Spaceflight Associated Neuro-ocular Syndrome (SANS): Clinical Update

William J. Tarver, MD, MPH¹; Tyson Brunstetter, OD, PhD²; Mary Van Baalen, PhD¹; Sara Mason³; Wafa Taiym⁴

Space Medicine Operations Division (SA)
¹NASA Johnson Space Center, Houston, TX; ²U.S. Navy, Houston, TX; ³MEI, Houston, TX; ⁴KBRwyle, Houston, TX

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SANS Clinical Update

- “SANS Incidence” Update
- Space naïve crewmember SANS data (vs. veteran crewmembers)
- Clinical Highlights – 2017
  - VIIP name change
  - “Optic disc changes” w/ long-duration spaceflight
  - Association between optic nerve head (ONH) cup volume and SANS diagnosis
  - International Fundoscopy Evaluation of Crewmembers (IFEC) Review
- Clinical Tasks – 2018
  - Deployment of next-gen Optical Coherence Tomography (OCT) device
  - Evaluating visual field (VF) testing for ISS
  - Update SANS case definition
Additional SANS signs not included: Optic nerve (ON) sheath distension, ON kinking/tortuosity, Retinal nerve fiber layer thickening, Retinal folds, Choroidal thickening. *Data analysis ongoing*
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Data analysis ongoing

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<tr>
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<th>All Crew</th>
<th>Space Naïve</th>
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<tbody>
<tr>
<td>D Edema</td>
<td>15%</td>
<td>17%</td>
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<tr>
<td>CWS</td>
<td>10%</td>
<td>11%</td>
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<tr>
<td>Scotoma</td>
<td>1.5%</td>
<td>0%</td>
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<td>R Heme</td>
<td>4%</td>
<td>17%</td>
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<tr>
<td>Chor Folds</td>
<td>23%</td>
<td>11%</td>
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<td>G Flattening</td>
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<td>11%</td>
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<tr>
<td>Ref Error Δ</td>
<td>19%</td>
<td>11%</td>
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**USOS Spaceflight Naïve Individuals w/ SANS Findings**

Expeditions 1-52

- Disc Edema: 18 (Occurred), 3 (Tested)
- Cotton Wool Spot: 18 (Occurred), 2 (Tested)
- Scotoma: 18 (Occurred), 2 (Tested)
- Retinal Hemorrhage: 18 (Occurred), 3 (Tested)
- Choroidal Folds: 18 (Occurred), 2 (Tested)
- Globe Flattening: 18 (Occurred), 2 (Tested)
- Refractive Error Δ: 18 (Occurred), 2 (Tested)
VIIP name change: Why?

“Vision Impairment Intracranial Pressure”
- Vision Impairment: Defined as the best-corrected visual acuity worse than 20/40 in the better-seeing eye (National Institutes of Health)
  - Not applicable to long-duration astronauts; all correctable to 20/20 or better
- Intracranial Pressure: Not conclusively tied to astronaut vision issues

“Spaceflight Associated Neuro-ocular Syndrome”
- More accurate, given current evidence
- More general; includes wider range of pathogenesis possibilities
“Optic disc changes” w/ long-duration spaceflight

- David Brown, MD – SANS Research & Clinical Advisory Panel (RCAP); Retinal specialist, Retinal Consultants of Houston
- Analyzed 14 crewmembers having complete pre-flight & on-orbit OCT data, **ALL** showed signs of:
  - Choroidal thickening
  - Venous engorgement
  - **Optic disc edema**, extending into the retinal nerve fiber layer
- Optic discs tend to expand forward *and backward*. This posterior displacement is opposite to that seen in terrestrial-based papilledema/idiopathic intracranial hypertension (IIH) cases
- Edema findings also reported by others (e.g., Nimesh Patel, OD, PhD; Brandon Macias, PhD; Steven Laurie, PhD)
Non-Case w/ "subclinical edema"
Non-Case w/ "subclinical edema"
Association between ONH cup volume & SANS diagnosis?

Source: Mayra Nelman & Simon Clemett, PhD
Association between ONH cup volume and SANS diagnosis?

• Appears that ONH edema (which occurs to some extent in most/all long-duration crewmembers):
  1. Engorges neurons just anterior to lamina cribrosa
  2. Edematous neurons fill cup (i.e., empty space)
  3. If occupies enough volume, “spills out” of ONH
  4. SANS diagnosed if edema extends ≥270-deg around disc (as visualized via fundoscopy)

• So, is a large ONH cup protective against SANS? Or are large cups just as susceptible to edema-induced vision loss…but are being under-diagnosed w/ SANS?
Clinical Highlights - 2017

  - Face-to-face mtg of SANS SubWG of MMOP’s Inflight Clinical Med WG
  - Goals: (1) Conduct retrospective, blinded eval of pre- & post-flight fundoscopic images for signs of SANS across long-duration ISS crewmembers. (2) Establish standard eval process for fundoscopic images across Partner Agencies
  • Face-to-face mtg of SANS SubWG of MMOP’s Inflight Clinical Med WG
  • Goals: (1) Conduct retrospective, blinded eval of pre- & post-flight fundoscopic images for signs of SANS across long-duration ISS crewmembers. (2) Establish standard eval process for fundoscopic images across Partner Agencies
  • Preliminary results:
    ▪ Results ranged from Frisen Grade 0 to 2. 10 of 52 crew rated Grade 1-2 (i.e., SANS)
    ▪ “Several Grade 0” crew showed edema, but not ≥ 270° (i.e., Grade 1)
    ▪ Wide inter-rater variability (very subjective)
  • All Partner Agencies agree:
    ▪ To use standardized Frisen scale to evaluate retinal images
    ▪ Frisen scale is useful, but inadequate for our needs. OCT + fundoscopy = synergy
    ▪ SANS case definition must be updated – Too limited; 100% based on fundo images; underestimates presence of SANS (i.e., Grade 0 ≠ No changes)
Clinical Tasks - 2018

- Deployment of next-gen Heidelberg OCT2 device
  - Same form & basic function as current on-orbit OCT
  - Head operates at 2X speed of current OCT = ~60% reduction in scan time
    - Permits denser datasets w/in same time rqmts
  - Deeper tissue penetration in standard scan mode
  - Angiography Module – 3D rep. of perfused retinal & choroidal vasculature
  - MultiColor imaging capability
    - May replace routine fundoscopy

ISS ETA: Summer 2018
Clinical Tasks - 2018

- Evaluating visual field (VF) testing for ISS
  - OCT: Gold standard for evaluating ocular **STRUCTURE**
  - VF testing
    - Measurement of retinal sensitivity over a visual area
    - A gold standard for evaluating visual **FUNCTION**
    - Performed *terrestrially* by NASA for >10 years; *not yet on-orbit*
  - Ocular structural changes occur during long-duration spaceflight; however, *functional losses are required before treatment can occur*. **VF testing may:**
    - Detect neuro defects (occurring btwn retina & occipital cortex)
    - Track progression of the pathology
    - Monitor effectiveness of med interventions

Example VF. NOT crewmember data
Update SANS case definition

- Diagnosis currently based solely on:
  - Optic disc edema of *Frisen grade of ≥ 1* (i.e., edema extending ≥ 270° around ONH) as evaluated via *fundoscopy*
    - Subjective / Binary / Ignores other SANS signs & diagnostic tech

- Most/all long-duration crewmembers have some “optic disc changes.” Suggests that SANS should be…
  - Described on a continuous scale, w/ a threshold btwn physiological/pathological
  - Measured more objectively (e.g., OCT)
  - Evaluated for edema, but also other [secondary] signs
Questions?

CAPT Tyson Brunstetter, MSC (AsO), USN
COM: 281-792-7705
Email: Tyson.J.Brunstetter@nasa.gov

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