Introduction to Spaceflight Associated Neuro-ocular Syndrome (SANS) and its Risk to NASA Astronauts

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Why We Do What We Do…
Recent SANS Headlines:

- Too much space travel is hazardous for your eyeballs
- Possible Mars Mission 'Showstopper': Vision Risks for Astronauts
- Spaceflight Bad for Astronauts' Vision, Study Suggests
- The mysterious syndrome impairing astronauts' sight
- Astronauts' eyes are at risk after too much time in space
- Astronauts Returning to Earth With Vision Problems
- Space travel is causing visual impairment for some astronauts. Will this prevent travel to Mars?
Background: *The Space Environment*

- Bottom-line: Not human friendly. For example…
  - **Vacuum**: No atmosphere; no air
  - **Gravity**
    - Gravity reduces w/ distance. ISS (@ ~200-250 mi) feels 90% of Earth’s gravity…But…
    - ISS moves at ~17,500 mph, in constant freefall = “Microgravity”
  - **Temperature extremes**
  - **Ionizing (high energy) radiation**: Galactic cosmic rays, solar proton events
  - **Orbiting space junk/debris**: >550K larger than 1cm
  - **Spaceflight Associated Neuro-ocular Syndrome (SANS)**
    - Formerly called Visual Impairment Intracranial Pressure (VIIP)
    - A top risk to Deep Space Journey (e.g., mission to Mars)
International Space Station (ISS)

- In use since 2000
  - 51 expeditions completed
- \(*n = 58\) (as of 31 Jan 17)
- Duration: \(~0.5\) to \(1\) y
- International partners
  - United States
  - Russia
  - European Union
  - Canada
  - Japan
- Crew: Typically 5-6
- “Low Earth orbit”

* Person flights; may include multiple-time flyers w/in program
Background: *The Future...*

- NASA to send humans to: An asteroid by 2025; Mars in the 2030s
Background: *SANS*

- Ocular testing has been performed pre- & post-flight
- Initial eye/vision testing capability on ISS was…
  - Ophthalmoscope (astro-physicians only)
  - Paper VA chart
  - Amsler grid
- **Sentinel SANS case discovered in 2005, post-flight**
  - Optic disc edema & cotton wool spot
- Surveillance/medical data collection has evolved
  - *Some* SANS-related testing began in 2008 (w/ Exp 18), but inconsistent
  - Feb 2010 (Exp 23): **Standardized medical monitoring** (i.e., “Eye MED B”) established
Ocular Surveillance
Ocular Surveillance

Terrestrially
- 3T MRI – Special “NASA Astronaut” protocol
- Visual Field (Threshold) Perimetry
- Cycloplegic Refraction

Terrestrially & On-Orbit
- Vision Exam
  - Distance visual acuity (ISS: Acuity Pro on laptop)
  - Near visual acuity (ISS: Handheld card)
  - Amsler grid (ISS: Laptop)
- Ocular Ultrasound
- Tonometry (when clinically indicated)
- Fundoscopy
- Optical Coherence Tomography (OCT)
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- Fundoscopy
- **Optical Coherence Tomography (OCT)**
Clinical Findings
USOS Individuals With Findings:
Expeditions 1-48

40 Individuals have one or more of these findings

![Bar chart showing the distribution of findings among USOS individuals.](chart.png)
USOS Individuals With Findings: Expeditions 1-48

40 Individuals have one or more of these findings

- Disc Edema
- ON Dilation/Edema
- Cotton Wool Spot
- RNFL Thickening
- Retinal Folds
- Scleroma
- Retinal Hemorrhage
- Choroidal Folds
- Choroidal Thickening
- Globe Flattening
- Refractive Error Shift
Pre-flight fundoscopic images of the optic discs

Post-flight images of optic discs, showing Grade 3 edema OD & Grade 1 edema OS
Clinical Findings: *Optic Disc Edema*

- *Terrestrially*: Optic disc edema is associated with:
  - **Unilateral**: Optic neuritis, optic neuropathy, retinal artery/vein occlusion
  - **Bilateral**: Increase in ICP…
    - IIH (→ “papilledema”)
    - Intracranial mass
    - Obstructive hydrocephalus
    - Cerebral edema
    - Increased CSF production
    - Decreased CSF absorption
    - Venous outflow obstruction
  - Typically reduces VA, enlarges blind spot, causes relative afferent pupillary defect & color impairment

Fundoscopic image of optic disc OD, 10 days after return to Earth
- Arrows: “C” shaped halo of edema
USOS Individuals With Findings: Expeditions 1-48

40 Individuals have one or more of these findings

- Disc Edema: 64
- ONSD Distention*: 10
- ON Tortuosity/Kinking*: 14
- Cotton Wool Spot: 47
- RPE1 Thickening*: 22
- Retinal Folds*: 37
- Scleritis: 12
- Retinal Hemorrhage: 7
- Choroidal Folds: 47
- Choroidal Thickening*: 2
- Global Flattening: 1
- Refractive Error Shift: 1

* Tested
** Affected
Post-flight ultrasound image of globe, optic nerve (ON; purple), and optic nerve sheath (green). Showing:
  - ON Sheath distention
  - ON tortuosity

**ON Sheath terrestrially:**
  - Normal diameter (ONSD) < 5.9 mm
  - Enlargement typically associated with increased ICP
USOS Individuals With Findings: Expeditions 1-48

40 Individuals have one or more of these findings

Post-flight OD

<table>
<thead>
<tr>
<th>Condition</th>
<th>Tested</th>
<th>Affected</th>
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<tr>
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<td>10</td>
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<tr>
<td>OND Distortion*</td>
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<tr>
<td>Cotton Wool Spot</td>
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<td>RNFL Thickening*</td>
<td>64</td>
<td>2</td>
</tr>
<tr>
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<td>64</td>
<td>11</td>
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<td>Globe Flattening</td>
<td>47</td>
<td>12</td>
</tr>
<tr>
<td>Refractive Error Shift</td>
<td>47</td>
<td>9</td>
</tr>
</tbody>
</table>
Clinical Findings: Choroidal Folds

- Choroidal thickening due to vessel engorgement \(\rightarrow\) induces choroidal (and sometimes retinal) folds
- Usually run horizontally (not concentrically around ONH)
- Can resolve post-flight or can persist (for 5+ yrs)
- So far, no clinically-significant impact on BCVA
- Terrestrially: Assoc. w/ choroidal tumors, scleritis, retrobulbar mass, papilledema/IIH
Clinical Findings: Retinal Nerve Fiber Layer Thickening

Post-flight OCT “circle scans” showing RNFL thickening consistent w/ observed optic disc edema OU
USOS Individuals With Findings:
Expeditions 1-48

40 Individuals have one or more of these findings
Clinical Findings: *Globe Flattening*

- **Case Example:**
  - Male, mid 40s at time of flight
  - No significant PMH/PSH/PFH
  - No meds
  - Normal BP (118/64)
  - Normal lipids
  - ECG Stress test normal w/ VO\textsubscript{2} max of 51ml/kg

- *Terrestrially:* Globe flattening associated w/ papilledema (i.e., disc edema 2\textdegree to increased intracranial pressure); typically bilateral
Clinical Findings: Globe Flattening

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6 days post-flight
Clinical Findings: *Globe Flattening*

- **Case Example:**
  - Male, mid 40s at time of flight
  - No significant PMH/PSH/PFH
  - No meds
  - Normal BP (118/64)
  - Normal lipids
  - ECG Stress test normal
    w/ VO$_2$ max of 51ml/kg

- *Terrestrially:* Globe flattening associated w/ papilledema
  (i.e., disc edema $2^o$ to increased intracranial pressure); typically bilateral

1 year post-flight
Clinical Findings: *Globe Flattening*

- **Case Example:**
  - Male, mid 40s at time of flight
  - No significant PMH/PSH/PFH
  - No meds
  - Normal BP (118/64)
  - Normal lipids
  - ECG Stress test normal w/ VO₂ max of 51ml/kg

- *Terrestrially*: Globe flattening associated w/ papilledema (i.e., disc edema 2° to increased intracranial pressure); typically bilateral
Clinical Findings: Hyperopic Shift

- Of the active astronaut population...
  - 80% wear vision correction (32% contact lenses)
  - Mean age = 47 yrs
  - Majority are presbyopic (i.e., a normal, age-related, progressively worsening inability to focus clearly on near objects)

- Post-flight questionnaires (1989 - 2011): 29% of short- & 60% of long-duration mission astronauts report a subjective degradation in vision, especially at near
  - Provided “Space Anticipation Glasses”
Why is this Happening?
Why is this Happening?

- Terrestrially → Fluid is pulled downward by gravity (i.e., hydrostatic pressure)
- Microgravity → Fluid is free to uniformly distribute (i.e., hydrostatic pressure is eliminated)

Consider how hydrostatic pressure affects fluid/blood distribution in humans…

And what happens in its absence…
Why is this Happening?

Microgravity $\rightarrow$ Cephalad fluid shift $\rightarrow$ Cerebral venous congestion (i.e., overfilling & distension)
Why is this Happening?

Microgravity → Cephalad fluid shift → Cerebral venous congestion (i.e., overfilling & distension)

- Hypothesis #1: *Increased intracranial pressure* (ICP)
  - e.g., Enough to cause an imbalance between ICP & intraocular pressure (i.e., translaminar pressure gradient)
- Hypothesis #2: *A local eye problem*
  - e.g., Compartmentalization of perioptic subarchnoid spaces
- Hypothesis #3: *Individual anatomical/genetic factors*
  - e.g., Altered folate-dependent 1-carbon metabolism
- Hypothesis #4: *Venous congestion* alters local physiology and/or places direct pressure on retinal axons
In-flight Exacerbating Factors??

Resistive Exercise

High Oral Sodium Intake
- Prepackaged Foods...
- Up to 5000+ mg/day

High CO₂
- ~10x terrestrial levels

In-flight Pharmaceuticals
Common Characteristics of the Cases
Almost all were “long duration” (i.e., >30 day) ISS mission crewmembers
  • One short-duration case w/ subtle disc edema (discovered retrospectively)
  • Severity related to flight duration?? [So…what about a 3-yr Mars mission??]

Normal past medical history:
  • Negative for uncontrolled systemic disease
  • None used medications before/during mission that would increase ICP
    (e.g., vitamin A, tetracycline, corticosteroids, or nalidixic acid)

ISS cabin
  • Normal pressure & oxygen
  • Elevated CO₂
    ▪ ~0.33-0.5% avg, w/ avg peak ~0.7%; 10x terrestrially: ~0.03-0.04%
Common Characteristics of the Cases

- All had *normal* pre-flight eye exams
- *None* experienced loss in BCVA, color vision, or stereopsis
- *None* complained of severe headaches, transient vision obscurations, double vision, pulsatile tinnitus, or vision changes during eye movements (i.e., classic symptoms of idiopathic intracranial hypertension)
- OD affected more than OS *in all cases*. *If monocular, always OD*
- For 14 crewmembers having complete pre-flight & on-orbit OCT data, regardless of SANS diagnosis, *ALL show signs of*:  
  - *Choroidal engorgement*, *Optic disc edema* (*subclinical or clinical*), extending into the retinal nerve fiber layer; *Retinal venous engorgement*
Clinical & Research Update
Ongoing SANS Efforts: Clinical/Research

**Clinical**

- “*Form & Function*”: Are there any RNFL thickness losses (*via OCT*)? If so, are there correlations w/ any reduction in visual sensitivity (*via visual field*)?
  - **KEY Concern/Risk**: Potential impact of *disc/retinal edema* during longer duration missions (>>12 months)

- **Deploy next-generation OCT:**
  - Faster (~60%); better signal-to-noise; MultiColor imaging

- **Consider deploying an ISS visual field device**

- **Consider possibility of *venous congestion* as a SANS contributing factor**

**Research**

- **Ocular Health Study & Fluid Shifts Study**
- **Clinical relevance of MRI-based findings**
- **Implementation of direct ICP measures** (Lumbar puncture pre- & post-mission)
- **Correlation btwn SANS & CO₂ using HDT (EnviHab)**
Lamina Cribrosa Movement

* Indicates Case

Source: Mayra Nelman & Simon Clemett, PhD

* Subject 5

Subject 8
Questions?

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