Rapamycin as a Novel Therapeutic for Alzheimer's Disease: An Imaging Assessment of Prevention and Treatment through in vivo Brain Vasculature, Metabolism, and Cognition

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The drug Rapamycin (Rapa) delays age-related diseases, increase lifespan, and inhibits the mechanistic target of Rapamycin, a kinase that prevents the clearance of Aß. However, the application of Rapa as a treatment for Alzheimer's disease (AD) remains unexplored. The first part of this study assessed Rapa's efficacy in preventing AD while the second objective leveraged neuroimaging for the early detection of AD. The final aim was to assess Rapa's efficacy later in the disease pathology. The mice were divided into two cohorts based on age: three months or seven months. Tests were conducted on two groups of transgenic mice: one that carries the apolipoprotein E4 gene, the strongest genetic risk factor for AD, and another that carries the neutral E3 gene. Methodology consisted of functional magnetic resonance imaging (fMRI), magnetic resonance spectroscopy (MRS), blood-brain barrier neuroinflammation determination, Radial Arm Water Maze, and Novel Object Recognition Test. Through fMRI, genetically predisposed AD mice exhibited vascular deficits at three months of age. Following sixteen weeks of treatment, genetically predisposed mice exhibited restored cerebral blood flow, significantly reduced neuroinflammation, and similar trends in metabolite concentration and cognition to control mice. In the older cohort, Rapa was less effective at repairing cognition in AD models, but remained effective in promoting healthy metabolites. These findings demonstrate that Rapa is a viable preventative for AD, especially in earlier stages of disease pathology, and that in vivo neuroimaging provides robust biomarkers.

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