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Author: Dr. Gabriela Alves Rodrigues  
Portugal

Prof. Thais Russomano  
Faculty of Medicine, University of Lisbon, United Kingdom  
Dr. Edson dos Santos Oliveira  
Portugal

UNDERSTANDING THE RELATION BETWEEN INTRACRANIAL PRESSURE AND SPACEFLIGHT  
ASSOCIATED NEURO-OCULAR SYNDROME (SANS)

**Abstract**

**INTRODUCTION:** Since 2011, neuro-ocular findings, such as globe flattening, optic disc edema or choroidal and retinal folds, have been one of the major concerns when talking about astronauts' health. These findings are, nowadays, called Spaceflight Associated Neuro-Ocular Syndrome (SANS). This systematic review aims to discuss the possible mechanisms involved on SANS' pathogenesis, such as intracranial pressure (ICP) variation, cerebrospinal fluid (CSF) compartmentalization and environment influence. We hypothesize that there is a relation between the variation of ICP and SANS development. Therefore, the question we want to answer is "Is the variation of ICP in astronauts who undergo long-duration spaceflights related to the development of SANS?".

**METHODS:** This systematic review was structured according to PRISMA 2020 checklist and based on the PICO method. The search was conducted in five databases, Pubmed, Web of Science, Scopus, Google Scholar and Wiley Online Library. The 852 results were then imported to RAYYAN for duplicate removal. Based on the eligibility criteria previously defined, two reviewers, independently and with blinding, screened the remaining 738 results, and together, after a final discussion, chose 240 results to be fully analyzed. The ones that didn't make a relation between the findings and SANS and/or ICP were excluded. To assess the risk of bias, each included study was evaluated, with specific tools, according to the type of study.

**RESULTS:** Twenty studies were reviewed. Nine establish a relation between the variation of ICP (increase, reduction or both) and SANS. Seven explain the existence of CSF compartmentalization after LDSF/analogs, where four defend that the glymphatic system is the responsible for this mechanism. Additionally, five correlate hypercapnia and/or exercise with SANS, while one suggests a direct association with intracranial venous congestion. Finally, one explores astronauts' genetics.

**DISCUSSION:** We believe that the studied theories are not mutually exclusive and that SANS has a multifactorial etiology, where ICP variation and its relation with CSF shifts, CSF compartmentalization and environmental factors have an important influence on the development of neuro-ocular changes. Despite some limitations, this work gives an interesting view on the development of this syndrome and it is a step forward to better understand it.