The Effects of Sex and Type 2 Diabetes on Alzheimer's Disease Pathology in Tg6799 Mouse Hippocampi and Cortices

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Alzheimer’s disease (AD) is a neurodegenerative disorder that causes progressively decreased verbal and visuospatial memory function. Previous research indicates that women are at greater risk for developing AD than are men, and that type 2 diabetes mellitus (T2DM) is a risk factor for AD. This study investigated how sex and T2DM affect AD pathology in the Tg6799 mouse model, inducing T2DM via high fat diet (HFD) administration. After six months, brain tissues were analyzed for AD pathologies via immunohistochemistry procedures and western blot. Results indicate that, when compared to males, female Tg6799 mouse hippocampi have: significantly more Aß, demonstrated by higher Aß ($p<0.01$) and ß-pleated sheet ($p<0.001$) levels; significantly more neurodegeneration ($p<0.01$); and significantly more neuroinflammation, shown by higher levels of activated microglia ($p<0.05$) and astrogliosis ($p<0.0001$). Female Tg6799 mouse cortices have more Aß, demonstrated by significantly higher ß-pleated sheet levels ($p<0.0001$), and significantly more neuroinflammation, demonstrated by upregulated microglia activation ($p<0.05$) and astrogliosis ($p<0.05$). Although metabolic data demonstrated that the HFD induced the onset of type 2 diabetes, this was not shown to affect AD pathology. This research strongly suggests that future AD models using Tg6799 mice should separate male and female data to avoid skewed results and advocates for a need for further investigation of AD pathology by sex.

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