

PHYSICAL EXERCISE AGAINST ALZHEIMER'S DISEASE: EXPERIMENTAL STUDIES IN 3XTG-AD MICE

C. Sanfeliu, Y. Garcia, S. Revilla, K. Buccieri,
J.C. Lopez-Ramos, J.M. Delgado-Garcia,
D. Acuna-Castroviejo, J. Vina, M. De la Fuente,
A. Ortega-Aznar, R. Cristofol, L. Gimenez-Llort

Institut d'Investigacions Biomediques de Barcelona, CSIC-IDIBAPS, Barcelona, Spain Institut de Neurociencias, Universitat Autònoma de Barcelona, Bellaterra, Barcelona, Spain; Division de Neurociencias, Universidad Pablo de Olavide, Sevilla, Spain; Departamento de Fisiologia, Instituto de Biotecnologia, Universidad de Granada, Granada, Spain; Departamento de Fisiologia, Facultad de Medicina, Universidad de Valencia, Valencia, Spain; Departamento de Fisiologia, Facultad de Biologia, Universidad Complutense de Madrid, Madrid, Spain; Departament d'Anatomia Patologica (Neuropatologia), Hospital Universitari Vall d'Hebron, Barcelona, Spain

Mouse models of Alzheimer's disease (AD) allow studying the brain and peripheral mechanisms underlying the proposed therapies against AD-related neurodegeneration. The triple transgenic mouse (3xTg-AD) harbors three mutant transgenes, PS1/M146V, APPSwe, and tauP301L (Oddo et al., Neuron 39:409-21, 2003), and reproduces the main hallmarks of AD. These mice develop severe AD pathology after 12 months of age, but early signs of cognitive impairment appear at 4-6 months. We have studied the effect of voluntary physical exercise in male and female 3xTg-AD mice and in ovariectomized female mice. Mice had free access to a running wheel. Also we have studied the effect of melatonin administered through the drinking water. NonTg mice with the same genetic background were used as a control. Melatonin was neuroprotective and its underlying mechanisms are under study. Physical exercise protected against cognitive decline at different mouse ages and improved the non-cognitive BPSD-like behaviors. Ovariectomy worsened the AD pathology of the mice, whereas a later physical exercise program reversed its deleterious effects. Amelioration of oxidative stress and reversion of aged-like neuroimmunoendocrine function were induced by physical exercise. Studies of gene and protein expression patterns are ongoing to fully understand the involved neuroprotective and anti-aging effects in brain and peripheral target organs. Therefore, experimental studies in AD mouse models allow assaying different temporal patterns of therapeutic treatments in the fight against the development of AD pathology with advancing age. Acknowledgments: SAF-2009-13093, MICINN; RD06/0013/1004, RD06/0013/0015, RD06/0013/0008, RD06/0013/0027, RD06/0013/0003 (RETICEF), ISCIII; and Fundacio La Marata de TV3/ 2006-062931.