SEEDING EFFECT OF PYROGLUTAMATE AMYLOID BETA 3-42 PROMOTES PLAQUE DEPOSITION AND BEHAVIOURAL DEFICITS IN A NOVEL MOUSE MODEL OF ALZHEIMER'S DISEASE

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N-terminally truncated amyloid beta (Aβ) peptides form a major fraction of Aβ within the brains of Alzheimer’s disease (AD) patients. Recent studies have suggested that one isoform of N-terminally modified Aβ, pyroglutamate Aβ (AβpE3-42), may be particularly relevant to the pathogenesis of AD. AβpE3-42 has a higher aggregation rate, increased resistance to proteolytic degradation and enhanced toxicity \textit{in vitro} relative to N-terminally-intact Aβ. Previous work from our lab has also demonstrated that AβpE3-42 can induce neurodegeneration in the TBA2 mouse line. In this study, we tested the hypothesis that AβpE3-42 is capable of seeding plaque formation \textit{in vivo} and augmenting behavioral deficits in an AD mouse model. To accomplish this, we crossed a mouse model expressing five familial AD mutations (5XFAD) to transgenic mice exclusively expressing Aβ3Q-42 (TBA42) in order to produce a new bigenic line (FAD42). FAD42 mice displayed enhanced behavioral impairments relative to the 5xFAD and TBA42 lines. In addition, Aβ plaque pathology in the FAD42 mice was noticeably increased in comparison to the 5xFAD animals. These data suggest that AβpE3-42 may be an important contributor to the development and progression of AD.