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Abstract

Sex-Dependent Hepatomegaly, and Increased Hepatic Oxidative Stress in Old Male and Female 3xTg-AD Mice as Compared to Mice with Physiological Aging †

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Abstract: When it comes to neurodegenerative disorders, Alzheimer's disease (AD) is one of the main causes of dementia in older people. Until now, studies have focused on alterations occurring in the brain. However, it has been shown that along with the accumulation of beta-amyloid plaques and tau proteins, oxidative stress and inflammation also play a role in this disease's pathophysiology. Peripheral organs such as the liver, the central organ regulating metabolism and supporting the immune system, could affect AD pathophysiological development and/or progress. We have previously described hepatic oxidative stress in 6-month-old 3xTg-AD mice, an age mimicking the prodromal stages of AD disease. In the present work, we studied the impact of AD-genotype and sex effects on liver dysfunction in 16-month-old male and female 3xTg-AD mice, an age mimicking advanced neuropathological stages of the disease, and as compared to age- and sex-matched non-transgenic mice with physiological aging. The mass index results showed hepatic damage as hepatomegaly in 3xTg-AD mice. A sex-dependent increase in hepatic tissue oxidative stress, measured through antioxidant enzymes glutathione reductase (Gr) and glutathione peroxidase (Gpx), and antioxidant compound glutathione (GSH), was found in 3xTg-AD mice. Furthermore, the correlations between the enzymes and the hepatic index also showed sex and genotype differences. These results indicate that liver status is affected in 3xTg-AD mice; it is affected in a sexually differential manner and could favor AD progression. Further ongoing analysis regarding β-amyloid and lipidic depositions on the liver would determine if these alterations correlate with a worse prognosis of the disease.

Keywords: Alzheimer's disease; aging; peripheral organs; liver; oxidative stress; sex differences

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