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Combined treatment with autophagy inducers rapamycin and trehalose as an experimental therapy for Alzheimer's disease-like pathology in mice

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Autophagy is considered to impede amyloid-β (Aβ) accumulation in Alzheimer's disease (AD). Autophagy can be induced through mTOR-dependent and mTOR-independent pathways (here, by means of rapamycin and trehalose respectively). In order to evaluate the contribution of these pathways to AD treatment, we studied the effects of autophagy inducers rapamycin (10 mg/kg, intraperitoneally, every other day, 14 days), trehalose (2 % solution in drinking water, 14 days), and their combination in a murine model of AD. Aβ fragment (25–35) was administered intracerebroventricularly in 2 days prior the start of treatment with autophagy inducers. The open-field, plus-maze, and passive avoidance tests were used for behavioral phenotyping. Neuronal density, amyloid accumulation, the expression of autophagy marker LC3-II and neuroinflammatory marker IBA1 were measured in the frontal cortex, hippocampus, and amygdala. mRNA levels of autophagy genes (Atg8, Becn1, Park2) were assessed in the hippocampus. Trehalose increased the autophagy gene expression and hence produced substantial and long-term autophagy induction. Both drugs efficiently prohibited microglia activation and Aβ deposition. Rapamycin and trehalose significantly reversed behavioral and neuronal deficits in Aβ-injected mice. Some parameters were better restored with the combined treatment. The results suggest that the trehalose alone or combined with rapamycin appeared to be a promising approach to therapy for AD.

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