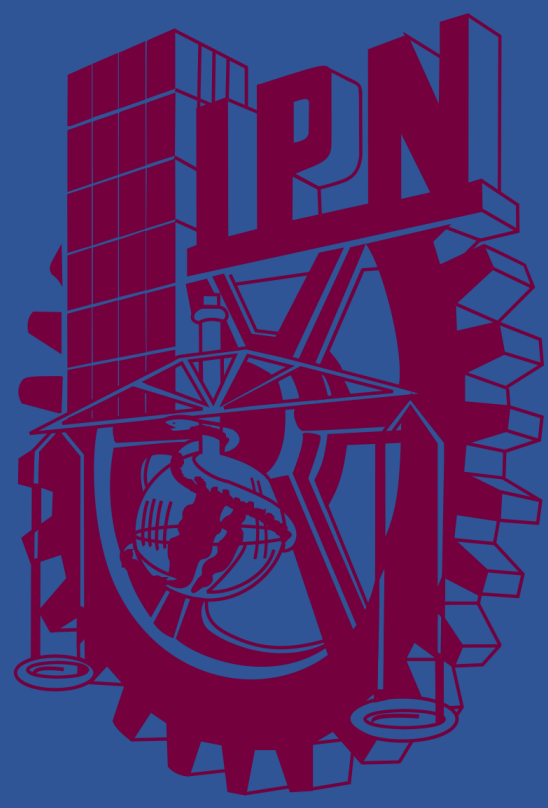




Dysregulated expression of APP mRNA and non-coding RNAs in an insulin-resistant Alzheimer's model

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Altered expression of miR-106a, miR-200b, APP, and glucose transporters (GLUT1/GLUT3) in 3xTg-AD mice with insulin resistance suggests a molecular link between metabolic dysfunction and Alzheimer's disease pathology.

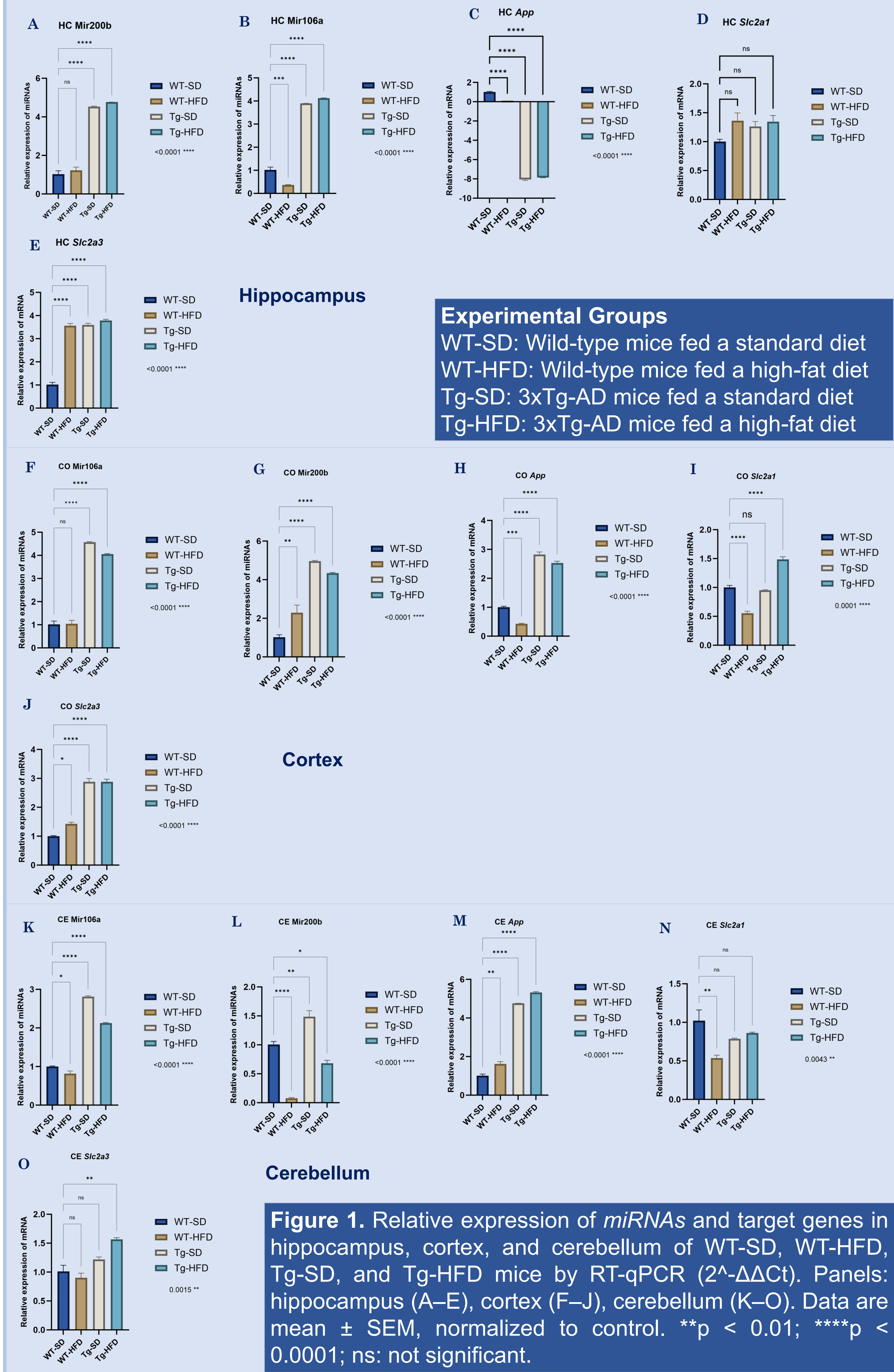
Introduction

Alzheimer's disease (AD) is the leading cause of dementia and is characterized by the accumulation of β -amyloid plaques derived from abnormal processing of the amyloid precursor protein (APP) ^{1,2}. Alterations in glucose metabolism and insulin resistance contribute to AD pathophysiology by impairing cerebral glucose uptake through transporters such as GLUT1 and GLUT3 ^{3,4}. MicroRNAs (miRNAs) are important post-transcriptional regulators involved in neurodegeneration, and previous studies have associated miR-106a and miR-200b with the regulation of APP expression and glucose metabolism ^{5,6}. However, their role in regulating AD-related genes under insulin-resistant conditions remains unclear.

Methods

A transgenic 3xTg-AD mouse model was used to evaluate the relationship between insulin resistance and the expression of AD-related genes. Insulin resistance was induced through a high-fat diet. Cognitive performance was assessed using the Morris water maze and the novel object recognition test. After behavioral assessment, the cortex, hippocampus, and cerebellum were dissected for total RNA extraction using TRIzol reagent. Expression levels of *App*, *Slc2a1*, *Slc2a3*, *Mir-106a*, and *Mir-200b* were determined by RT-qPCR, and statistical analyses were performed using GraphPad Prism.

Results



Conclusion

These findings indicate that insulin resistance in 3xTg-AD transgenic mice modulates the expression of the *App* transcript and the glucose transporters *Slc2a1* and *Slc2a3* differentially in brain regions, while microRNA expression is overexpressed in almost all brain regions, potentially suggesting regulation in some brain region associated with Alzheimer's disease.

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