Optic Disc Edema after 30 Days of Strict Head-down Tilt Bed Rest

As of 2017, optic disc edema has been identified from funduscopy images in 10 of 68 astronauts (15%) flying long-duration missions to the International Space Station (ISS). Optic disc edema is one of the ocular findings that characterizes the spaceflight-associated neuro-ocular syndrome (SANS); however, it has not manifest during prior experiments using the spaceflight analog 6° head-down tilt bed rest (HDTBR). To more closely replicate the ISS environment, we studied 11 subjects (5 women) before and after 30 days of strict HDTBR in a mild hypercapnic environment (3.8 mmHg ambient partial pressure of carbon dioxide [PCO2]). Subjects remained in the strict head-down tilt position 24 hours per day and were instructed to not lift their head or raise onto an elbow during meals and use of a standard pillow was prohibited. After approval by the Institutional Review Boards at the National Aeronautics and Space Administration’s (NASA) Johnson Space Center and the Institute for Aerospace Medicine at the German Aerospace Center, optical coherence tomography (OCT) (Spectralis Flex Module OCT2, Heidelberg Engineering, Heidelberg, Germany) images (20°×20°; 25 lines, ART = 25, HR mode) were obtained in seated subjects before HDTBR and on the first day of recovery approximately 2 to 3 hours after assuming upright posture. The Early Treatment Diabetic Retinopathy Study analysis grid was manually centered over the optic disc and total retinal thickness (TRT) from each quadrant surrounding the central 1-mm disc was measured, as previously described.

Based on preliminary review of OCT images, undilated fundus images were obtained in 5 subjects suspected of ocular structural changes. For the first time, we report the development of optic disc edema using an Earth-based spaceflight analog. Four subjects were diagnosed with a Modified Frisén Scale grade1 of 1, and 1 subject was diagnosed with a grade of 2; the edema was observed bilaterally. Analysis of OCT images provided evidence of a significant increase in peripapillary TRT from pre- to post-HDTBR in all quadrants. The mean change (95% confidence interval) for each quadrant for all subjects was as follows: inferior, 39 (18–60) µm; superior, 53 (26–79) µm; nasal, 42 (14–70) µm; and temporal, 22 (11–33) µm. This increase in TRT is approximately 4 to 5 times greater than that observed after the 70-day HDTBR study when standard pillow use was permitted and a mild hypercapnic environment was not used (Fig 1).

This study design of strict HDTBR and a mild hypercapnic environment was chosen by NASA to most closely match conditions on the ISS to develop a model of SANS using an Earth-based analog. As a result, the study design was not intended to differentiate which factor(s) were responsible for the outcomes described here. We speculate that strict head-down tilt and the associated hydrostatic pressure gradient at the level of the eye contributed to the optic disc edema. Data from patients with Ommaya reservoirs demonstrate that placing the head on a pillow while supine consistently reduced intracranial pressure (ICP) from 14 to 10 mmHg.4 This finding suggests that previous HDTBR studies that allowed subjects use of a standard pillow during daily activities, and allowed them to lift the upper torso during meals, may have temporarily relieved the cephalad venous congestion and lowered ICP, thus mitigating the development of optic disc edema. Accordingly, because astronauts are unable to “lift their head or stand up” while in weightlessness, the impacts of the sustained headward fluid shift may underlie the development of optic disc edema during spaceflight. When subjects in this study maintained a strict head-down tilt position without use of a standard pillow and were not allowed to lift their head and upper body, to eat during meals, they too demonstrated optic disc edema. Future studies should be conducted to differentiate the effects of the strict head-down tilt from the mild increase in ambient PCO2.

The direct role of a mild increase in ambient PCO2 on the development of optic disc edema on ISS is unexplored. Arterial blood gas measurements have not been conducted during spaceflight. However, end-tidal PCO2 (PETCO2) measurements acquired in astronauts during spaceflight, when the ambient PCO2 was similar to that used in this study (3.8 mmHg), were similar to PETCO2 measured in the supine position on Earth before and after spaceflight when breathing room air.5 Similarly, in the current study PETCO2 measured in the 6° head-down tilt position before and on the final day of bed rest (mean ± standard deviation) was 42.1 ± 3.3 mmHg and 41.7 ± 3.4 mmHg, respectively. These data indicate that our spaceflight analog did not alter arterial PCO2 levels, which would likely be necessary for the hypercapnic environment to contribute to the development of optic disc edema. Comparison of arterialized and/or PETCO2 values throughout HDTBR in control subjects not breathing elevated ambient PCO2 is necessary to confirm these observations.

We observed Frisén Grade edema in ~45% of our subjects after 30 days of HDTBR, which is higher than the 15% reported in astronauts after ISS missions.1 Both during weightlessness and after 24 hours of HDTBR, jugular vein area increases without a corresponding increase in ICP,3 suggesting a potential direct effect on venous drainage of the eye. Conversely, the hydrostatic pressure column during 24 hours of HDTBR leads to a sustained ICP similar to supine posture, but weightlessness causes ICP to decrease in the supine posture.4 Whether these factors contributed to differences in edema incidence between HDTBR and weightlessness, or to the lack of other SANS symptoms observed here, requires further investigation.

We document the development of optic disc edema and quantified peripapillary TRT after 30 days of strict HDTBR in a mildly hypercapnic environment, suggesting that this novel spaceflight analog may lead to retinal structure changes similar to SANS. This model should be considered for testing possible countermeasures on Earth that this may prevent or reverse these findings. Whether longer-duration HDTBR studies will lead to the development of additional ocular changes associated with SANS, or to a greater incidence or magnitude of change, is unknown. This model of experimentally induced optic disc edema in human subjects
provides new opportunities to investigate the pathophysiology and potential treatment options for optic disc edema, both for NASA and for patients on Earth.

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Abbreviations and Acronyms:
- **HDTBR** = 6° head-down tilt bed rest; **ICP** = intracranial pressure; **ISS** = International Space Station; **NASA** = National Aeronautics and Space Administration; **OCT** = optical coherence tomography; **PCO₂** = partial pressure of carbon dioxide; **PETCO₂** = end-tidal partial pressure of carbon dioxide; **SANS** = spaceflight-associated neuro-ocular syndrome; **TRT** = total retinal thickness.

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**References**


**Figure 1.** Optic disc edema and increased total retinal thickness. Funduscopic images of the retina and optic disc from both eyes from A, the single subject diagnosed with Frisén grade 2 and B, one of the other subjects who received a diagnosis of Frisén grade 1 in both eyes (and a choroidal nevus in the right eye). A, The Frisén grade 2 was classified based on the grayish circumferential halo observed completely around the optic disc, while (B) the Frisén grade 1 was classified based on the grayish C-shaped halo with a temporal gap. C, Change in global total retinal thickness (TRT) from pre- to post-6° head-down tilt bed rest (HDTBR). Means and 95% confidence intervals are plotted for each peripapillary quadrant from the current and previous studies. Data from the current study in which subjects maintained strict head-down tilt and were in a mild hypercapnic environment are plotted at 30 days of HDTBR (filled symbols). Data plotted at 14 days and 70 days of HDTBR (open symbols) were from subjects that did not maintain strict head-down tilt and were in a normocapnic environment. Note: Data from each study were collected after exactly 14, 30, and 70 days, respectively, and the symbols have been shifted to prevent overlap and improve visualization. Data from 14 and 70 days of HDTBR are adapted from Taibbi et al.³