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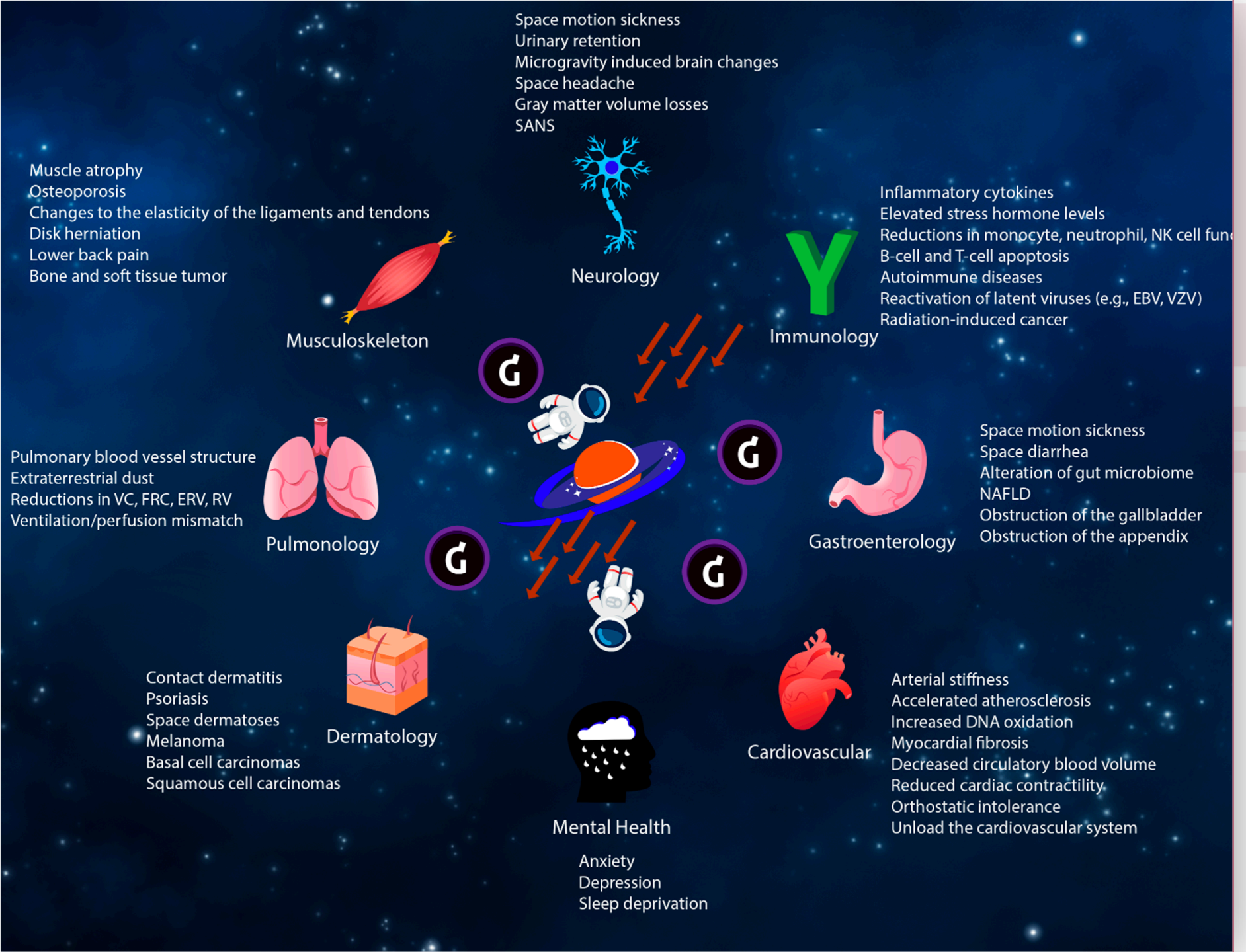
Action 4 Space: Rescue from brain waste clearance system disruption

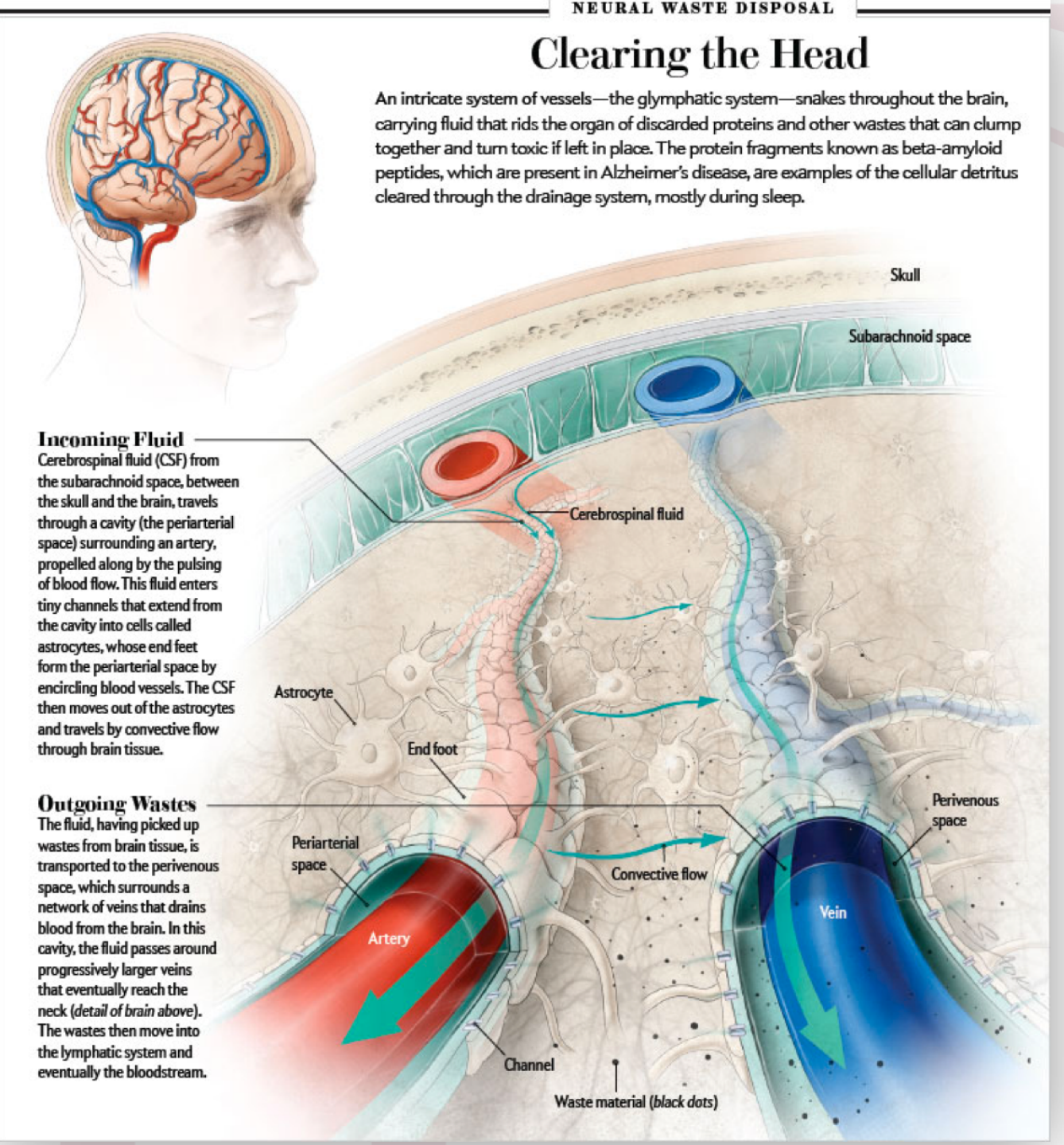
Cristina Lanni

Simposio di "Biomedicina Spaziale per le Future Missioni di Esplorazione Umana dello Spazio: *a Call to Action*"

Potential effects of the space environment on each organ system



Krittanawong C. et al., Cells 2023



The glymphatic system

Glymphatic system controls the clearance of waste products, including beta-amyloid (Aβ), in the central nervous system during the sleep and its function is suppressed in several neurodegenerative diseases such as Alzheimer's disease.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5347443/

The glymphatic system: a glial-dependent perivascular network controlled by circadian system

ARTICLE

https://doi.org/10.1038/s41467-020-18115-2 OPEN

Circadian control of brain glymphatic and lymphatic fluid flow

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- The glymphatic system is **more effective during sleep**, but whether sleep timing promotes glymphatic function remains unknown.
- We here show **glymphatic influx and clearance exhibit endogenous, circadian rhythms peaking** during the mid-rest phase of mice.
- The **perivascular polarization of AQP4** is highest during the rest phase and loss of AQP4 eliminates the day-night difference in both glymphatic influx and drainage to the lymph nodes.
- We conclude that **CSF distribution is under circadian control** and that **AQP4 supports this rhythm.**

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Working hypothesis

Whether a prolonged exposure to spaceflight causes a reduction and/or disruption of the glymphatic system functionality, this could trigger reactive neurovascular and neuroinflammatory events (not necessarily reversible), thus compromising the performance and long-term health.

- Alteration of the molecular clockwork machinery in mouse colon after DSS treatment
- Alteration of the molecular clockwork machinery in mouse brain areas after DSS treatment
- Impairment in circadian glymphatic clearance
- Alteration of the astrocyte-mediated fluid drainage – *ex vivo* evaluation
- Study of the functional consequences of the molecular alterations observed in the expression of the main astrocytic components: *in vivo* MRI
- Alterations in brain metabolites by magnetic resonance spectroscopy
- Waste products deposition in specific brain areas as a consequence of a derangement in glymphatic system clearance

Data not available since they are undergo Embargo for publication

Brain, Behavior, and Immunity 89 (2020) 357–370

Contents lists available at ScienceDirect

Brain, Behavior, and Immunity

journal homepage: www.elsevier.com/locate/ybrbi

Full-length Article

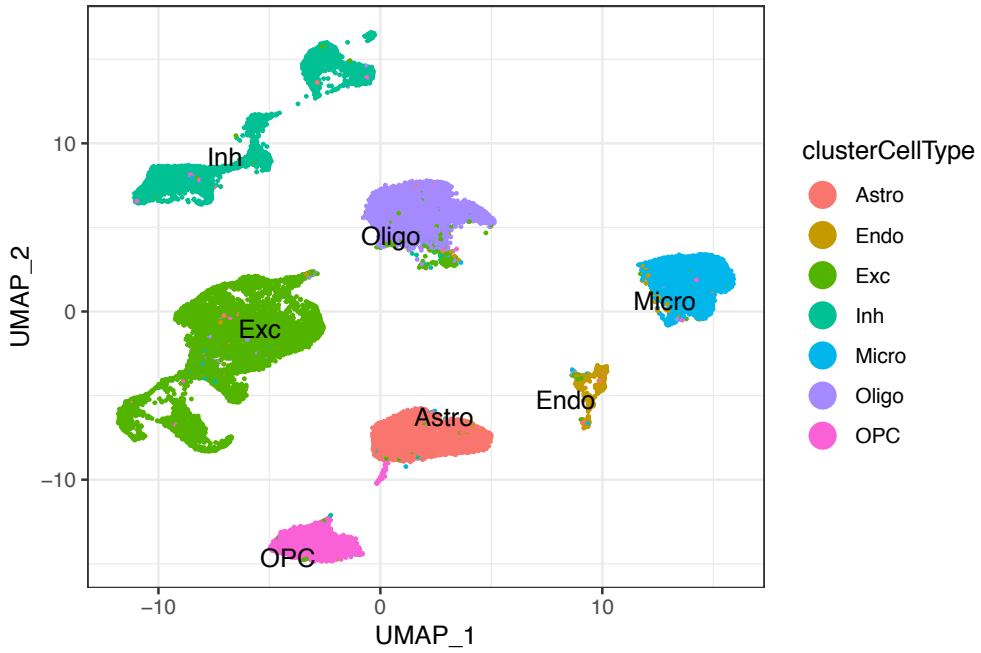
Polyunsaturated fatty acid supplement alleviates depression-incident cognitive dysfunction by protecting the cerebrovascular and glymphatic systems

Xinghua Liu[a,b,1], Jiahuan Hao[a,1], Ensheng Yao[a], Jie Cao[a], Xiaolong Zheng[a], Di Yao[a], Chenyan Zhang[a], Jia Li[a], Dengji Pan[a], Xiang Luo[a], Minghuan Wang[a,*], Wei Wang[a,c,*]

Future perspectives

Animal experimental settings that simulate the zero-G to study the molecular and functional alterations of the glymphatic system, by analyzing:

(i) core astrocytic components functionally coordinate the transport of cerebrospinal fluid and interstitial fluid,
(ii) the dynamics of the functionality of the glymphatic system in the brain by means of in vivo imaging,
(iii) the transcriptomic profile in order to identify potential biomarkers,
(iv) the effect of treatments able to correct the alterations of the glymphatic system induced by the procedure.

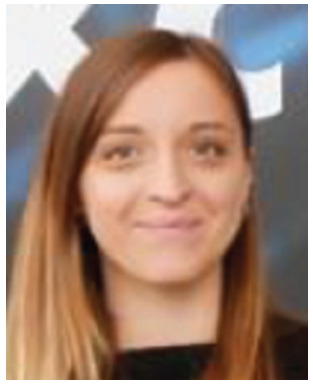


The biomolecular evaluation of the transcriptomic profiles on different brain areas of mouse models exposed to environments and procedures that simulate the zero-G will allow to profile specific molecular signatures related to the disorganization of the wasting and clearance processes that could trigger a self-sustaining and non-reversible neuroinflammatory process of neurodegeneration

Acknowledgements

Stefano Govoni

Marta Filibian



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PRIN 2020SCBBN2_005