The impact of microgravity and gravitational countermeasures on the gut microbiome of humans enrolled in the AGBRESA study

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The Artificial Gravity Bed Rest Study – AGBRESA – was the first joint study conducted by DLR, ESA and NASA to simulate the effects of microgravity on healthy subjects. Moreover, the study included the use of artificial gravity protocols in a short-arm human centrifuge as a measure to counteract the negative effects of weightlessness. The health of the gut translates into the overall wellbeing since the disruption of the gut symbiotic networks – dysbiosis – could be due to either diet, antibiotic ingestion, sleep disturbance, physical activity or psychological stresses. In recent times, the gut microbiome has changed from being a complementary addition to our digestive tract to a potentially life-changing role by directly being the source of stimuli which revealed to impact neurochemistry, behavior and overall physiological status. Combined, microbial fluctuations could alter the intestinal microbiota composition and bacterial metabolite production, or more severely, in the disruption of host intestinal barrier integrity and the immune system activity, triggering intestinal inflammation syndromes and making the gut a very relevant organ to be studied in the context of spaceflight.

Thus, 12 subjects, 8 males, were subjected to bed rest at negative 6-degree inclination for a period of 60 days with a preceding baseline of 15 days and posterior recovery period of 14 days. In other to characterize the gut microenvironment of healthy humans in simulated microgravity, fecal samples were collected during the baseline stage (once), during the head-down tilt treatment (at days 10, 30, and 50) and during the recovery period (once), and the samples were then processed for 16S rRNA sequencing and taxonomic analysis of the gut microenvironment.

The characterization of the prokaryote flora was conducted 1) throughout time in contrast to the baseline reference and 2) in the context of the gravitational countermeasure vs the bed-rest-only control. The analysis revealed the detection of commensal microorganisms described to positively impact the gut such as *Bifidobacterium spp., Lactobacillus spp., Akkermansia spp. and Enterococus spp.*. Interestingly, we were able to detect pathogens like *Campylobacter hominis* which has been linked to severe bowel diseases ulcerative colitis and Crohn's disease. Also, opportunistic microorganisms such as *Fusobacterium spp., Prevotella spp., Pseudomonas spp., Staphylococcus and Streptococcus spp.*, could potentially indicate an imbalance of the microbial networks and be a good an indicator of dysbiosis. Additionally, we set aside samples to undergo proteomic and metabolite analysis to improve the characterization of the gut microenvironment under microgravity simulation and the extent of the gravitational countermeasure recovery on bowel condition.

Overall, the microgravity simulation performed on the AGBRESA study did not impact dramatically the fitness of the participants. Nonetheless, the analysis of the gut provides important insights on the triggers that occur during the adaptation of human physiology to long term exposure to spaceflight conditions and whether these relate to the described complications associated with gut disease.