THE VISUAL IMPAIRMENT INTRACRANIAL PRESSURE SYNDROME IN LONG DURATION U.S. ASTRONAUTS: EPIDEMIOLOGY AND PATHOPHYSIOLOGY

Lead Scientist, NASA VIIP Risk

Universities Space Research Association, Houston, TX,

Sensorimotor Workshop
NSBRI, Houston, TX
Thursday August 29, 2013.
Visual Impairment Intracranial Pressure Syndrome Signs

- **Hyperopic Shifts**
  - Up to +1.75 diopters

- **Choroidal Folds**
  - Parallel grooves in the posterior pole

- **Globe Flattening**

- **Optic Disc Edema (swelling)**

- **Altered Blood flow**
  - "cotton wool" spots

- **Increased Optic Nerve Sheath Diameter**

MRI Orbital Image showing globe flattening

Normal Globe

Flatten Globe
VIIP Clinical Findings

• To date 15 U.S. ISS long-duration spaceflight astronauts have developed some or all of the following findings:

  - Hyperopic shift
  - Choroidal folds
  - Cotton wool spots
  - Optic Nerve Sheath Distention
  - Globe flattening
  - Edema of the Optic disc (papilledema)

Signs of elevated intracranial pressure

• High postflight intracranial pressure in four crew members:
  • 15.4-21.3mmHg (Normal: 7-15mmHg) or,
  • 21-29 cmH2O, Normal: 9.5-20.4cmH2O
Initial Identification of the VIIP: Subjective Changes in Vision

- 50% of long-duration (ISS) mission astronauts report a subjective degradation in vision, primarily increasing *farsightedness*

- **Hyperopic shift**
  
  Decreased near visual acuity, distant vision intact

(1 mm decrease in axial length is equivalent to a 3 diaper hyperopic shift)
Pre to Post Flight Papilledema: A Clinical Sign of Raised Intracranial Pressure

Pre Flight
Fundoscopic images of the right and left optic disc.

Post Flight
Fundoscopic images of the right and left optic disc showing Grade 3 edema right and Grade 1 edema left.
In Flight B-scan Ultrasound
Because of a variable pressure-diameter relationship, the clinical relevance of this method relies on the demonstration of ongoing enlargement on serial US studies.

78 measures
$r = 0.71$
$p < 0.0001$
ISS Inflight Crew Ultrasound Imaging: Additional Signs of Raised Intracranial Pressure

1. Increased Optic Nerve Sheath Diameter

Terrestrial Normal < 5.9 mm

2. Posterior Globe Flattening

Preflight

Postflight

Flattening of Posterior Globe

3. Raised Optic Disc

Postflight
Choroidal Folds

- Thickening of the choroid secondary to venous blood engorgement from uG fluid shift.
## VIIP Clinical Practice Guideline Case Definition

<table>
<thead>
<tr>
<th>Class 1</th>
<th>( \geq .50 ) diopter cycloplegic refractive change and/or cotton wool spot</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Class 2</strong></td>
<td>( \geq .50 ) diopter cycloplegic refractive changes or cotton wool spot</td>
</tr>
<tr>
<td></td>
<td>• Choroidal folds and/or optic nerve sheath distension and/or globe flattening and/or scotoma</td>
</tr>
<tr>
<td><strong>Class 3</strong></td>
<td>( \geq .50 ) diopter cycloplegic refractive changes and/or cotton wool spot</td>
</tr>
<tr>
<td></td>
<td>• Optic nerve sheath distension, and/or globe flattening and/or choroidal folds and/or scotoma</td>
</tr>
<tr>
<td></td>
<td>• Papilledema of Grade 0-2.</td>
</tr>
<tr>
<td><strong>Class 4</strong></td>
<td>( \geq .50 ) diopter cycloplegic refractive changes and/or cotton wool spot</td>
</tr>
<tr>
<td></td>
<td>• Optic nerve sheath distension, and/or globe flattening and/or choroidal folds and/or scotoma</td>
</tr>
<tr>
<td></td>
<td>• Papilledema Grade 2 or above.</td>
</tr>
<tr>
<td></td>
<td>• Presenting symptoms of new headache, pulsatile tinnitus and/or transient visual obscurations</td>
</tr>
<tr>
<td></td>
<td>• CSF opening pressure &gt;25 cm H2O</td>
</tr>
</tbody>
</table>
Current U.S. ISS VIIP Incidence:

41 U.S. ISS astronauts flown to date as of Expedition 32:
- **Unclassified astronauts N=16** (*No MRI, OCT or ocular US*)
- Non-cases N=6
- **Confirmed cases: 19**

**Clinical Classification:**

- Class One N=2
- Class Two N=11
- Class Three N=2
- Class Four N=4

\[
\begin{align*}
68.4 \% & \text{ Class 1&2} \\
31.6 \% & \text{ Class 3&4}
\end{align*}
\]

Increasing severity

Current VIIP Incidence as a % of U.S. ISS astronauts tested= 76.0%
Visual Impairment and Elevated Intracranial Pressure in Spaceflight

Primary Systems Involved

Cardiovascular + CNS + Ocular

Cardiovascular

CNS

Ocular
Cephalad Fluid Shift

On ground 1G → Initial stage in space
Loss of Hydrostatic Drainage & Cerebral Venous Congestion

Adapted from Rowell, 1988

Loss of Hydrostatic Drainage & Cerebral Venous Congestion

Adapted from Hargens & Richardson, Respiratory Physiology & Neurobiology. 2009

1G

0G

1G Supine

Adapted from Rowell, 1988
Tilt Angle vs ICP & CVP: Positional Fluid Shifts

2. Hemodynamic changes due to Trendelenburg positioning and pneumoperitoneum during laproscopic hysterectomy, Acta *Anaesthesiologica Scandavica*. 1995
Redistribution of Venous Pressures From 1G to 0G

Standing 1G

\[ ICP = CSF_{out\ resistance} \times CSF_{formation} + SSS_{pressure} \]

0G

venous pressure (mmHg)

\[ \begin{array}{c}
-20 \\
0 \\
20 \\
40 \\
60 \\
80 \\
100 \\
\end{array} \]

venous pressure (mmHg)

\[ \begin{array}{c}
15-20 \\
7-9 \\
\end{array} \]

9.8m/s²

Cranium is rigid
Venous congestion
Obligate arterial flow
Transcapillary leak
++ICP~30-40

Jugular Vein Pressure & ICP Increases in Simulated Microgravity

- Jugular bulb pressure approximates dural sinus pressure
- Jugular vein pressure measured in 7 animals during 4.5s free drop
- Loss of hydrostatic pressure gradient increased JVP 1.3mmHg
  - i.e. loss of hydrostatic assisted venous drainage
- Similar study, ICP increased in 5 rats from 4.8 to 7.3 mmHg =52% increase in ICP
- Factors that may further raise ICP:
  - Complete cephalad fluid shift, Increased CO2


VIIP Ocular Findings in ISS Astronauts

- Flattening: 64%
- ΔCR ≥ 0.5 Diopter: 50%
- Distension: 36%
- Choroidal Folds: 33%
- Disc Edema: 17%
- CWS*: 8%
- Scotoma: 3%

# of Crewmembers
IIH MRI Signs vs VIIP

<table>
<thead>
<tr>
<th>Imaging Assessment</th>
<th>Present in IIH (Specificity)</th>
<th>Seen in VIIP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venous Stenosis Score</td>
<td>100%</td>
<td>?</td>
</tr>
<tr>
<td>Flattening of Posterior Globes</td>
<td>100%</td>
<td>Yes</td>
</tr>
<tr>
<td>Optic Nerve Protrusion</td>
<td>100%</td>
<td>Yes</td>
</tr>
<tr>
<td>Partially Empty Sella</td>
<td>95.3%</td>
<td>Yes</td>
</tr>
<tr>
<td>Optic Nerve Sheath Distension</td>
<td>88.4%</td>
<td>Yes</td>
</tr>
<tr>
<td>Optic Nerve Tortuosity</td>
<td>86%</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Vascular Capacitance: Venous & Arterial

20% = 1L

70-80% = 4L
Venous Compliance

\[ C = \frac{\Delta V}{\Delta P} \]

Vein

Volume

Pressure

Vein

Artery

Volume

Pressure
Factors Increasing Venous Tone will Increase Cerebral Venous Outflow Resistance

- Resting Tone of Venous Vessels Influenced by:
  - SNS tone $\uparrow$
    - Resting Blood Pressure
  - Endothelin $\uparrow$
  - Nitric oxide $\downarrow$
  - Inflammatory cytokines $\uparrow$

$\text{Although effects of tone less on venous side vs arterial, volume is much greater}$
Metabolic Syndrome

Hypertension

Hyperglycemia

Hypertriglyceridemia

Elevated LDL

Decreased HDL

Impaired Fibrinolysis

Hypercoaguability

Oxidative Stress

ROS 02-

Endothelial Dysfunction

↓NO2

Inflammation

Proliferation

↑CRP

Vascular Dysfunction
Occupational Surveillance Data Mining: Percentage Body Fat

VIIP Classification vs %Fat
(Annual Preflight Exam)

Best Fit (curvilinear) for Cases; $R^2 = .38$, p<.01
N=35, 13 Cases, total observations=35
Estimated & Observed CPG Scores

Non-Linear Estimation of CPG for Cases

* Antihypertensive Medication

Sig. association of SBP with CPG score
p=.0002 R²= 31%

Confirmed non-cases (Green) & unclassified (Blue)
Not included in model, for reference only

N=35, Cases=13
○ cases △ non-cases

Pre-flight Systolic Blood Pressure Non-Cases vs Cases per CPG
Occupational Surveillance Data Mining:
Resting Pulse Pressure (Sitting)

Cases per CPG vs Pulse Pressure
(Annual Preflight Exam 4-Year Mean)

Estimated & Observed CPG Scores

Pre-Flight Pulse Pressure

Confirmed non-cases (Green) & unclassified (Blue)
Not included in model, for reference only

Best Fit (curvilinear) for Cases; $R^2 = .45$ (including BP meds predictor), $p < .01$
Self Reported ISS Inflight Daily Sodium Intake

- Current recommended daily sodium limit = 2300mg/day
- If 51y or high BP, recommended limit=1500mg/day
- Applies to majority of U.S. adults

<table>
<thead>
<tr>
<th>Subject's Mean Reported Na Intake per Flight</th>
<th>Confirm non-case</th>
<th>CPG-1</th>
<th>CPG-2</th>
<th>CPG-3</th>
<th>CPG-4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3512</td>
<td>3506</td>
<td>4843</td>
<td>3661</td>
<td>5281</td>
</tr>
</tbody>
</table>

Jackknife

<p>| Sodiummgday  | Coef.  | Std. Err. | z     | P&gt;|z| | 95% Conf. Interval |
|--------------|--------|-----------|-------|-----|---------------------|
| cpg_revised  | 0.2186 | 0.1105    | 1.98  | 0.048 | 0.0020036…yes … positive, but weak |</p>
<table>
<thead>
<tr>
<th>Cardiovascular Variable</th>
<th>Significant Correlation Across CPG Classification</th>
<th>R²</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Biochemistry:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL</td>
<td>✓</td>
<td>0.43</td>
<td>P&lt;0.02</td>
</tr>
<tr>
<td>HDL</td>
<td>-</td>
<td>0.22</td>
<td>P&lt;0.09</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin A1c</td>
<td>✓</td>
<td>-</td>
<td>P&lt;0.01</td>
</tr>
<tr>
<td>Fasting serum glucose</td>
<td>✓</td>
<td>0.125</td>
<td>P&lt;0.008</td>
</tr>
<tr>
<td>Homocysteine</td>
<td>✓</td>
<td>-</td>
<td>P&lt;0.01</td>
</tr>
<tr>
<td>Oral sodium intake</td>
<td>✓</td>
<td>0.22</td>
<td>P&lt;0.05</td>
</tr>
<tr>
<td><strong>Body Composition:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>✓</td>
<td>0.41</td>
<td>P&lt;0.01</td>
</tr>
<tr>
<td>Percentage Body Fat</td>
<td>✓</td>
<td>0.38</td>
<td>P&lt;0.01</td>
</tr>
<tr>
<td><strong>Cardiac:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resting systolic blood pressure (pre-in-post flight)</td>
<td>✓</td>
<td>0.31</td>
<td>P&lt;0.0002</td>
</tr>
<tr>
<td>Pulse Pressure (pre-in-post flight)</td>
<td>✓</td>
<td>0.45</td>
<td>P&lt;0.01</td>
</tr>
<tr>
<td>CT Coronary Calcium Score</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Aerobic Capacity:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased Maximal Oxygen Uptake</td>
<td>✓</td>
<td>-</td>
<td>P&lt;0.04</td>
</tr>
</tbody>
</table>
Key Brain Areas Affected by Fluid Shift

- CSF Production
- CSF Resorption (AG-Venous/Lymphatic)
- Venous Congestion
- Interstitial fluid
Pressure and Compliance Changes in the Craniospinal Axis

Resistance to cerebral venous drainage

\[ ICP = CSF_{out \text{ resistance}} \times CSF_{formation} + SSS_{pressure} \]

CVR = CPP/CBF

CPP = MAP - ICP
Venous Congestion May Cause Increased Transcapillary Pressure & Decreased Absorption
Venous Congestion & Interstitial Edema Inhibit Lymphatic CSF Drainage-Impacts on Optic Nerve
The Translaminar Pressure Gradient: A Mechanism for Papilledema

Area of Interest:

Optic nerve
Retina
Lens

Area of Magnification

Translaminar Pressure Gradients:

1G 0G

Translaminar Pressure Gradient

CSFp

IOP

retinal pigmented epithelium (RPE)

optic disc (or optic papilla)

dural sheath of optic nerve

optic nerve

retina vessels

lamina cribrosa

vitreal cavity
OCT: Average RNFL Change in VIIP Cases Pre to Postflight

![Graph showing OCT: Average RNFL Change in VIIP Cases Pre to Postflight](image)

- **RNFL Pre & Post ISS by CPG Classification**

- **Observed and Modeled RNFL with 95% CI**

- **Clinical Practice Guidelines Classification (0-4)**

- **Mean (95%CI) Pre**

- **Mean (95%CI) Post**

- **RNFL Pre**

- **RNFL Post**

- **Sig difference in RNFL Pre to Postflight for CPG 3&4. p<0.01**
IOP for Six Shuttle Missions (12 Subjects)

Pre-flight, In-flight-Post-flight

- Ocular Hypertension
- Ocular Hypotension

Sources:
- Mission 1 A
- Mission 1B
- Mission 2
- Mission 3
- STS 55 1
- STS 55 2
- STS 90 1
- STS 90 2
- STS 90 3
- STS 90 4
- STS 95

Glaucoma Medically Controlled
Mean IOP Pre & Postflight in ISS Crew per VIIP CPG: Does Low IOP Predispose to Papilledema Formation?

Sig difference between CPG 3-4 vs CPG 0
Postflight p<0.04 (All 5 CPG 3-4 cases represented Pre/Post)

N=34, 13 cases, 7.9 Obs/subject
Translaminar Pressure Difference & Visual Field Defect

Examples:

<table>
<thead>
<tr>
<th>ICP</th>
<th>IOP</th>
<th>TLP</th>
<th>Delta</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>15</td>
<td>-5</td>
<td>5</td>
</tr>
<tr>
<td>25</td>
<td>17</td>
<td>+8</td>
<td>13</td>
</tr>
<tr>
<td>35</td>
<td>17</td>
<td>+18</td>
<td>23</td>
</tr>
</tbody>
</table>

- Amount of glaucomatous visual field defect correlated positively with the TLP pressure difference ($P < 0.005$) $r=0.69$
CO$_2$ Levels on ISS

- **CO$_2$ is an extremely potent vasodilator**
  - Every 1mmHg increase PaCO$_2$ = 4% increase in dilation

- **CO$_2$ mission average=3.56mmHg (0.33%)**
  - 10x normal sea level atmospheric: 0.0314%
  - Average Peak CO$_2$=8.32mmHg (0.7%) (20x)

- **CO$_2$ may cause increased CSF production due to increased flux of HCO$_3^-$ across choroid plexus & accompanying H$_2$O**

Adapted from Alperin et al. Radiology, 2000
Increased BP with Elevated CO2 Causing Decreased Compliance

CPP = MAP - ICP
Cerebral Blood Volume Change with Changing PaCO2

@ 37, CBV = 0.041 Paco, + 2 = 3.52
@45mmHg CBV = 0.041 Paco, + 2 3.85
Diff = .33ml/100 .33x12 4ml
Cerebral Blood Flow Velocity During Hypercapnia & $10^\circ$ HDT + Hypercapnia

**PART ONE: HYPERCAPNIA ON CEREBRAL BLOOD FLOW—SLIWKA ET AL.**

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**Cerebral Blood Flow Velocity (CBFv): Left Middle Cerebral Artery (MCA)**

Mean CBFv MCA [cm/s]: $10^\circ$ HDT + Rebreathing Test

---

**Cerebral Blood Flow Velocity (CBFv): Left Middle Cerebral Artery (MCA)**

Mean CBFv MCA [cm/s]: $10^\circ$ HDT + Rebreathing Test

---

**Mean CBFv MCA [cm/s]: $10^\circ$ HDT + Rebreathing Test**

- Exposure to CO$_2$

---
Data mining - Contributions of CO$_2$ to the VIIP syndrome

- **PI:** TBD

- **Aims:** This retrospective data mining effort will evaluate the in-flight CO$_2$ levels during flight with the time course of identified visual changes experienced by crew members to determine if increase CO$_2$ levels could be a contributing factor to the VIIP syndrome.

- Zwart et al. 2012 found a difference in CO2 concentrations between cases and non-cases:
  - In-flight cabin CO2 concentrations were higher ($P < 0.05$) for OC+ (N=5) than OC- astronauts (N=15).

<table>
<thead>
<tr>
<th></th>
<th>FD15</th>
<th>FD30</th>
<th>FD60</th>
<th>FD120</th>
<th>FD180</th>
</tr>
</thead>
<tbody>
<tr>
<td>OC-</td>
<td>2.6 ± 1.4</td>
<td>2.9 ± 1.3</td>
<td>2.9 ± 0.9</td>
<td>2.6 ± 1.2</td>
<td>2.9 ± 0.6</td>
</tr>
<tr>
<td>OC+ *</td>
<td>3.6 ± 0.7</td>
<td>3.7 ± 0.5</td>
<td>3.8 ± 0.5</td>
<td>3.3 ± 0.8</td>
<td>3.1 ± 1.1</td>
</tr>
</tbody>
</table>

* $P < 0.05$

Limit Resistive Training:

Resistive Exercise
Does in-flight resistance training cause additional transient elevations in ICP?

Resistive Exercise Repetitions causing spikes in ICP
(1 hour x 5 sessions per week)

Max 2-Leg Press with Valsalva  CVP↑ 56mmHg
Max 2-Leg Press no Valsalva  CVP↑ 9mmHg

Microgravity Dose Response for the VIIP?

- N=27 Astronauts, mean time to MR imaging was 606 days +/- 822
- 18 group 1 astronauts underwent imaging more than 100 days after flight
- Consistently higher percentage of findings for group with greater microgravity exposure, and increased severity of findings.

| Cumulative Lifetime Exposure to Microgravity Relative to Imaging Findings |
|---|---|---|---|---|---|---|
| **Time in UG** | **No. Subjects** | **Globe Flattening** | **Optic Nerve Sheath Kinking** | **ONSD>5.9 mm** | **Optic Disc Protrusion** | **Moderate or Greater Pituitary Concavity** |
| <30d (Short) | 12 | 1 | 1 | 5 | 0 | 0 |
| >30d (Long) | 15 | 6 | 3 | 9 | 4 | 3 |
A Working Model: Potential Interaction of the CNS, Vascular, & Ocular System in the VIIP

[Diagram showing the interaction of the CNS, vascular, and ocular systems with labels for Spinal subarachnoid space, Fourth ventricle, Third ventricle, Lateral ventricles, Choroid plexus, Cortical subarachnoid space, Arachnoid granulations, Cerebral venous blood, Cerebral venous congestion, Loss of hydrostatic drainage, 8 m/s², Adapted from Rekate]
Supplemental O2 as a Treatment Option

- As the arterial tension of CO2 rises, CBF increases, when it is reduced vasoconstriction is induced.
- Hyperventilation can lead to a mean reduction in intracranial pressure of about 50% within 2-30 minutes.

Supplemental O2 to drive down PaCO2 & venous congestion/ICP
Correlation of ONSD & Visual Field Deficit

- 20 patients with IIH (mean age=47) papilledema grade 1.1(range 0-4), 20 controls
- CSF pressure=260-320mmH2O, Mean duration disease=7.65 years
- Perimetric defects in 70% of eyes (28/40)
- Deficit associated with papilledema grade

**MD:** Average deviation from age matched controls

**PSD:** Measure of visual field irregularities
Blind Spot Enlargement Following Papilledema

- 24 IIH patients, symptoms present 1-30 months
- Median CSFp=25mm Hg (range 8-45), all had papilledema initially
- Followed for 49 months, treated with Diamox and diuretics 6-18 months
- Patients who regained normal disc (50%) had shorter duration of disease (median=4 months) vs those who developed chronic changes (median=12 months)
- Visual field testing not conducted
Visual Loss Associated with Papilledema Grade

- 9 IIH patients (mean age=31.8) with asymmetric papilledema 2+ grade diff.
  - High grade=3 (2-5) vs Low grade=1 (0-2)
- Mean CSFp=347.2 mm H2O
- Visual loss most prominent in eye with higher grade papilledema
- High grade papilledema should be regarded as a risk factor for visual loss

The Visual Island

Depression of the visual island with increasing papilledema grade
Mild Papilledema and Visual Field Loss

- N=22, mean age=40, recent diagnosis of IIH
- Mild papilledema, mean= Frisen 2 (range 1-3)
- Mean CSFp=35cmH2O (range 25.5-45)
- 1 Year follow-up:
  - Perimetry: 66% normal VF, 18% enlargement blind spot, 16% irreversible field loss
  - OCT: 10 RNFL thinner than normal (3 visual field constriction, 3 inferonasal defects, 1 had a scotoma)
- RNFL swelling and attrition may occur simultaneously
- Perimetry needed with OCT, since OCT cannot distinguish between decreased swelling vs axonal loss
- *Both OCT and perimetry required for F/U*

- 23 IIH patients, mean age 33.8, 23 controls
- Mean follow-up in patients with regression of papilledema=27 months
- 8/13 (63%) regressive papilledema group had mild-moderate concentric visual field damage—superior and inferior regions
- Patients with papilledema, only 1/10 detectable visual field loss
- Data show significant reduction RNFL as a sign of axon loss in patients with apparently treated papilledema
- Minor loss of axons will be masked by structure of retina, with overlapping receptive fields. Thus, 40% of RNFL may be lost before occurrence of visual field damage
Microgravity Dose Response for the VIIP?

- N=27 Astronauts, mean time to MR imaging was 606 days +/- 822
- 18 group 1 astronauts underwent imaging more than 100 days after flight
- Consistently higher percentage of findings for group with greater microgravity exposure, and increased severity of findings.

### Cumulative Lifetime Exposure to Microgravity Relative to Imaging Findings

<table>
<thead>
<tr>
<th>Time in UG (Days)</th>
<th>No. Subjects</th>
<th>Globe Flattening</th>
<th>Optic Nerve Sheath Kinking</th>
<th>ONSD&gt;5.9 mm</th>
<th>Optic Disc Protrusion</th>
<th>Moderate or Greater Pituitary Concavity</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30d (Short)</td>
<td>12</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>&gt;30d (Long)</td>
<td>15</td>
<td>6</td>
<td>3</td>
<td>9</td>
<td>4</td>
<td>3</td>
</tr>
</tbody>
</table>
Monroe Kelly Principle & ICP

Accommodation of up to 120ml volume change while maintaining normal ICP
Fluid Shift & Inadequate Cerebral Venous & CSF Accommodation May Increase ICP in 0G

0G Cephalad fluid shift causes venous blood & CSF outflow resistance
Increased CSF Vol., Venous Congestion, & Increased interstitial Vol.

  - 3D volumetric MR imaging
  - N=11 IIH newly diagnosed non-treated women vs N=11 overweight healthy women

### Cranial Volumetric Measurements

<table>
<thead>
<tr>
<th></th>
<th>ICCSF (mL)</th>
<th>EVCSF (mL)</th>
<th>GM (mL)</th>
<th>ICV (mL)</th>
<th>Nor VCSF (%)</th>
<th>Nor EVCSF (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (n = 11)</td>
<td>238 ± 25</td>
<td>220 ± 24</td>
<td>557 ± 31</td>
<td>1332 ± 81</td>
<td>1.4 ± 0.5</td>
<td>16 ± 1</td>
</tr>
<tr>
<td>IIH (n = 11)</td>
<td>309 ± 56</td>
<td>290 ± 52</td>
<td>602 ± 57</td>
<td>1438 ± 124</td>
<td>1.3 ± 0.4</td>
<td>20 ± 2</td>
</tr>
<tr>
<td>P value</td>
<td>0.002</td>
<td>0.0011</td>
<td>0.038</td>
<td>0.029</td>
<td>0.511</td>
<td>0.0007</td>
</tr>
</tbody>
</table>


### Arterial & Venous Volumetric Flow Rate Measurements

<table>
<thead>
<tr>
<th></th>
<th>TCBF (mL/min)</th>
<th>Total IJV (mL/min)</th>
<th>Nor IJV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control (n = 11)</td>
<td>789 ± 116</td>
<td>628 ± 72</td>
<td>81 ± 10</td>
</tr>
<tr>
<td>IIH (n = 11)</td>
<td>823 ± 68</td>
<td>532 ± 87</td>
<td>65 ± 7</td>
</tr>
<tr>
<td>P value</td>
<td>0.414</td>
<td>0.011</td>
<td>0.001</td>
</tr>
</tbody>
</table>

- Less venous volume draining via the IJV
- Likely increased drainage via secondary vessels
- Implying an increased resistance to venous outflow
Prolonged Elevations in ICP and Impaired Cognition

  - Prospective
  - N=5, mean papilledema 2, mean ICP 25.6 mmHg.
  - Difficulties in learning and memory for 6-30 months.
  - Testing showed a slight impairment in verbal tests.
  - At 12 month follow-up, after intensive medical or surgical treatment in 4/5 subjects the intellectual impairment reversed, and papilledema had resolved in 4 patients

  - Prospective
  - N=9, All subjects experienced mild deficits in short term memory and auditory processing of linguistic information.
  - Particular difficulty in following complex directions containing prepositional information and in immediate recall of words or numbers.

- Retrospective N=10. Cognitively tested at presentation.

  - 80% had an impairment in memory and learning:

- Concept of cognitive reserve in mild Cognitive Impairment

- Prolonged Elevations in ICP and Impaired Cognition - Cont’d

• Concept of cognitive reserve in mild Cognitive Impairment
THE VISUAL IMPAIRMENT INTRACRANIAL PRESSURE SYNDROME IN LONG DURATION U.S. ASTRONAUTS: EPIDEMIOLOGY AND PATHOPHYSIOLOGY

Lead Scientist, NASA VIIP Risk

Universities Space Research Association, Houston, TX,