HALLMARKS OF ALZHEIMER'S DISEASE IN SENESCENCE ACCELERATED MICE P8: AN IN VIVO AND IN VITRO APPROACH

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As the average population age increases, the need for an enhanced understanding of Alzheimer's disease (AD) becomes of vital importance. Several mouse models focus on the overexpression of mutated AD-associated genes, but there are no models for spontaneous neurodegenerative changes associated with age-related/AD. The senescence-accelerated mouse prone strain (SAMP8) displays remarkable pathological similarities to AD such as amyloid-ß (beta) modifications, gliosis, tau phosphorylation, and oxidative stress in reference to control strain SAMR1. We found that SAMP8 mice generate multiple forms of hyperphosphorylated tau and cdk/5/p35/GSK3ß (beta) activation. Studies performed in cultured cortical neurons and in astrocytes from SAMP8 and SAMR1 showed that most of the parameters mentioned above and oxidative stress mimic the findings in vivo. One of putative strategies to prevent/ameliorate the AD progress is caloric restriction (CR). We demonstrate that in vivo CR reduced tau phosphorylation and GSK3ß (beta) activation in SAMP8. Accordingly, cultures of SAMP8 astrocytes treated with serum from CR rats showed a change on gene expression that correlated to an amelioration of the mitochondrial function. In conclusion SAMP8 displays the notable traits of aging, but also those of AD. It has also been showed that hallmarks of AD can be reproduced in in vitro assays. Therefore, SAMP8 is currently the most viable model in biogerontology for modelling the links between aging and AD and its findings can be translated to human benefit against AD.
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