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ASTROCYTES AGED IN VITRO DISPLAY AN IMPAIRED NEUROPROTECTIVE CAPACITY ON CORTICAL NEURONS: A TOOL IN SCREENING FOR NEUROTOXICITY

Alterations in astrocyte function that may affect neuronal viability and neurotoxic response occur with brain aging. In this study, we evaluate the neuroprotective capacity of astrocytes in an experimental model of in vitro aging. Changes in oxidative stress, glutamate uptake and protein expression were evaluated in rat cortical astrocytes cultured for 10 and 90 days in vitro (DIV). Levels of glial fibrillary acidic protein and S100b increased at 90 days when cells were positive for the senescence β -galactosidase marker. In long-term astrocyte cultures, the generation of reactive oxygen species was enhanced and mitochondrial activity decreased. Simultaneously, there was an increase in proteins that stained positively for nitrotyrosine. The expression of Cu/Zn-superoxide dismutase (SOD-1) and haeme oxygenase-1 (HO-1) proteins and inducible nitric oxide synthase (iNOS) increased in aged astrocytes. Glutamate uptake in 90-DIV astrocytes was higher than in 10 DIV ones, and was more vulnerable to inhibition by H₂O₂ exposure. Enhanced glutamate uptake was probably because of up-regulation of the glutamate/aspartate transporter protein. Astrocyte neuroprotection was tested by measuring neocortical neuronal survival in cocultures with young and long-term astrocyte cultures. Aged astrocytes had a highly significant reduced ability ($p < 0.001$) to maintain survival of neocortical neurons. These findings indicate that astrocytes may partially lose their neuroprotective ability during aging. The results also suggest that aged astrocytes may contribute to exacerbating neuronal injury in age-related neurodegenerative processes and during exposure to neurotoxic agents such as methylmercury and organotins. Therefore, they may be a useful tool for in vitro coculture neurotoxicity testing and studies on mechanisms of neurotoxic action.

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Poster

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