



Spaceflight Associated Neuro-ocular Syndrome (SANS)

A Briefing for Astronaut Candidates

Tyson Brunstetter, OD, PhD, MBA
SANS Clinical Lead (Eyes/Vision)
Space and Occupational Medicine Branch (SD3)



The SANS Team



Clinical

Bill Tarver, MD, MPH
Tyson Brunstetter, OD, PhD
Ann Tsung, MD, MPH
Bob Gibson, OD

Medical Surveillance

Sara Mason
Suzi Osborne, MPH
Wafa Taiym, MS

*Lifetime Surveillance of
Astronaut Health (LSAH)*

Crew Training

Rachel Richardson, BSN, RN
Molly Freedman, BSN, RN
Christopher Schubert, LP, NRP

Biomedical Engineering

Daniel Marburgh
Amirah Mathin, MS
Anna Mendiola
Amanda Boudreaux
Elizabeth Talburt
Will Misek

Research

Brandon Macias, PhD
Steve Laurie, PhD

*Cardiovascular &
Vision Laboratory*



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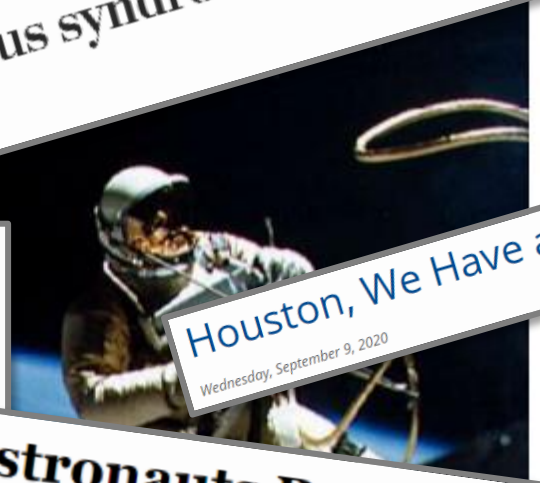
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By SPACE.com Staff | March 13, 2012 12:00am ET

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By Mike Wall, Senior Writer | April 8, 2014 07:00am ET

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Wednesday, September 9, 2020

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By Mike Wall published January 30, 2017

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What's So Special About the Eye?

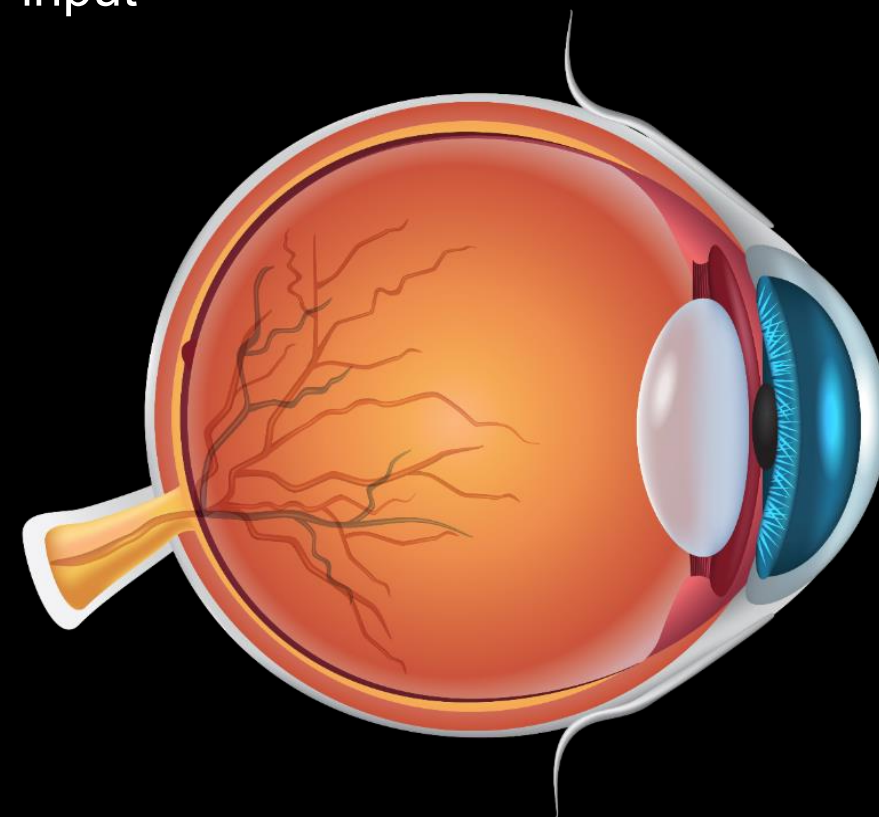


Image credit: NASA



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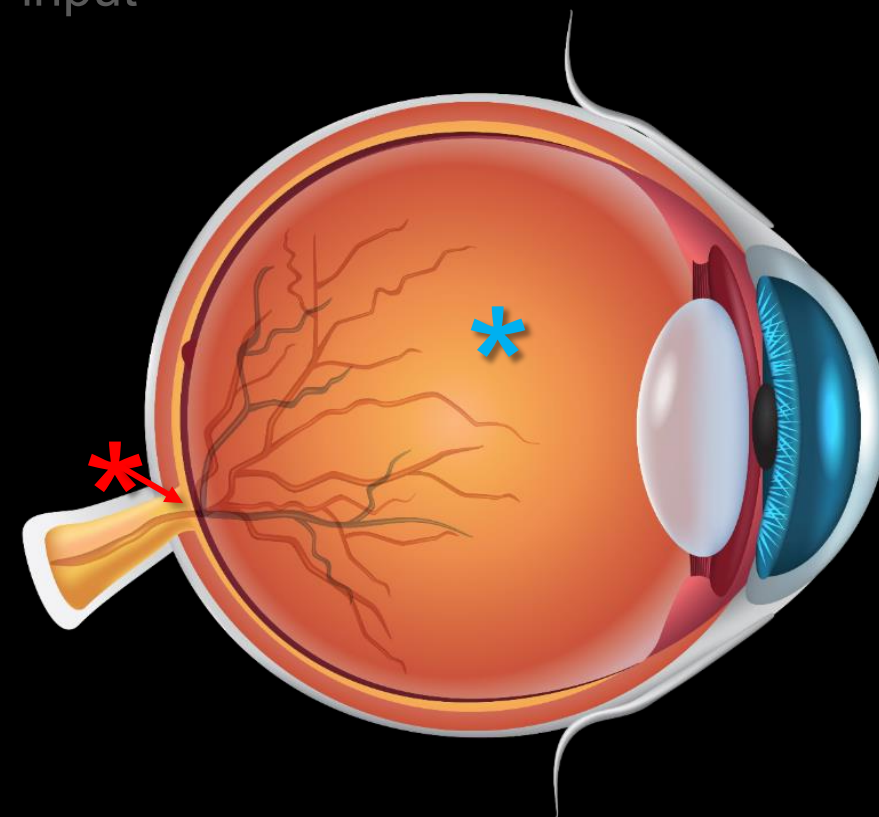
- Only 1" in diameter, but provides ~80% of our total sensory input
- Retina and optic disc (aka optic nerve head)...
 - Convert light energy into neural signals, transmit information to brain via optic nerve fibers → "vision"
 - Extremely high metabolism, requires reliable & sustained blood supply
 - Affected by spaceflight in most crewmembers (SANS)
 - Central nervous system (CNS)
 - Susceptible to *permanent loss*





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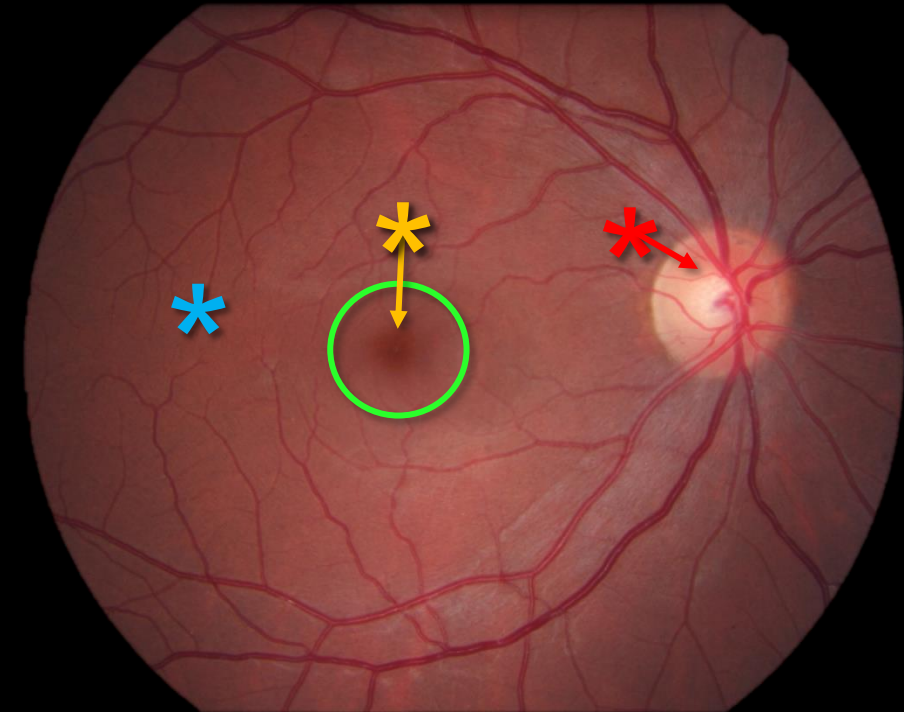
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 - Includes retina's area of central vision: **fovea** & **macula**





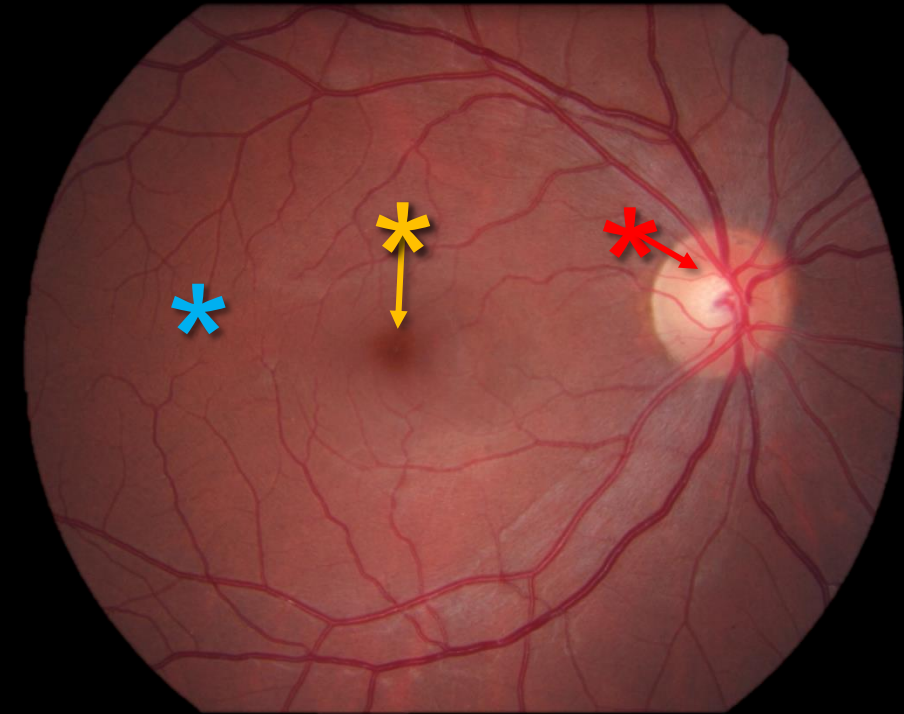
What's So Special About the Eye?

Optical coherence tomography (OCT)

- Our most critical tool to detect & monitor SANS
- Onboard ISS since 2013
- Provides non-invasive, high resolution, cross-sectional images



Image credit: NASA



Retina Optic disc Fovea



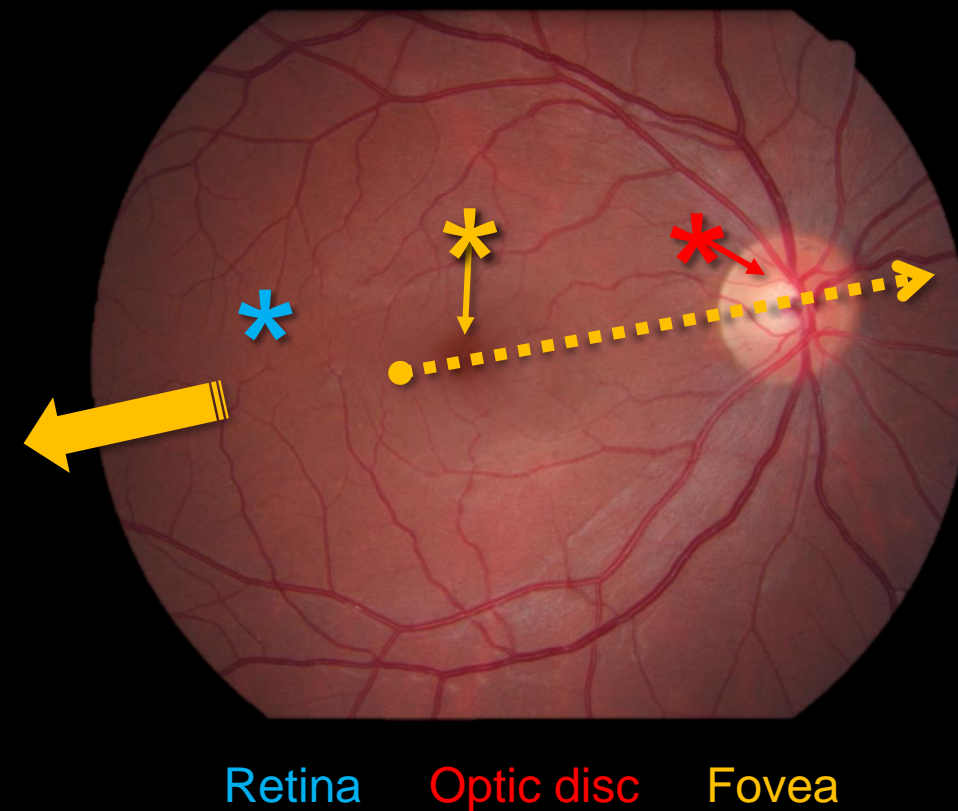
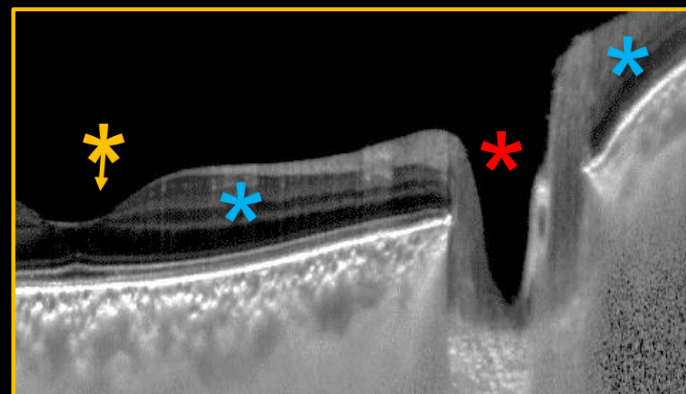
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Image credit: NASA





Spaceflight Associated Neuro-ocular Syndrome (SANS)



Image credit: NASA



SANS Signs: *The Big Four*



Globe flattening

Refractive error shift

Optic disc edema

Chorioretinal folds



SANS Signs: *The Big Four*



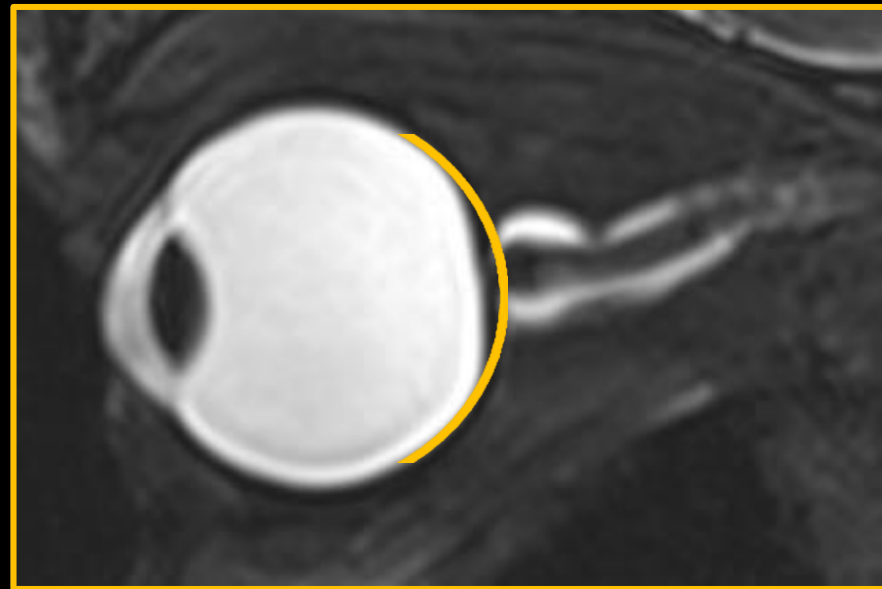
Globe flattening

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- Mild-to-severe cases: **23% of ISS crewmembers**
- **Risk**: May change refractive error (power of glasses), but otherwise, no known risks
- **Can become permanent** (moderate-to-severe cases)





SANS Signs: *The Big Four*

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- “Hyperopic shift” (likely driven by globe flattening)
 - $\geq +0.75$ diopter (D) shift: 15% of ISS crewmembers
 - Largest single-mission shift: +2.00D
- **Risk:** May blur near vision* (and/or distance vision)
 - In near-sighted (myopic) crew, may *improve* distance vision!
 - Bottom-line: *Report vision changes to your crew surgeons*
- **Countermeasure:** “Space anticipation glasses” (SAGs)
 - SAGs: Extra glasses supplied for mission, each w/ increasing power
 - *If vision degrades, select SAG that clears vision*
 - With proper correction, vision remains 20/20 or better
- **Can become permanent** (moderate-to-severe cases)



<https://en.excimerclinic.ru/babyvision/longsight/>



SANS Signs: *The Big Four*



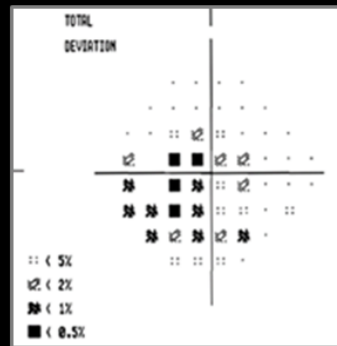
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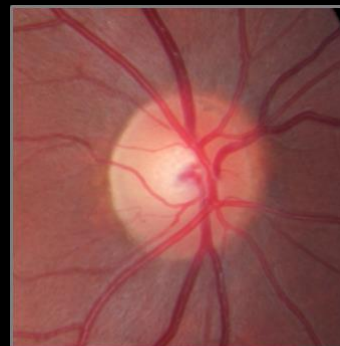
Optic disc edema

Chorioretinal folds

- Swelling of optic nerve head (CNS)
- Mild-to-severe cases: **66% of ISS crewmembers**
- **Risk: Visual field loss** (enlarged blind spots)
 - Detected in 3% of ISS crew, immediately post-flight – Resolved
 - With extended duration and/or severity, *has potential* to become permanent
- **Typically resolves** ~3-12 months after return to 1G



Visual field defect, post-flight



Normal optic disc



SANS optic disc edema



Elevated optic disc



SANS Signs: *The Big Four*

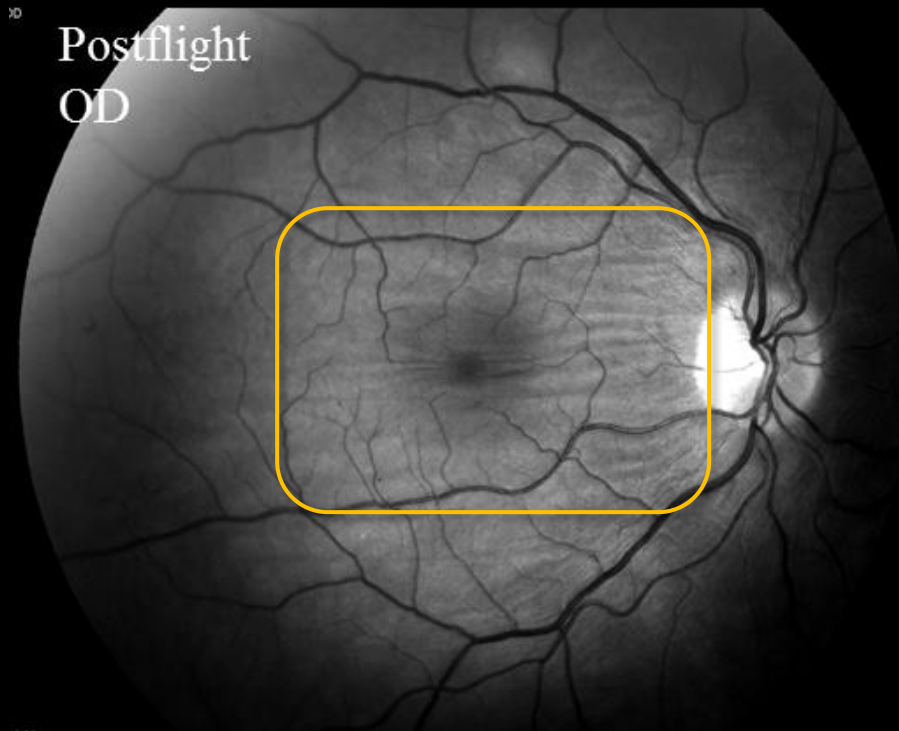
Globe flattening

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Optic disc edema

Chorioretinal folds

- Folds within & below retina (CNS)





SANS Signs: *The Big Four*



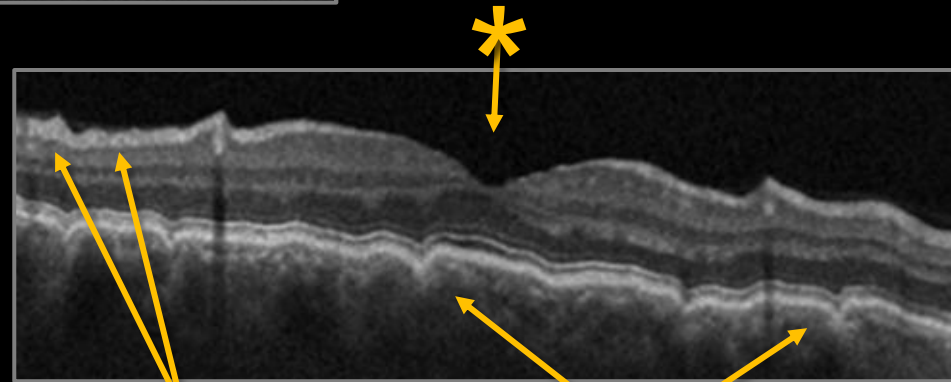
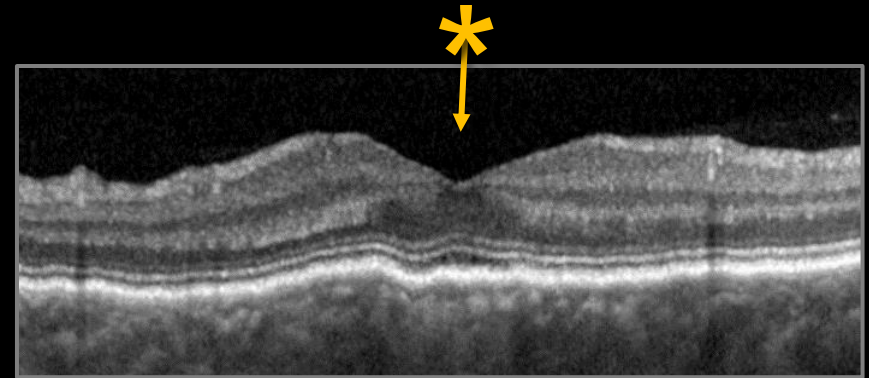
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Chorioretinal folds

- Folds within & below retina (CNS)



* Fovea

Retinal folds

Choroidal folds

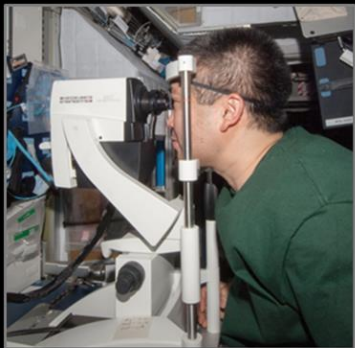


Image credit: NASA



SANS Signs: *The Big Four*

Globe flattening

Refractive error shift

Optic disc edema

Chorioretinal folds

- Folds within & below retina (CNS)
- Mild-to-severe cases: **16% of ISS crewmembers**
 - Folds in fovea: **5% of ISS crewmembers**
- **Can become permanent** (moderate-to-severe cases)

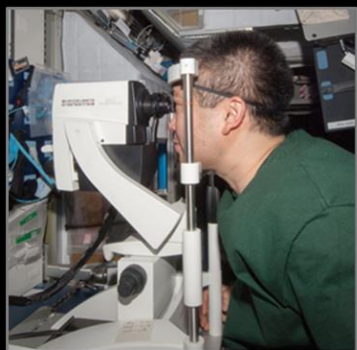
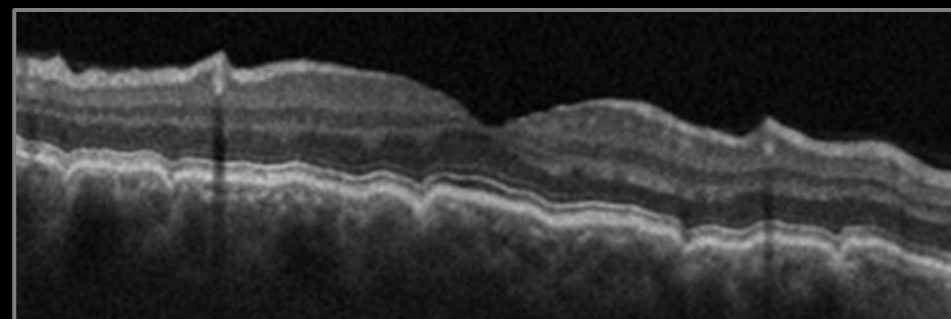
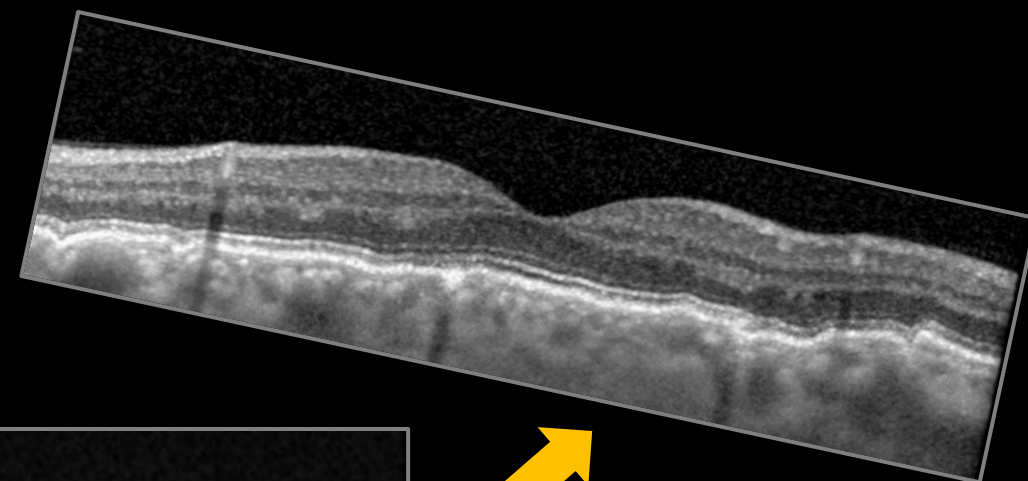


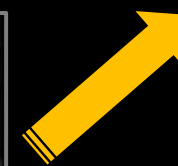
Image credit: NASA



R+1/3d



R+>5y





SANS Signs: *The Big Four*



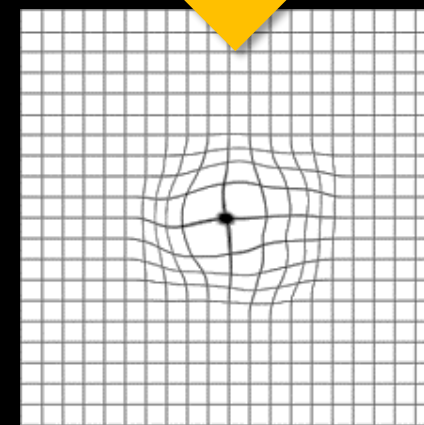
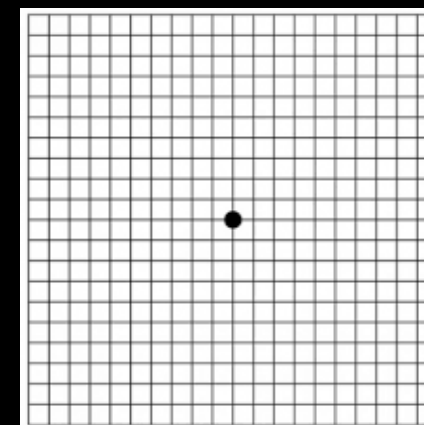
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Chorioretinal folds

- Folds within & below retina (CNS)
- Mild-to-severe cases: **16% of ISS crewmembers**
 - Folds in fovea: **5% of ISS crewmembers**
- **Can become permanent** (moderate-to-severe cases)
- **Risk: Distorted central vision, if severe folds located in macula/fovea**
 - Detected in **0%** of ISS crew
 - With increased duration and/or severity, *has potential* to become permanent, cause retinal damage





SANS Signs: *The Big Four*

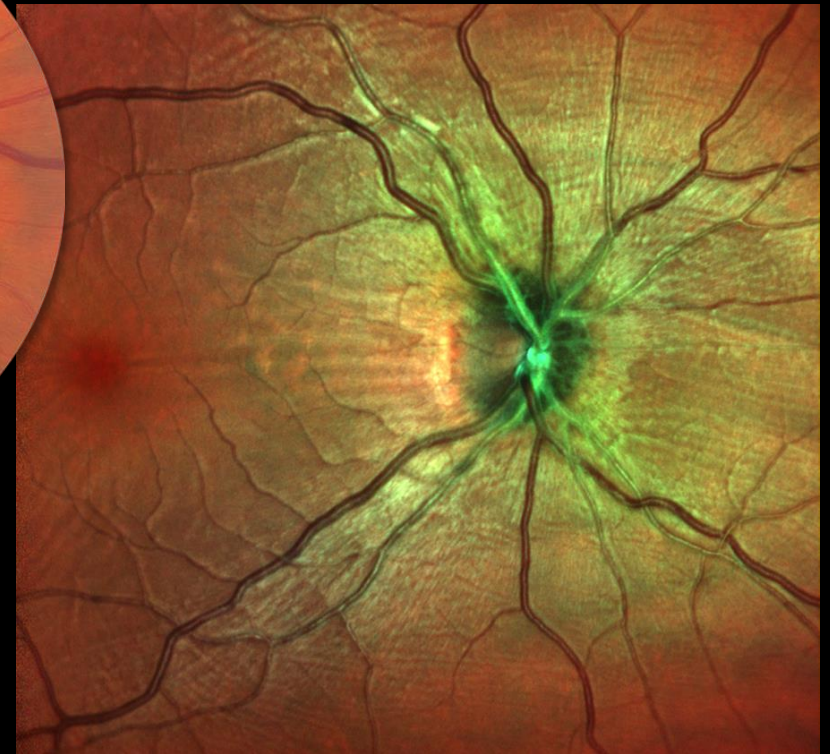
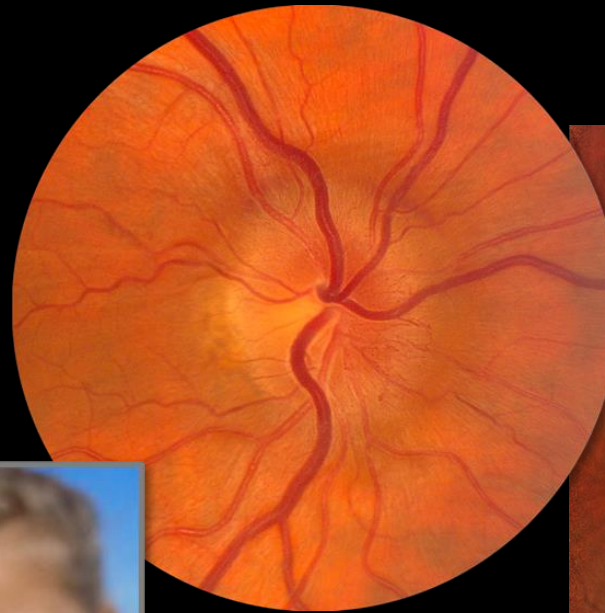
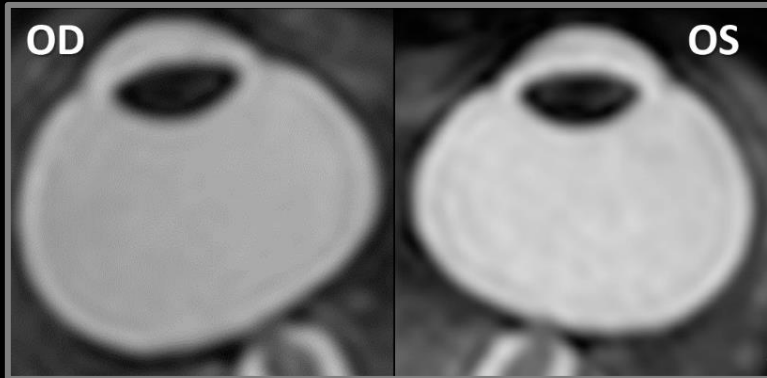


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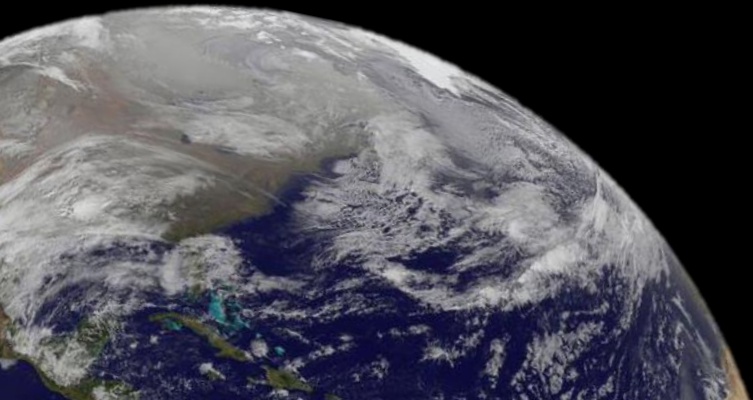
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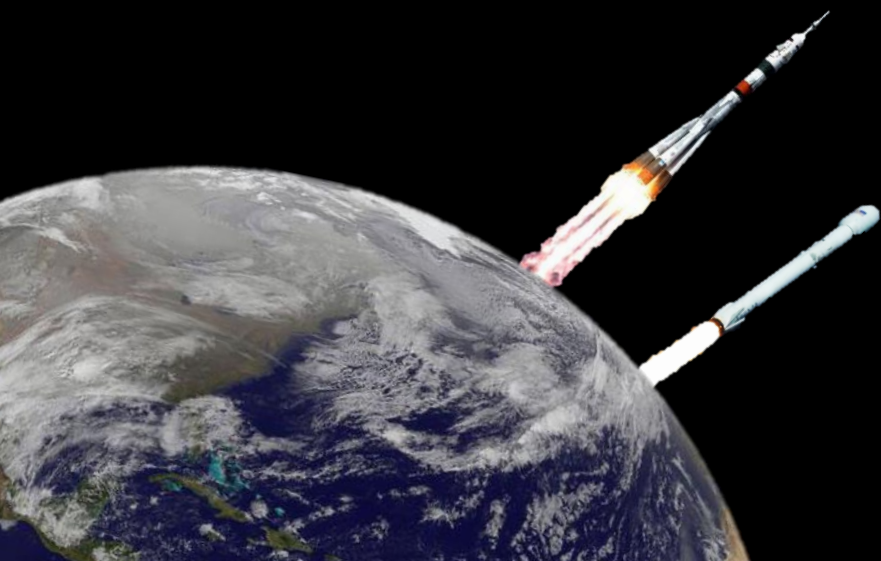
What *in the world* is going on?





Mission Duration: *Long* (~6-12 mo)

Micro-
gravity





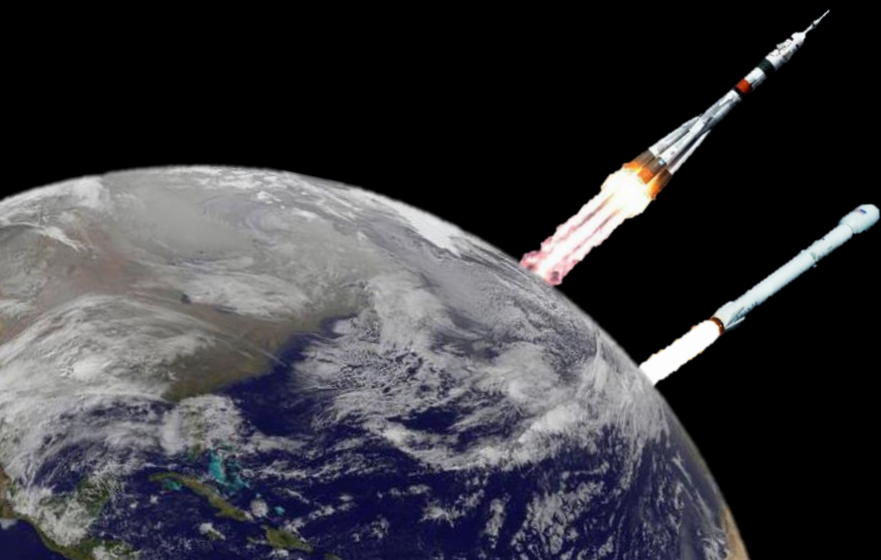
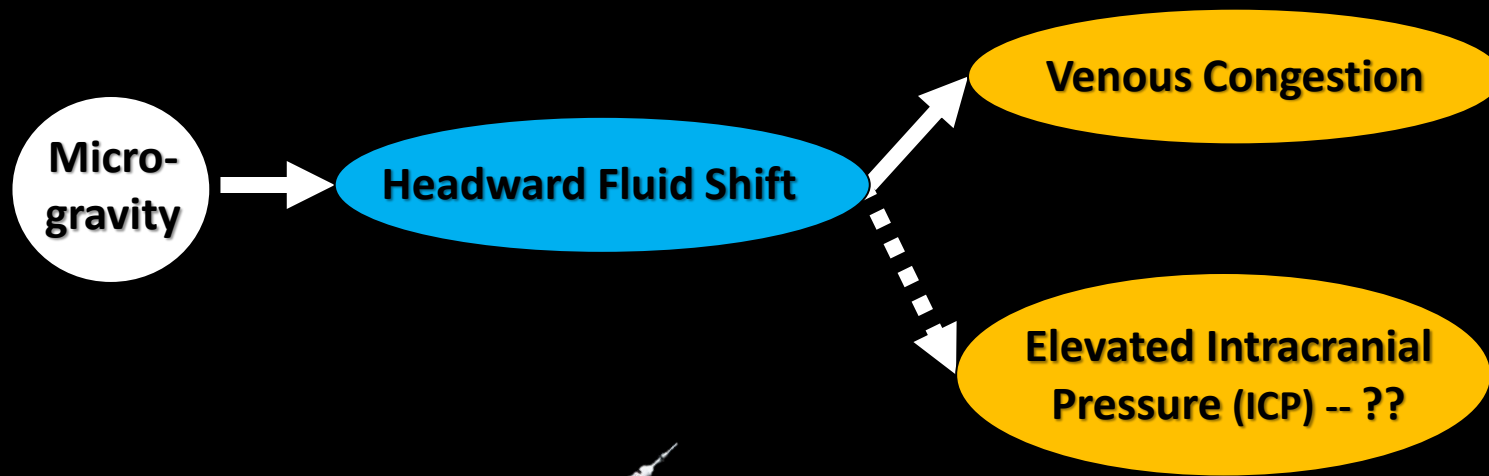
Mission Duration: *Long* (~6-12 mo)



“Puffy Face Syndrome”

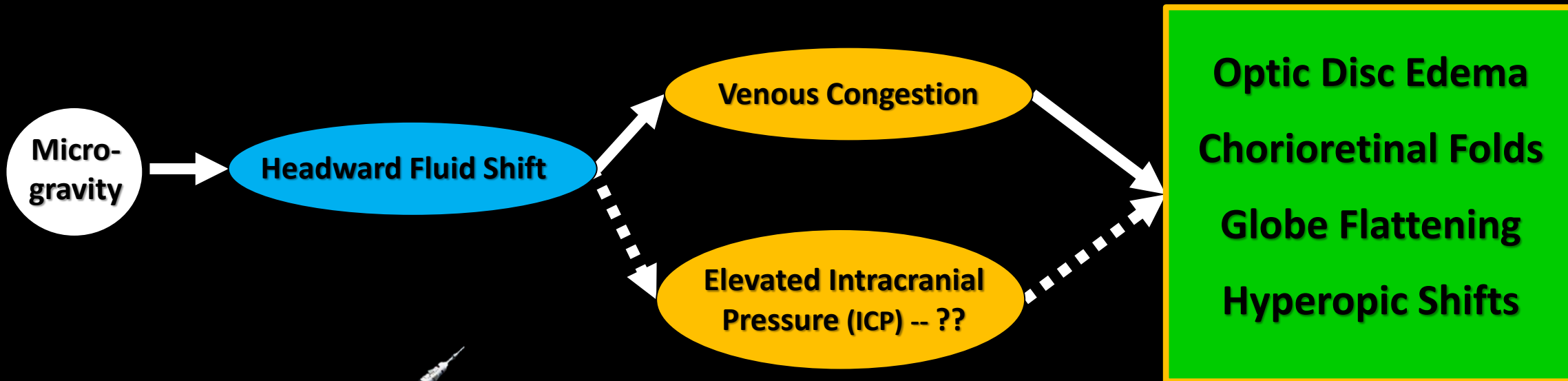


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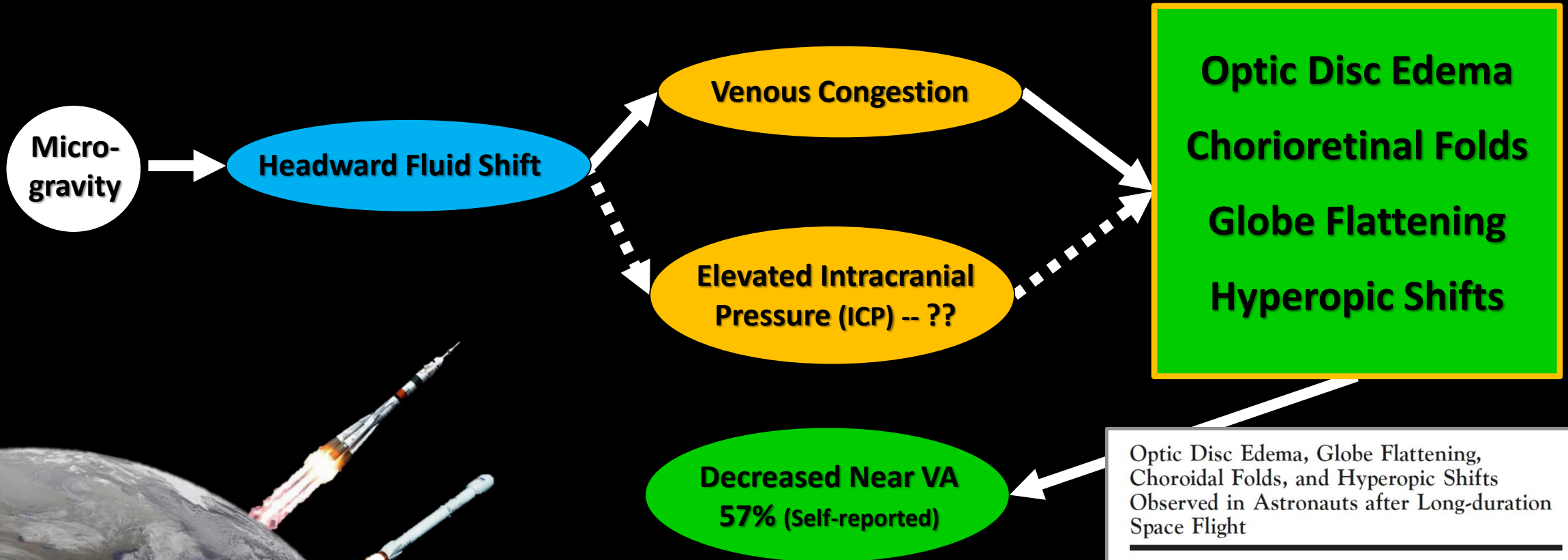


Optic Disc Edema, Globe Flattening, Choroidal Folds, and Hyperopic Shifts Observed in Astronauts after Long-duration Space Flight

Thomas H. Mader, MD,¹ C. Robert Gibson, OD,² Anastas F. Pass, OD, JD,³ Larry A. Kramer, MD,⁴ Andrew G. Lee, MD,⁵ Jennifer Fogarty, PhD,⁶ William J. Tarver, MD,⁶ Joseph P. Dervuy, MD,⁶ Douglas R. Hamilton, MD, PhD,⁷ Ashot Sargsyan, MD,⁷ John L. Phillips, PhD,⁸ Duc Tran, DO,² William Lipsky, MD,² Jung Choi, OD,² Claudia Stern, MD, PhD,⁹ Raffi Kizyanjian, MD,¹⁰ James D. Polk, DO⁹



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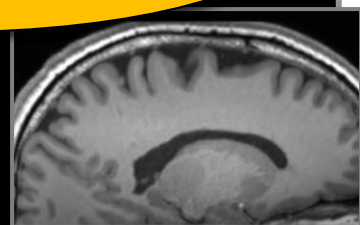
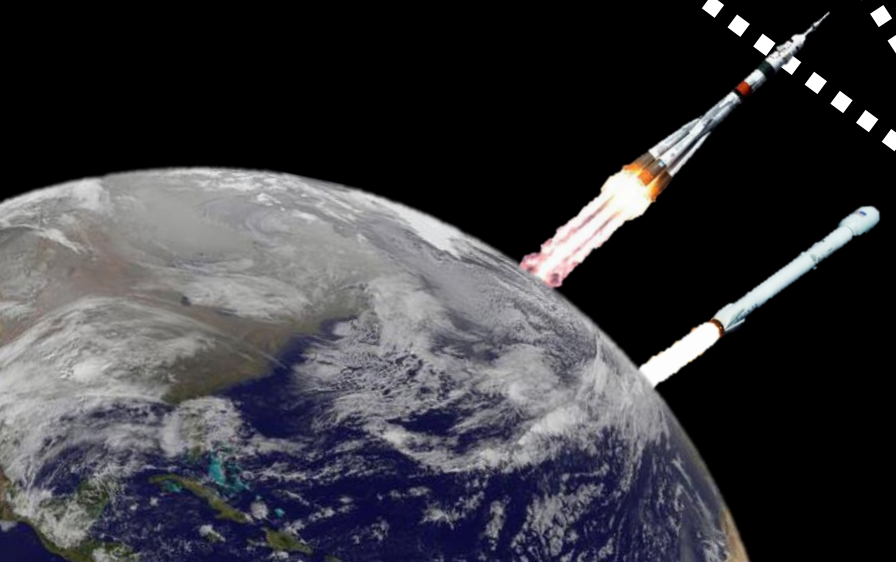
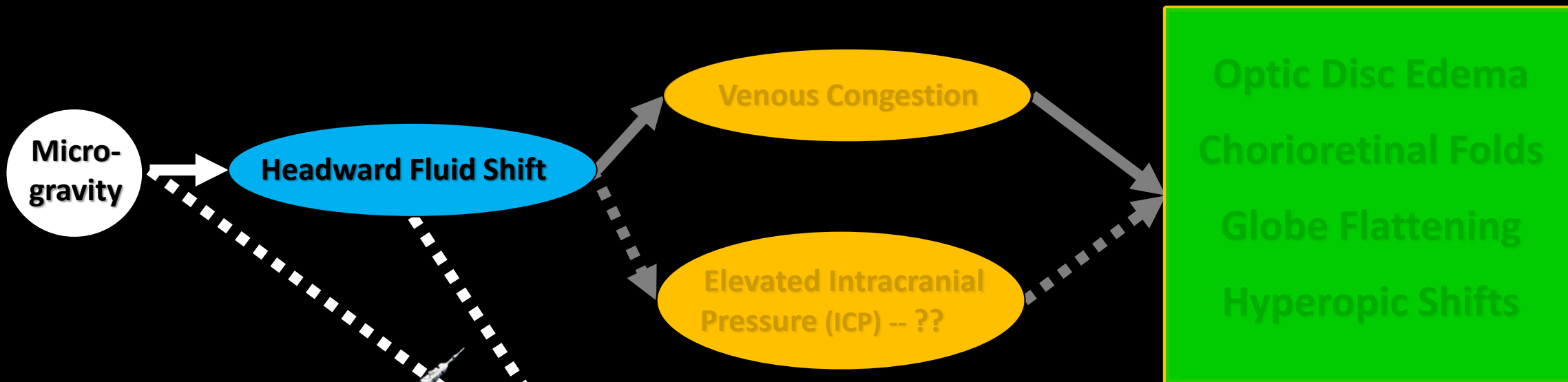


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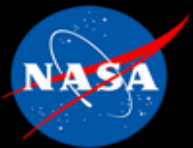


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

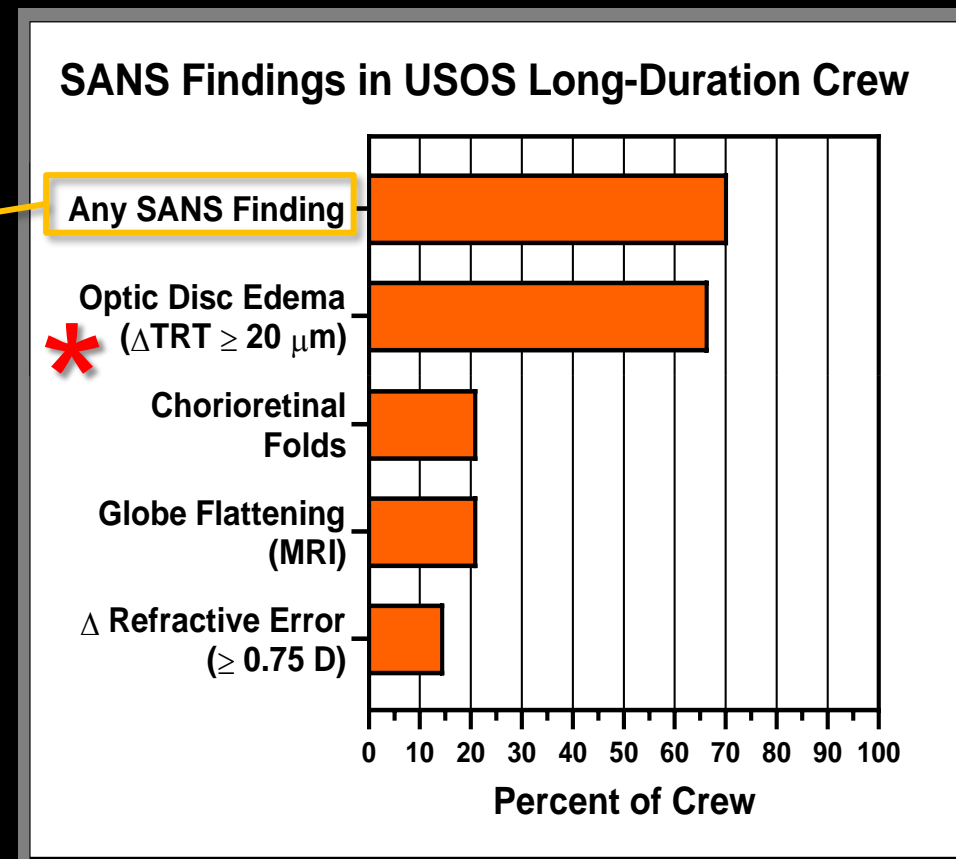
Effects of Spaceflight on Astronaut Brain Structure as Indicated on MRI

Donna R. Roberts, M.D., Moritz H. Albrecht, M.D., Heather R. Collins, Ph.D., Davud Asemani, Ph.D., A. Rano Chatterjee, M.D., M. Vittoria Spampinato, M.D., Xun Zhu, Ph.D., Marc I. Chimowitz, M.B., Ch.B., and Michael U. Antonucci, M.D.



Mission Duration: *Long* (~6-12 mo)

- No permanent loss of vision or cognitive function yet detected in any crew
- About 70% of long-duration crewmembers present w/ signs of SANS (from mild to severe)
 - Diagnosed in males *and* females, in novice & veteran crewmembers, in either/both eyes
 - *Can't yet predict* who will develop SANS
- Severity *related to mission duration*
- Some changes can become *permanent* (i.e., globe flattening, hyperopic shifts, choroidal folds)



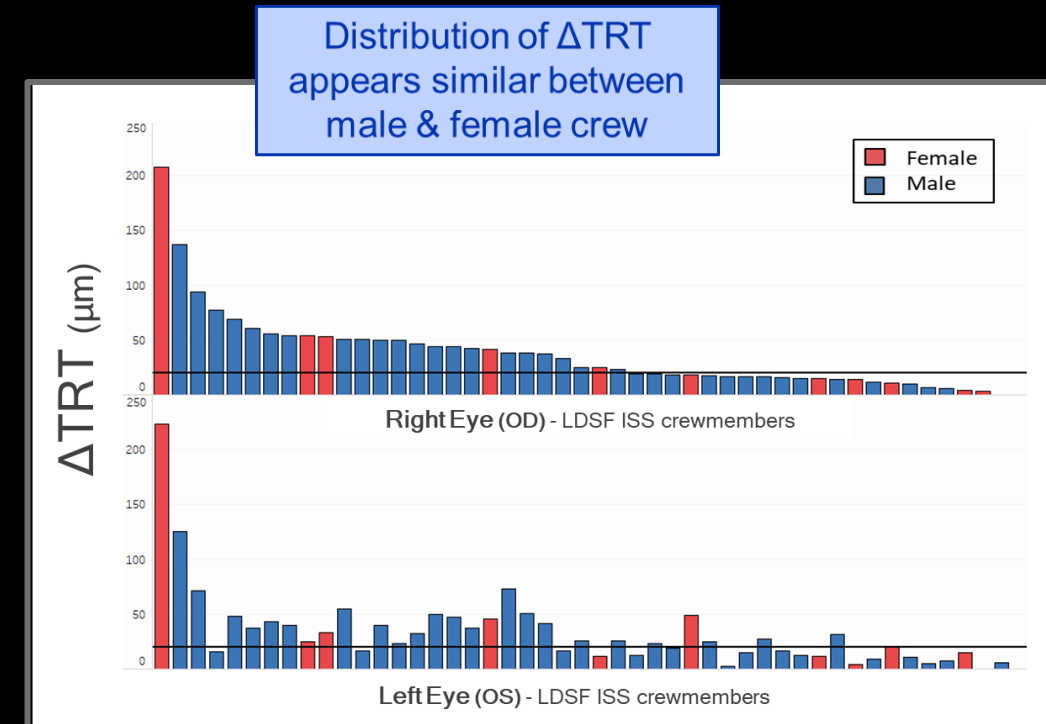
Data courtesy of NASA LSAH

* ΔTRT = Change in total retinal thickness near optic disc (vs. pre-flight). Objectively quantifies optic disc edema



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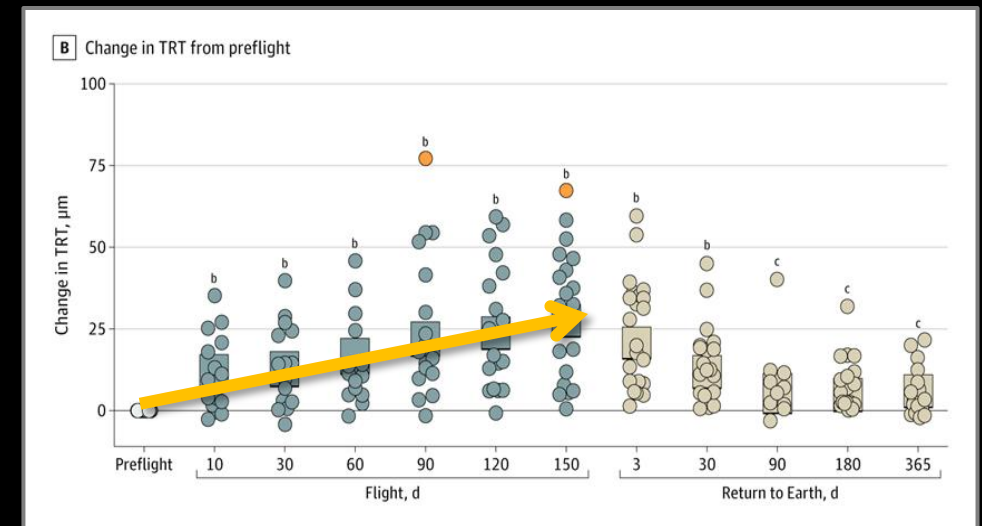


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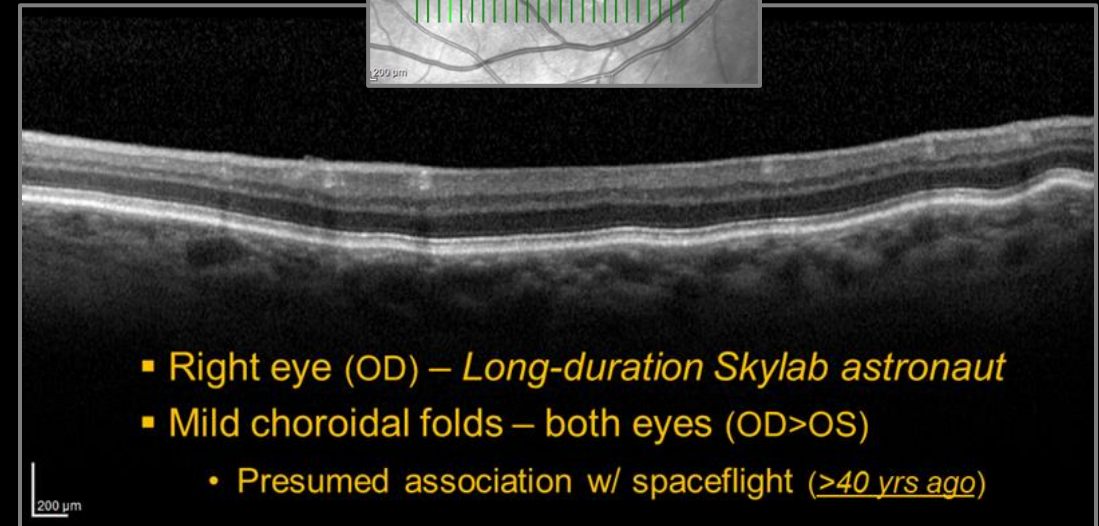
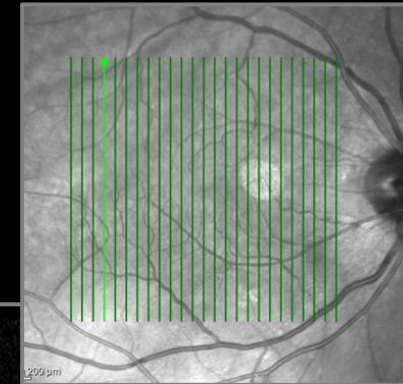


Macias BR, et al. Association of long-duration spaceflight with anterior and posterior ocular structure changes in astronauts and their recovery. JAMA Ophthalmol. 2020 Apr 02



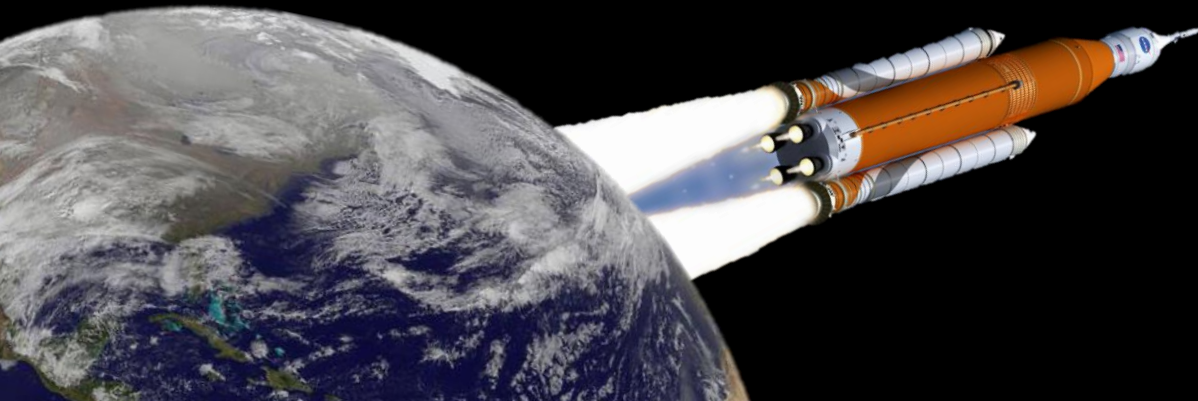
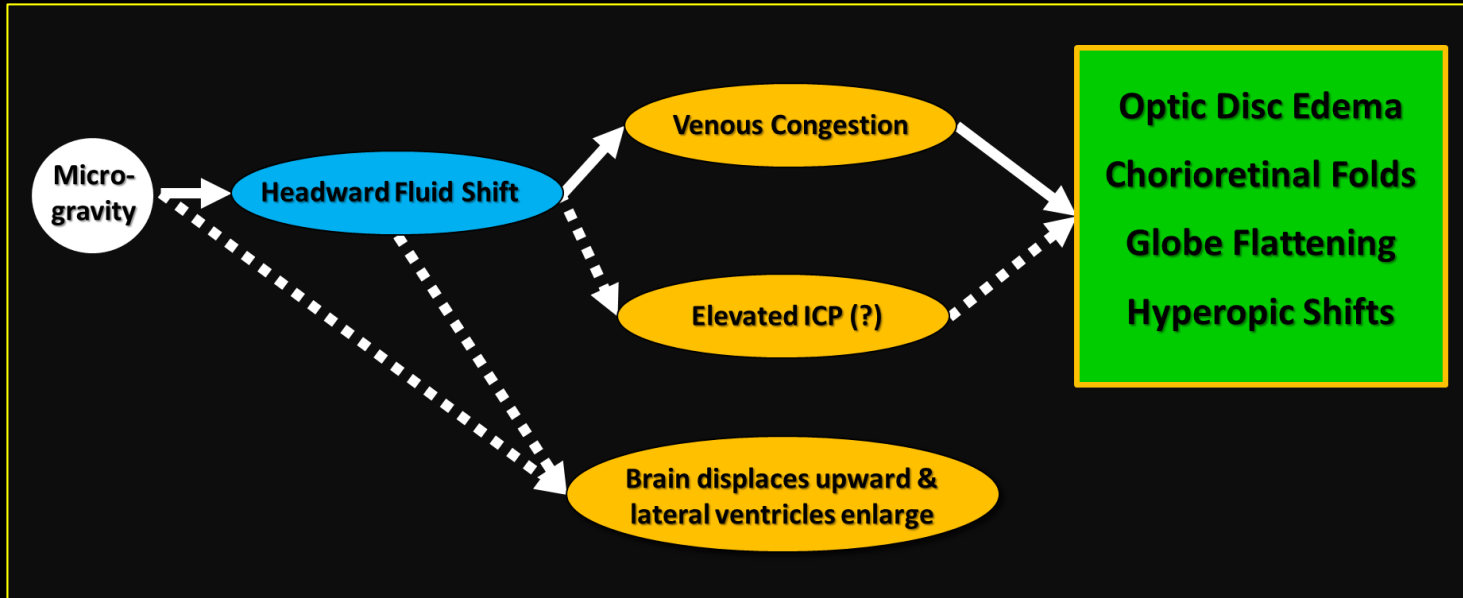
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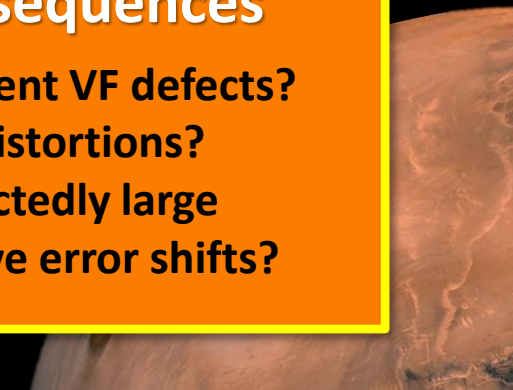
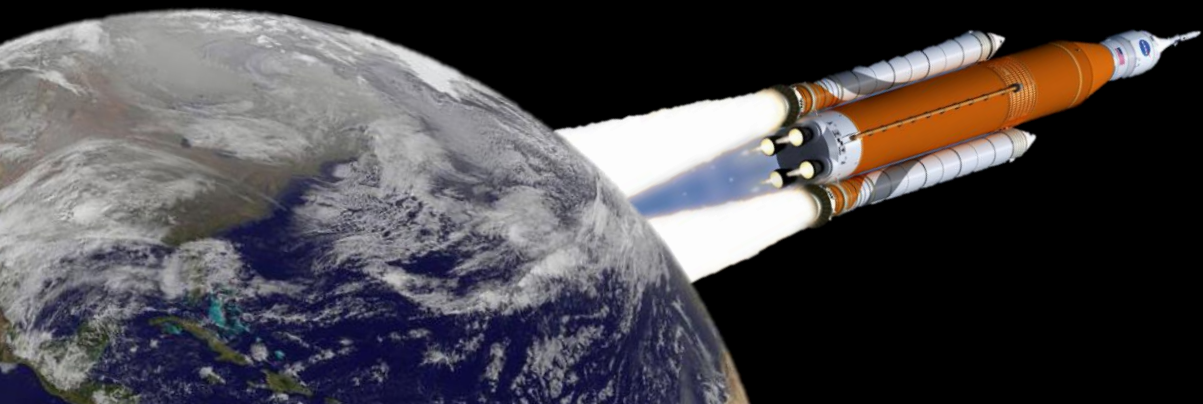
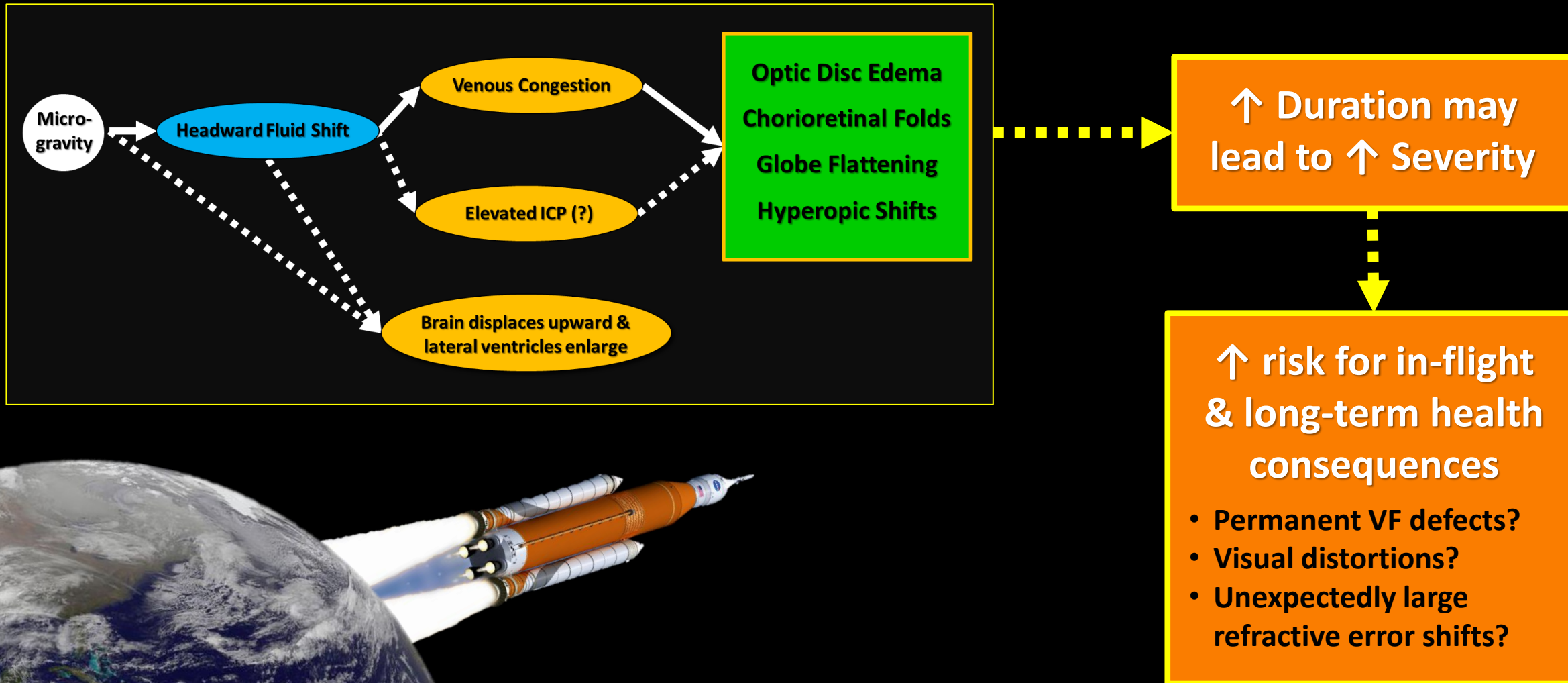


Mission Duration: *Exploration* (~2–3 years)





Mission Duration: *Exploration* (~2–3 years)





Medical Testing & Surveillance



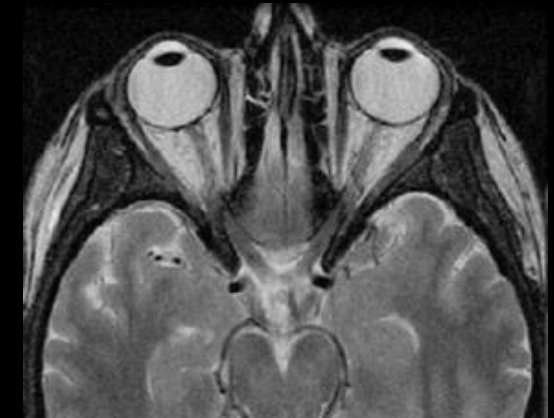
Image credit: NASA



Medical Testing & Surveillance



Primary SANS/Ocular Tests	Pre-flight	On-orbit			Post-flight
		FD30	FD90	R-30	
3T MRI – Head & Orbits	X	--	--	--	X
Comprehensive Eye Exam	X	--	--	--	X
Visual Field	X	Not yet on-orbit			X
Vision Screening – VA, Amsler grid, Survey	X	X	X	X	X
Retinal Photography – “Fundoscopy”	X	X	X	X	X
Optical Coherence Tomography	X	X	X	X	X
Ocular Ultrasound	X	X	X	X	X
Tonometry – Intraocular Pressure	X	X	X	X	X
		<u>Note:</u> ESA only; ACI otherwise			



<https://www.opthalmicmart.com/product/humphrey-field-analyzer-3/>

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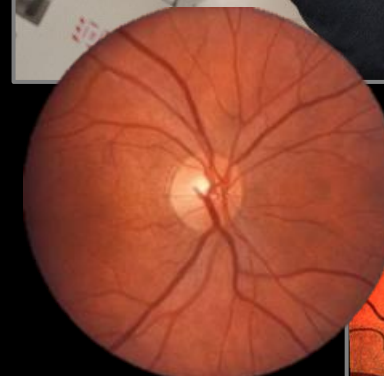
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Optical Coherence Tomography	X	X	X	X	X
Ocular Ultrasound	X	X	X	X	X
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Image credit: NASA





Medical Testing & Surveillance



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Retinal Photography – “Fundoscopy”	X	X	X	X	X
Optical Coherence Tomography	X	X	X	X	X
Ocular Ultrasound	X	X	X	X	X
Tonometry – Intraocular Pressure	X	X	X	X	X
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Image credit: NASA



Medical Testing & Surveillance



Primary SANS/Ocular Tests	Pre-flight	On-orbit			Post-flight
		FD30	FD90	R-30	
3T MRI – Head & Orbits	X	--	--	--	X
Comprehensive Eye Exam	X	--	--	--	X
Visual Field	X	Not yet on-orbit			X
Vision Screening – VA, Amsler grid, Survey	X	X	X	X	X
Retinal Photography – “Fundoscopy”	X	X	X	X	X
Optical Coherence Tomography	X	X	X	X	X
Ocular Ultrasound	X	X	X	X	X
Tonometry – Intraocular Pressure	X	X	X	X	X
		<u>Note:</u> ESA only; ACI otherwise			



Image credit: NASA



Medical Testing & Surveillance



Primary SANS/Ocular Tests	Pre-flight	On-orbit			Post-flight
		FD30	FD90	R-30	
3T MRI – Head & Orbits	X	--	--	--	X
Comprehensive Eye Exam	X	--	--	--	X
Visual Field	X	Not yet on-orbit			X
Vision Screening – VA, Amsler grid, Survey	X	X	X	X	X
Retinal Photography – “Fundoscopy”	X	X	X	X	X
Optical Coherence Tomography	X	X	X	X	X
Ocular Ultrasound	X	X	X	X	X
Tonometry – Intraocular Pressure	X	X	X	X	X
		Note: ESA only; ACI otherwise			



Image credit: NASA



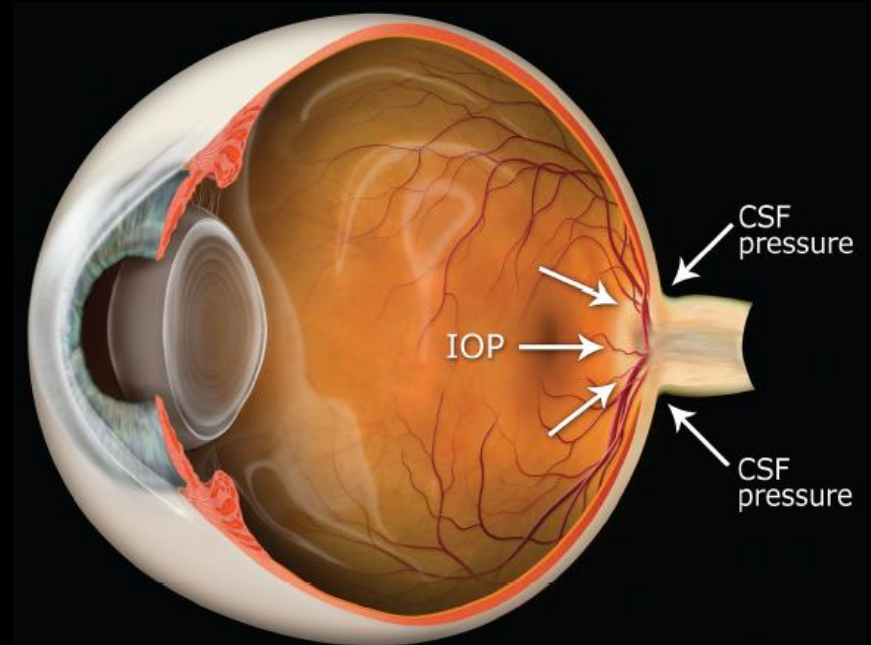
Why is this Happening?



Image credit: NASA

Top SANS Pathogenesis Theories

- Hypothesis #1: *Increased optic nerve sheath pressure*
 - Due to an overall increase in ICP or localized to the perioptic subarachnoid space (e.g., due to compartmentalization)
 - Enough to cause an imbalance between ICP & intraocular pressure (i.e., a translaminar pressure gradient)
- Hypothesis #2: *Venous congestion* alters local physiology, reduces blood perfusion, and/or places direct pressure on retinal axons
- Hypothesis #3: *Individual anatomical/genetic factors*
 - e.g., Altered folate-dependent 1-carbon metabolism





Mitigation Strategies

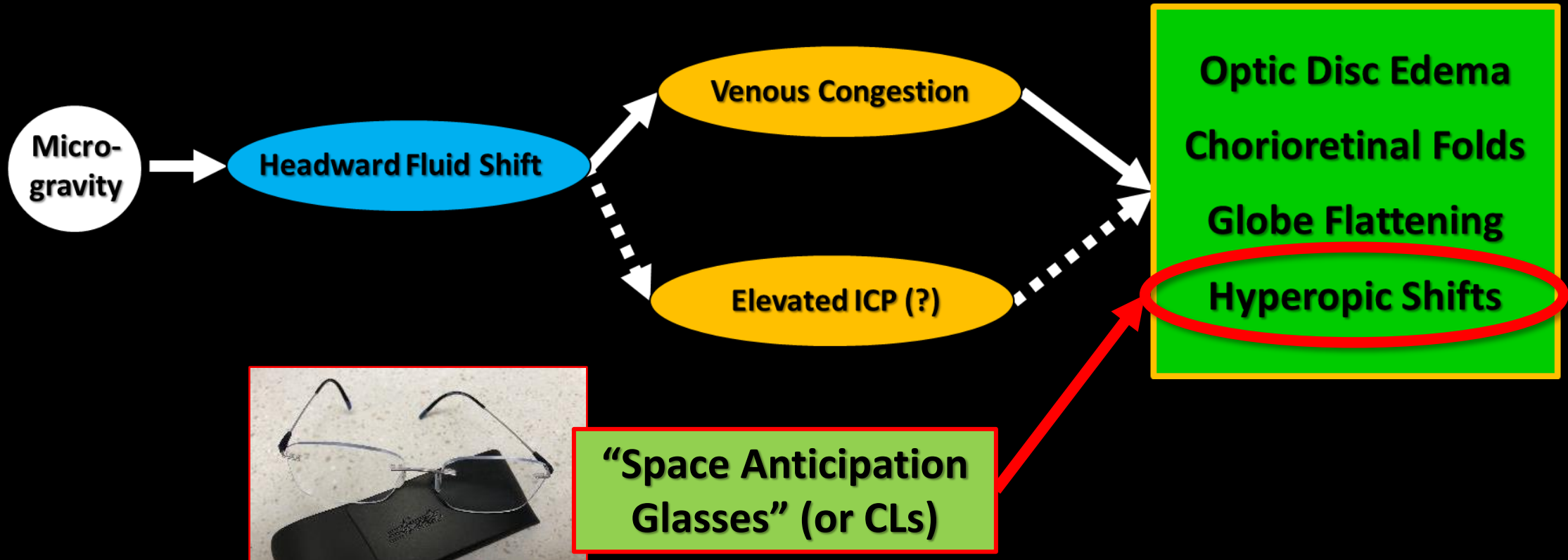


Image credit: NASA





SANS Mitigation Strategies





SANS Mitigation Strategies

- Artificial Gravity
- Lower Body Negative Pressure (?)
- Thigh Cuffs (?)

Micro-gravity

Headward Fluid Shift

Venous Congestion

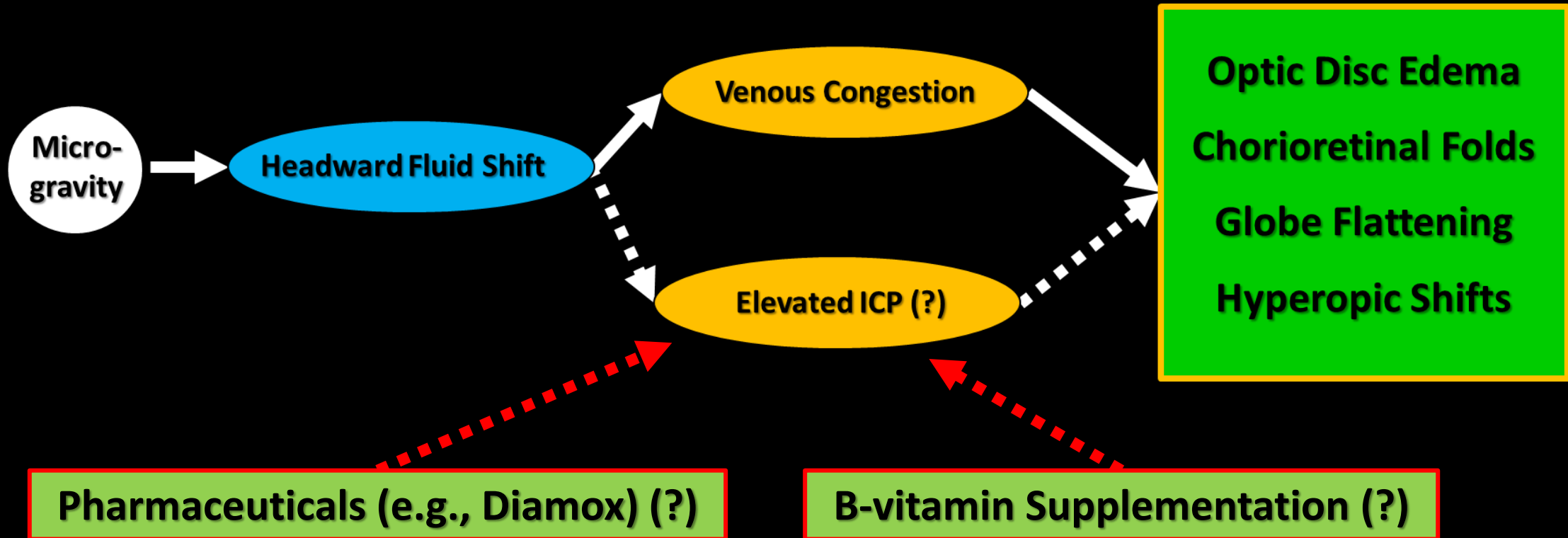
Elevated ICP (?)

Optic Disc Edema
Chorioretinal Folds
Globe Flattening
Hyperopic Shifts





SANS Mitigation Strategies





Bottom-line Messages: SANS



Image credit: NASA

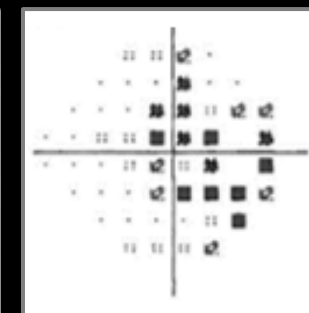
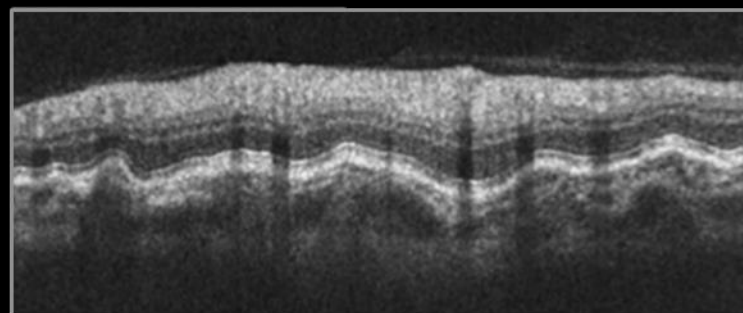
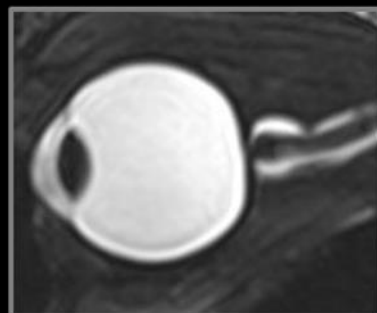




Bottom-line Messages: SANS



- Currently, *no evidence* of cognitive impairment or permanent vision loss in *any* astronauts
- No mission has lost objectives secondary to SANS
- 70% of ISS crewmembers diagnosed w/ SANS, while *18% develop clinically-concerning SANS*
- Cases are typically *asymptomatic* unless they develop *blurred vision*
 - Inform your crew surgeons about any vision changes
- SANS countermeasures are being aggressively pursued & studied
 - Please consider volunteering for SANS research (e.g., ISAFE)
- SANS severity is related to mission duration. SANS poses a significant risk during extended-duration spaceflight (e.g., a >2-yr Mars mission)





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SANS Prevalence



Feature of SANS	DIAGNOSTIC THRESHOLDS FOR SANS							
	<i>Earliest indication</i>	72%	<i>Clinically Concerning</i>	18%	<i>Pathological: Acute Functional Impact</i>	6%	<i>Pathological: Affecting Long-Term Health</i>	0%
OPTIC DISC EDEMA	≥ +20 μm ΔTRT and/or evidence of mild edema not meeting Frisè grade 1	66%	≥ +55 μm ΔTRT and/or Frisè grade ≥ 1 <i>Note: Post-flight lumbar puncture recommended</i>	17%	Visual field loss (e.g., enlarged blindspot) <i>Associated anatomical signs to be determined</i>	3%	Permanent visual field loss and/or reduced retinal nerve fibre layer (RNFL) thickness	0%
CHORIORETINAL FOLDS	Any evidence of folds (i.e., choroidal, retinal or peripapillary wrinkles)	16%	Sharp folds in vicinity of macula	5%	Distorted central vision <i>Associated anatomical signs to be determined</i>	0%	Permanently distorted central vision, atrophy of retinal pigment epithelium (RPE) or photoreceptors, and/or choroidal neovascularization	0%
GLOBE FLATTENING	Any evidence of posterior globe flattening (centered at optic nerve) and/or decreased axial length (centered at fovea)	23%	Moderate change	12%	RE shift <i>beyond</i> power of available in-flight “Space Anticipation Glasses”	--	Currently unknown	--
REFRACTIVE ERROR (RE) SHIFT	≥ +0.75 diopters	15%	≥ +1.50 diopters (i.e., RE shift <i>approaching</i> power limit of available in-flight “Space Anticipation Glasses”)	5%		2%	Currently unknown	--

Data courtesy of LSAH (Sara Mason)

Note: Percentages rounded to whole numbers



Questions?

Tyson Brunstetter, OD, PhD¹
SANS Clinical Lead (Eyes/Vision)
Email: Tyson.J.Brunstetter@nasa.gov

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- William J. Tarver, MD, MPH¹ — SANS Clinical Lead (CNS)
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- Steven S. Laurie, PhD² — SANS Research Lead
- Brandon R. Macias, PhD¹ — SANS Deputy Research Lead

- Amanda Boudreaux²
- David M. Brown, MD³
- Molly Freedman, BSN, RN²
- C. Robert (Bob) Gibson, OD^{2,4}
- Stephen F. Hart, MD¹
- Andrew G. Lee, MD⁵
- Thomas Mader, MD²
- Daniel A. Marburgh²
- Sara S. Mason⁶
- Amirah M. Mathin, MS²
- Anna M. Mendiola²
- William T. Misek²
- Suzy Osborne, MPH²
- Rachel Richardson, BSN, RN²
- Ashot Sargsyan, MD²
- Christopher Schubert, LP, NRP²
- Wafa F. Taiym, MS²
- Elizabeth Talburt²
- Mary Van Baalen, PhD¹
- Julia A. Wells, BSN, RN²

1. NASA Johnson Space Center, Houston, TX
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