FRAILTY IN 5XFAD MOUSE MODEL OD ALZHEIMER'S DISEASE: THE INFLUENCE OF AGE AND PROTEASOME ACTIVATION

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Objectives: Increased frailty is associated with the progression of Alzheimer's disease (AD), characterized by the accumulation of amyloid plaques composed of aggregated amyloid-beta (Abeta) peptides, mainly Abeta 42. 18 alpha- glycyrrhetinic acid (18-alpha GA) has been shown to enhance activity of ubiquitin-proteasome system responsible for the removal of proteins, and to decrease Abeta deposits in model organisms. We examined the effect of 18-alpha GA supplementation on APP processing and generation of Abeta 42 in the 5xFAD transgenic AD mouse model, characterized by the deposition of plaques in the cortex and hippocampus as early as at 2 months of age.

Methods: Both female and male mice were exposed to the 18-alpha GA treatment for six months, starting from 2-months of age which is considered an early phase of AD pathology, suitable for therapeutics application. Frailty was determined in control young (2 months) and old (12-13 months of age) mice, as well in those treated with 18-alpha-GA, by using phenotype frailty score (FS) and clinical frailty index (FI).

Results: Obtained results showed a significant increase in frailty in aged 5xFAD mice. Significant differences were observed between males and females. 18-alpha-GA treatment increased activity of the proteasome in the cortex and hippocampus of 5xFAD mice, decreased the number of Abeta plaques and decreased frailty level.

Conclusions: Results indicate that 18-alpha-GA has a therapeutic potential in treatment of AD pathology.