A Serious And Possible Limiting Problem With Visual Impairment From Protracted Space Flights: Increased Intracranial Pressure As A Possible Cause And What Can Be Done About It

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I Have No Disclosures

Slides Courtesy of
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Visual Impairment Intracranial Pressure (VIIP) 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

VIIP Clinical Findings

• To date 22 U.S. ISS long-duration spaceflight astronauts have developed some or all of the following findings:

  • Hyperopic shift
  • Cotton wool spots
  • Choroidal folds
  • Optic Nerve Sheath Distention
  • Globe flattening
  • Edema of the Optic disc (papilledema)
  • Partially Empty Sella
  • Post flight elevated CSF pressure

Initial Identification of the VIIP: Subjective Changes in Vision

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

  • Hyperopic shift
    Decreased near visual acuity, distant vision intact

Normal Eye

Hyperopic Eye

(1 mm decrease in axial length is equivalent to a 3 diopter hyperopic shift)

Dose Response for VIIP: Shuttle vs ISS

- N=27 Astronauts
  - Consistently higher percentage of findings for group with greater microgravity exposure, and increased severity of findings.

<table>
<thead>
<tr>
<th>Time in UG</th>
<th>Subjects</th>
<th>Globe Flattening</th>
<th>Optic Nerve Sheath Distention</th>
<th>Optic Disc Edema (papilledema)</th>
<th>Partially Empty Sella</th>
<th>Post flight elevated CSF pressure</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>
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<tr>
<td>&gt;30d (Long)</td>
<td>15</td>
<td>6</td>
<td>3</td>
<td>9</td>
<td>4</td>
<td>3</td>
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Greater incidence and severity of findings in ISS vs Shuttle astronauts suggest dose response effect.
Current U.S. ISS VIIP Incidence:

48 U.S. ISS astronauts:
- Unclassified astronauts N=15 (No MRI, OCT or ocular US)
- Known non-cases: N=11 (33.3%)
- Confirmed cases: N=22 (66.7%)

Clinical classification of cases:
- Class One: N=2
- Class Two: N=13
- Class Three: N=3
- Class Four: N=4

Current VIIP Incidence as a % of U.S. ISS astronauts tested= 66.7%
Males: 80%, mean CPG severity= 2.1 ; Females: 55%, mean CPG severity=0.9

Globe Flattening and Axial Length

Finding | Present in IH | Present in IIH | Present in VIIP
--- | --- | --- | ---
Increased Pressure Retro-orbital space | √ | | |

Pre to Post Flight Papilledema
(First case 2005. N=6)

Implications for Deep Space Missions

1. Normal Visual Field with normal blind spot (in black)
2. Early Defect, Enlarged Blind Spot and Inferior Nasal Loss
3. Severe Visual Constriction

Prolonged Disc Edema may lead to Peripheral Visual Field Loss
Fundamental Mechanism:
Cephalad Fluid Shift

Fluid Shift, Loss of Hydrostatic Drainage & Cerebral Venous Congestion

NASA Crewmember LPs to Date

ICP in Space Flight

CVP & ICP Increases with Acute Cephalad Fluid Shift During HDT

ICP has never been directly measured in humans during microgravity:
- Russians measured ICP invasively in a Macaque monkey in 1992, during a 10-day Bion satellite flight, with an intracranial (epidural) probe
- ICP increased as high as 30% compared with preflight measurements
- CO2 did not exceed 1mmHg, ISS mission average=3.56mmHg

ISS Inflight CO2 Levels:
- CO₂ mission average = 3.56 mmHg (0.33%) (10x normal sea level atmosphere: 0.0314%)
- Average Peak CO₂ = 8.32 mmHg (0.7%) (20x)

ISS Commander Jeff Williams working on CSFM unit.

Cephalad fluid Shift Exacerbates CO2 Challenge on ISS

How Intracranial Pressure and Intraocular Pressure Interact to Cause Disc Edema

The Translaminar Pressure Gradient: A Mechanism for Papilledema

Inflight Ocular Ultrasound a Surrogate for Intracranial/Retro-Orbital Pressure
Raised Intracranial Pressure—Qualitative Measurement with ONSD

Elevated ICP transmitted to optic nerve

Optic Nerve Sheath Distension

Case Report - Increased Optic Nerve Sheath Diameter On-Orbit

T1 MRI orbital imaging of the right eye. Pre flight (left) and Post flight (right) showing flattening of the posterior globe.

Case Report: MRI Globe Imaging

What are we doing about it?
- Monitoring
- Research
- Countermeasures

Case Report - Flattening of Posterior Wall - and Raised Optic Disc

Elevation of optic disc
**MedB Ocular Testing Requirements for all US Astronauts**

*Vision Testing includes Visual Acuity, Amsler Grid, Contrast Sensitivity, & Threshold Visual Fields. The latter is measured at Coastal Eye for ground testing.*

**Post-flight Exams**

R+1-3 Victory Lakes MRI

**Pre-flight Exams**

L-21/18 mo L-12-3 mo Victory Lakes MRI

Ocular Ultrasound at L-12/9 and 6/3 mo; All other tests at L-9/6 mo

**In-flight Exams**

L+90

L+30 R-30

Ocular Ultrasound

Fundoscopy

OCT

Vision Testing*

• Fundoscopy

• OCT/A-Scan

• Vision Testing*

• Refraction

• Pupil Reflexes

• Extra-Ocular Muscle Bal.

• IOP (Tonometry)

Coastal Eye Assoc:

• OCT/A-Scan

• Biomicroscopy/Hi Res Photogr.

**Mechanical Countermeasures: Lower Body Negative Pressure**

Luca Parmitano (ESA) on ISS wearing Russian Chibis-M suit

Blood is sucked down into lower body

LBNP Reverses fluid shift creating a 1G-like fluid distribution while in space

**Considerations for Inflight Treatment: ↓ICP**

- **Supporting human ground data:**
  - Non-Drug:
    - Lower salt intake: ↓volume of fluid shifted towards the head
    - Decrease CO2: reduces cerebrovascular dilation
  - Drug:
    - Acetazolamide (alveolar/altitude med): ↓CSF production
    - Elevates urinary calcium (countermeasures: K citrate & renal US)
    - Steroids (potential last resort to delay unscheduled deorbit)
  - Non-Drug:
    - Reduce ARED exposure: decreases frequent ICP ↑ associated with resistance training

- **Conceptual (Human or animal data):**
  - Drug:
    - Prilosec (common human antacid med): used to ↓ICP in veterinary medicine
    - Angiotensin Converting Enzyme Inhibitors
    - Hydrochlorothiazide
  - (common BP meds): ↓volume of fluid shifted towards the head
  - Non-Drug:
    - Reduce ARED exposure: decreases frequent ICP ↑ associated with resistance training

**Mechanical Countermeasures: Braslet Occlusion Cuff**

Sequesters venous blood in the legs decreasing amount of volume shifted towards the head

**Ocular Coherence Tomography (OCT)**

Sequesters venous blood in the legs decreasing amount of volume shifted towards the head

**Tonometry**
Exercise with the Advanced Resistive Exercise Device (ARED), along with adequate energy intake and Vitamin D helps to prevent loss of bone mass density in ISS crewmembers.

Dilemma: Must perform exercise to protect bone, but straining increases intracranial pressure.

MTRR A66G

Based on preflight blood chemistry differences between astronauts and without vision/eye issues, Dr. Smith et al. looked at a handful of genes which affect this pathway.

Everyone with the one form of genes (for the MTRR enzyme) developed ophthalmologic issues (but not everyone with issues had those genes).

MTRR: Methionine Synthase Reductase

Genotype, B-vitamin status, and androgens affect space flight–induced ophthalmic changes.

AMERICA’S NEXT GIANT LEAP