Reduction of the expression of the late-onset Alzheimer's disease (AD) risk-factor *BIN1* does not affect amyloid pathology in an AD mouse model

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**Contents:**

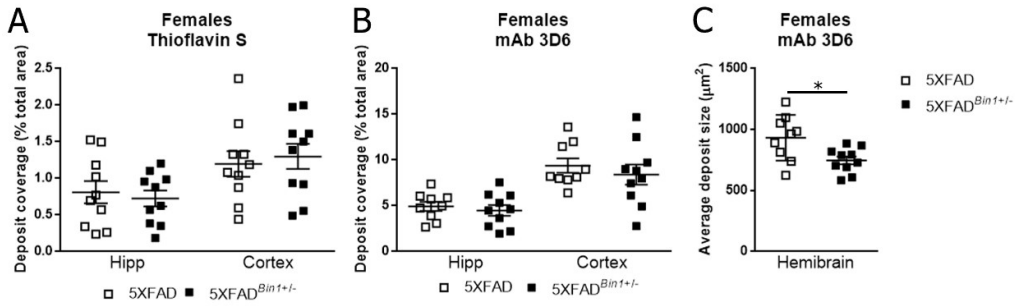


**Figure S1.** A) Quantitative analysis of Thioflavin S-positive amyloid burden in the hippocampus (Hipp) or cortex of 4-month-old females 5XFAD and 5XFAD$^{Bin1+/-}$ mice ($n$ = 10 per genotype). B) Quantitative analysis of amyloid burden identified by mAb 3D6 in the hippocampus (Hipp) or cortex of females 5XFAD and 5XFAD$^{Bin1+/-}$ mice ($n$ = 10 per genotype). C) Quantitative analysis of the average deposit size in the hemibrain identified by mAb 3D6 in female 5XFAD and 5XFAD$^{Bin1+/-}$ mice ($n$ = 10 per genotype).

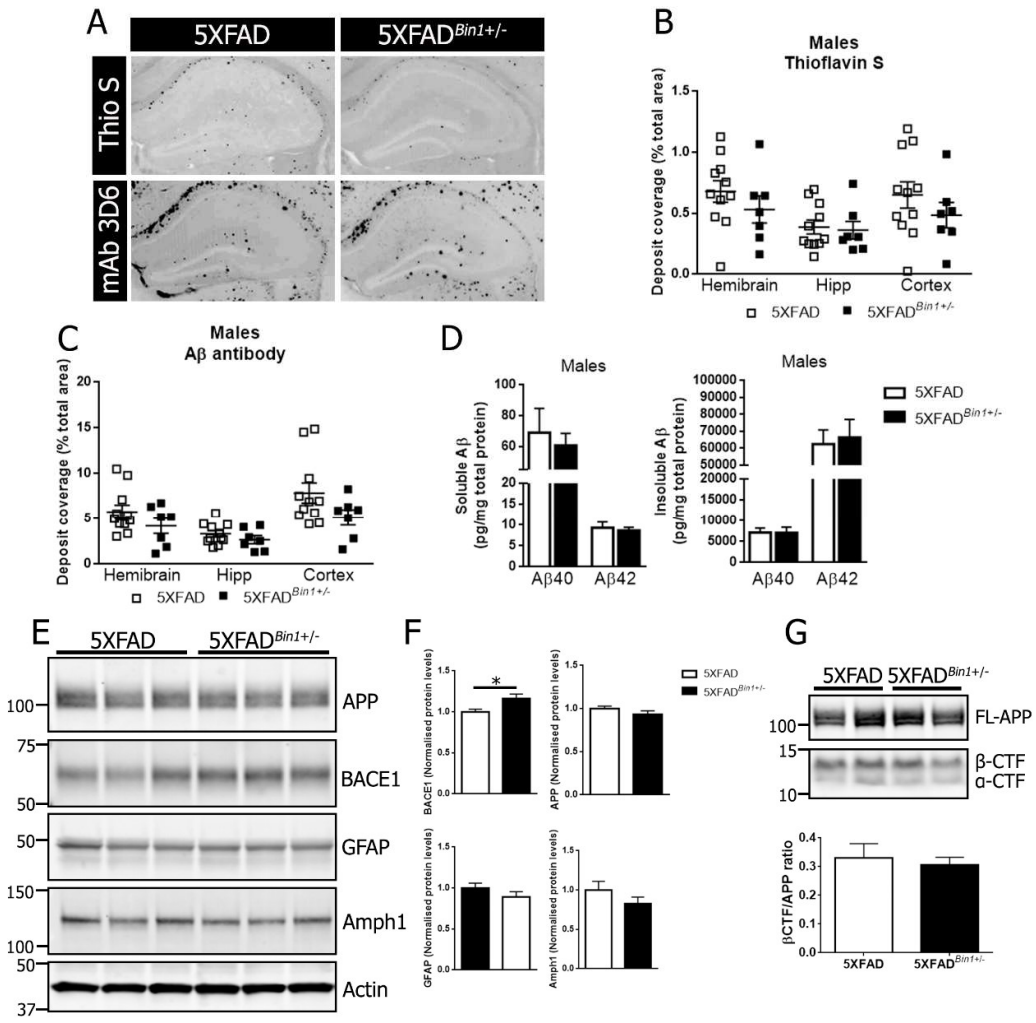


**Figure S2.** A) Representative images of Thioflavin S and mAb 3D6 staining in the hippocampus of 4-month-old male 5XFAD and 5XFAD$^{Bin1+/-}$ mice. B and C) Quantification of amyloid burden by Thioflavin S staining and by mAb 3D6 staining, respectively ($n$ = 11 5XFAD and 7 5XFAD$^{Bin1+/-}$) in the hemibrains, hippocampus (Hipp) and cortex. D) TBS soluble (left) and insoluble, formic acid extracted Aβ40 and Aβ42 (right) were measured by V-PLEX 6e10 immunoassay ($n$ = 11 5XFAD and 7 5XFAD$^{Bin1+/-}$). E) Immunoblot analysis of APP, BACE1, GFAP and Amph1 levels in 5XFAD and 5XFAD$^{Bin1+/-}$ male mice. F) Quantification of the levels of BACE1, APP, GFAP and Amph1 in forebrain homogenates, normalized to actin ($n$ = 8 per genotype). G) Immunoblot analysis of full-length APP (FL-APP) and APP C-terminal fragments (CTF) and quantification of β-CTF normalized to FL-APP ($n$ = 4 per genotype).

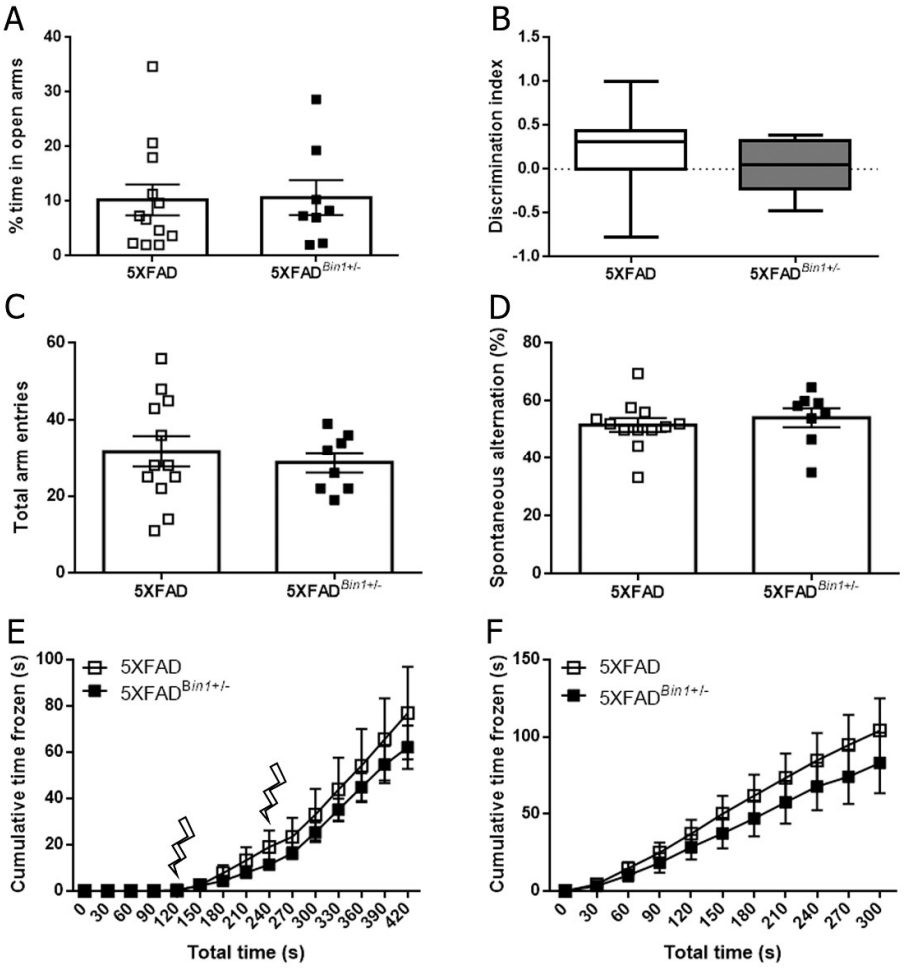


**Figure S3. Reduction of BIN1 does not alter behavioural deficits in male 5XFAD mice**

A) The percentage of time in the open arms of the elevated-plus maze was quantified for 4-month-old male 5XFAD and 5XFAD$^{Bin1+/-}$ mice. B) Discrimination index score from novel object recognition for male 5XFAD and 5XFAD$^{Bin1+/-}$ mice. C) The number of arm entries over the 8 min Y-Maze trial. D) The number of spontaneous alternations in the Y-maze over the 8 min trial period. E) Freezing behaviour in male 5XFAD and 5XFAD$^{Bin1+/-}$ mice during day 1 of fear conditioning. Lightning bolts represent delivery of the shock stimulus. F) Freezing behaviour in male 5XFAD and 5XFAD$^{Bin1+/-}$ mice on day 2 of fear conditioning, 24 h after shock application ($n$ = 12 5XFAD and 8 5XFAD$^{Bin1+/-}$ mice for all analyses).

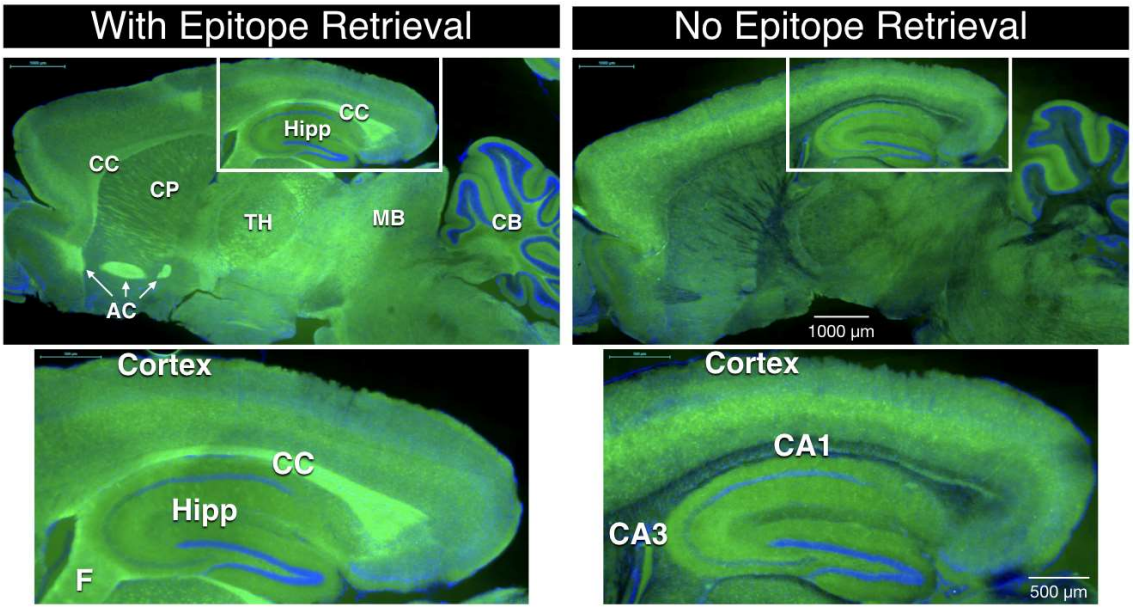


**Figure S4. Preferential labelling of neuronal BIN1 in the absence of epitope retrieval**

Sagittal mouse brain sections were processed for immunohistochemical staining of BIN1 using mAb 13463 (green). Nuclei were stained with Hoechst (blue). The slides were scanned using CRi Pannoramic Scan Whole Slide Scanner and analyzed by Pannoramic Viewer (3DHISTECH). The boxed region is shown at a higher magnification at the bottom. *Left panels*: floating brain sections were subjected to epitope retrieval by incubation in 10 mM trisodium citrate pH 6 and 0.05 % Tween 20 for 30 min at 90°C prior to blocking and staining with the primary antibody. Under these conditions, BIN1 staining of white matter predominates. *Right panels*: immunostaining performed without the epitope retrieval step reveals preferential neuronal BIN1 staining. AC = anterior commissure; CA1 = *Cornu Ammonis* area 1; CA3 = *Cornu Ammonis* area 3; CB = cerebellum CC = corpus callosum; CP = caudate putamen; F = fimbria; Hipp = hippocampus; MB = midbrain; TH = thalamus.