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AN *IN SILICO-IN VIVO* FRAMEWORK FOR THE ACUTE OCULAR AND CARDIOVASCULAR RESPONSE TO 6° HEAD-DOWN TILT

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Introduction

Ensuring the healthiness of astronauts undergoing long-term missions in space is of primary importance for the aerospace community. Spaceflight associated neuro-ocular syndrome (SANS) has been widely acknowledged to cause severe ocular disorders in astronauts returning from long permanence in weightlessness [1].

In this context, head-down tilt (HDT) has gained large popularity to resemble the cardiovascular response to microgravity, as well as to study SANS [2].

We propose a novel multiscale numerical framework to simulate the acute response to 6° HDBR – with *in vivo* validation – to help shed light on SANS onset.

Methods

We developed a new cardiovascular model integrating our previously validated *in silico* framework [3] with a lumped model of the eye [4] and of the cerebrovascular circulation [5]. The global model presents a 1D description of the arterial tree combined with 0D analogues of the remaining vasculature, accounting for short-term homeostatic control and for the action of gravity during posture changes. Using this model, we simulated a tilt maneuver between 80° head-up tilt (HUT) and 6° HDT.

In vivo measures were taken at the Bioastronautics and Human Performance (BHP) Laboratory at Texas A&M University (TX, USA). Six healthy male subjects were positioned upright (80°) on an inversion table, tilted down to -6° HDT for approximately 10 minutes and eventually tilted back upright to 80°. Subjects' arterial pressure, heart rate, cardiac output, stroke volume, and intraocular pressure measures were collected at each position. Seated baseline measures of the same parameters were also acquired.

Results

The model results in response to acute 6° HDT – and tilt back to 80° – are shown in Figure 1. The corresponding *in vivo* mean and standard deviation ($\mu \pm \sigma$) of subjects' parameters are also depicted in Figure 1.

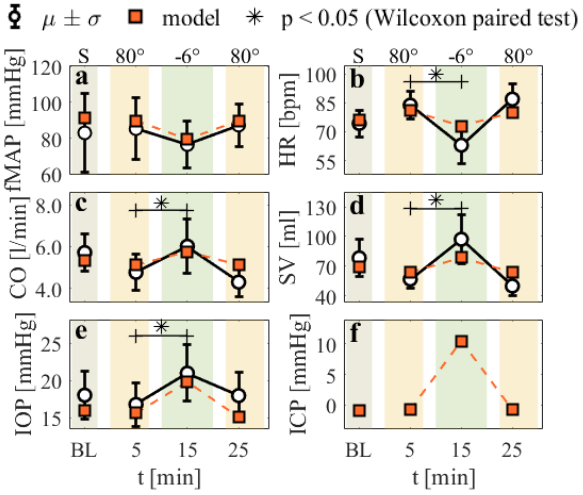

Figure 1: Model results and experimental data for finger mean arterial pressure at brachial level (fMAP, panel a), heart rate (HR, panel b), cardiac output (CO, panel c), stroke volume (SV, panel d) and intraocular pressure (IOP, panel e). ICP (panel f) is the simulated intracranial pressure. S: baseline seated.

Discussion

The model results reproduce the *in vivo* acute ocular and cardiovascular response to 6°HDT. In addition, the model offers novel insights into the hemodynamic mechanisms related to intraocular pressure and intracranial pressure – in terms of average and pulsatile values – both at steady-state and during the transient dynamics.

As also observed upon entering microgravity, the initial fluid shift associated with 6° HDT leads to a sudden increase in SV and CO accompanied by a drop in HR. While arterial pressure does not show wide variations, IOP rises by 4.2 mmHg (model) compared to 80° upright (21.0 ± 3.8 at 6° HDT vs. 18.0 ± 3.2 at 80° HUT). In addition, the model simulates an ICP increase of 11.3 mmHg in response to 6° HDT [6-7] which is much larger than the observed IOP increase. As a result, our model predicts that the translaminar pressure IOP-ICP is markedly reduced during acute HDT (-43%) [6-8]. These results may contribute to the understanding of SANS among astronauts experiencing analog ocular and vascular responses upon long-term space missions.

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