Supporting Information

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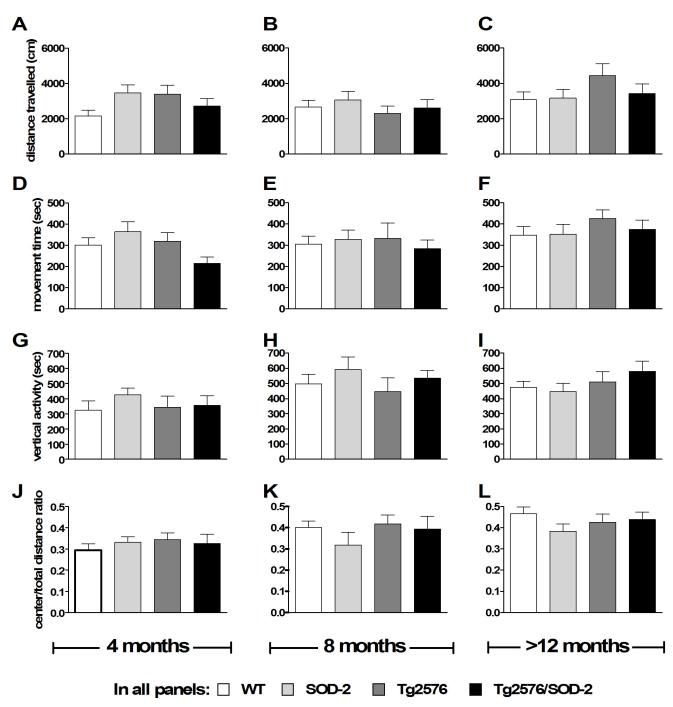


Fig. S1. Superoxide dismutase (SOD-2) overexpression and the Swedish amyloid precursor protein (APP) mutation do not affect the locomotor activity in the open field. (A–C) Total distance traveled in the testing arena. This is an indicator of mouse locomotor activity. (D–F) Total movement time in the testing arena, also indicative of locomotor activity. (G–I) Vertical activity, indicative of rearing behavior, as measured by vertical laser beam interruption. (I–I) Graphs represent the center-to-total-distance ratio which can be used as an indicator of anxiety-related behavior. (I–I) All measurements performed in 4-, 8-, and >12-month-old WT, SOD-2, Tg2576, and Tg2576/SOD-2 animals. Significance was assessed by one-way ANOVA with Tukey's post test. For WT, SOD-2, Tg2576, and Tg2576/SOD-2 mice, respectively, I = 6, 8, 8, and 8 at 4 months of age; I = 10, 8, 9, and 10 at 8 months of age; and I = 18, 16, 17, and 19 at >12 months of age.

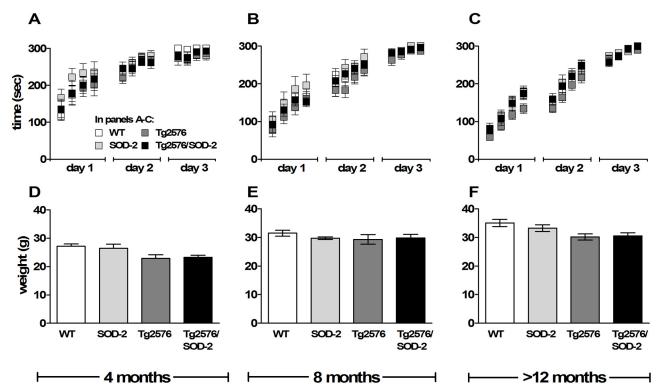


Fig. S2. SOD-2 overexpression and the Swedish APP mutation do not affect the motor coordination and balance of mice in the accelerating rota-rod test. (A–C) Graphs represent the time spent walking balanced on top of the rotating rod on each test-day for 4-, 8-, and >12-month-old WT, SOD-2, Tg2576, and Tg2576/SOD-2 mice. (D–F) Graphs represent the weights of 4-, 8-, and >12-month-old WT, SOD-2, Tg2576, and Tg2576/SOD-2 mice. The weight of the mice was measured to rule out its effect on balance performance during the rota-rod test. Significance was assessed by one-way ANOVA with Tukey's post test. For WT, SOD-2, Tg2576, and Tg2576/SOD-2 mice, respectively, n = 6, 8, 8, and 8 at 4 months of age; n = 10, 8, 9, and 10 at 8 months of age; and n = 18, 16, 17, and 19 at >12 months of age.

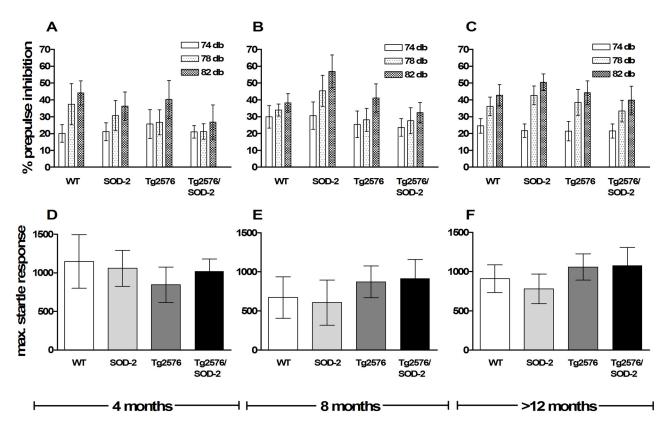


Fig. S3. SOD-2 overexpression and the Swedish APP mutation do not affect the startle response and the prepulse inhibition of the startle of mice. (A–C) Prepulse inhibition of the startle response with acoustic prepulses of 74, 78, and 82 dB of 4-, 8-, and >12-month-old WT, SOD-2, Tg2576, and Tg2576/SOD-2 mice. (D–F) Graphs represent the maximum startle response in the absence of an acoustic prepulse of 4-, 8-, and >12-month-old WT, SOD-2, Tg2576, and Tg2576/SOD-2 mice. Significance was assessed by one-way ANOVA with Tukey's post test. For WT, SOD-2, Tg2576, and Tg2576/SOD-2 mice, respectively, n = 6, 8, 8, and 8 at 4 months of age; n = 10, 8, 9, and 10 at 8 months of age; and n = 18, 16, 17, and 19 at >12 months of age.

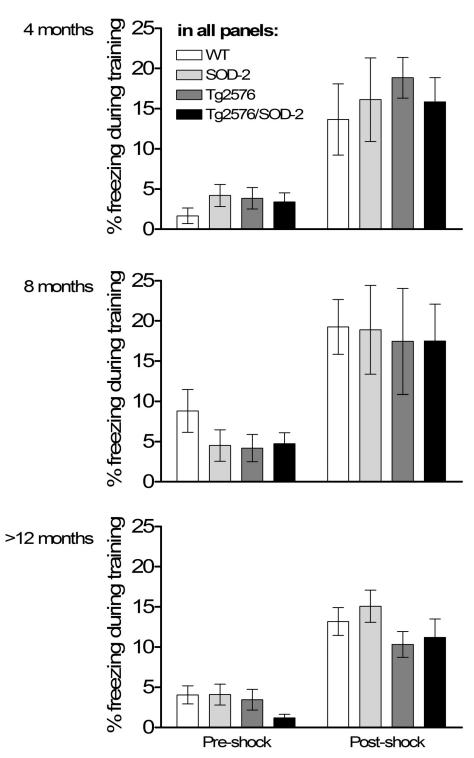


Fig. S4. Tg2576 animals have normal shock sensitivity. Graphs represent the freezing reaction of 4-, 8-, and >12-month-old WT, SOD-2, Tg2576, and Tg2576/SOD-2 mice, before and after a foot shock during the fear-conditioning training session. Significance was assessed by one-way ANOVA with Tukey's post test. For WT, SOD-2, Tg2576, and Tg2576/SOD-2 mice, respectively, n = 6, 8, 8, and 8 at 4 months of age; n = 10, 8, 9, and 10 at 8 months of age; and n = 18, 16, 17, and 19 at >12 months of age.

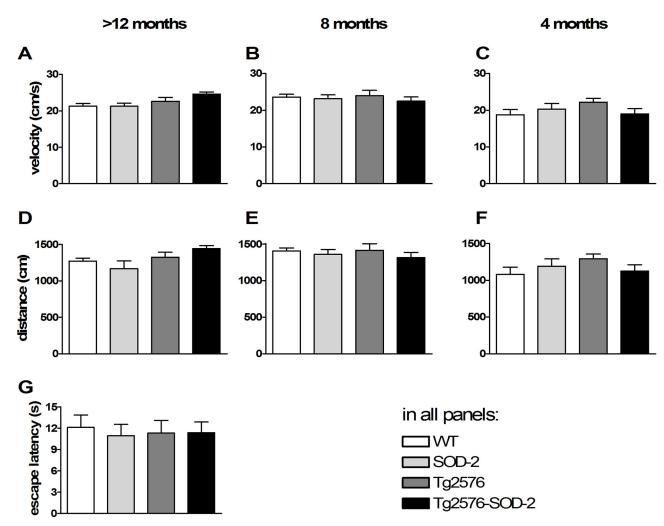


Fig. S5. SOD-2 overexpression and the Swedish APP mutation do not affect the swim speed, distance traveled, or the visual acuity of mice in the Morris water maze. (A–C) Swimming velocity of 4-, 8-, and >12-month-old WT, SOD-2, Tg2576, and Tg2576/SOD-2 mice. (D–F) Total distance traveled in the pool of 4-, 8-, and >12-month-old WT, SOD-2, Tg2576, and Tg2576/SOD-2 mice. (G) Graphs represent the latency to find the platform in the pool in the presence of a visual cue. The >12-month-old WT, SOD-2, Tg2576, and Tg2576/SOD-2 mice were tested to rule out the possibility of losing visual acuity with age. Significance was assessed by one-way ANOVA with Tukey's post test. For WT, SOD-2, Tg2576, and Tg2576/SOD-2 mice, respectively, n = 6, 8, 8, and 8 at 4 months of age; n = 10, 8, 9, and 10 at 8 months of age; and n = 18, 16, 17, and 19 at >12 months of age.

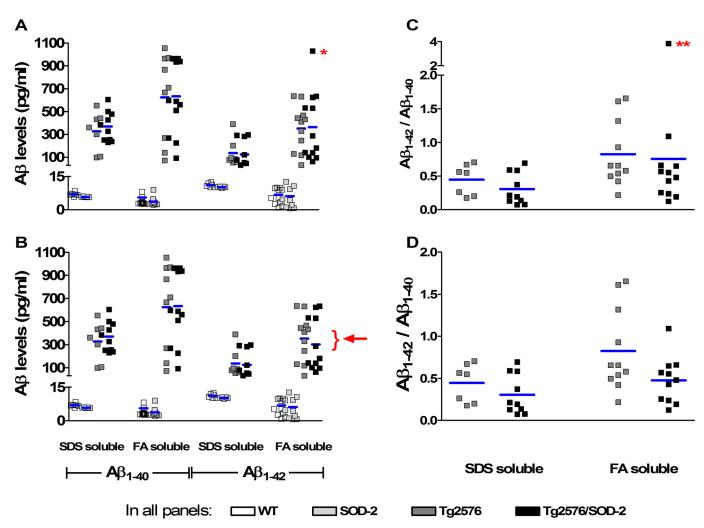


Fig. 56. Outlier analysis for the amyloid-β (Aβ) level measurements by ELISA. (A) The scatter plot represents the distribution of the SDS-soluble and formic acid (FA)-soluble $Aβ_{1-40}$ and $Aβ_{1-42}$ levels presented in Fig. 4A for the 12-month-old WT, SOD-2, Tg2576, and Tg2576/SOD-2 mice. Means within each group are indicated by a blue line. One value from the FA-soluble $Aβ_{1-42}$ of the Tg2576/SOD-2 group (marked with *) falls furthest from the rest without being a significant outlier and hence potentially masks decreases in $Aβ_{1-42}$ levels of this group. (B) Had this value been discarded, the trend toward decreased $Aβ_{1-42}$ levels in the Tg2576/SOD-2 group would have appeared (indicated by a red bracket and arrow). (C) The scatter plot represents the distribution of the SDS-soluble and FA-soluble $Aβ_{1-42}/Aβ_{1-40}$ ratios presented in Fig. 4B for the 12-month-old WT, SOD-2, Tg2576, and Tg2576/SOD-2 mice. The outlying value discussed in A becomes a significant outlier when the ratios are computed (marked with **). This value was therefore rejected, leading to a significant decrease in the $Aβ_{1-42}/Aβ_{1-40}$ ratio of the Tg2576 mice (represented in D).