews performed at baseline and after 1, 2, 3 and 12 months. Parallel changes in papilledema were assessed by optical coherence tomography (OCT). All patients had comprehensive neuro-ophthalmological examinations including automated perimetry.

Results: Forty-four patients were included. Thirty-five patients completed the 12-month follow-up. Dramatic improvement in headache occurred within the first weeks after diagnosis. After 1 year, 15 patients reported no or only infrequent head-
## Predictors of headache outcome

<table>
<thead>
<tr>
<th>Predictor</th>
<th>OR estimate</th>
<th>95% confidence intervals</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache outcome, 12 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increasing age, years</td>
<td>1.14</td>
<td>1.02 - 1.28</td>
<td>0.03</td>
</tr>
<tr>
<td>Increasing ICP, cmH$_2$O</td>
<td>0.86</td>
<td>0.75 - 0.99</td>
<td>0.03</td>
</tr>
<tr>
<td>Declining BMI, kg/m$^2$</td>
<td>1.53</td>
<td>0.96 - 2.44</td>
<td>0.07</td>
</tr>
<tr>
<td>Preexisting headache, y/n</td>
<td>0.50</td>
<td>0.07 - 3.56</td>
<td>0.49</td>
</tr>
</tbody>
</table>

>2 headache days /month

≤1 headache days/month
Summary: Prognostic factors

- Sustained long-term headache after resolution of papilledema suggest that headache is caused by more complex mechanisms than ICP elevation alone.

- Chronic IIH headache mimic chronic tension-type headache.

- High ICP and younger age at onset may predict a better headache outcome.

- Visual damage seems to be sufficiently prevented by standard treatment regime. Thus the main challenge in IIH management is to prevent and treat the headache.
BMJ Open  Cognitive function in idiopathic intracranial hypertension: a prospective case–control study

Hanne Maria Yri,1 Birgitte Fagerlund,2 Hysse Birgitte Forchhammer,3 Rigmor Højland Jensen1


ABSTRACT

Objective: To explore the extent and nature of cognitive deficits in patients with idiopathic intracranial hypertension (IIH) at the time of diagnosis and after 3 months of treatment.

Design: Prospective case–control study.

Setting: Neurological department, ophthalmological department and a tertiary headache referral clinic at a Danish university hospital.

Participants: 31 patients with definite IIH referred

Strengths and limitations of this study

- The first study to assess a broad range of cognitive functions in more than 10 patients.
- Prospective controlled design and a well-defined study population.
- Controls were matched for age, sex and premorbid intelligence, and for comparisons of cognitive measures we adjusted for education and headache at time of testing.
Diagnosis

- Executive function
- Working memory
- Visuospatial memory
- Processing speed
- Attention
- Reaction time

** But widely unchanged after 3 months despite ICP normalisation and improved headache **
Possible pathophysiological mechanisms in IIH

Obesity

- Adipocytes:
  - Cytokines
  - Adipokines (leptin)
  - 11β-HSD1
  - Vitamin A

Female gender

Steroid hormones
Endocrine dysfunctions

Obesity → Adipocytes: Cytokines, Adipokines (leptin), 11β-HSD1, Vitamin A → Elevated ICP

CSF production? → Elevated ICP → CSF drainage?

Ventricles → Brain → Ventricle

Choroid plexus epithelial cells → Ependymal cells

Sagittal sinus → Olfactory bulb → Sagittal sinus

Cribriform plate → Nasal mucosa → Nasal lymphatics

Subarachnoid space → Arachnoid granulations → Perivascular efflux (lymphatics) and the dural lymphatics
Water channels involved in CSF-regulation

H Damkjær et al 2015; Uldall et al 2017
Validation of epidural ICP-method

A novel method for long-term monitoring of intracranial pressure in rats

Maria Uldall\textsuperscript{a,b}, Marianne Juhler\textsuperscript{c}, Anders Daehli Skjolding\textsuperscript{c}, Christina Kruuse\textsuperscript{b,d}, Inger Jansen-Olesen\textsuperscript{a,b}, Rigmor Jensen\textsuperscript{a,*}

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\textsuperscript{c} Department of Neurosurgery, The National Hospital, Rigshospitalet, University of Copenhagen, Blegdamsvej 9, 2100 Copenhagen \textit{Ø}, Denmark
\textsuperscript{d} Department of Neurology, Herlev Hospital, University of Copenhagen, Herlev Ringvej 75, 2730 Herlev, Denmark
Obesity-induced intracranial hypertension in rats?

![Rats with increased intracranial pressure](image1)

**Graph:**
- **ICP (mmHg):** Days post surgery
- **BMI (g/cm²):** Days 0 and 31
- **Obese** vs. **Lean**

*Significant differences:* **** (p < 0.0001)
Novel therapeutic targets

**Glucagon like peptide-1 (GLP-1)**

- Gut neuropeptide
- Produced by:
  - Proximal small bowl post meal (L cells)
  - In brain - nucleus of the solitary tract (NTS)
- Actions:
  - Stimulates insulin secretion
  - Reduces appetite (brain)
Effects of GLP-1 agonist treatment

Evaluated the signalling pathway

Rodent primary choroid plexus cells treated with Exenadin-4 (GLP-1R agonist)

Findings:
- Reduced Na\(^+\)K\(^+\) ATPase activity indicating reduced CSF secretion
- GLP-1 signals via a cAMP / PKA pathway

PKI = protein kinase A (PKA) inhibitor
- PKI abolishes the reduction in Na\(^+\)K\(^+\)ATPase activity
- Effect mediated via PKA

Botfield et al, Sci Trans Med, 2017
GLP-1 agonist reduce ICP in conscious rats

- GLP-1 significantly lowered ICP compared to saline within 10 minutes of treatment
- Effect lasted for full 60 minutes at least

Day 0
- Surgery - rats are fitted with an epidural ICP pressure

Day 2
- Rat is sedated and a 15 minute ICP baseline is recorded
- Rat receives a subcutaneous injection of either saline or 20µg/kg GLP-1 agonist
- 60 minute ICP recording of saline or GLP-1 treatment. Spikes in the trace represent when the animal is moving (*)

Botfield et al, Sci Trans Med, 2017
TREATMENT & FOLLOW-UP

• Balance CSF production and absorption?
  • Medical
    - acetazolamide
    - weight reduction
  • Surgical
    - Shunt or ONSF?
• Follow-up
  - symptoms
  - optic disc/vision

PROBLEMS:
• Identification
• Compliance
• Weight loss
• Headache
Acetazolamide

- Carbon anhydrase inhibitor
- Decreases CSF production

First line of treatment

Starting dosage 1500 mg, eg. 500 mg 3 times per day
Increase slowly - up to a maximum of 4000 mg per day

Effect of Diamox on ICP

- Diamox 200 mg, n = 6 SD
- Saline, n = 6 SD

Uldall et al Neuroscience Methods 2017
Weight loss is therapeutic in IIH

• Prospective cross over study
• Weight reduction 15%
• Significant reduction in ICP
• Significant reduction in headache
• Significant improvement in vision

Sinclair et al. 2010. BMJ;341:c2701
Case

- 17 y.o. woman
- Increasing headache and visual blurring during 14 days
- ICP >>50 cm H₂O
- Chart note: pt can now (after lp) better see faces...possibly pale papilla
- Ophthalmologist: Next week
- Visual fields: central defect
- Acuity: 1/36 (0.06)
- Relative afferent pupill defect
- Decreased color vision

Indication for action! Must have acute intervention!!!
Surgery

Optic nerve sheath fenestration

Censer et al. 2014 World Neurosurg Nov;82(5):745-50..

Unilateral endoscopic optic nerve decompression for idiopathic intracranial hypertension: a series of 10 patients.
Surgery

Ventriculo-peritoneal

Lateral Ventricle
Valve
Subcutaneous Tunnel
Peritoneal Cavity

Lumbo-peritoneal

Lumbar Subarachnoid Space
Peritoneal Cavity
Valve
<table>
<thead>
<tr>
<th>Procedures</th>
<th>Number of studies</th>
<th>Number of cases</th>
<th>Follow-up (months)</th>
<th>Headache improvement (range)</th>
<th>Visual acuity improvement (range)</th>
<th>Visual field improvement (range)</th>
<th>Papilledema improvement (range)</th>
<th>Revision rate of procedure (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optic nerve sheath fenestration</td>
<td>8</td>
<td>432</td>
<td>20</td>
<td>26% (13%–90%)</td>
<td>42% (17%–100%)</td>
<td>72% (48%–100%)</td>
<td>92% (79%–100%)</td>
<td>6.5% (5%–21%)</td>
</tr>
<tr>
<td>CSF diversion</td>
<td>7</td>
<td>209</td>
<td>39</td>
<td>55% (21%–92%)</td>
<td>56% (40%–93%)</td>
<td>77% (64%–100%)</td>
<td>70% (56%–87%)</td>
<td>44% (8%–85%)</td>
</tr>
<tr>
<td>Cerebral sinus endovascular stent</td>
<td>9</td>
<td>174</td>
<td>23</td>
<td>77% (58%–100%)</td>
<td>89% (69%–100%)</td>
<td>79% (77%–79%)</td>
<td>93% (50%–100%)</td>
<td>NA</td>
</tr>
</tbody>
</table>

Recommendations: The least invasive procedure first

*Pain Res 2016; 9:87-99*
Treatment strategy of IIH

**Mild**
Intact visual fields/no papilledema

- Diamox
  - 1000-1500 mg/døgn

**Mild-moderate defects in visual fields**

- Diamox
  - 2250-3000 mg/døgn (+ Topimax/Furix)

**Severe or malignant visual impairment**

- Acute intervention
  - ONF or V-P shunting

- Dietary counselizing and weight reduction
- Frequent follow-up in headache center and neuroophthalmologists for at least 1 year

_DHC standard and Ball et al J Neurol 2011_
IIH is a task for specialists

- IIH is not always idiopathic and is not always benign
- Chronic Headache
- Cognitive dysfunction
- Impaired QoL
- Diagnosis and treatment can be difficult
- BUT

- Exciting research field
- Team up with ophthalmologist and neurosurgeon
- Centralized for 5-10 millions
Invitation to Master in Headache Disorders

Join us for the 2. Master course starting in September 2018

Endorsed by

International Headache Society; European Headache Federation; European Academy of Neurology; Lifting The Burden; European Headache Alliance; Migraine Trust; Danish Headache Society; Patient Organizations
Concluding thoughts

- Is IIH truly idiopathic?
- Does one pathogenesis account for all cases?

- Potential role for:
  - Obesity
  - Androgens

- Novel Therapies
  - GlP-1 R agonists to lower ICP & reduce obesity
Take Home message IIH

• The incidence of IIH is rapidly increasing in the wake of the obesity epidemics
• Exciting model of ICP regulation and headache?
• IIH (former benign intracranial hypertension) is not **benign** and not always **idiopathic**
• Active treatment with high doses of azetazolamid and weight loss are required
• Close follow up visits are needed to prevent relapse
IIH & pregnancy

• Diamox teratogenic in one rat study

• No increased prevalence of birth defects in humans

• No increase risk of complications at birth and delivery

• No contraindications for vaginal delivery

• No contraindications for spinal anesthesiology
ICHD-3-beta

7.1.1 *Headache attributed to IIH*

A Any headache fulfilling criterion C

B Idiopathic intracranial hypertension (IIH) has been diagnosed, with CSF pressure > 250 mm CSF (measured by lumbar puncture performed in the lateral decubitus position, without sedative medications, or by epidural or intraventricular monitoring)

C Evidence of causation demonstrated by at least two of the following
1. Headache has developed in temporal relation to IIH, or has lead to its discovery
2. Headache is relieved by reducing intracranial hypertension
3. Headache is aggravated in temporal relation to increase in intracranial pressure

D Not better accounted for by another ICHD-3 diagnosis
Testing the diagnostic headache criteria

<table>
<thead>
<tr>
<th></th>
<th>ICHD-2</th>
<th>ICHD-3 beta</th>
<th>Proposed criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sensitivity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IIH</td>
<td><img src="1" alt="Venn Diagram" /></td>
<td><img src="2" alt="Venn Diagram" /></td>
<td><img src="3" alt="Venn Diagram" /></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>60%</td>
<td>86%</td>
<td>95%</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td><img src="4" alt="Venn Diagram" /></td>
<td><img src="5" alt="Venn Diagram" /></td>
<td><img src="6" alt="Venn Diagram" /></td>
</tr>
<tr>
<td>Specificity</td>
<td>86%</td>
<td>53%</td>
<td>65%</td>
</tr>
</tbody>
</table>

Note that while ICHD-2 requires all criteria fulfilled the ICHD-3-beta and the criteria proposed by the authors require only fulfilment of respectively two of three and three of four C criteria.
Headache in IIH

- Many do not have the classical features of raised ICP
- Progressive, daily, diffuse, non-pulsatile headache with aggravation by coughing

<table>
<thead>
<tr>
<th>Exacerbated by</th>
<th>IIH (n=44)</th>
<th>Controls (n=34)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bending</td>
<td>50%</td>
<td>44%</td>
</tr>
<tr>
<td>Cough / strain</td>
<td>70%</td>
<td>35%</td>
</tr>
<tr>
<td>Morning</td>
<td>20%</td>
<td>29%</td>
</tr>
<tr>
<td>Physical activity</td>
<td>64%</td>
<td>74%</td>
</tr>
</tbody>
</table>

- Most frequent descriptions of headache:
  - Daily 86%
- Migrainous features common
  - 68%

Controls from a headache clinic with normal ICP and no papilloedema

Yri and Jensen. Cephalalgia. 2014
Aquaporins in rat CP (brain slices)

AQP1

AQP4
AQP1 expression in choroid plexus

AQP1 mRNA in CP

AQP1 protein expression in CP

p = 0.08, Mann-withney

p = 0.43, Mann-withney

Na/K ATPase

NKCC1

NBCe2 (Na/HCO3)

AQP4
Idiopathic intracranial hypertension: Clinical nosography and field-testing of the ICHD diagnostic criteria. A case-control study

Hanne M Yri and Rigmor H Jensen

Abstract
Aims: The aims of this article are to characterize the headache in idiopathic intracranial hypertension (IIH) and to field-test the ICHD diagnostic criteria for headache attributed to IIH.
Materials and methods: We included 44 patients with new-onset IIH. Thirty-four patients with suspected but unconfirmed IIH served as controls. Headache and other IIH-related symptoms were assessed by a detailed standardized interview. In participants referred before diagnostic lumbar puncture (n = 67), we recorded headache intensity before and after
IIH headache diagnostic criteria

Diagnostic criteria:

7.1.1 Headache attributed to idiopathic intracranial hypertension (IIH)

Diagnostic criteria:
A. Any headache fulfilling criterion C
B. Idiopathic intracranial hypertension (IIH) has been diagnosed, with CSF pressure >250 mm CSF (measured by lumbar puncture performed in the lateral decubitus position, without sedative medications or by epidural or intraventricular monitoring)
C. Evidence of causation demonstrated by at least two of the following:
   1. headache has developed in temporal relation to IIH, or led to its discovery
   2. headache is relieved by reducing intracranial hypertension
   3. headache is aggravated in temporal relation to increase in intracranial pressure
D. Not better accounted for by another ICHD-3 diagnosis.

Headache characteristics are very variable in IIH

<table>
<thead>
<tr>
<th></th>
<th>ICHD-2</th>
<th>ICHD-3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>60%</td>
<td>86%</td>
</tr>
<tr>
<td>Specificity</td>
<td>86%</td>
<td>53%</td>
</tr>
</tbody>
</table>

Yri and Jensen. Cephalalgia. 2014
# IIH surgery systematic review

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Studies</th>
<th>Number patients</th>
<th>Visual field ↑ (%)</th>
<th>Papiledema ↓ (%)</th>
<th>Headache ↓ (%)</th>
<th>Shunt revisions</th>
</tr>
</thead>
<tbody>
<tr>
<td>VP shunt</td>
<td>4</td>
<td>61</td>
<td>68</td>
<td>86</td>
<td>63</td>
<td>33%</td>
</tr>
<tr>
<td>LP Shunt</td>
<td>9</td>
<td>287</td>
<td>78</td>
<td>60</td>
<td>75</td>
<td>45%</td>
</tr>
<tr>
<td>ONS Fenestrations</td>
<td>11</td>
<td>332</td>
<td>72</td>
<td>90</td>
<td>37</td>
<td>-</td>
</tr>
<tr>
<td>Stents</td>
<td>7</td>
<td>132</td>
<td>NR</td>
<td>97</td>
<td>82</td>
<td>-</td>
</tr>
</tbody>
</table>

Headache attributed to IIH and SIH (ICHD-3 beta version 2013)

**Headache attributed to IIH**

(A) Any headache fulfilling criterion C

(B) Idiopathic intracranial hypertension (IIH) has been diagnosed, with CSF pressure >250 mm CSF (measured by lumbar puncture performed in the lateral decubitus position, without sedative medications, or by epidural or intraventricular monitoring)

(C) Evidence of causation demonstrated by at least two of the following:

1. Headache has developed in temporal relation to IIH, or led to its discovery
2. Headache is relieved by reducing intracranial hypertension
3. Headache is aggravated in temporal relation to increase in intracranial pressure

(D) Not better accounted for by another ICHD-3 diagnosis

**Headache attributed to SIH**

(A) Any headache fulfilling criterion C

(B) Low CSF pressure (<60 mm CSF) and/or evidence of CSF leakage on imaging

(C) Headache has developed in temporal relation to the low CSF pressure or CSF leakage, or has led to its discovery

(D) Not better accounted for by another ICHD-3 diagnosis
Effect of Diamox on ICP

Percentage change from baseline

Baseline

Minutes post treatment

Baseline 30 min

60 min and ICP average measured every 5 min
Results

![Diagram showing headache index over weeks after diagnosis.]

- Headache index is plotted against weeks after diagnosis.
- The x-axis represents diagnosis (1 to 13).
- The y-axis represents hours/week x intensity (VAS).

The diagram illustrates the variation in headache index over time following diagnosis.
### Papilledema

- **Diagnosis**
  - 1 month
  - 3 months
  - 12 months
- **Healthy controls**
  - 200
  - 400
  - 600
  - 800

**p = 0.2**

### Headache

- **Frequency, n(%)**
  - **Daily**
    - 1 month: 38 (86)
    - 3 months: 16 (41)
    - 12 months: 18 (45)
  - **<2 days/month**
    - 1 month: 0
    - 3 months: 11 (28)
    - 12 months: 13 (33)
  - **No headache**
    - 1 month: 0
    - 3 months: 10 (26)
    - 12 months: 10 (25)

- **Intensity, median (IQR), VAS**
  - **Constant or daily headache**
    - 1 month: 7.5 (4.6 - 8.4)
    - 3 months: 5.0 (4.0 - 5.8)
    - 12 months: 5.5 (4.1 - 6.4)
  - **Episodic headache**
    - 1 month: 8.5 (5.5 - 9.8)
    - 3 months: 4.3 (3.0 - 6.0)
    - 12 months: 3.8 (3.0 - 4.8)

- **BMI, median (IQR), kg/m²**
  - 1 month: 35.5 (31.6 - 39.2)
  - 3 months: 34.8 (31.2 - 38.9)
  - 12 months: 33.0 (30.0 - 38.1)

**p = 0.2**

*Retinal Nerve Fiber Layer Thickness*
Diskogenic microspurs as a major cause of intractable spontaneous intracranial hypotension.
Beck, Jurgen; Ulrich, Christian; Fung, Christian; Fichtner, Jens; Seidel, Kathleen; Fiechter, Michael; Hsieh, Kety; Murek, Michael; Bervini, David; Meier, Niklaus; Mono, Marie-Luise; Mordasini, Pasquale; Hewer, Ekkehard; ZGraggen, Werner; Gralla, Jan; Raabe, Andreas

DOI: 10.1212/WNL.0000000000003122
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Take Home Message?

- A systematic interview and work up are essential
- Use of diaries/calendars can be recommended
- A patient may have more than one headache
- Avoid medication overuse
- Follow-up visits are essential
- Diamox/Topiramate are used
- Limited evidence

Generally I'm very brave, only today I happen to have a headache!
GLP-1 in a raised ICP model

No animal models of IIH

Hydrocephalus rodent model generated
- Kaolin was injected into the cisterna magna to induce hydrocephalus

Raised ICP model

Rat receives a subcutaneous injection of either saline or 20µg/kg GLP-1 agonist

Exendin-1 (GLP-1R agonist) reduces ICP in rats with raised intracranial pressure

Repurposing existing GLP-1 drugs may represent a novel therapeutic strategy for raised ICP and IIH

In raised ICP rodents ICP was 56.6 ± 5.7% of baseline p<0.0001

Botfield et al, Sci Trans Med, 2017
GLP-1 in the kidney and choroid plexus

- Increases Na\(^+\) excretion
- Drives diuresis

Can GLP-1 modulate fluid secretion in the choroid plexus?
Localisation and expression of the GLP-1R in the choroid plexus

Human Choroid Plexus

GLP-1R antibody

Rat Choroid Plexus

Fluorescently tagged Exendin-4 (GLP-1R agonist)

GLP-1R localises to human & rat choroid plexus

Botfield et al, Sci Trans Med, 2017
Chronic migraine: Principles of management—Can we use in IIH-headache?

• Accurate diagnosis (only 20% receive accurate diagnosis of chronic migraine according to a survey of 520 chronic migraine sufferers)\(^1\)
  • Assess all headache days that the patient is experiencing, not just migraine attacks **SO USE A CALENDER OR DIARY** \(^2\)

• Identification and minimisation/elimination of trigger and aggravating factors\(^3\)

• Identification and management of coexistent, comorbid disorders, and other factors that influence prognosis\(^3,4\)

• Thorough understanding of patient’s current medication use\(^3\)

• Establishment of treatment plan\(^1,3\)
  • Nonpharmacologic
  • Pharmacologic (acute and preventive); establish limits on acute and rescue therapy
  • Limit the use of acute medication to <3 days/week\(^1\)

---

Treatment:
1. Non-pharmacological

2. Acute: Simple analgesics maximum 3 days/week, mainly NSAIDS and PCM

3. Prevention: Amitriptyline, Mirtazapine, Venlafaxin for CTTH only
### Table 3. Mean and median visual field grades at the initial visit and at the end of the third, sixth and twelfth months in the two treatment groups (a) right eye (b) left eye

<table>
<thead>
<tr>
<th></th>
<th>Visual field grade (topiramate)</th>
<th>Visual field grade (acetazolamide)</th>
<th>(P^a)</th>
<th>(P^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Right eye</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial visit</td>
<td>3 (2–3)</td>
<td>3 (1–3)</td>
<td></td>
<td>0.921</td>
</tr>
<tr>
<td>Third month</td>
<td>2 (1–3)</td>
<td>2.5 (1–3)</td>
<td>0.008</td>
<td>0.93</td>
</tr>
<tr>
<td>Sixth month</td>
<td>2 (1–3)</td>
<td>2 (0–3)</td>
<td>&lt;0.001</td>
<td>0.74</td>
</tr>
<tr>
<td>Twelfth month</td>
<td>1 (0–3)</td>
<td>1 (0–3)</td>
<td>&lt;0.001</td>
<td>0.873</td>
</tr>
<tr>
<td>(b) Left eye</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial visit</td>
<td>3 (2–3)</td>
<td>3 (1–3)</td>
<td></td>
<td>0.248</td>
</tr>
<tr>
<td>Third month</td>
<td>2.5 (1–3)</td>
<td>2 (1–3)</td>
<td>0.08</td>
<td>0.41</td>
</tr>
<tr>
<td>Sixth month</td>
<td>2 (1–3)</td>
<td>2 (0–3)</td>
<td>&lt;0.001</td>
<td>0.63</td>
</tr>
<tr>
<td>Twelfth month</td>
<td>1.5 (1–3)</td>
<td>1 (0–3)</td>
<td>&lt;0.001</td>
<td>0.4</td>
</tr>
</tbody>
</table>

\(P^a\) values found by comparison of the visual field grades on follow-up visits with the grades at the initial visit in each treatment group.

\(P^b\) values found by comparison of the visual field grades between the two treatment groups at the initial and follow-up visits.
Perspectives for IIH-headache

- Precise diagnosis?
- Mechanisms?
- Chronic headache despite ICP-normalization?
- Treatment of secondary IH-headaches?
- Earlier Intervention?

- Octreotide 5 ptts *Clin Neurol Surg* 2016?
- Neuromodulation 4 ptts *Neurol India* 2016?
- Craniectomi?
Chronic migraine: multifaceted approach to therapy

1-3

Lifestyle modifications, behavioral therapy

Education, support, managing expectations, and close follow-up

Pharmacologic therapy (acute and preventative)

Chronic migraine management

## Headache characteristics

<table>
<thead>
<tr>
<th></th>
<th>Diagnosis (n=44)</th>
<th>1 month (n=39)</th>
<th>3 months (n=40)</th>
<th>12 months (n=35)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with headache, n</td>
<td>44</td>
<td>29</td>
<td>30</td>
<td>22</td>
</tr>
</tbody>
</table>

### Headache characteristics, n (%)

#### Aggravated by:

- **Cough or strain**: 31(70), 15(52), 15(52), 16(73)
- **Bending forward**: 23(52), 13(45), 15(52), 11(50)
- **Physical activity**: 28(64), 19(66), 19(66), 14(64)
- **Nausea**: 33(75), 14(48), 13(43), 7(32)
- **Photofobia**: 29(66), 15(52), 18(60), 16(73)
- **Phonofobia**: 32(73), 12(41), 16(53), 14(64)

- **“Fullfills criteria” of**
  - **Migraine**: 30(68), 17(59), 17(57), 11(50)
  - **Migraine – attacks<4 hours included**: 36(82), 18(62), 19(63), 12(55)
  - **Tension-type headache**: 11(25), 17(59), 17(57), 12(55)
  - **Migraine and tension-type**: 4(9), 6(21), 6(20), 3(15)
Overdiagnosis of idiopathic intracranial hypertension.
Fisayo, Adeniyi; Bruce, Beau; MD, PhD; Newman, Nancy; Biousse, Valerie

DOI: 10.1212/WNL.0000000000002318

Diagnostic errors in idiopathic intracranial hypertension (IIH)
### Table 2
Characterization of patients referred with a preexisting diagnosis of IIH (group I)

<table>
<thead>
<tr>
<th>Characterization</th>
<th>Total (n = 84)</th>
<th>With IH</th>
<th>Without IH</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. patients</td>
<td>84</td>
<td>52</td>
<td>34</td>
</tr>
<tr>
<td>Male</td>
<td>5</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Female</td>
<td>79</td>
<td>45</td>
<td>32</td>
</tr>
<tr>
<td>Mean age, y</td>
<td>34</td>
<td>31</td>
<td>30</td>
</tr>
<tr>
<td>Age range, y (QR)</td>
<td>10-90 (25-42)</td>
<td>10-65 (25-33)</td>
<td>10-90 (25-49)</td>
</tr>
<tr>
<td>Mean BMI, kg/m²</td>
<td>35.7</td>
<td>36.3</td>
<td>34.9</td>
</tr>
<tr>
<td>BMI range, kg/m²</td>
<td>18.4-76.8 (25.9-40.2)</td>
<td>18.4-76.8 (31.1-40.5)</td>
<td>19.1-66.8 (27.4-39.6)</td>
</tr>
<tr>
<td>Referring provider</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ophthalmologist</td>
<td>5</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Neurologist</td>
<td>32</td>
<td>17</td>
<td>15</td>
</tr>
<tr>
<td>Neuro-ophthalmologist</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Neurosurgeon</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Otorhinolaryngologist</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Emergency department</td>
<td>3</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Primary provider</td>
<td>3</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Self-referral</td>
<td>4</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Specialists seen prior to referral</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average no. seen</td>
<td>2.8</td>
<td>2.9</td>
<td>2.8</td>
</tr>
<tr>
<td>Ophthalmologist</td>
<td>69</td>
<td>46</td>
<td>23</td>
</tr>
<tr>
<td>Neurologist</td>
<td>60</td>
<td>35</td>
<td>25</td>
</tr>
<tr>
<td>Otorhinolaryngologist</td>
<td>40</td>
<td>26</td>
<td>14</td>
</tr>
<tr>
<td>Neuro-ophthalmologist</td>
<td>31</td>
<td>18</td>
<td>13</td>
</tr>
<tr>
<td>Neurosurgeon</td>
<td>8</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Emergency department</td>
<td>20</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Other</td>
<td>3</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Symptoms reported by patient</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average no. symptom</td>
<td>2.3</td>
<td>2.5</td>
<td>1.9</td>
</tr>
<tr>
<td>Headache</td>
<td>68</td>
<td>44</td>
<td>24</td>
</tr>
<tr>
<td>Vision disturbance</td>
<td>60</td>
<td>38</td>
<td>22</td>
</tr>
<tr>
<td>TVO</td>
<td>28</td>
<td>20</td>
<td>8</td>
</tr>
<tr>
<td>Pulseless tinnitus</td>
<td>27</td>
<td>19</td>
<td>8</td>
</tr>
<tr>
<td>Diplopia</td>
<td>13</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>Testing performed prior to referral</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lumbar puncture</td>
<td>77</td>
<td>50</td>
<td>27</td>
</tr>
<tr>
<td>CSF OR IIH on x-ray, MRI brain, or CT venogram</td>
<td>60</td>
<td>46</td>
<td>13</td>
</tr>
<tr>
<td>MRI orbits</td>
<td>19</td>
<td>14</td>
<td>5</td>
</tr>
<tr>
<td>MRI or CT venogram</td>
<td>30</td>
<td>22</td>
<td>8</td>
</tr>
<tr>
<td>MRI angiogram head</td>
<td>7</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>MRI angiogram neck</td>
<td>3</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Short or optic nerve sheath fenestration requested</td>
<td>5</td>
<td>4</td>
<td>1</td>
</tr>
</tbody>
</table>

*Overdiagnosis of idiopathic intracranial hypertension.*

Fisayo, Adeniyi; Bruce, Beau; MD, PhD; Newman, Nancy; Biousse, Valerie

DOI: 10.1212/WNL.0000000000002318

Table 2 - A Characterization of patients referred with a pre-existing diagnosis of IIH (Group I)
Patients suspected of having IIH
n=92*

Normal ICP
n=41

Subjects with headache
n=34

IIH confirmed
n=45

OCT controls
n=37

QST controls
n=28

Eligible for QST testing
n=28

Eligible for cognitive testing
n=31

Cognitive controls
n=31

Study I

Study II

Study III

Study IV

*Patients with identified secondary causes (n=6) were excluded.
From episodic to chronic migraine: external factors

- If the frequency of headaches increases, chronic migraine can develop.
- Every year, between 2.5 and 4.6% of people with episodic migraine experience progression to chronic migraine.
- Approximately the same proportion regress from chronic migraine to episodic migraine spontaneously.

Various external and intrinsic factors can favor migraine chronification:

- Low frequency episodic migraine: 0-9 headache days/month
- High frequency episodic migraine: 10-14 headache days/month
- Chronic migraine: ≥ 15 headache days/month

Lipton RB. *Neurology* 2009;
Tension-Type Headache
Diagnostic criteria ICHD-III beta

- Headache has at least two of the following criteria
  - bilateral location
  - pressing/tightening quality
  - mild or moderate intensity
  - not aggravated by routine physical activity

- Both of the following
  - no nausea or vomiting
  - no more than one of photophobia or phonophobia

Infrequent ETTH
<1 headache Days/month

Frequent ETTH
1-14 headache days/month

Chronic TTH
≥ 15 headache days/month
Headache diagnosis in controls – classification paper

<table>
<thead>
<tr>
<th>Headache Diagnosis</th>
<th>n, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Migræne, episodic</td>
<td>5(15)</td>
</tr>
<tr>
<td>Migraine, chronic</td>
<td>13(38)</td>
</tr>
<tr>
<td>Tension-type, episodic</td>
<td>2(6)</td>
</tr>
<tr>
<td>Tension-type, chronic</td>
<td>12(29)</td>
</tr>
<tr>
<td>Medication overuse headache</td>
<td>10(35)</td>
</tr>
<tr>
<td>Not classified</td>
<td>5(15)</td>
</tr>
</tbody>
</table>

ICHDI-3-beta n=34
Clinical characteristics

<table>
<thead>
<tr>
<th></th>
<th>Diagnosis</th>
<th>3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracranial pressure</td>
<td>41.0 cmH₂O</td>
<td>25.9 cmH₂O</td>
</tr>
<tr>
<td>(ICP)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>ICP &gt; 25 cmH₂O</em></td>
<td>100%</td>
<td>50%</td>
</tr>
<tr>
<td>Body mass index</td>
<td>35.7 kg/m²</td>
<td>34.0 kg/m²</td>
</tr>
<tr>
<td>Headache</td>
<td>71%</td>
<td>48%</td>
</tr>
<tr>
<td>Headache intensity</td>
<td>2.6 VAS</td>
<td>1.8 VAS</td>
</tr>
</tbody>
</table>
Reduction in headache after CSF withdrawal – classification paper

<table>
<thead>
<tr>
<th>Subject, n</th>
<th>Patients</th>
<th>Controls</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median headache reduction, % (range)</td>
<td>86 (30-100)</td>
<td>48 (11-100)</td>
<td>0.054</td>
</tr>
</tbody>
</table>
Methods and subjects

- 28 patients with newly diagnosed IIH
- 28 healthy sex-matched controls
- Exclusion criteria
  - medication overuse
  - headache prophylactic therapy
- Quantitative sensory testing (QST)
Methods

• Pressure pain
  • Finger – extra cephalic
  • Temple – cephalic

• Electrical stimulation
  • Anterio tibial muscle

• Supra threshold stimulation
  • 1.5 times the individual threshold
Results

Suprathreshold stimulation, patients and healthy controls

Pain rating (VAS)

- Pressure, extra cephalic: p=0.09
- Pressure, cephalic: p=0.52
- Single electrical: p=0.30
- Repetitive electrical: p=0.46
## Results

<table>
<thead>
<tr>
<th></th>
<th>Baseline n=28</th>
<th>1 month n=21</th>
<th>3 months n=25</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily headache&lt;sup&gt;a&lt;/sup&gt;, n(%)</td>
<td>25 (89)</td>
<td>13 (62)</td>
<td>15 (60)</td>
</tr>
<tr>
<td>Intensity:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>daily headache, mean (IQR), VAS</td>
<td>7.2 (5.4–8.8)</td>
<td>4.5 (4.0–5.5)</td>
<td>5.2 (4.0–6.3)</td>
</tr>
<tr>
<td>episodic headache, mean (IQR), VAS</td>
<td>7.4 (5.0–9.5)</td>
<td>4.9 (3.0–7.5)</td>
<td>5.4 (4.2–6.9)</td>
</tr>
<tr>
<td>Headache index&lt;sup&gt;b&lt;/sup&gt;, hours/week*VAS</td>
<td>839 (217–1344)</td>
<td>418 (161–614)</td>
<td>328 (27–588)</td>
</tr>
<tr>
<td>ICP&gt; 25 cmH&lt;sub&gt;2&lt;/sub&gt;O, n(%)</td>
<td>28 (100)</td>
<td></td>
<td>11 (44)</td>
</tr>
</tbody>
</table>
Results

Changes in suprathreshold stimulation from diagnosis to the 3-month follow-up, patients with IIH

- Pressure, extra cephalic: p=0.32
- Pressure, cephalic: p=0.09
- Single electrical: p=0.78
- Repetitive electrical: p=0.98
Conclusions

• We found no convincing evidence of increased pain sensitivity in patients with IIH

• This suggest that chronification of IIH headache may be caused by other mechanisms than central sensitization

• Further investigation of headache pathophysiology is needed for identification of possible targets for treatment
Background and signs of IIH

- papilledema
- headache
- obese ♀
- progressive
- permanent visual loss
25 IIH-patients and 25 controls
Most sensitive findings:
Empty sella and nerve sheath distension = most reliable signs.
Posterior globe flattening: specific but not sensitive. No changes in lateral ventricles (+VBM) and no relation to clinical presentations.

Jan Hoffmann et al Cephalalgia 2013
Idiopathic Intracranial Hypertension is not always Idiopathic

– Sinus venous trombosis
– Infections
– Inflammation
  • Sarcoidosis
– Endokrinological
  • parathyroid, thyroid, growth hormone, corticosteroid
– Neoplastic
– Uremia
– Toxic:
  • Tetracycline, steroids, vitamin A
Treatment strategy of IIH

- **Mild**
  - Intact visual fields/no papiledema
  - Diamox 1000-1500 mg/døgn

- **Mild-moderate**
  - Defects in visual fields
  - Diamox 2250-3000 mg/døgn (+ Topimax/Furix)

- **Severe or malignant visual impairment**
  - Acute intervention and V-P shunting

- **Dietary counselling and weight reduction**
  - Frequent follow-up in headache center and neuroophthalmologists for at least 1 year

*DHC standard and Ball et al J Neurol 2011*
Take Home message IIH

- The incidence of IIH is rapidly increasing in the wake of the obesity epidemics
- Exciting model of ICP regulation and headache?
- IIH (former benign intracranial hypertension) is not **benign** and not always **idiopathic**
- Active treatment with high doses of azetazolamid and weight loss are required
- Close follow up visits are needed to prevent relapse
Treatment strategy of IIH

Mild
Intact visual fields/no papilledema

Diamox
1000-1500 mg/døgn

Mild-moderate defects in visual fields

Diamox
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Severe or malignant visual impairment

Acute intervention and V-P shunting

• Dietary counselling and weight reduction
• Frequent follow-up in headache center and neuroophthalmologists for at least 1 year

DHC standard and Ball et al J Neurol 2011
Case 10 (Yri et al BMJ cases 2014)

- 32 year old male

- Trauma to the head and neck 3 months followed by headache, aggravation of neck pain, and blurred vision.

- Posttraumatic Headache?

- Present again with 2 weeks aggravated headache, retrobulbar pain and blurred vision on the right eye.

- Positional vertigo and short lasting loss of vision

- ?
Signs

- BMI 23.5 kg/m²
- Bilat papiledema

(Yri et al BMJ cases 2014)
Paraclinical Findings (Yri et al BMJ cases 2014)

- MR i.a
- Spinal Tap: 28 cmH2O
- CSV: protein 0.44, erythrocyttes 0, leukocytes 5
- Visual Field: enlarged blind spots, otherwise normal
- Visus: 1/0.5
Case 10  (Yri et al BMJ cases 2014)

- Additional history: weeks before headache start had an episode of scarlatina
- Thrunkal erythema, possible small genital ulcers (chancre), fever and neck stiffness, Improved headache during antibiotics
- ??
- CSF: Positive for Syfilis
- 2 weeks of high dose i.v. penicillin
- OBS: IIH is a diagnosis of exclusion and be alert with atypical phenotype
Secondary causes to Increased Intracranial Pressure

- Sinus venous trombosis
- Infection
- Inflammation
  - Sarcoidosis
- Endocrinological
- parathyroidea, thyroidea, growth hormone, cushing (steroids)
- Neoplasms/ Carcinomatosis
- Uremia
- Pharmacological tetracyklin, steroids, a-vitamine
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<th>Clinical feature</th>
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Yri and Jensen. Cephalalia. 2014