MRI of Hydrocephalus with Thoughts on the Etiology of NPH

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Hydrocephalus

- MR findings: Interstitial edema
- CSF Flow: Functional (Shuntability)

- Forms:
  - Obstructive (tumor, inflammation)
  - Communicating (SAH, meningitis)(NPH)
Colloid Cyst
Communicating Hydrocephalus
Aqueductal Stenosis
No flow void!
Aqueductal Stenosis

- Abnormally small aqueduct
- Totally obliterated aqueduct
- Membrane formation
- Forking with multiple diverticuli
Benign External Hydrocephalus
Benign External Hydrocephalus
Tectal Glioma

How does the CSF get out??
How Does CSF Get Out?

- Through pia?
- Via aquaporins?
- Via VR spaces?
- Via lymphatics?
- Solute transport?
Callosal Sulcus
Callosal Sulcus
Normal Pressure Hydrocephalus

- Described by Hakim, Adams, et al (1965)
- 50% known cause (SAH, meningitis)
- 50% idiopathic (older)
- Diagnosis primarily clinical: Gait apraxia, dementia, incontinence
- Radiology: communicating hydrocephalus
Physiologic Tests for NPH

• Nuclear cisternography
  – Communicating hydrocephalus
• Pressure monitoring
  – Waterhammer pulse
  – Plateau waves
• Saline Infusion (outpatient)
  – If resistance > 4mmHg/ml/min, 82% respond to ELD
• 50 cc Tap test: PPV 73-100%; sensitivity 26-62%
• External lumbar drainage (inpatient)
External Lumbar Drainage

- 16 gauge lumbar puncture; catheter drainage
- 10 cc/hour for 3 days; gait assessed
- Of 151 patients* with iNPH, 100 improved with ELD
  - Gait only (88%), gait/dementia (84%), triad (59%)
- Of responders, 90% improve with VP shunt
- Of nonresponders, 22% improve with shunt

NPH
Atrophy
Gait Disturbance in NPH

Paracentral fibers corticospinal tracts?

Parkinson’s from pressure on substantia nigra?
Enlarged 3rd Ventricle in NPH
Quantification of CSF Flow Void

- Signal loss (dephasing) due to
  - CSF velocity
  - Orientation
  - Gradient strength
- Extent of flow void
  - More important than magnitude
CSF Flow
Void
Proposed Causes of CSF Motion

- Production by choroid plexus (500 ml/day)
- Cardiac pulsations
  - Choroid plexus (Bering, 1959)
  - Large arteries
  - Cerebral hemispheres (phase-contrast MRI)
CSF Flow Void vs. Surgical Response

- 20 patients shunted for presumed NPH (1984)
- All had gait disturbance and dementia
- 17/20 had incontinence
NPH vs CSF Flow Void

- Surgical Response graded (1984)
  - Excellent-good
  - Fair-poor
- CSF flow graded (1989)
  - Absent-mild
  - Moderate-severe
Materials and Methods

• Surgical Response Compared to:
• CSF Flow Void on Routine MRI
  – 1984
  – No flow compensation
Normal
(1984)
Hyperdynamic flow (1984)
### CSF Flow Void

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<thead>
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<th>Surgical Response</th>
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<tr>
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<td>8</td>
<td>1</td>
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<tr>
<td>Poor</td>
<td>2</td>
<td>9</td>
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Fisher’s Exact Test $p < 0.003$
To shunt or not to shunt (1984)

Enlarged Sylvian cisterns in NPH
Association of DWMI and NPH: Clinical

• Some cases of L’etat Lacunaire (Marie, 1901) may have been NPH (Fischer, 1981)

• Coexistence of NPH and Hypertensive Cerebrovascular Disease Noted Previously (Earnest 1974, Goto 1977, Graff-Radford 1987)
### DWMI: Normal vs NPH Incidence

<table>
<thead>
<tr>
<th>DWMI</th>
<th>GROUPS</th>
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<tr>
<td>3</td>
<td>NPH (Groups I &amp; II)</td>
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<tr>
<td>2</td>
<td>NORMAL (Group IV)</td>
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<td>1</td>
<td>NPH (Groups I &amp; II)</td>
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<td>4</td>
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<td>15</td>
<td>26</td>
<td>21</td>
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\[ X^2 = 18.44, \ p < .001 \]
“Multiple deep cerebral infarctions may be the initial pathologic process in some cases of NPH”

• Earnest, 1974
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<td>Good</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Poor</td>
<td>8</td>
<td>3</td>
</tr>
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</table>

Fischer’s Exact Test: Not significant
Conclusion

• There is a significantly greater incidence of DWMI in patients with NPH than in age-matched controls.

Conclusions

• CSF flow void is useful indicator of favorable response to CSF diversion
• Presence of DWMI is not contraindication to shunting
• NPH and DWMI may be related
CSF Flow Void
CSF Flow Measurement

- CSF flow void on conventional MR images represents average motion during 256 spin echo acquisitions.
- Since CSF motion is due to cardiac pulsations, it is better evaluated using cardiac gated techniques.
Phase Contrast CSF Velocity Imaging

• “Velocity” is speed plus direction
• Flow sensitization along craniocaudal axis
  – Flow up: shades of black
  – Flow down: shades of white
  – No flow: gray
  – Set aliasing velocity
  – Quantification of velocity or flow
Qualitative CSF Velocity Imaging
Quantitative CSF Flow Study

- 512x512; 16 cm FOV
- .32 mm pixels
- 4mm slice angled perpendicular to aqueduct
- Velocity-encode in slice direction
- Retrospective cardiac-gating (not EKG triggering)
Quantitative CSF Velocity Imaging
Quantitative CSF Flow Study

- Through-plane flow-encoding
- Venc = 10, 20, 30 cm/sec (NPH)
- Venc = 5 cm/sec (shunt malfunction)
Quantitative CSF Velocity Imaging
Communicating Hydrocephalus
CSF Velocity Imaging

Magnitude image

Phase contrast image
Phase Contrast CSF Flow
Quantitative CSF Flow

- GE: Cine PC 40/min/30 degrees
- Siemens: Retrospective Cardiac Gating
  - Flash 100/10/15 degrees
- Both: 18 Cine Frames
Quantitative CSF Velocity Imaging
Quantitative CSF Velocity Imaging

- Calculates “Aqueductal CSF stroke volume”
- Stroke volume: microliters of CSF flowing back or forth over cardiac cycle
- Verified by pulsatile flow phantom using ultrasound flow meter (Mullin, 1993)
Materials and Methods

- 20 Patients (age 54-85)
- Suspected NPH
- Routine MRI of Brain
- Quantitative CSF Velocity Imaging
- VP Shunt
- Follow up at 1 month

Results

• Of 20 shunted patients:
  • 14 had hyperdynamic flow
    – (SV>42 microliters; NB: machine specific!)
    – 13 had a good surgical response
    – 1 did not (chronic MS)
  • 6 had normal or decreased flow
    – (SV<42 microliters)
    – 3 had a good surgical response
    – 3 did not (concomitant atrophy)

NPH (SV = 121 μL)
Results

• Only 7 of 14 (50%) patients with hyperdynamic flow had prominent aqueductal CSF flow void or routine MR images

• Ubiquitous Flow Compensation; FSE
NPH: preshunting

- 75-year-old
- Gait disorder
- Cognitive impairment
  - For about 6 months
- No tremor
- Bilateral forced grasp

Courtesy of Joseph Masdeu, MD, PhD, NIH
Hydrocephalus: Before and After

- Treated with a ventriculo-peritoneal shunt
Improved Gait and Cognition After Shunting
78 Year Old Woman with Suspected NPH
CSF Flow Study: No Flow
CISS: Aqueductal Stenosis
Normal Aqueduct: CISS
Aqueductal Stenosis: FIESTA

64 yo woman R/O NPH
What Causes Idiopathic NPH?

• Consider normal bulk flow of water in brain
• Consider association of deep white matter ischemia (DWMI) and NPH
Normal Bulk Flow of Extracellular Brain Water

- Water leaves upstream arterioles under pressure-osmotic gradients (eg, mannitol)
- Normal and excess water resorbed by downstream capillaries and venules
- Vasogenic edema flows centripetally to be absorbed by ventricles
- Interstitial edema flows centrifugally to subarachnoid space via extracellular space
Idiopathic NPH and DWMI

- Both diseases of elderly
- Significant association now shown by many
- CBF reduced in NPH and DWMI
- Acetazolamide challenge: no increase in CBF
  - Arterioles already maximally dilated (esp WM)
- DWMI more extensive than T2 abnormality
  - Magnetization transfer ratio decreased
  - Apparent diffusion coefficient increased
  - Increased lactate on proton spectroscopy
Possible Etiology of NPH

• Hypothesis: NPH patients have always had large ventricles (“slightly enlarged”)
  – Decreased CSF resorption (saline infusion test)
  – Unrecognized benign external hydrocephalus?
• No evidence for previous SAH or meningitis
• Significant CSF resorption pathway is via extracellular space of brain (like tectal gliomas)
• Everything fine until “second hit”: DWMI

• Bradley WG, Neurosurgical Clinics of North America 36:661-684;2001
DWMI is “Second Hit” in NPH

- No symptoms until DWMI occurs later in life
- Resistance to peripheral CSF flow through extracellular space increases slightly due to DWMI
  - Loss of myelin lipid: more hydrophilic environment
  - Greater attraction of outflowing CSF to myelin protein
- CSF production continues unabated
  - Accumulates in ventricles - hydrocephalus worsens
  - Increased tangential shearing forces
  - NPH symptoms begin

- Bradley, WG Neurosurgical Clinics of North America 36:661-684;2001
Aqueductal Stenosis in Elderly

- Also rely on extracellular space of brain for CSF drainage
- DWMI is second hit by increasing resistance to CSF outflow
- Sx: headaches plus triad of NPH
- ?Mechanism in 30-ish women (Mayo series)

constant current generator ~ 500 cc/day
Normal 4th ventricular Outflow of CSF

Normal Suction
Low Resistance
Good Flow

Reduced 4th ventricular Outflow of CSF

Normal Suction
High Resistance
Low Flow

Increasesd CSF Outflow through 4th Ventricle and Extracellular Space

Normal Suction
Lower Resistance
Better Flow
Flow versus increasing resistance in normal pathway

Flow (cc/day)

$F_{\text{normal}}$

$F_{\text{fcs}}$

$R_{\text{normal}}$ (mmH2O*day/min)
Increasing Resistance to Extracellular CSF Flow vs Ventricular Volume

Recs vs. Vvent

Recs

0 2 4 6 8 10 12

Vvent

0 200 400 600 800 1000 1200

Recs
Hypotheses

- If NPH patients had benign external hydrocephalus before 1 year of age, their intracranial volumes should still be larger than sex-matched controls.
- If they rely on drainage of CSF through the extracellular space of the brain, the ADC should be elevated for a given degree of DWMI.
Materials and Methods

• Intracranial volumes measured from T2WIs using workstation (Vital Images)
• 22 men with clinical NPH vs 55 controls
  – Ave stroke volume: 159 uL (normal: 42 uL)
• 29 women with NPH vs 55 controls
  – Ave stroke volume: 127 uL

Results: Intracranial Volumes

- NPH men (n= 22): 1682 cc
- Control men (n=55): 1565 cc
- NPH volumes significantly larger (p<.003)
  - 117 cc (7.5%)
- NPH women (n=29): 1493 cc
- Control women (n=55): 1405 cc
- NPH volumes significantly larger (p<.002)
  - 88 cc (6.5%)
Implication

- Patients with “slightly enlarged ventricles” for no apparent reason should be observed carefully for onset of gait disturbance in later years
- Probable window of opportunity to treat
ADC: NPH vs Controls

• Apparent Diffusion Coefficient (ADC) profile in 10 pixel wide coronal sections through axial slices through upper lateral ventricles

• ADC measurements in centrum semiovale controlled for a given degree of DWMI
ADC Profile: Mid/Posterior Coronal Location
ADC Profile: NPH vs Control
Anterior Coronal Location

Blue: NPH
Red: Control
ADC vs NPH vs Control

AVIM: Asymptomatic Ventriculomegaly with features of iNPH on MRI
67 yo man will be shunted for NPH in 19 years; currently walking 20 miles a day

1982 CT for giant cell arteritis
1985: Still no NPH symptoms (now age 70)
1991: Pt (now 76) will develop NPH in 10 years.
**Follow up**

**TO:** Bradley  
**FROM:** Dr. Brian Johnson  
**DATE:** 1/30  
**TIME:** 3:30 PM  
**PHONE:** ( )  
**CELL:** (50) 6916-5515  
**FAX:** ( )  

**MESSAGE:**

Father had normal pressure hydrocephalus.  
Follow up post shunt.  
His father can walk several miles a day.

**SIGNED:** [Signature]

**EMAIL ADDRESS:**  
**PHONE:** Y  
**RETURNED CALL:** Y  
**WANTS TO SEE YOU:**  
**WILL CALL AGAIN:**  
**WAS IN:**  
**URGENT:**
Testimonial from 86 yo physician with NPH

• Dr Bradley,

• Your optimistic verbal report to me re: the result of my CSF flow study proved accurate. Ventriculo-peritoneal shunt resulted in substantial improvement. Would it be possible for me to receive a written report for my records.

• Thank you.
55 yo r/o Metastatic Melanoma: Future NPH Patient?
Conclusions

• NPH diagnosed by symptoms, not MRI
• MRI used to confirm diagnosis of shunt-responsive NPH
• Asymptomatic patients may have dilated ventricles and elevated CSF flow: Pre NPH?
• Not everyone with benign external hydrocephalus gets NPH
• Keep your extracellular space open