

## **Vision Changes after Space Flight Are Related to Alterations in Folate-Dependent One-Carbon Metabolism**

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About 20% of astronauts on International Space Station missions have developed measurable ophthalmic changes after flight. This study was conducted to determine whether the folate-dependent 1-carbon pathway is altered in these individuals. Data were modeled to evaluate differences between individuals with ophthalmic changes ( $n=5$ ) and those without them ( $n=15$ ). We also correlated mean preflight serum concentrations of the 1-carbon metabolites with changes in measured refraction after flight. Serum homocysteine (HCy), cystathionine, 2-methylcitric acid, and methylmalonic acid concentrations were 25%-45% higher ( $P<0.001$ ) in astronauts with ophthalmic changes than in those without them. These differences existed before, during, and after flight. Preflight serum HCy and cystathionine, and in-flight serum folate, were significantly ( $P<0.05$ ) correlated with postflight change in refraction, and preflight serum concentrations of 2-methylcitric acid tended to be associated ( $P=0.06$ ) with ophthalmic changes. The biochemical differences observed in those with vision issues strongly suggests impairment of the folate-dependent 1-carbon transfer pathway. Impairment of this pathway, by polymorphisms, diet or other means, may interact with components of the microgravity environment to influence these pathophysiologic changes. This study was funded by the NASA Human Research Program.