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Ocular rigidity and choroidal thickness changes in response to microgravity: A case study

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ABSTRACT

Purpose: To evaluate ocular rigidity and choroidal thickness changes in response to microgravity and the Valsalva maneuver in a private astronaut.
Methods: Ophthalmological examination and Optical Coherence Tomography were performed before, during, and after space flight. Choroidal thickness was measured at all time points at rest and during the Valsalva maneuver. Ocular rigidity was obtained before and after flight using a non-invasive method enhanced with deep learning-based choroid segmentation.
Results: Ocular rigidity decreased after space flight compared to baseline. There was an increase in average choroidal thickness during the Valsalva maneuver compared to the resting condition before, during, and after space flight, and such increase was greater when the Valsalva maneuver was performed during space flight.
Conclusions and importance: The data indicates biomechanical changes to ocular tissues because of space flight and greater choroidal thickness increase. The findings could lead to a better understanding of space flight-associated neuro-ocular syndrome and may have repercussions for short duration missions in a nascent industry.

1. Introduction

Space flight-associated neuro-ocular syndrome (SANS) consists of a group of ophthalmological symptoms and signs which can manifest following microgravity exposure. It has been reported, based on National Aeronautics and Space Administration (NASA) data, that up to 23 % of all astronauts present symptoms of SANS, rising to 48 % of astronauts who participated in long-term missions (>30 days).[1]

The physio pathological changes in microgravity vary among different subjects, with the most prevalent findings being optic disc edema, globe flattening, choroidal and retinal folds, hyperopic refractive error shifts, and focal areas of retinal ischemia.[1,2] Choroidal alterations in Spaceflight-Associated Neuro-ocular Syndrome (SANS) have been demonstrated, but there remains a need to better understand their origin, especially as they have been gaining more traction in terrestrial diseases and have been described in SANS as a growing risk factor.[3] While the tools to explore the choroid are still in development, choroidal thickness has served as a biomarker in ophthalmology since the optical coherence technology (OCT) evolved to provide sufficient quality for detecting the choroid-sclera interface.[3] Consequently, it could serve as an objective means of observing vascular changes in SANS.

In addition to the findings that can be obtained from static images, such as choroidal thickness, the biomechanical properties of ophthalmic tissues have been identified as potential factors of interest in ophthalmic diseases.[4] Specifically, ocular rigidity has emerged as a novel risk factor that provides information on both scleral compliance and volumetric changes in the choroid.[5,6] Therefore, the application of this tool could be of great value in the study of Spaceflight-Associated Neuro-ocular Syndrome (SANS). Given the increasing prevalence of short-duration exposure to microgravity as a target of the new private industry and the effects on ocular health are still virtually unexplored.

2. Material and methods

We primarily sought to evaluate choroid thickness (CT) and ocular rigidity (OR)[5] changes following short duration space flight. Secondly,

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we aimed to study whether Valsalva maneuvers, which are almost unavoidable when performing strength exercise to failure or performing exercise requiring relatively high force output[7–9] could trigger substantial choroidal changes in space.[7,10] Following the integration of the Advanced Resistance Exercise Device at the International Space Station (ISS), into astronauts' training regimen in 2008, some hypothesized that SANS could be at least in part associated with strenuous exercise.[11]

We obtained ophthalmological data including Optical Coherence Tomography (OCT) images from a 53-year-old male private astronaut who sojourned 15 days aboard the ISS. A complete ophthalmological examination was performed before (128 days) and after flight (10 days).

Static images were captured using a Spectralis device with the OCT 1 software before and after flight and a OCT2 software in orbit. The images are compatible, and the acquisition modality was the same in all circumstances. Vertical macular cubes, size 20°x20° centered on the fovea were acquired to assess retinal anatomy and choroidal thickness before, during and after flight. For the optic nerve head evaluation, a vertical block, same size centered on the region was obtained before and after the mission.

OCT videos were obtained using a Spectralis imaging device equipped with the OCT2 Module (Heidelberg Engineering, Heidelberg, Germany). OR was measured using a non-invasive method[5] newly enhanced with deep learning-based choroid segmentation. Macular B-scans were acquired before (57 days), during (6 days after docking), and after space flight, both at rest and during Valsalva maneuver.

2.1. Participant consent

This study was approved by the institutional review board of the Maisonneuve-Rosemont Hospital and performed in accordance with the 1964 Declaration of Helsinki and its amendment. The participant provided both verbal and written consent for their medical information and images to be included and submitted as part of a scientific report.

3. Results

Slit lamp examination showed no relevant findings. Visual acuity was 1.0 logMAR OU without correction, before and after space flight. There were no changes in axial length or pathological findings in the macular and optic nerve head OCT.

Intraocular pressure (IOP) before and after the flight was 17 mmHg and 14.9 mmHg for the right eye (OD), and 14 mmHg and 14.8 mmHg for the left eye (OS), respectively (Fig. 1). There was a decrease in ocular pulse amplitude, the change of IOP during systole, measured with a Pascal tonometer, of 54.8 % OD and 33.3 % OS after flight compared to baseline measurements (Fig. 1).

We observed an increase in average resting CT of 13 % OD and 11 % OS after 6 days on the ISS compared to pre-flight. A decrease in average resting CT from pre-flight values of 9.78 % OD and 3.57 % OD was observed 10 days post-flight.

We systematically observed an increase in CT during Valsalva before, during and after flight; for the OD the increases were of 7.1 μm (3.3 %), 7.8 μm (3.2 %) and 9.8 μm (5 %), respectively, and for the OS 3.5 μm (1.8 %), 5.2 μm (2.4 %) and 1.7 μm (0.9 %). Choroidal thickness maps corresponding to rest and Valsalva were generated for all time points, along with CT difference surface plots (Fig. 2). An analysis of variance was performed to assess the difference between the 3 conditions in both eyes in Valsalva and resting state showing a statistically significant difference (0.02 and 0.05 respectively).

Additionally, ETDRS region analysis was performed to investigate localized CT differences within the scan area, suggesting accentuated CT increase in the central and superior regions OU (zones 2 and 6) in microgravity compared to postflight conditions (Fig. 2).

Finally, OR was measured in both eyes before (128 days) and 10 days after the flight. In the OD, the OR coefficients were 17 mL^{-1} and 11 mL^{-1} before and after the flight, respectively, and for the OS the coefficients were 18 mL^{-1} and 12 mL^{-1}. These represent decreases in OR of 33 % for both eyes (Fig. 1). A mixed effect model for the data acquired from both eyes showed a significant difference for the change in OR after space flight.

4. Discussion

SANS is a complex condition that includes changes in refraction, macular and optic nerve anatomy.[1] The pathophysiology of SANS has been challenging to establish due to the limited number of subjects studied. However, the main hypothesis revolves around elevated intracranial pressure and compartmentalization of cerebrospinal fluid (CSF)

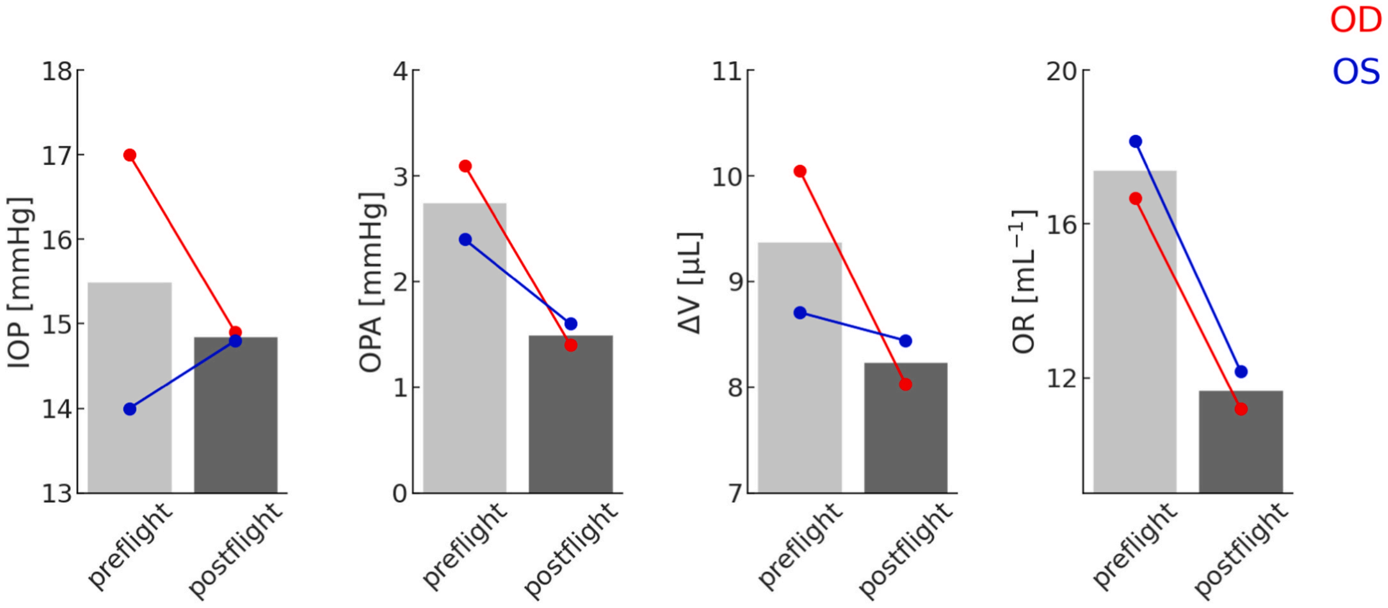

Fig. 1. Ocular rigidity and associated measurements for both eyes before and after space flight. Intraocular pressure (IOP), ocular pulse amplitude (OPA), pulsatile change in choroid volume (ΔV) and ocular rigidity (OR) clinical parameters for both eyes (OD and OS) before and after space flight are shown. Decreased OR was observed after space flight compared to the same measurement before space flight.

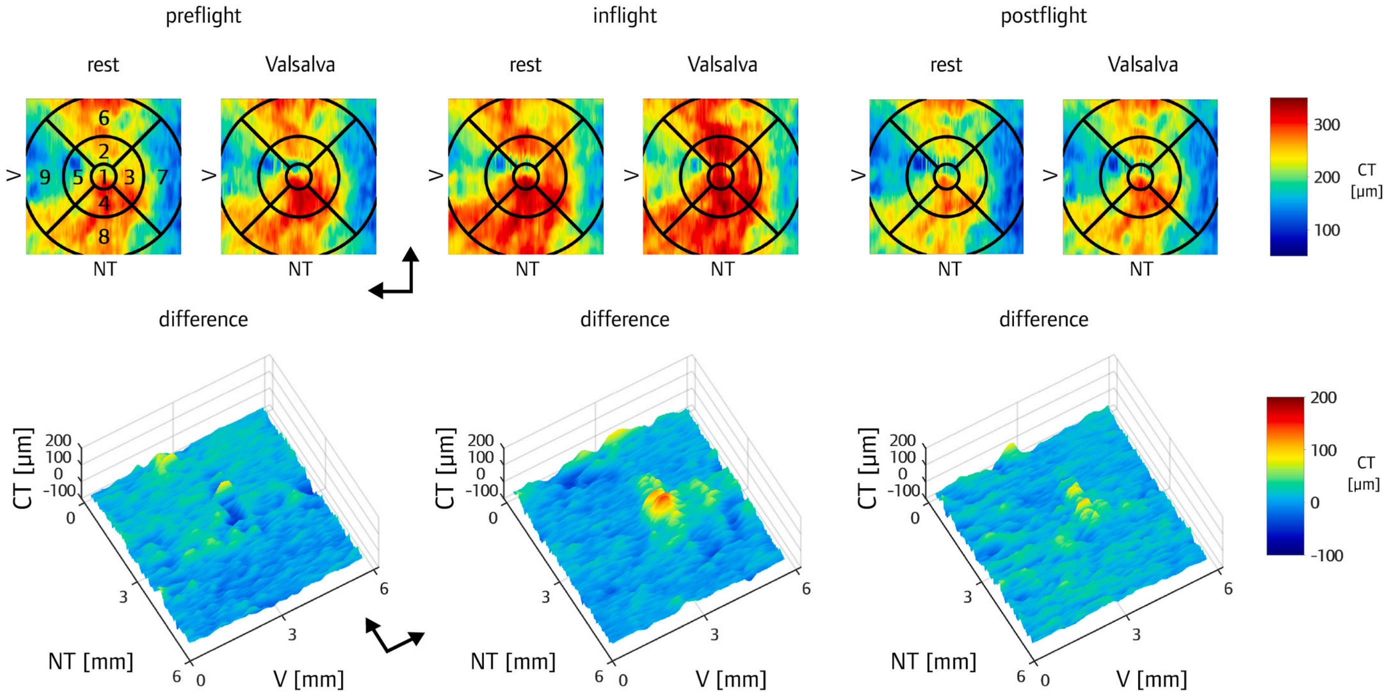

Fig. 2. Choroid thickness maps and thickness difference surface plots for the right eye at all time points. Choroid thickness (CT) maps with dimensions 6 mm × 6 mm for the right eye at rest and during the Valsalva maneuver, before, during and after space flight are displayed (top). Vertical (V) axis and naso-temporal (NT) axis directions are shown. An increase in average CT was observed during the Valsalva Maneuver for all three time points. CT difference (ΔCT) surface plots for each time point are shown. The greatest localized CT increases are observed in microgravity in the central (1) and superior (2 and 6) regions.

to the globe.[1,12] These factors are not mutually exclusive and differences in baseline biomechanical properties of the eyes could act as risk factors for their development.

Our data suggests that microgravity can accentuate the increase in CT during Valsalva particularly in some zones of the macular region. While there exists conflicting reports, incremental CT increase during Valsalva has been described.[13–15] It is believed that chronic cephalad fluid shift occurs during space flight causing blood congestion and choroidal enlargement which may in turn, alter biomechanical forces in the ocular tissues.[15] The Valsalva maneuver has been suggested as a potential tool to assess acute choroidal changes[16,17] but its effects in microgravity conditions have not been described.

Our findings are compatible with the physiological effects on the choroid that would be expected from Valsalva-induced thoracic pressure increase and altered vascular load in microgravity conditions. Given the accentuated increase in CT during Valsalva in microgravity and the association of Valsalva with resistive exercise, the routine use of a muscle strength maintenance device on the ISS may be a relevant risk factor for ocular changes during and after space flight.

Additionally, ocular rigidity has previously been described as a biomechanical biomarker with clinical relevance.[5,18] We detected a decrease in ocular rigidity suggesting a change in the mechanical properties of the sclera during and after being exposed to microgravity conditions. A change in scleral biomechanics, especially if it persisted a month or more after landing, could help understand SANS physiopathology and potentially lead to its prevention. The measurements obtained as part of the present case study should be included in future studies aiming to investigate SANS pathology in a larger population. By doing so, we may identify individuals at higher risk of developing SANS and implement preventive measures. Further research is needed to clarify the relationship between ocular biomechanics and SANS and to develop effective countermeasures to prevent or mitigate the condition.

In addition to the obvious limitation regarding the sample size, it is important to consider biological factors that impact vascular regulation and cardiac output in microgravity conditions. Despite NASA's strict regimen of electrolyte and fluid intake (2.5 L/day of water for direct consumption and food rehydration),[19,20] there is still a risk of mild dehydration even during short space flights. Another factor that could affect choroidal volume is the volumetric changes in the circadian cycle. However, these two factors decrease choroidal thickness,[21,22] potentially leading to an underestimation of our results. In physiological conditions where these factors are absent, a larger choroidal increase would likely be observed.

5. Conclusion

We analyzed Valsalva's effects on the choroid during short-time spaceflight. Of additional relevance to SANS pathophysiology, we found a reduction in OR after exposure to microgravity. Our findings need to be supported with more data to further ascertain and better understand microgravity exposure-associated biomechanical changes. Despite limitations, they represent the first step towards understanding the role of ocular biomechanics in SANS.

Author's contribution

MMS: Conceptualization, Methodology, Writing- Original draft preparation **CBN.:** Software, Writing. **RM**: Software. **MRL***:* Conceptualization Supervision, Writing and editing.**:** **SC**: Conceptualization Supervision, Writing and editing.

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The funding sources had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Additional contributions

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This study was approved by the institutional review board of the Maisonneuve-Rosemont Hospital and performed in accordance with the 1964 Declaration of Helsinki and its amendment.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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