Mechanisms of Headache in Intracranial Hypotension

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Overview

• What are the different pain fibers?
• Which are involved in pain transmission?
• What role does sensitization play in pain and headache?
• What causes headache?
• What causes low CSF pressure?
• What causes low CSF pressure headache?
  – Increased compliance?
    • HIP drift?
# Sensory Nerve Fibers

<table>
<thead>
<tr>
<th>Fiber type</th>
<th>Myelinated</th>
<th>Conduction velocity (meters/sec)</th>
<th>Sensory Information</th>
<th>Neurotransmitters</th>
</tr>
</thead>
<tbody>
<tr>
<td>A-β</td>
<td>Yes</td>
<td>30-100</td>
<td>Touch, vibration</td>
<td>EAA (NPY, GAL, CCK, SP, following activation or injury)</td>
</tr>
<tr>
<td>A-δ</td>
<td>Yes</td>
<td>12-30</td>
<td>Initial sharp pain, touch, pressure</td>
<td>EAA</td>
</tr>
<tr>
<td>C</td>
<td>No</td>
<td>0.5-2</td>
<td>Dull pain, temperature</td>
<td>Glutamate, SP, CGRP, NKA</td>
</tr>
</tbody>
</table>
Acute Pain

C fiber

Aδ fiber

First pain

Second pain

Pain intensity

Time
Sensitization

- Increased responsiveness to stimuli
  - **Hyperalgesia**: Increase in pain sensitivity
  - **Allodynia**: Nonpainful stimuli now painful
- Peripheral sensitization
  - Increased sensitivity of nociceptive receptor
- Central sensitization
  - Increased spontaneous neuronal discharge
  - Expanded nociceptive receptive fields
Sensitization

Peripheral Sensitization
- Glu, Sp, CGRP, NA, NGF
- BK, PGs, HA, 5-HT, H⁺
- Adenosine, NO

Central Sensitization
- Glu
- Sp

WDR Neuron

Impulses
- C-fiber
- Aβ fiber

DRG
- Trigeminal Ganglion

CNS

Modulator
- NE
- 5-HT

PNS

Nucleus Trigeminal Caudalis
What Causes Headaches?

1. Traction, tension, or displacement of pain-sensitive structures

2. Distention/dilation of intracranial arteries, veins or venous sinuses

3. Inflammation of pain-sensitive structures

4. Obstruction of CSF pathways

5. Primary central pain: involvement of pain-modulating systems
Anatomy of Headache Pain
Pain Sensitive Cranial Structures

Scalp and its Blood supply
Dura
Venous Sinus
Large Arteries
Pain sensitive fibers of 5th, 9th, and 10th cranial nerves
Head and Neck Muscles
Intracranial Hypotension

• Normal pressure:
  70 to 200 (250?) mm H$_2$O

• Intracranial hypotension/hypovolemia
  – Symptoms with pressures < 70 mm H$_2$O
    • At times pressure not measurable
    • At times pressure normal
  – Most common cause LP
Intracranial Hypotension: Causes

A. LP: diagnostic, myelography and spinal anesthesia

B. Traumatic: head or back trauma (+ CSF leak)

C. Postoperative: craniotomy, spinal surgery, postpneumonectomy

D. Malfunctioning CSF shunt

E. Spontaneous CSF leak

F. Systemic illness: dehydration, diabetic coma, hyperpnea, meningoencephalitis, uremia, severe systemic infection
Intracranial Hypotension Headache Mechanisms

1. Downward brain displacement due to loss of CSF buoyancy?
   – Could cause traction on pain-sensitive structures (esp. dura)

2. Intracranial CSF volume loss
   – Can cause compensatory dilation pain-sensitive intracranial venous structures

But Headache aggravated by jugular compression

• Increases intracranial pressure and venous dilatation
• Headache not caused by intracranial hypotension alone
Headache Mechanisms: Buoyancy Loss

- CSF cushions the brain
  - Does loss ↓ upward buoyant force and cause brain sag when patient is erect?
  - Sag increases tension on veins that anchor brain to dural venous sinuses

- But no evidence to support this
  - Despite CSF loss, brain remains surrounded by fluid, so no decrease in upward buoyant force

Headache Mechanisms: Monroe-Kellie hypothesis

- Sum of brain, CSF, and intracranial blood volume constant
  - ↓ in one causes ↑ in one or both of remaining two.
- CSF loss → ↓ CSF pressure but not venous pressure
  - Pressure difference causes veins to dilate
    - More dilatation in upright posture
- Dilatation of pain sensitive intracranial venous structures
  - → orthostatic headache
- Evidence:
  - Pial veins of anesthetized cat dilate with CSF removal
  - Jugular venous compression increases headache intensity
  - Acute venous sinuses distension produces pain

Forbes HS, Nason GI. Vascular responses to hypertonic solutions and withdrawal of CSF Arch Neurol Psychiatry 1935;34:533–47.
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Arch Neurol Psychiatry 1935;34:533–47.
Intracranial Hypotension or Intracranial Hypovoleemia or Neither?

**CSF Pressure**
- Orthostatic headache can occur with normal pressure
- No correlation between CSF pressure and headache
- Jugular compression raises pressure and worsens headache

**CSF Volume**
- Loss correlates to post-LP headache

**Craniospinal Elasticity (Compliance)**
- Altered distribution due to spinal loss of CSF
Pressure Volume Curves and Compliance

- volume - pressure curve (less compliant)
- pressure-volume curve (more compliant)
- Distensibility: slope of volume–pressure curve.
  - ↑ Compliance → ↑ Distensibility
  - ↓ pressure → ↑ Compliance
Compliance of Membranes Enclosing CSF

Different throughout system

• Rostral component (covered by rigid skull)
  – Depends upon compressibility of intracranial venous and capillary vessels

• Caudal component
  – Depends on degree of filling of spinal dural sac

• Increased lumbar compliance (more give) causes HIP to be displaced caudally

Hydrostatic Indifferent Point (HIP)

• Point were upright CSF pressure = CSF recumbent pressure  
  – Normally between C7 and T5
• CSF leak may increase lumbar compliance (more give)  
  – Increased lumbar compliance shifts HIP downward  
  – Independent of decreased CSF volume or opening pressure
• Upright ICP more negative: equals distance HIP displaced  
  – Decrease in addition to that resulting from loss of filling pressure
• Change in lumbar compliance alone (without CSF leak) could cause orthostatic headache

Hydrostatic Indifferent Point

Located along upright CSF axis where CSF pressure = supine CSF opening pressure

**CSF Leak: Increased Caudal Compliance of CSF Space Relative To Cranial End**

- **Lumbar dural sac compliance increases with CSF leak**
  - Causes caudal HIP displacement
  - Upright ICP more negative equal to distance HIP displaced
  - Decrease in addition to that due to loss of filling pressure

- **Cranial compliance decreases with CSF leak**
  - Cerebral veins normally slightly collapsed, because CSF pressure exceeds dural sinuses pressure
  - \( \downarrow \) CSF pressure \( \rightarrow \) venous engorgement
    - Walls become stiffer and less compressible

CSF Leak and Dural Compliance

Lumbar dura usually resists stretch
  – Limits distensibility of caudal CSF space

1. **Large holes** increase lumbar compliance by
  – Exposing CSF to more compliant epidural space
    • Epidural veins, epidural fat, and paravertebral soft tissue

2. ↓ **filling pressure** increases lumbar compliance
  – Lumbar dural sac collapses and becomes more compliant
    • Creates space to accommodate CSF when patient upright

Does CSF Rhinorrhea Produce Headache?

Rostral CSF leak displaces HIP less than that due to LP

- Only 9cm caudally

WHY?

- Increased rostral CSF space should move HIP rostrally
- But ↓ filling pressure → ↑ caudal dural sac compliance
  - Overcomes effects of rostral anatomic change.
  - Thus rostral leaks may not lower HIP enough to cause headache

Lumbar Puncture
LP Causes Caudal Displacement of HIP

- **Initial** CSF pressure: 18 cm recumbent and 53 cm sitting
  - HIP 35 cm (53-18)
- **Post LP** CSF pressure: 5.5 cm recumbent and 28 cm sitting
  - HIP now 22.5 cm (28-5.5)
    - HIP displaced 12.5 cm (35-22.5) caudally
- **Filling pressure** ↓ 12.5 cm (18-5.5)
- **ICP** ↓ 12.5 cm recumbent, but ↓ 25 cm (12.5+12.5) upright
- **Standing** → marked ↑ in transmural venous pressure
  - Intracranial veins distend acutely
    - More distension due to loss of filling pressure
- **Acute orthostatic venous distention causes orthostatic headache**

Hydrostatic Indifferent Point

Location along the upright CSF axis where CSF pressure = supine CSF opening pressure
Normal

- -

C7

T5

HIP

+

+ +

Increased compliance of lower CSF space

HIP

- -

+++

+
Normal

Increased compliance of lower CSF space

Back  Replay
Spinal CSF Compartments: Cervical

• Cervical subarachnoid space differs from lumbar
  – Lumbar CSF space collapses but cervical CSF space expands with Valsalva maneuver
  – Opposite may occur in LPH
• Caudal HIP displacement
  – Cervical CSF pressure decreases
  – Cervical dura collapses but cervical epidural veins dilate
• Cervical dura compliance ↓
  – But does not overcome caudal HIP displacement from ↑ lumbar compliance
Spinal CSF Compartments: Cervical

- Standing: CSF from cervical and intracranial compartments move into more compliant lumbar sac
- Cervical dura partially collapses with compensatory acute distension of cervical *epidural veins*
  - Can cause orthostatic posterior cervical pain
  - Intracranial veins dilate causing orthostatic headache
- Young children and older adults: have stiffer caudal space
  - Less increase in caudal compliance with dural tear
    - HIP displaced less and post LP headache less common
Intracranial Hypotension Headache: Conclusion

- **Cause:** abnormal distribution of craniospinal elasticity
- **↑ lumbar compliance** → HIP to move caudally → **more** intracranial hypotension and venous dilation in erect position

- **Can explain:** orthostatic character of headache
  - Spinal not cranial leakage produces headache
  - Imperfect correlation between CSF pressure and headache
  - Near absence in very young and elderly due to **↑** epidural space stiffness at these ages