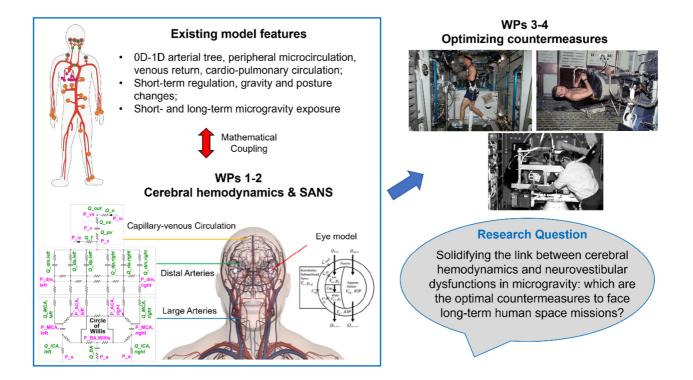
## Optimizing countermeasures against cardiovascular deconditioning and cerebral hemodynamics changes in long-term human spaceflights

Long-term human spaceflight induces a number of cardiovascular alterations, from blood volume reduction to cardiac atrophy, leading to *cardiovascular deconditioning*, that is the adaptation of the cardiovascular system to a less demanding environment [1-4]. The main driver of these changes is the fluid shift from lower to upper body, which is as well believed to be the underlying cause of the Spaceflight Associated Neuro-ocular Syndrome (SANS), classified today among the major risks of the human space exploration [5,6].

For none of the countermeasures - currently adopted or investigated to mitigate cardiovascular deconditioning in view of future Moon/Mars missions - definitive findings on the optimal functioning are known [7,8]. In particular, though artificial gravity is one of the most promising countermeasures [9], the current knowledge mainly relies on ground-based analogs [10]. Moreover, being the association between cerebral hemodynamics and SANS a recent frontier for which the underlying mechanisms are barely understood, no *ad hoc* strategies to contrast cerebral hemodynamic alterations have been so far implemented [8, 11].

We here propose to develop a computational approach, based on our validated multiscale cardiovascular model able to accurately reproduce the hemodynamic response to short- and long-term microgravity exposure [12-14]. Our aims are to: (i) investigate the altered cerebral hemodynamics at broad and then its role on the onset of SANS; and (ii) individuate the optimal countermeasure configuration, among the currently implementable, against cardiovascular deconditioning and neurovestibular dysfunctions induced by hemodynamic alterations (e.g., SANS) for the next manned missions. Results will shed light on the underlying mechanisms altering cerebral hemodynamics and contribute to the design of the most effective cardiovascular countermeasures for long-term missions (including short-term adaptations to each spaceflight phase) to Moon/Mars.



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