IAF MICROGRAVITY SCIENCES AND PROCESSES SYMPOSIUM (A2)
Life and Physical Sciences under reduced Gravity (7)

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AN INVESTIGATION ON THE DIFFERENCES BETWEEN BETA AMYLOID AGGREGATES FORMED ON BOARD THE INTERNATIONAL SPACE STATION AND ON EARTH

Abstract

Microgravity induces several physiological and metabolic changes in cells, organs, and apparatuses, resulting in several undesirable modifications in the normal functioning of living organisms. These changes may become troublesome for professionals engaged in future, long-term space missions. Ever since early animal studies, there has been a growing interest in the effects of microgravity on the Central Nervous System (CNS), resulting in several publications describing changes in the homeostasis of the CNS, including biochemical and cellular alterations associated with neurodegenerative processes typical of age-related pathologies like Alzheimer's Disease (AD). This knowledge, and the observation that microgravity may alter the normal behavior of proteins (including the folding properties of amyloidogenic proteins associated with neurodegeneration), drove the attention of national space agencies on the relationship between microgravity, amyloids and the molecular pathogenesis of neurodegeneration. One elementary approach to this complex issue is to study the aggregation of proteins involved in AD under microgravity conditions by using a simple and well-defined in vitro system. In our ASI-granted (Italian Space Agency) Amyloid Aggregation project, we studied the mode of aggregation of two most representative AD-associated peptides, namely Aβ40, Aβ42 (and a mixture thereof), by a customized test tube system operated on the International Space Station by ESA astronaut Luca Parmitano during the "Beyond" mission in 2019. After manual activation of the tubes, peptides were allowed to aggregate at RT for incubation times encompassing 0-29 hours. At the end of each incubation period, reactions were stopped by freezing tubes in the MELFI. Samples stayed at ultra-low temperature until biochemical and microscopical analyses. When compared to identical samples operated on Earth in the same experimental conditions, we found differences in size distribution and in the shape of aggregates, thus confirming and expanding previous results obtained on similar preparations sent to the ISS by other authors. Mass spectrometry analyses did not evidence any covalent modification in our ISS peptides, supporting the hypothesis that differences between ISS and Earth aggregates derive from the effects of microgravity on the formation of supramolecular peptide structures. These results suggest that the mode of aggregation of different types of Aβ peptides is significantly affected by microgravity and paved the way to a cognate project (named Beta-Amyloid Aggregation) whose first part has been completed in January 2024 by the Italian Air Force Col. Walter Villadei during the Ax-3 mission. ISS samples are expected to return to Earth in spring 2024 for appropriate analyses.