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>
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

Modulator
- NE
- 5-HT

PNS
- C-fiber
- Aβ fiber
- DRG (Trigeminal Ganglion)

CNS
- WDR Neuron
- Nucleus Trigeminal Caudalis

Impulses
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 Pressure

• Normal pressure:
  70 to 200 (or 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.
Pial Vessels Dilate as CSF Pressure Decreases

Forbes HS, Nason GI. Vascular responses to hypertonic solutions and withdrawal of CSF
Arch Neurol Psychiatry 1935;34:533–47.
Intracranial Hypotension or Intracranial Hypovolemia 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


Normal

Increased compliance of lower CSF space
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
  - ↓ CSF pressure → 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

Magnaes B. Body position and cerebrospinal fluid pressure
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

65 – 150 – 195

C7

T5

Brain

Spinal fluid

HIP
Increased compliance of lower CSF space
Normal

Increased compliance of lower CSF space
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