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

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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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* All Crew | Space Naïve
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D Edema | 15% | 17%
CWS | 10% | 11%
Scotoma | 1.5% | 0%
R Heme | 4% | 17%
Chor Folds | 23% | 11%
G Flattening | 23% | 11%
Ref Error Δ | 19% | 11%

USOS Spaceflight Naïve Individuals w/ SANS Findings*
Expeditions 1-52

* Data analysis ongoing
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
Clinical Highlights - 2017

- “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?

* SANS Case

* Non-Case w/ "subclinical edema"

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

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• 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
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
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?

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