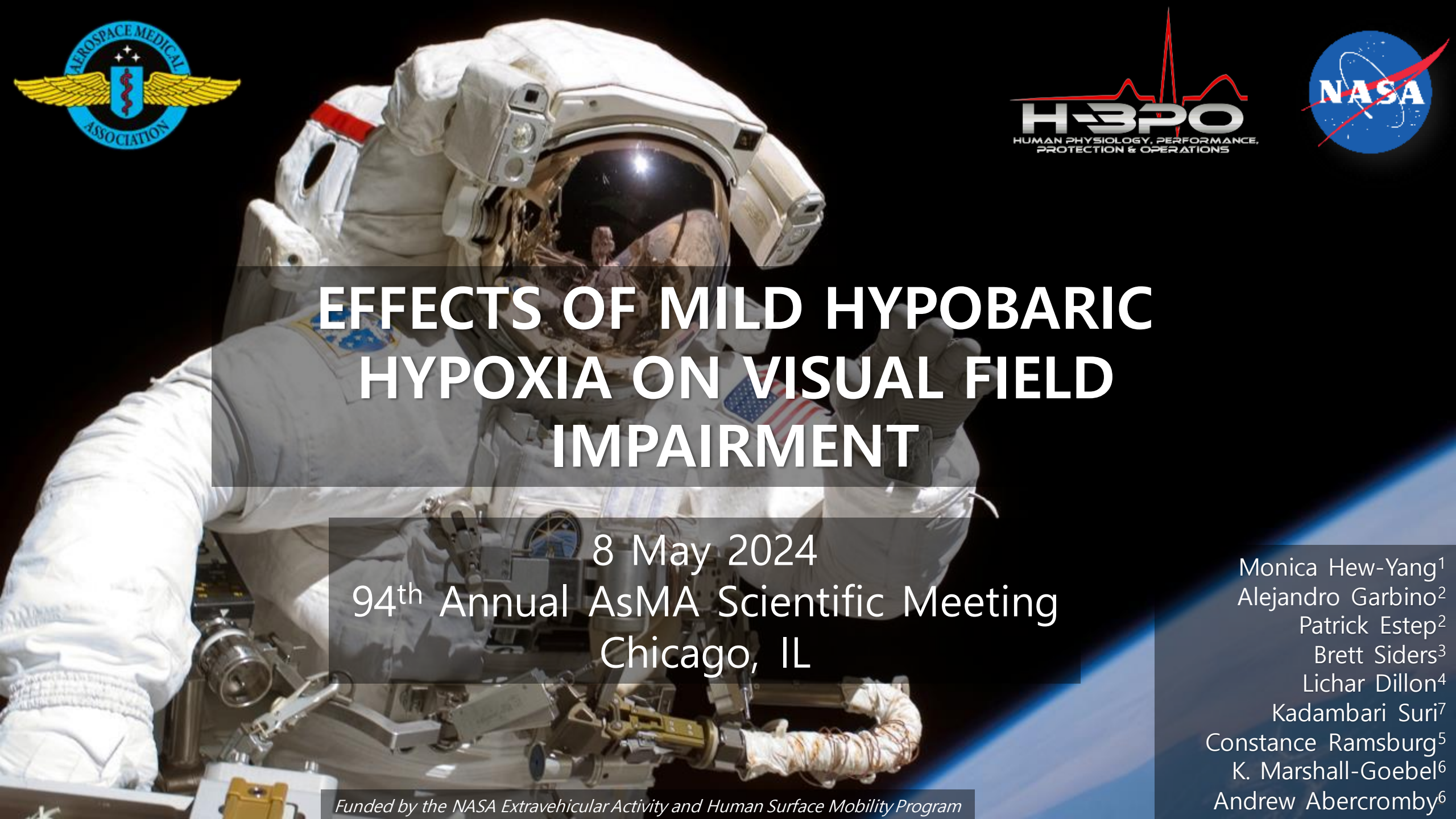




EFFECTS OF MILD HYPOBARIC HYPOXIA ON VISUAL FIELD IMPAIRMENT

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Disclosure Information

94th Annual Scientific Meeting

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I have no financial relationships to disclose.

I will not discuss off-label use and/or investigational use in my presentation.

*The opinions discussed are mine and mine alone, they do not
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Exploration Atmosphere Study – Mission 2



- **Subjects:** 7 test subjects (including 2 Doppler Techs)
 - Mean age: 37.9 ± 9 years, 4 females
- **Location:** 20-foot hypobaric chamber facility, Building 7 NASA Johnson Space Center (JSC)
- **Timeframe:** May-June 2023
- **Protocol:** 11-day Exposure to a possible Lunar habitat “exploration atmosphere” consisting of lower pressure (8.2 psia) and higher O_2 (34%) [partial pressure (P_{IO_2}) = 128 mmHg]
 - Equivalent air altitude = 4000 ft
- **Primary purpose:** validate a prebreathe protocol to reduce decompression sickness (DCS) risk during extravehicular activities and **characterize hypoxic effects of the Exploration Atmosphere (EA)**



20-Foot Chamber Facility Exterior, NASA JSC
Photo Credit: NASA/H-3PO

Note: Chamber is NOT intended to represent a flight-like habitat



Impacts of Hypoxia on Visual Field Performance



- The visual system has long been recognized as being particularly susceptible to hypoxia, both in terms of time to impairment and functional complications.^{11,14,16}
- The three hypoxia zones harbor predictable visual system effects:

Altitude	Hypoxia Zones (equivalent %O2/piO2)	Photopic (day) Vision	Mesopic (twilight) Vision	Scotopic (Night) Vision (more sensitive to hypoxia)
Sea level to 3,000 m (9,842 ft)	Indifferent zone (21 - 14.3%O ₂) (149 -100mmHg)	1. Vision unaffected ^{3,14} 2. CS is relatively resistant to mild hypoxia at < 10,000 ft. ^{8,9,10} 3. Improvement in CS seen w/ short-term hypobaric hypoxia. ⁵	1. Statistically significant ↓ (minimal clinical significance) in contrast VA at 6,000-8000 ft ⁷ . 2. CS is resistant to mild hypoxia at mild mesopic condition. ^{8,9,10}	1. Average vision performance ↓: 5% at 1,100 m, 18% 2,800 m. ¹¹ 2. Visual impairment shown to occur at ~4,000-5,000 ft. ¹⁶
3000 m to 5000 m (16,404 ft)	Adaptation Zone (14.3 -11.4%O ₂) (100 -75 mmHg)	1. Visual impairment is common at 10,000-15,000 ft ¹⁶ 2. Impairment can be mostly overcome, and visual tasks can still be carried out.	1. Significant low contrast VA ↓ at 10,000 ft ⁷ 2. High/low contrast VA at 10,000 ft → minor unanticipated improvement @ 7 hr, but no overall relevant clinical Δ over 12 hr. ^{4,6}	Average vision performance ↓: 35% at 4,000 m. ¹¹
>5,000 m (>16,404 ft)	Inadequate Compensation (< 11.4%O ₂) (< 75 mmHg)	1. Physiological adaptations can no longer compensate for the decreased oxygen available. 2. Impaired accommodation and convergence, more overt diplopia, and delayed respond to visual stimuli ^{11,16}		



Objectives



- Hypoxia is associated with slight decrements in visual performance. This study explores whether an 8.2psi/34% O₂ exploration atmosphere causes significant visual impairment.
- Hypothesis: There is no clinically significant negative change in visual performance while living in the exploration atmosphere compared to sea level.





Methods (1/2)



- **Equipment**

- Distance (2.0 m) w/ controlled lighting (pre-calibrated), 1-3cd/m² (photopic vision)
 - Artemis crew are likely to operate in photopic conditions (e-screen in dim cabin)
- Surface Pro tablets with Freiburg Vision Test 'FrACT₁₀' test battery (5-10 min)



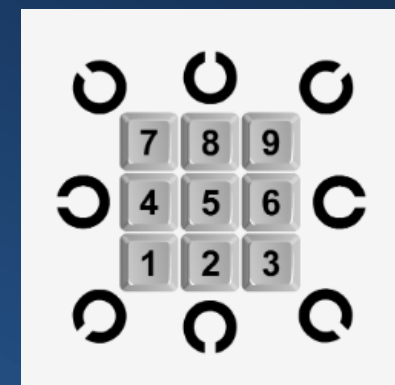
- **Protocol**

- Subject enters the space and light-adapts for 3 min in test space
- **Dependent Variables:** FrACT visual test battery for three sessions
 - Visual Acuity at 100%cW contrast (high contrast)
 - Visual Acuity at 50%cW contrast (low contrast)
 - Contrast Sensitivity (fixed size w/ varying luminance) → contrast sensitivity threshold



- **Statistics: statistical significance at $\alpha = 0.05$**

- Equivalence testing, one-way repeated measures ANOVA and paired t-tests
- Clinical significance thresholds for evaluating photopic vision:
 - Visual acuity at 100% contrast (VA_{100%}): +/- 0.06 LogMAR (= 3 letters in an eyechart line)
 - Visual acuity at 50% contrast (VA_{50%}): +/- 0.1 LogMAR (= 1 eye chart line)
 - Contrast Sensitivity (CS): +/- 10% (logCS Weber) difference from baseline

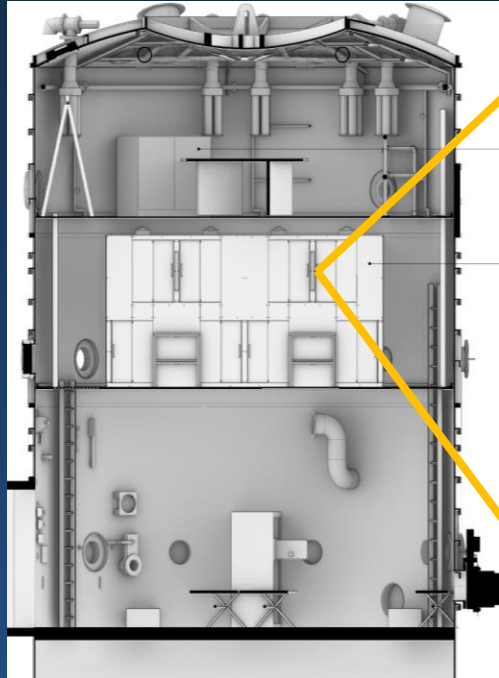




Method (2/2) – Protocol/Timeline



- Measurements (11 in test, 1 pre)
 - FrACT Test: AM (☀), PM (☾)
 - VA and CS at each test
 - Test Day (TD)
 - x1 fam training session
- Equivalent Air Altitude = 4000 ft
- Distance = 2 m
- Repeated subjects (n =7)



Pre Mission
TD 0
☾

		EVA		EVA		EVA		EVA		EVA
TD 1	TD 2	TD 3	TD 4	TD 5	TD 6	TD 7	TD 8	TD 9	TD 10	TD 11
☾	☀ ☾		☀ ☾		☀ ☾		☀ ☾		☀ ☾	

Sea Level (14.7 psia/21%O2)
baseline, P_iO₂ 149.7 mmHg

Exploration Atmosphere (8.2 psia/34%O2)
mild hypoxic, P_iO₂ 128 mmHg

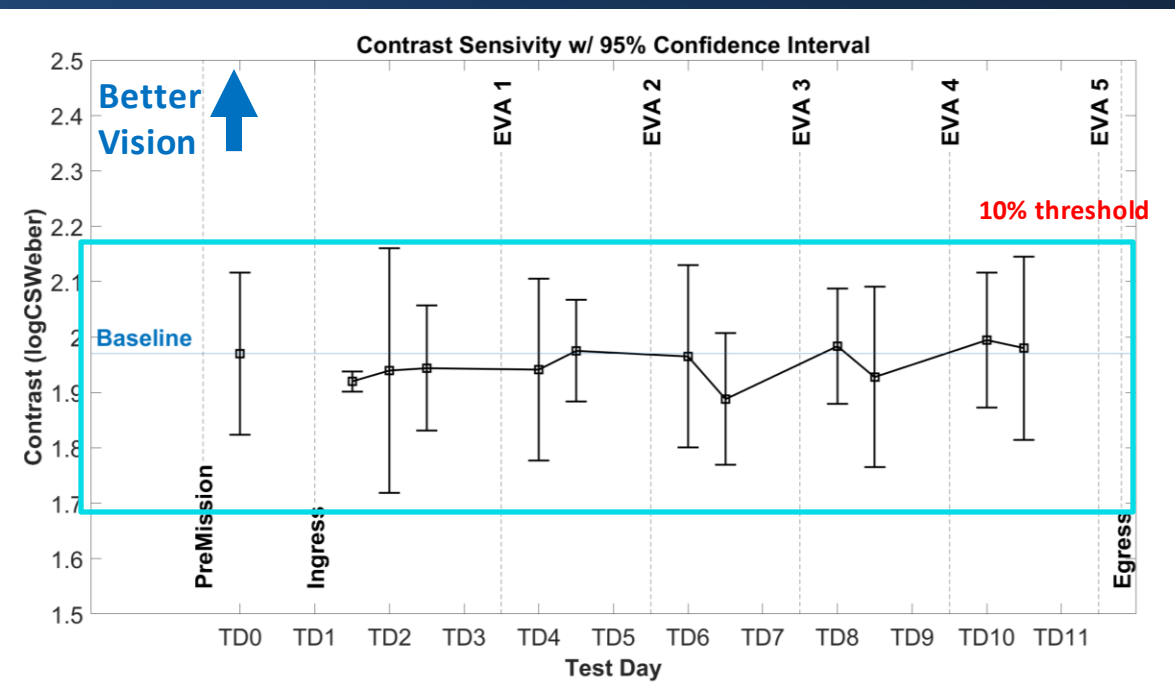
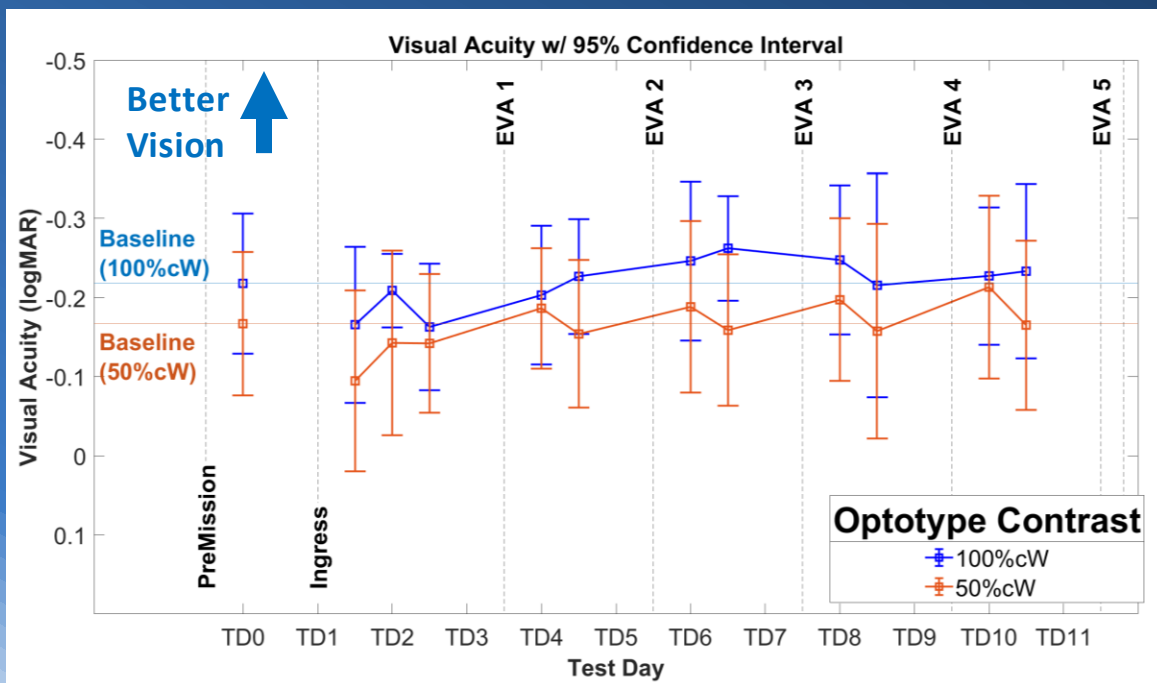
EVA (4.3 psia/85%O2) – 6 hr
mild hyperoxia, P_iO₂ 149 mmHg



Results: Adaptation to the EA (1/2)

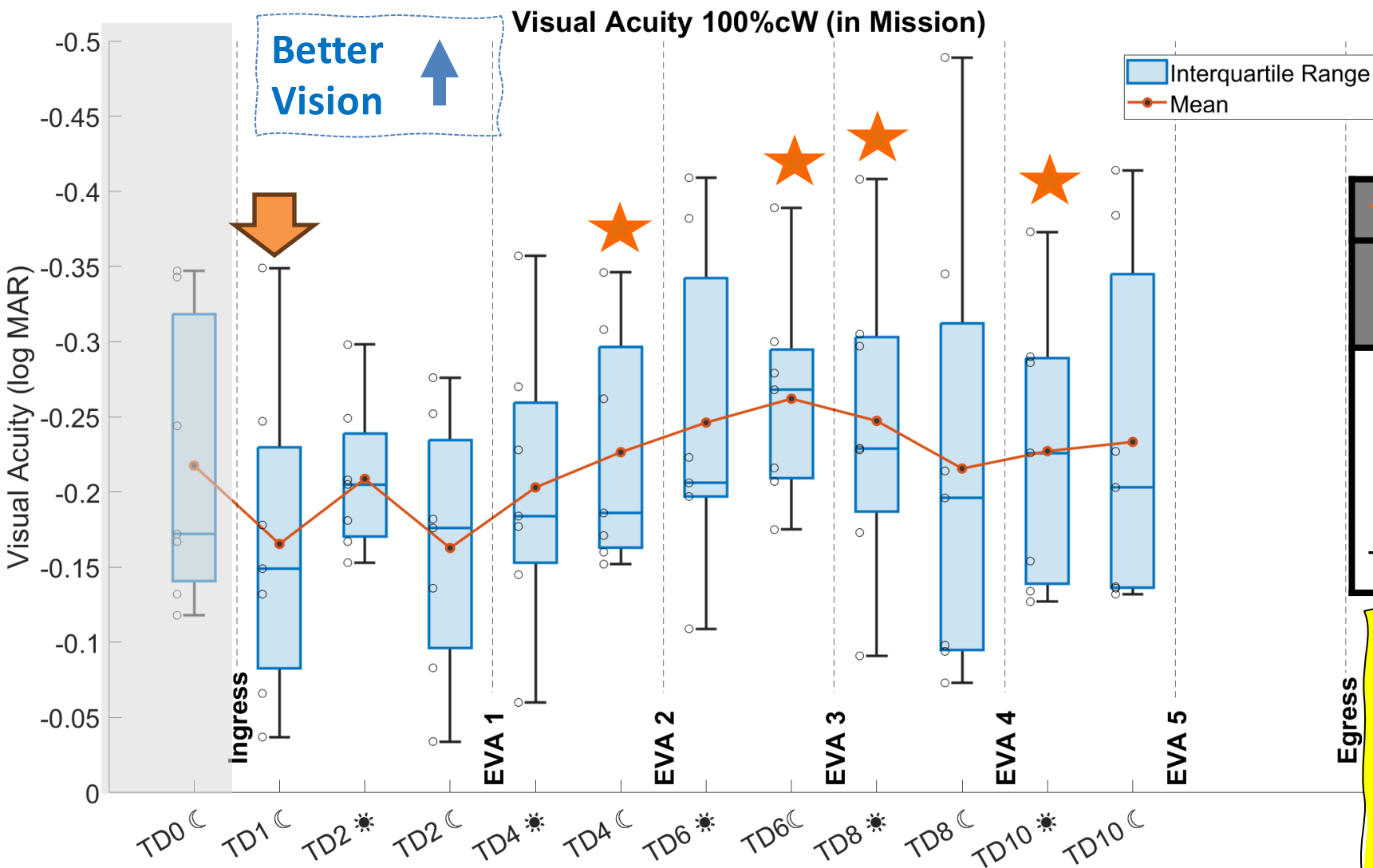


- **There was no clinically significant negative change in visual performance in EA when compared to pre-mission baseline (sea level)**
 - **VA50, CS:** statistically significant for equivalence within the ± 0.1 logMAR of baseline
 - **VA100:** No statistically significant equivalence (90% CI $\Delta = [-0.0804, -0.00641]$) between baseline and TD10
 - No statistically significant **vision degradation** per clinical significance level
 - Observed clinically (marginally) significant **vision improvement**: $\Delta = -0.08$ LogMar (~4 letters)
→ **Possible recovery/training effect within mission**





Results: Adaptation to the EA (2/2)



★ Clinically/Stats Significant	
TD1 vs.	Mean Δ (Log MAR) (% wrt TD1)
TD4 PM	0.06 (37.5%)
TD6 PM	0.1 (62.5%)
TD8 AM	0.08 (50%)
TD10 AM	0.06 (37.5%)

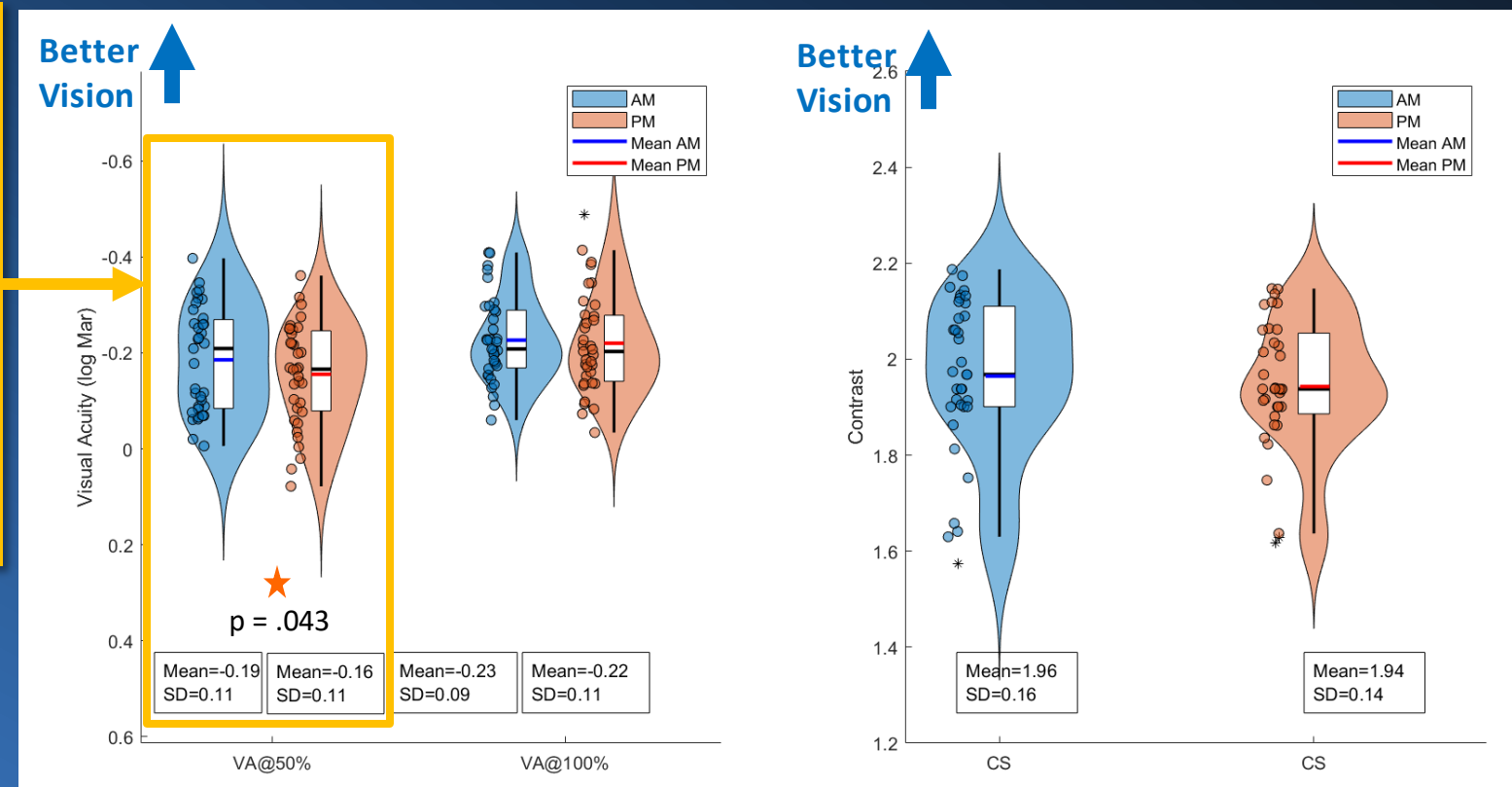
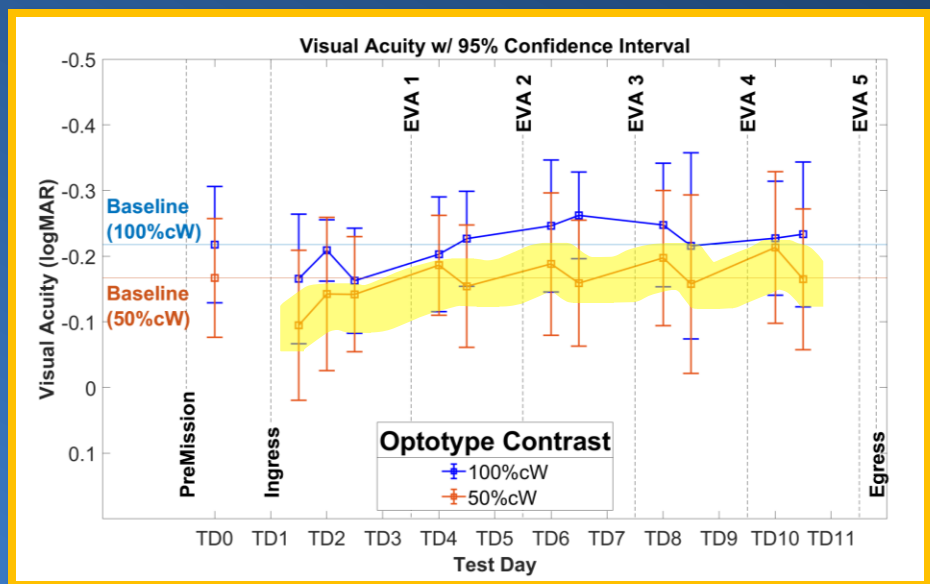
Possible adaptation/recovery/training effect within mission: TD1 shows clinically and statistically significant vision improvement after TD 4



Results: Time of Day Effect



- Paired t-test showed statistically significant difference within mission between AM/PM for VA 50% only
 - Low contrast visual acuity measurements: Slight degradation in PM (vs. AM)
 - The difference is only 1.5 letter on average ($\Delta = +0.03$ logMAR), and thus it is **not clinically significant**.





Conclusion and Future Work



- Preliminary analysis suggests that the EA-2 mild hypobaric hypoxic environment **did not cause clinically significant negative impacts** to participants' visual field performance.
- Visual acuity and contrast sensitivity **did not meaningfully differ** between pre-mission (sea level) and during exposure to the Exploration Atmosphere (8.2psi, 34% O₂, 128mmHg piO₂)
- Potential in-mission recovery/training effects observed in **high contrast visual acuity**
 - Slight vision improvement: statistically significant in not worse than the clinical significance bound ($\Delta VA_{100\%} = -0.08 \text{ LogMAR}$)
- EA-1 data revealed large variance and recording errors and was removed from the analysis.
- **Future Work**
 - Lighting condition and training effect calibration in work
 - Mini-study to investigate and characterize the potential training effect
 - Increase statistics by increasing number of subjects in future studies
 - Update from +/- 0.06 (54%) to +/-0.067 LogMar (80%) to be fully powered for equivalency testing
 - OR increase number of subject from 7 to 13



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Acknowledgement

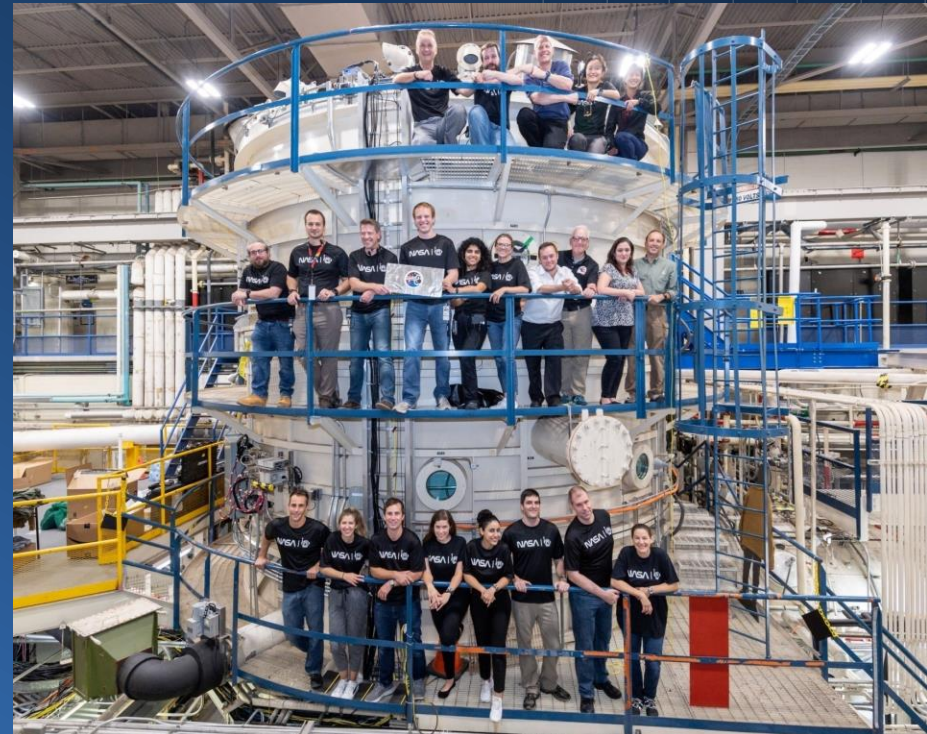
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- Dr. Tyson Brunstetter and Dr. Matthew Yang for their inputs on visual field performance
- Dr. Millennia Young of the SK Biostatistics Laboratory for supporting statistical analysis
- JSC Exploration Atmosphere 20ft chamber test and support teams



Thank you!

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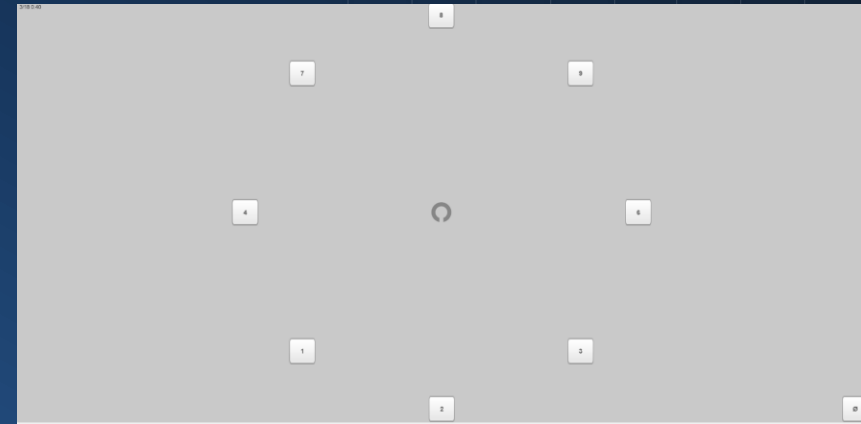
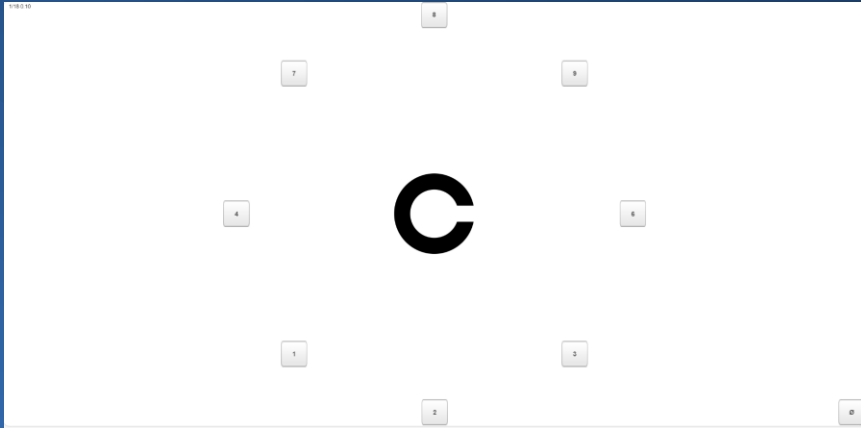


BACKUP SECTION

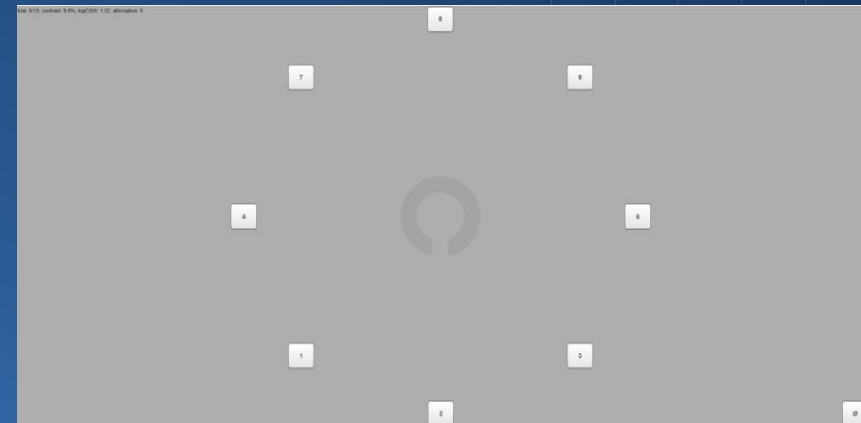
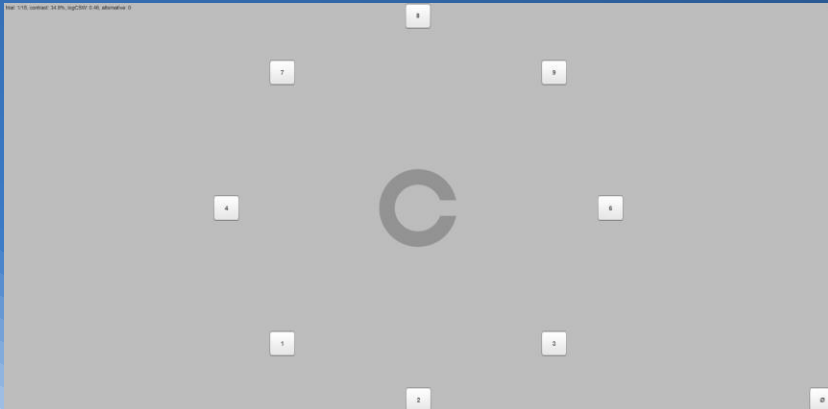
Example VAC Test



- Optotype 100 vs 50

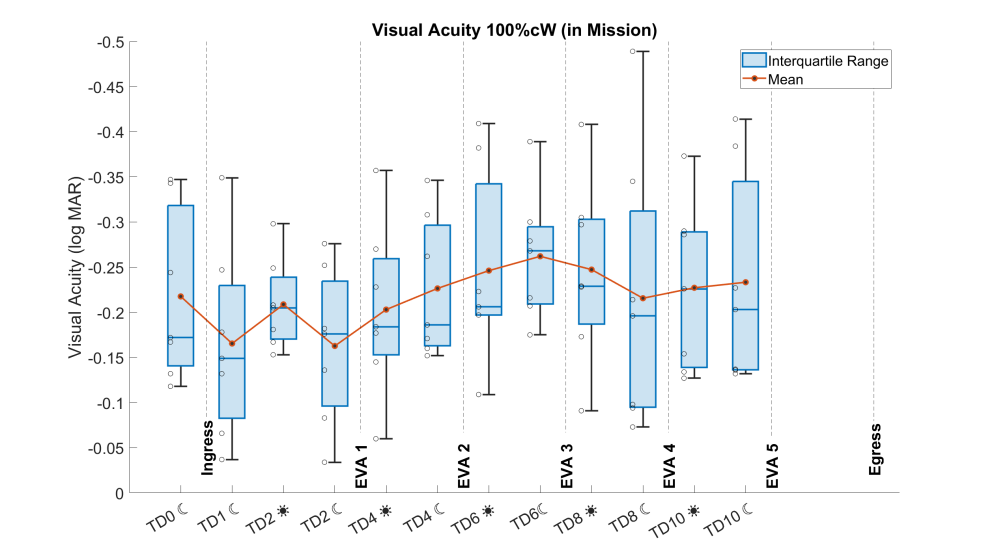


- Optotype 50, contrast assessment





Backup: Visual Acuity at 100% Contrast - Improvement



Possible recovery/training effect within mission: TD1 shows clinically and statistically significant differences after TD 4

Paired T-test	1.5 vs 4.5	1.5 vs. 6.5	1.5 vs. 8	1.5 vs 10
P-value	0.042	0.012	0.005	0.022
t	2.57	3.54	4.3	3.06
95% CI of the difference btw the pair	[0, 0.12]	[0.03, 0.16]	[0.04, 0.13]	[0.01, 0.11]
Effect Size	$d = 0.97$ (large)	$d = 1.34$ (large)	$d = 1.63$ (large)	$d = 1.16$ (large)
Mean Δ (Log MAR) (% change wrt TD1.5)	0.06+/-0.06 (37.5%)	0.1+/- 0.07 (62.5%)	0.08+/-0.05 (50%)	0.06/- 0.05 (37.5%)
Statistical Sig delta	0.0582	0.0938	0.0815	0.058



Additional References



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- [2] *Aviation Visual Perception* (Ashgate Studies in Human Factors for Flight Operations), pp35
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- [9] Connolly DM. Oxygenation state and twilight vision at 2438 m. *Aviat Space Environ Med* 2011; 82: 2 – 8 .
- [10] Connolly DM, S Erle WP. Assisted night vision and oxygenation state: 'steady adapted gaze.' *Aviat Space Environ Med* 2014; 85:120 – 9.
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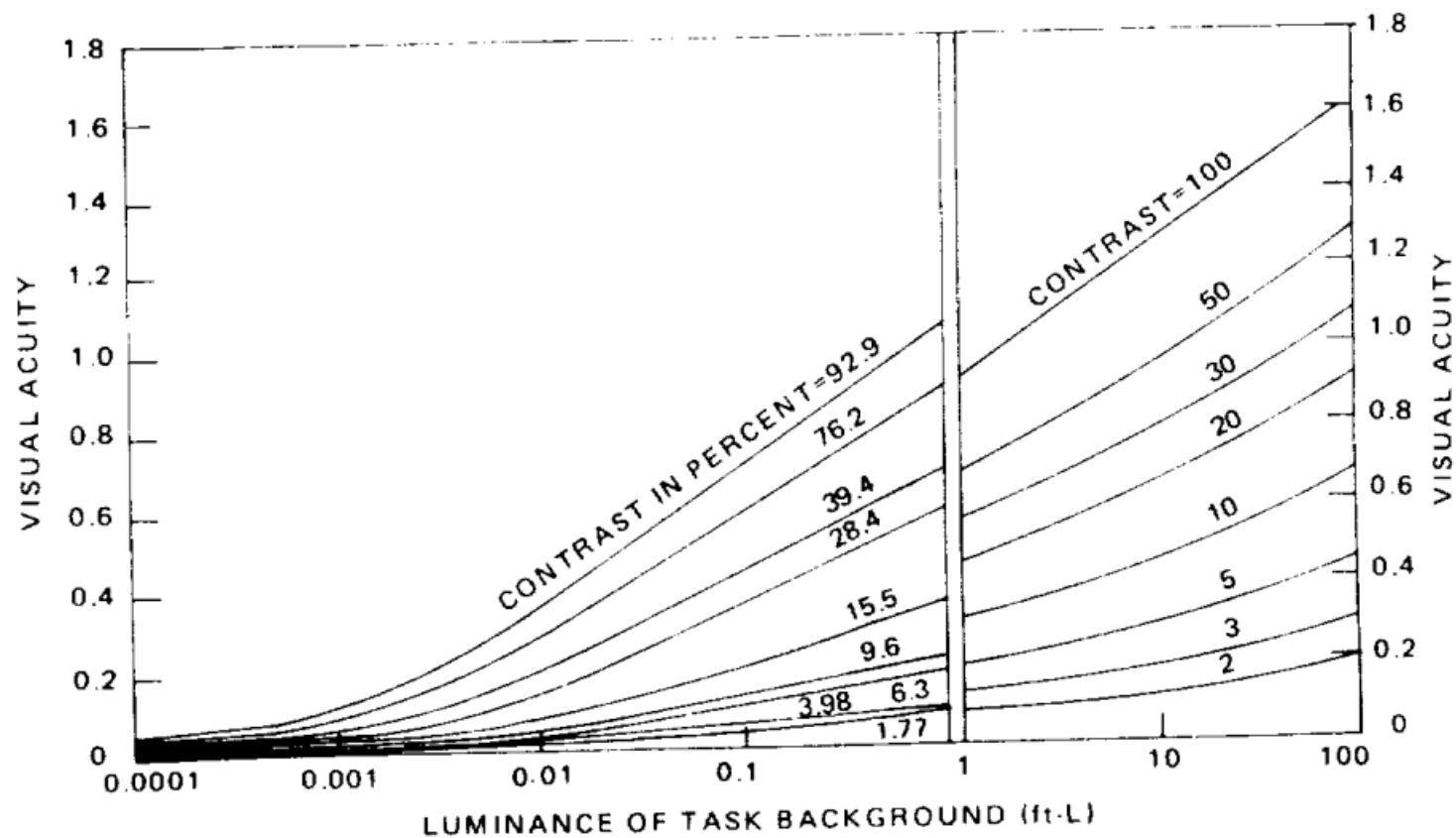


Figure 13-19. Visual acuity as a function of background luminance for a number of contrast levels, here expressed as percentages. (Data on left from Conner & Ganoung, 1935; on right from Cobb & Moss, 1948)



Contrast sensitivity

CS was assessed using Weber CS. At baseline mean Weber CS was 1.28 ± 0.16 (mean $\pm$ SD) logCS. Mean intraindividual logCS differences of Weber contrast were -0.16 ± 0.22 (CI 95% -0.26 to -0.07 ; mean logCS = 1.03 ± 0.14 , 0.01) on the day of ascent to 4559 m, -0.10 ± 0.20 (CI 95% -0.19 to -0.01 ; mean logCS = 1.09 ± 0.07 , $p=0.049$) on day 2 and -0.12 ± 0.19 (CI 95% -0.22 to -0.03 ; mean logCS = 1.07 ± 0.08 , $p=0.03$) on day 3 during high altitude exposure compared with baseline (figure 3).

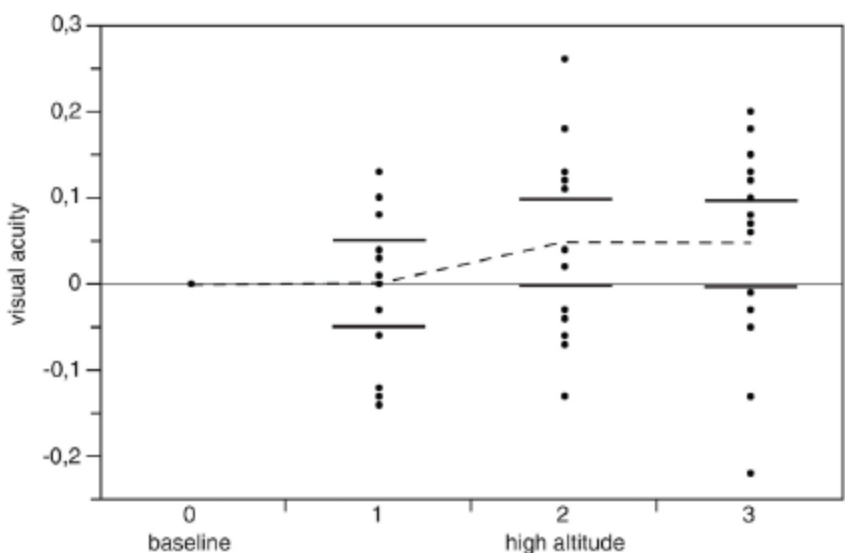


Figure 2 BCVA Intraindividual logMAR values of BCVA during high altitude exposure (days 1–3) compared with baseline (0). Horizontal bars mark the 95% CI. Visual acuity remained unchanged during high altitude exposure. BCVA, best-corrected visual acuity.

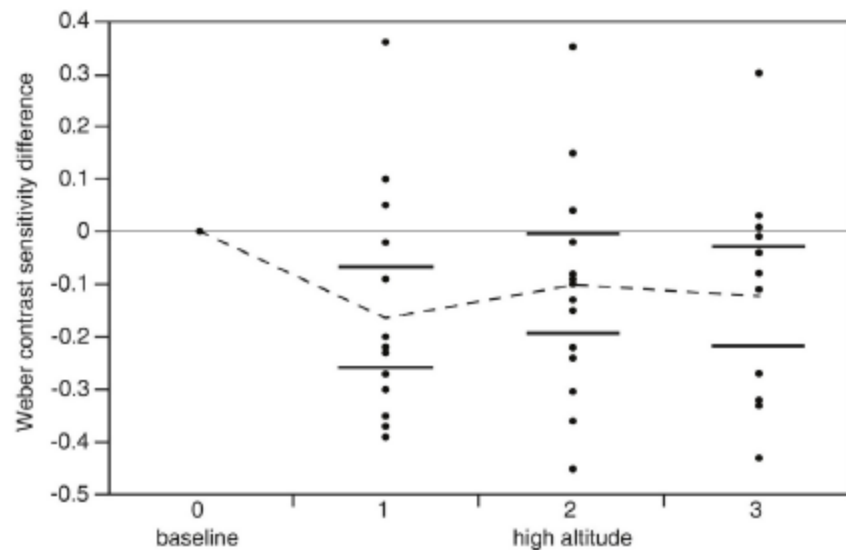


Figure 3 Contrast sensitivity. Weber CS illustrated as logCS was assessed during high altitude exposure (days 1–3) compared with baseline (0). There was a significant decrease in CS at high altitude. Horizontal bars mark the 95% CI. CS, contrast sensitivity.

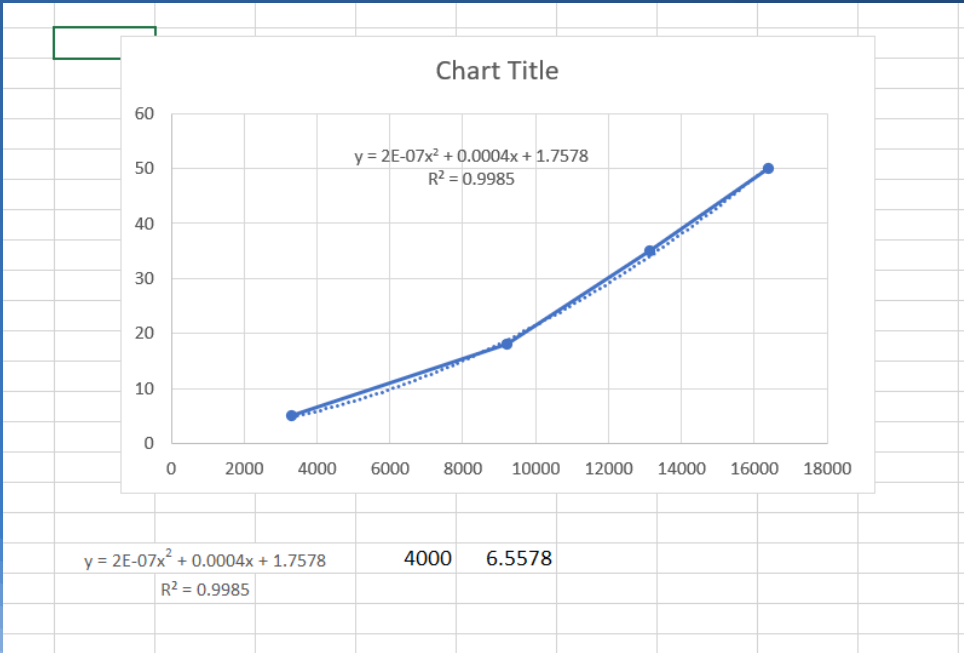
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[2] Aviation Visual Perception (Ashgate Studies in Human Factors for Flight Operations), pp35



Tredici and Ivan (2008) presented the following altitudes along with their corresponding reductions in visual capability (see Table 2.1). Basically, a reduction in oxygen can be equivalent to excessive fatigue or smoking, all resulting in reduced visual capability. Smoking is especially bad for a pilot prior to night flying because it increases carbon monoxide levels. According to Tredici and Ivan, a 5 percent saturation level of carbon monoxide is similar to flying at 3,000 m (9,840 ft) without oxygen, and smoking 3 cigarettes prior to a night flight increases carbon monoxide saturation levels to 4 percent, reducing night vision performance by 18 percent. This value is significant when considering the difficulty in visual perception at night even when fully prepared and physiologically healthy.

Table 2.1 Altitudes along with their corresponding reductions in visual capability

Altitude	Reduction in dark visual capabilities
1,100 m (~3,300 ft)	5%
2,800 m (~9,200 ft)	18%
4,000 m (~13,120 ft)	35%
5,000 m (~16,400 ft)	50%



Clinical Significance for Visual Performance



- Clinical significance for these three parameters
 - Power analysis by Millenia to confirm if we have enough power to see the clinical significance
 - Or do the Confidence interval – approach – see slides
- Proposed numbers for clinical significance: These are the three parameters we measured for photopic vision.
 - Visual acuity at 100% contrast: **+/- 0.1 (unit : LogMAR)** (note: visual degradation means increasing LogMAR)
 - Visual acuity at 50% contrast: **+/- 0.1 (unit : LogMAR)** (note: visual degradation means increasing LogMAR)
 - Contrast Sensitivity: **+/- 10% difference from baseline** (unit: logCS Weber) (note: visual degradation means decreasing logCSWeber)
 - Note: baseline = TD0 values at sea level; some first order unidentified results plotted below.
- Is there any “asymmetry” in the clinical significance level ? (e.g., +0.05/-0.1 for visual acuity)

[1] pp 358, [2] pp35:
I saw the following, but I couldn’t trace back the literature where these numbers came from, and am not sure what parameter is measured as visual capability in this table (calculated in %). Do you recall or know anything about this ?

Tredici and Ivan (2008) presented the following altitudes along with their corresponding reductions in visual capability (see Table 2.1). Basically, a reduction in oxygen can be equivalent to excessive fatigue or smoking, all resulting in reduced visual capability. Smoking is especially bad for a pilot prior to night flying because it increases carbon monoxide levels. According to Tredici and Ivan, a 5 percent saturation level of carbon monoxide is similar to flying at 3,000 m (9,840 ft) without oxygen, and smoking 3 cigarettes prior to a night flight increases carbon monoxide saturation levels to 4 percent, reducing night vision performance by 18 percent. This value is significant when considering the difficulty in visual perception at night even when fully prepared and physiologically healthy.

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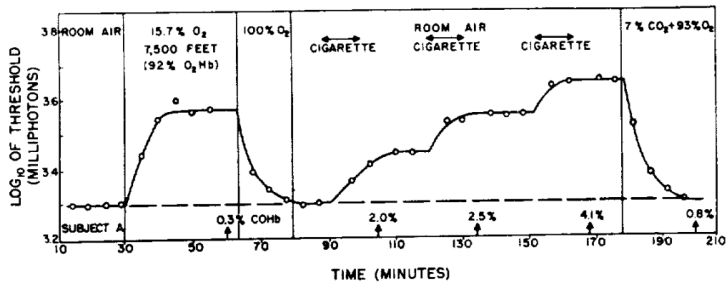


Figure 13-36. Effects of altitude, smoking, and oxygen inhalation on luminance sensitivity. (From *Human factors in air transport design* by R. A. McFarland. Copyright 1946 by The McGraw-Hill Book Company. Used by their permission)



Visual Acuity Unit Conversion Charts



20 ft	6 m	Decimal	logMAR
20/630	6/190	0.032	+1.5
20/500	6/150	0.04	+1.4
20/400	6/120	0.05	+1.3
20/320	6/95	0.06	+1.2
20/250	6/75	0.08	+1.1
20/200	6/60	0.1	+1.0
20/160	6/48	0.125	+0.9
20/125	6/38	0.16	+0.8
20/100	6/30	0.2	+0.7
20/80	6/24	0.25	+0.6
20/63	6/19	0.32	+0.5
20/50	6/15	0.4	+0.4
20/40	6/12	0.5	+0.3
20/32	6/9.5	0.63	+0.2
20/25	6/7.5	0.8	+0.1
20/20	6/6	1.0	0
20/16	6/4.8	1.25	-0.1
20/12.5	6/3.8	1.6	-0.2
20/10	6/3	2.0	-

LogMAR	VA _{dec}	Snellen (ft)	Snellen (m)	Category
-0.30	2.0	20/10	6/3.0	
-0.20	1.6	20/12.5	6/3.8	
-0.10	1.26	20/16	6/4.8	
0.00	1.0	20/20	6/6.0	
0.10	0.8	20/25	6/7.5	
0.20	0.63	20/30	6/9.5	
0.30	0.5	20/40	6/12	
0.40	0.4	20/50	6/15	(mild impairment ¹)
0.50	0.32	20/60	6/19	(moderate impairment ¹)
0.60	0.25	20/80	6/24	
0.70	0.2	20/100	6/30	
0.80	0.16	20/125	6/38	
0.90	0.13	20/160	6/48	
1.00	0.10	20/200	6/60	(severe impairment ¹)
1.10	0.08	20/250	6/75	
1.20	0.063	20/300	6/95	
1.30	0.050	20/400	6/120	

Luminance Impact on Vision

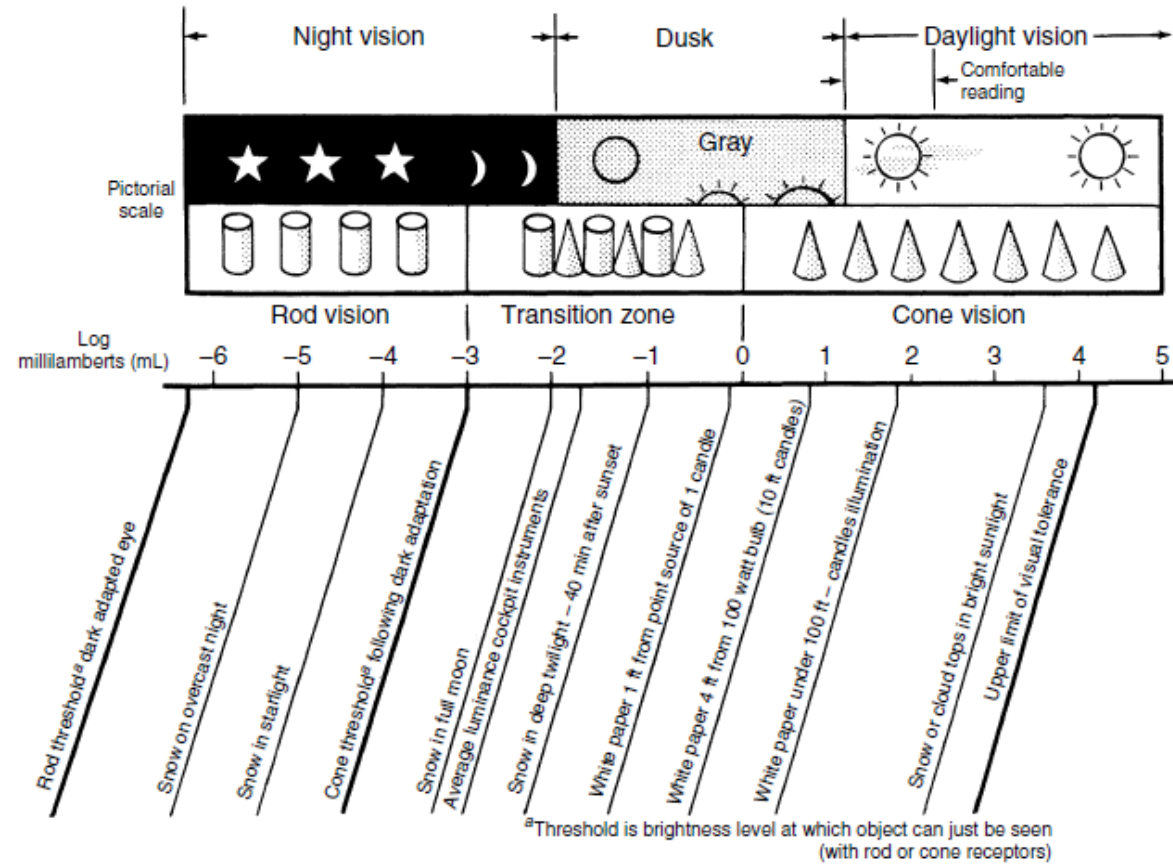


FIGURE 14-7 Luminance under varying conditions of illumination.