

ANALYSES OF MAGNETIC RESONANCE IMAGING OF CEREBROSPINAL FLUID DYNAMICS PRE AND POST SHORT AND LONG-DURATION SPACE FLIGHTS

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Background

Long-Term Goal: Determine the role of the cerebrospinal fluid (CSF) in Visual Impairment and Intracranial Pressure (VIIP) Syndrome.

Cephalad fluid shift is currently considered a primary factor in VIIP. The term fluid shifts refers to the redistribution of blood volume within the cardiovascular system, or translocation of fluids from the lower body to the thorax and cephalic regions due to elimination of the hydrostatic blood pressure gradients. **Figure 1a** from Hargens et al (1) summarizes the concept of fluid shift in the absence of hydrostatic pressure gradients. The fluid components being considered are the blood volume, the plasma and interstitial fluids. Fluid shifts' impacts on the cardiovascular functions resulting from decreased plasma and stroke volumes are well documented. In contrast, a mechanism by which fluid shifts cause VIIP remains elusive.

The role of microgravity-induced redistribution of CSF within the cranio-spinal system as a potential factor in VIIP has not yet been carefully investigated. The cranio-spinal CSF, shown in **Figure 1b**, extends over a large portion of our body, and therefore, is strongly influenced by the hydrostatic pressure gradient and its absence in space. Furthermore, cranial and spinal canal CSF plays an important role in idiopathic intracranial hypertension (IIH) (2,3), a terrestrial condition that shares several similarities with VIIP, especially those related to the structural ocular changes seen in VIIP (e.g., globe flattening, optic disc edema, optic nerve sheath distension and protrusion). In fact, the CSF between the cranium and the orbits is likely the mediator for the structural ocular changes in VIIP, as shown in **Figure 2**.

The Current Study:

This limited directed retrospective study focuses on quantitative analysis of specialized magnetic resonance imaging (MRI) scans of NASA crewmembers performed before and after the completion of their spaceflights. The MRI scans were obtained between October 2010 and early 2014. At present, seventeen subjects have given consent for inclusion in the study; 9 of whom flew short-duration missions on the space shuttle, and 8 who flew long-duration missions on the International Space Station (ISS). Because VIIP is associated with long exposure to microgravity, comparing the magnitude of changes occurring after short and long duration spaceflights may provide hints related to etiology of VIIP.

The MRI study protocol included dynamic velocity-encoded imaging of the pulsatile blood and CSF flow to and from the cranium during the cardiac cycle (**Figure 3**) from which important cerebral hemodynamics and craniospinal hydrodynamics measures can be calculated (3,4). The study aims to compare pre-to-postflight changes between the short and long-duration spaceflight cohorts. Second, the study attempts to identify association between the magnitude of pre-to-postflight change in specific quantitative MRI measures and the presence and severity of signs and symptoms indicative of the VIIP syndrome. The main quantitative cerebral hemodynamics and craniospinal hydrodynamics measures include 1) total cerebral blood flow, 2) venous outflow, 3) craniospinal CSF flow and stroke volume, 4) craniospinal compliance distribution, and 5) MR-derived intracranial pressure (MRICP).

Measurements of blood flow are an integral part of investigations of the CSF flow dynamics because the cranio-spinal CSF flow is driven by the difference between the arterial inflow and venous outflow to and from the brain (5).

Fig. 3. The net transcranial blood flow is the driving force for the craniospinal CSF pulsatile flow (Alperin et al 1996).

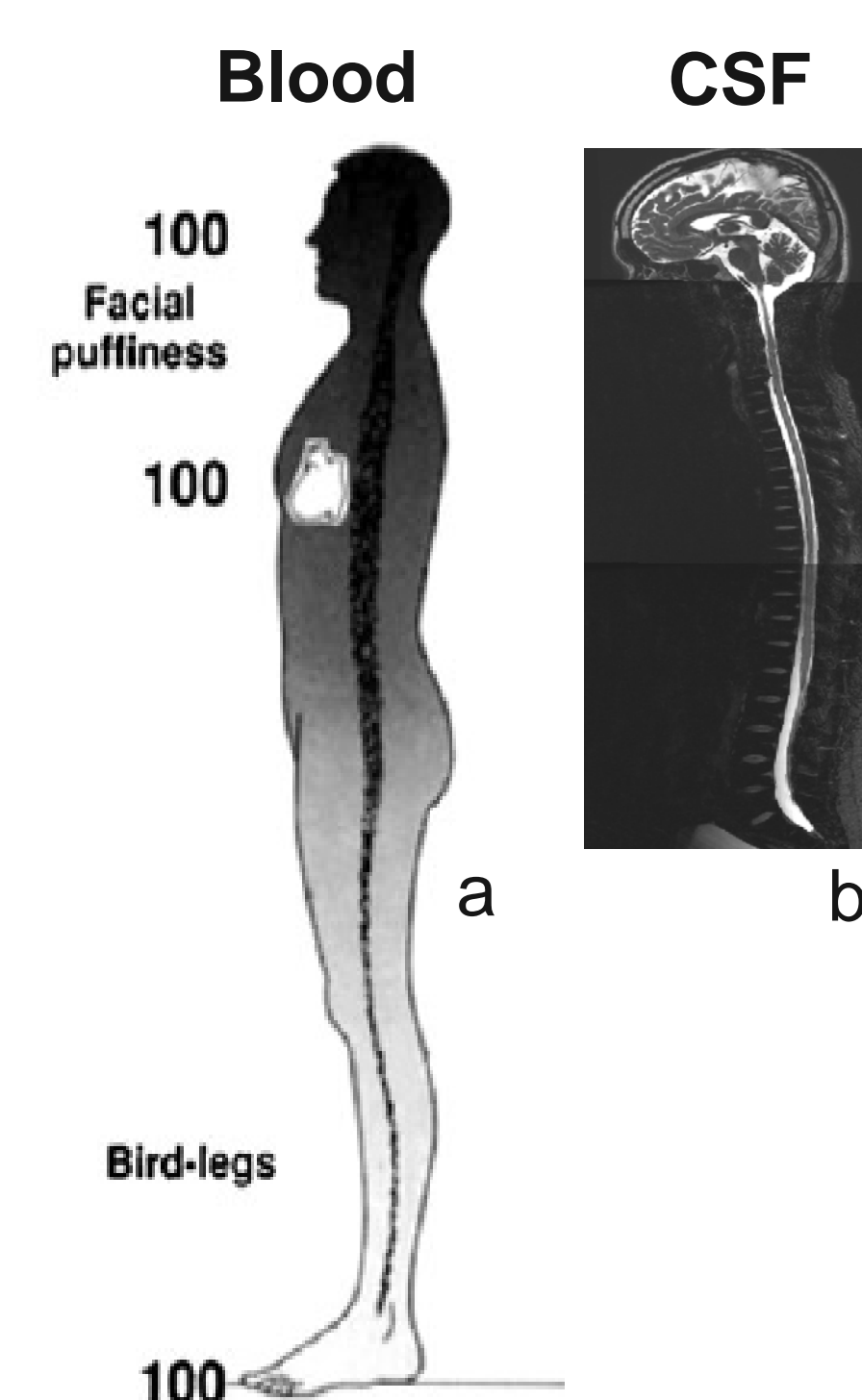
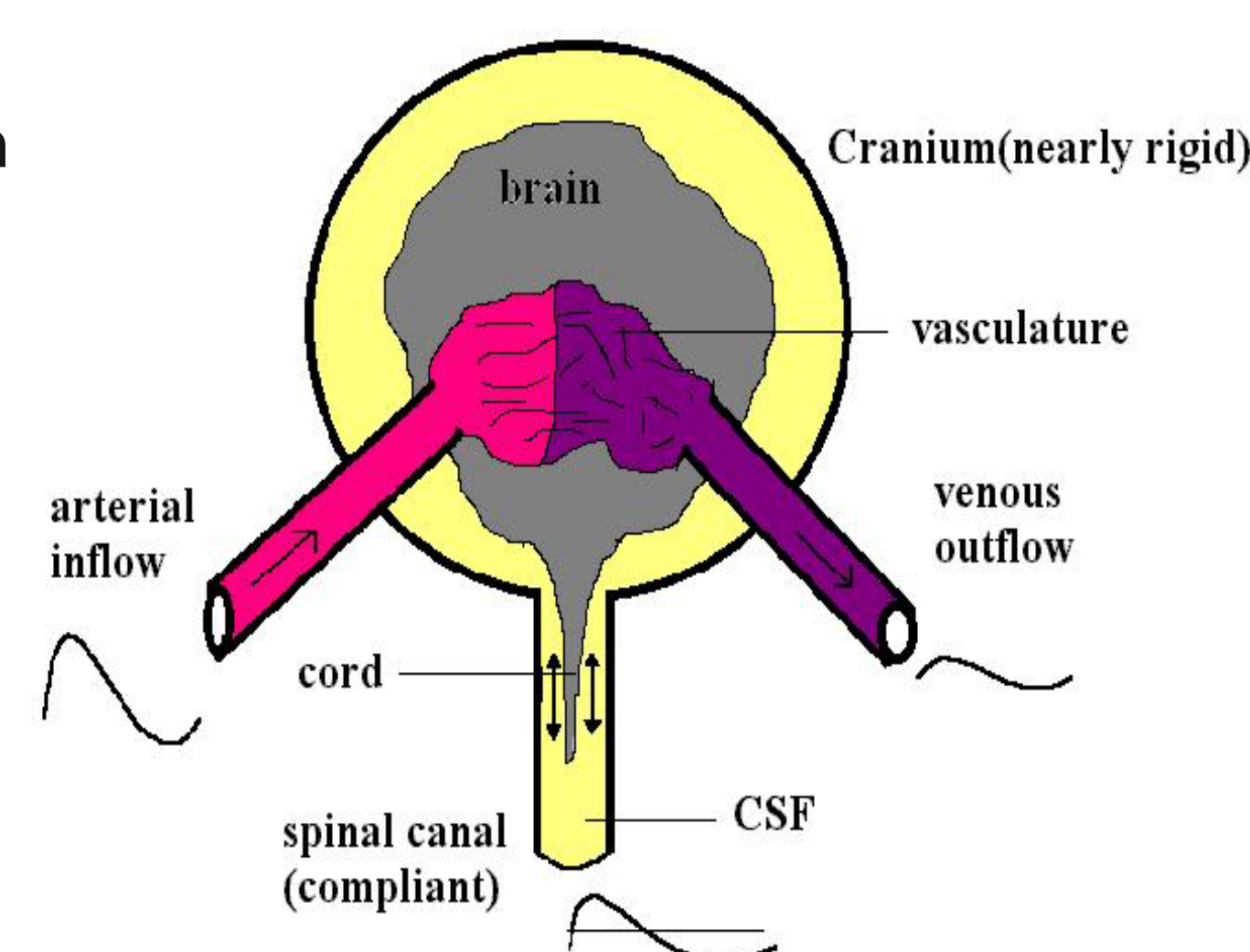
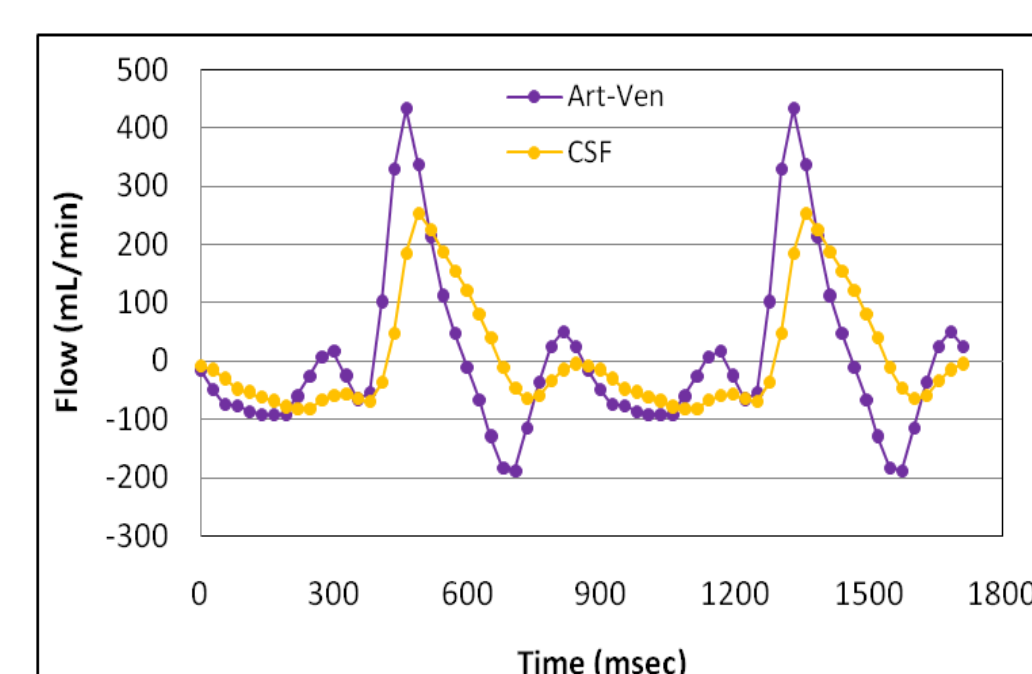


Fig. 1. a) Fluid shift in microgravity. b) The cranio-spinal CSF volume (white) has not yet been evaluated in VIIP.

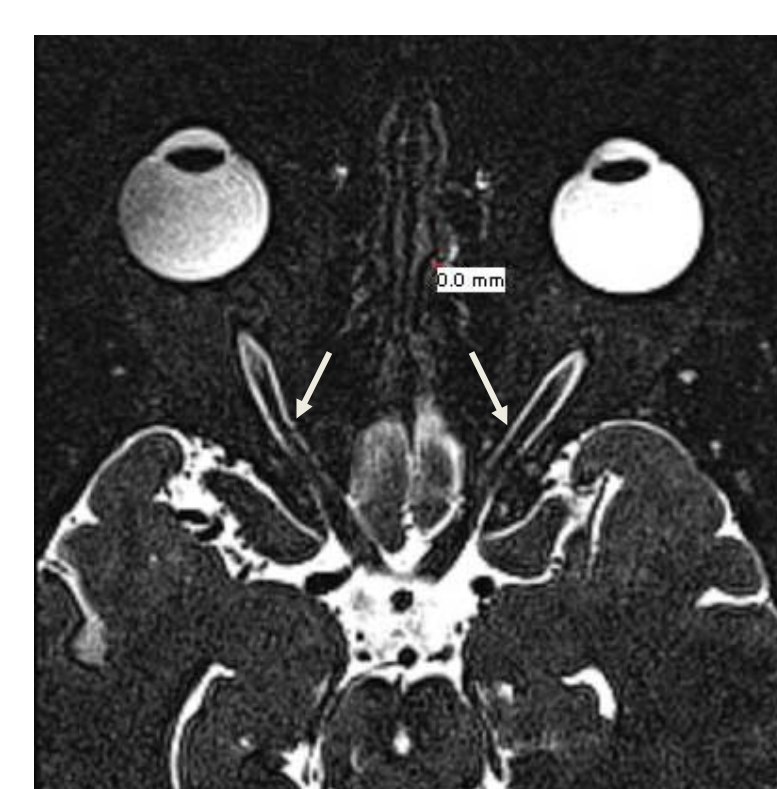


Fig. 2. MR image of the CSF pathways between the cranium and the orbits.

Material and Methods

Preliminary results are based on analyses of data from 17 crewmembers. The initial analysis compares pre to postflight changes in total cerebral blood flow (CBF) and cranio-spinal CSF flow volume. Total CBF is obtained by summation of the mean flow rates through the 4 blood vessels supplying the brain (right and left internal carotid and vertebral arteries). Volumetric flow rates were obtained using an automated lumen segmentation technique shown to have 3-4-fold improved reproducibility and accuracy over manual lumen segmentation (6). Two cohorts, 5 short-duration and 8 long-duration crewmembers, who were scanned within 3 to 8 days post landing were included (4 short-duration crewmembers with MRI scans occurring beyond 10 days post flight were excluded). The VIIP Clinical Practice Guideline (CPG) classification is being used initially as a measure for VIIP severity. The CPG classification is shown in the table below:

Class	Criteria
Class 1	<ul style="list-style-type: none"> ≥ .50 diopter cycloplegic refractive change and/or cotton wool spot No evidence of papilledema, nerve sheath distention, choroidal folds, globe flattening, scotoma compared to baseline. CSF opening pressure (if measured) ≤ 25 cmH2O
Class 2	<ul style="list-style-type: none"> ≥ .50 diopter cycloplegic refractive changes or cotton wool spot Choroidal folds and/or optic nerve sheath distension and/or globe flattening and/or scotoma No evidence of papilledema CSF opening pressure ≤ 25 cm H2O (if measured)
Class 3	<ul style="list-style-type: none"> ≥ .50 diopter cycloplegic refractive changes and/or cotton wool spot Optic nerve sheath distention, and/or globe flattening and/or choroidal folds and/or scotoma Papilledema Grade 0-2. CSF opening pressure ≤ 25 cm H2O
Class 4	<ul style="list-style-type: none"> ≥ .50 diopter cycloplegic refractive changes and/or cotton wool spot Optic nerve sheath distention, and/or globe flattening and/or choroidal folds and/or scotoma Papilledema Grade 2 or above. Presenting symptoms of new headache, pulsatile tinnitus and/or transient visual obscurations CSF opening pressure >25 cm H2O

Results

Median CPG scores of the short and long-duration cohorts were similar, 2. Mean preflight total CBF for the short and long-duration cohorts were similar, 863±144 and 747±119 mL/min, respectively. Percentage CBF changes for all short duration crewmembers were 11% or lower, within the range of normal physiological fluctuations in healthy individuals. In contrast, in 4 of the 8 long-duration crewmembers, the change in CBF exceeded the range of normal physiological fluctuation. In 3 of the 4 subjects an increase in CBF was measured. Large pre to postflight changes in the craniospinal CSF flow volume were found in 6 of the 8 long-duration crewmembers. Box-Whisker plots of the CPG and the percent CBF and CSF flow changes for the two cohorts are shown in **Figure 4**. Examples of CSF flow waveforms for a short and two long-duration (CPG 0 and 3) are shown in **Figure 5**.

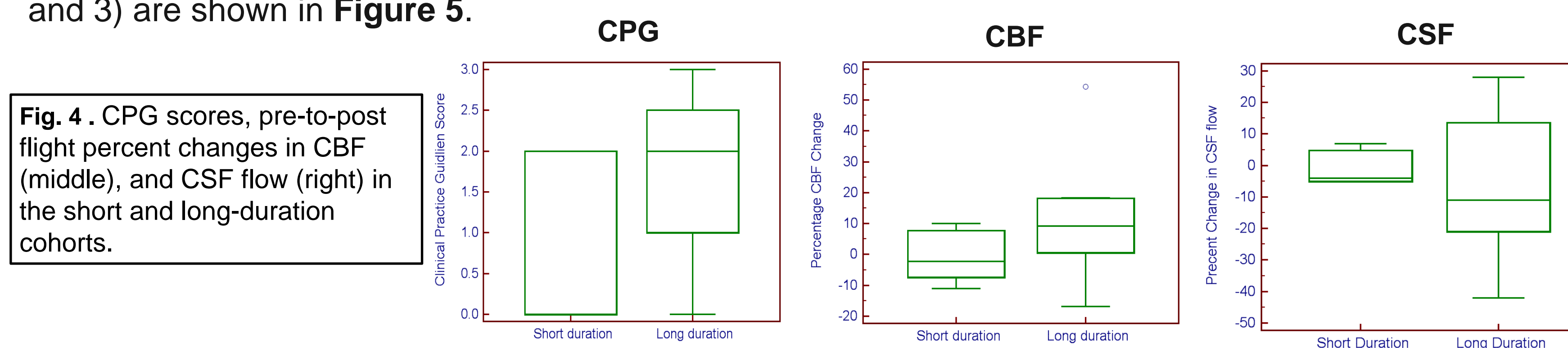


Fig. 4. CPG scores, pre-to-post flight percent changes in CBF (middle), and CSF flow (right) in the short and long-duration cohorts.

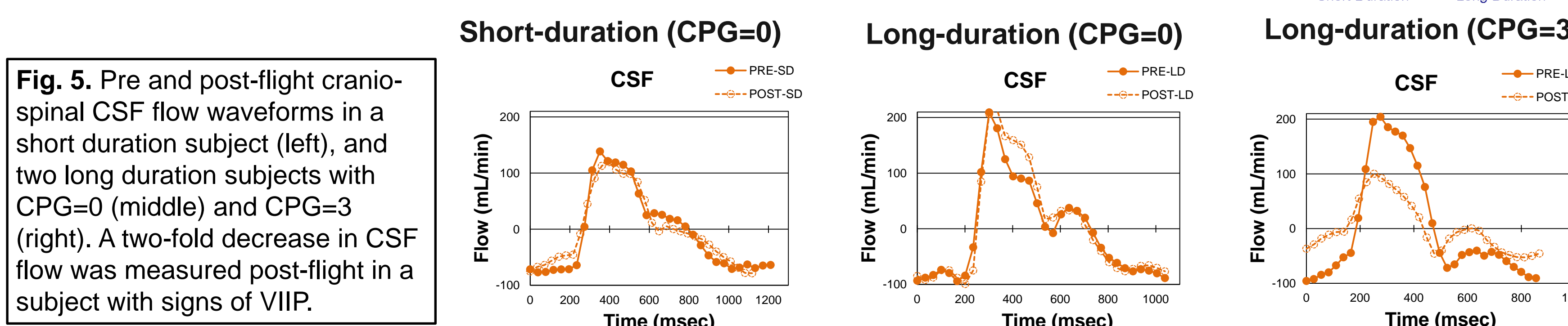


Fig. 5. Pre and post-flight cranio-spinal CSF flow waveforms in a short duration subject (left), and two long duration subjects with CPG=0 (middle) and CPG=3 (right). A two-fold decrease in CSF flow was measured post-flight in a subject with signs of VIIP.

Conclusion

Changes in CBF and CSF flow dynamics larger than normal physiological fluctuations were observed in the long-duration crewmembers. Changes in CSF flow were more pronounced than changes in CBF. Decreased CSF flow dynamics were observed in a subject with VIIP signs. Study limitations include a slightly longer landing-to-MRI scan period for the short-duration cohort and limited sensitivity of the subjective discrete ordinal CPG scale. This limitation can be overcome by using imaging based parametric measures of VIIP severity such as globe deformation measures (7).

References and Acknowledgements

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