Neuronal activity regulates the regional vulnerability to amyloid-β deposition

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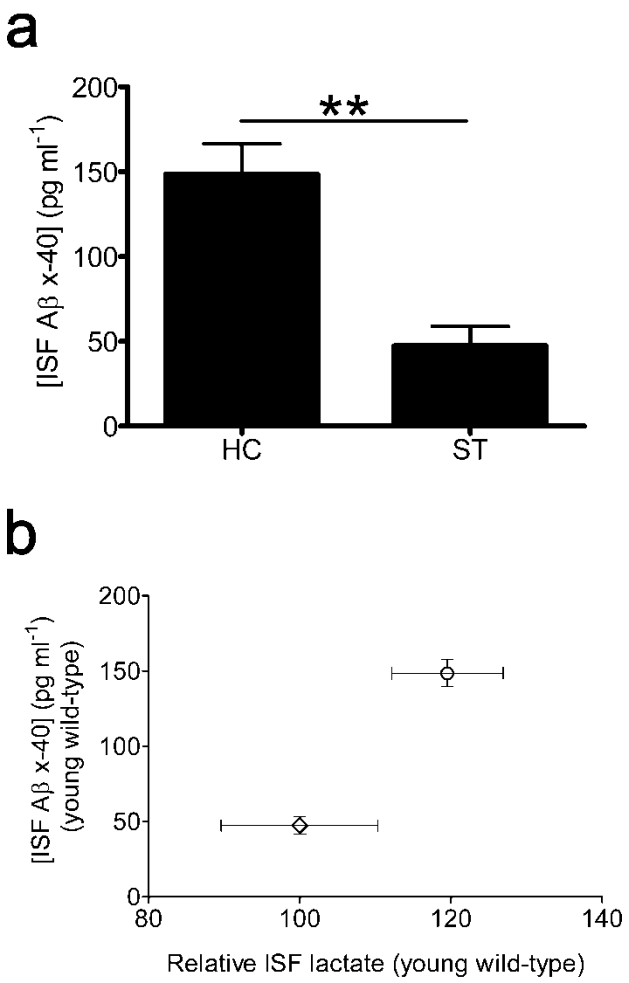
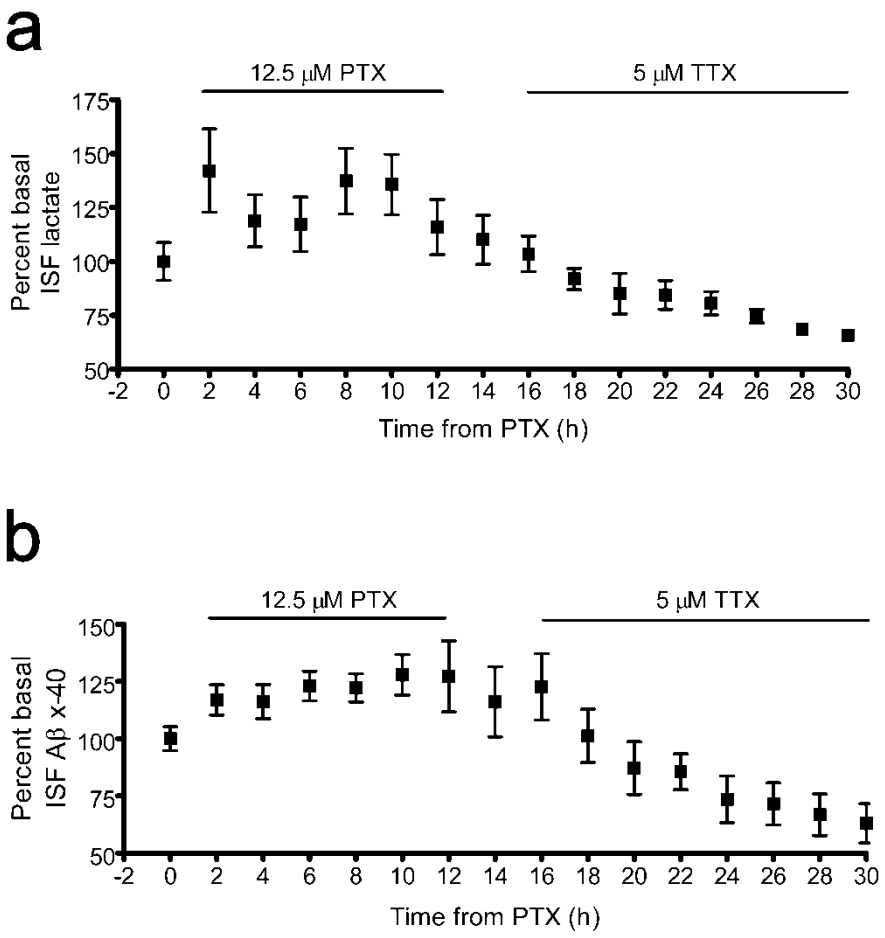
Supplemental Information:

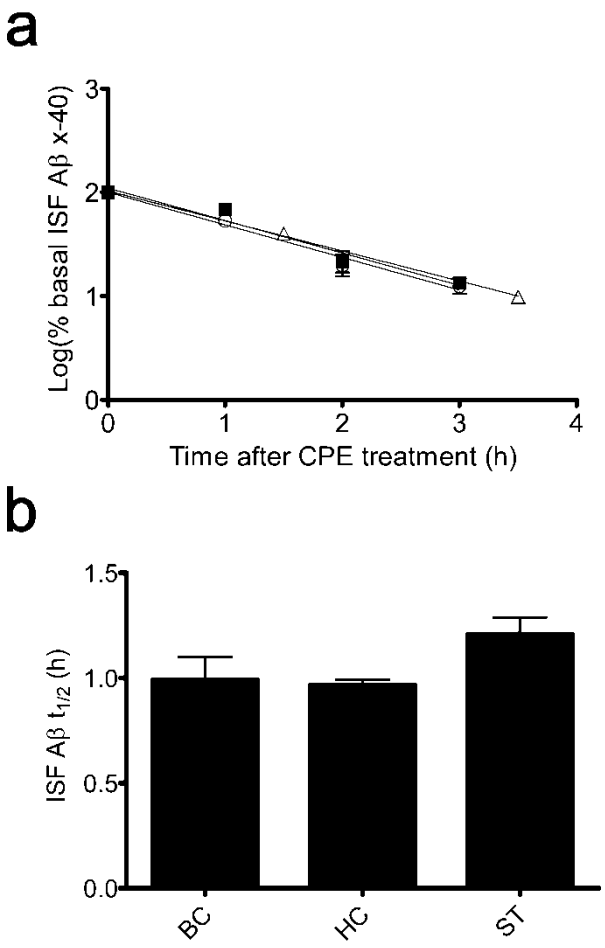
Supplementary Figures 1–5



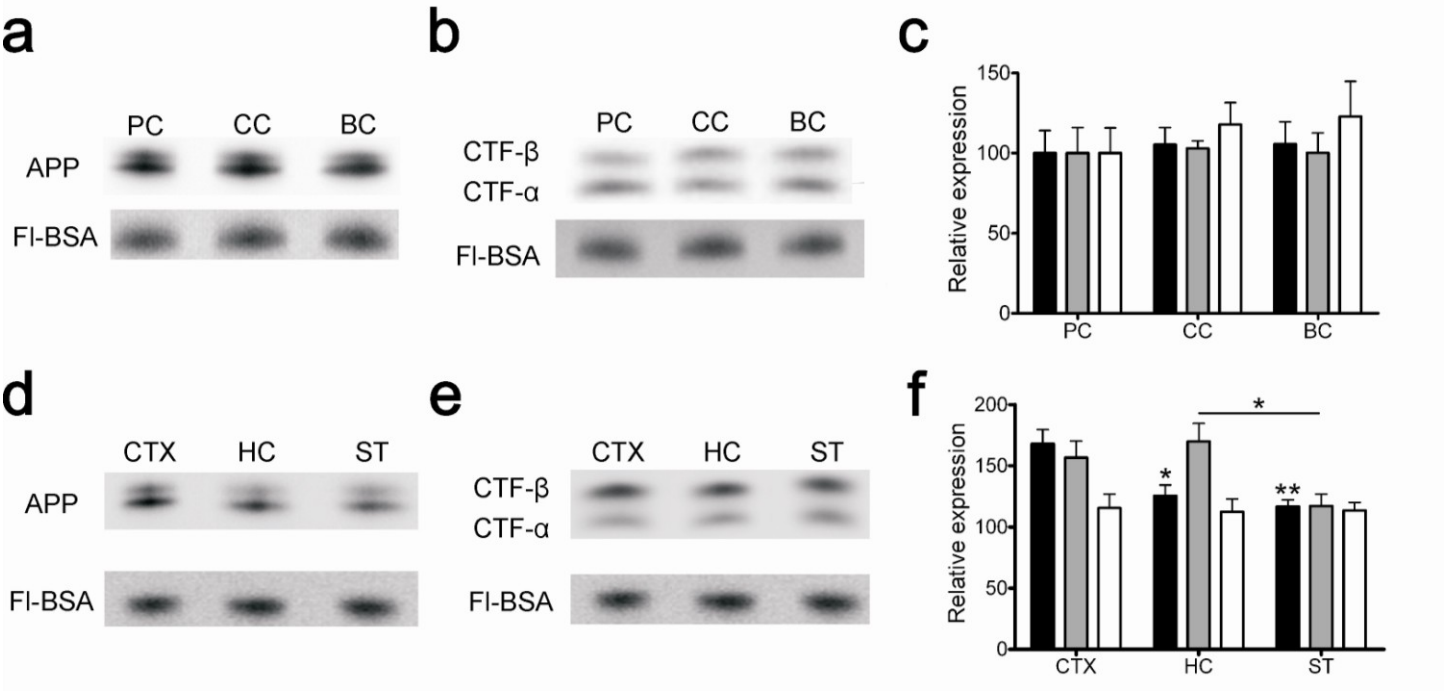
Supplementary Figure 1 Regional ISF Aβ and lactate levels in wild-type (B6SJL) mice. (**a**) In vivo microdialysis was performed in hippocampus and striatum of 5.5 ± 0.5 month-old wild-type (B6SJL) mice. Murine ISF $A\beta_{x\text{-}40}$ levels were significantly greater in hippocampus compared to striatum (n = 4 per group; two-tailed t-test). (**b**) Murine ISF $A\beta_{x\text{-}40}$ levels were closely associated with ISF lactate levels in a region-specific manner (n = 4). ◊, striatum; ○, hippocampus. **, $P < 0.01$. Values represent mean ± SEM.



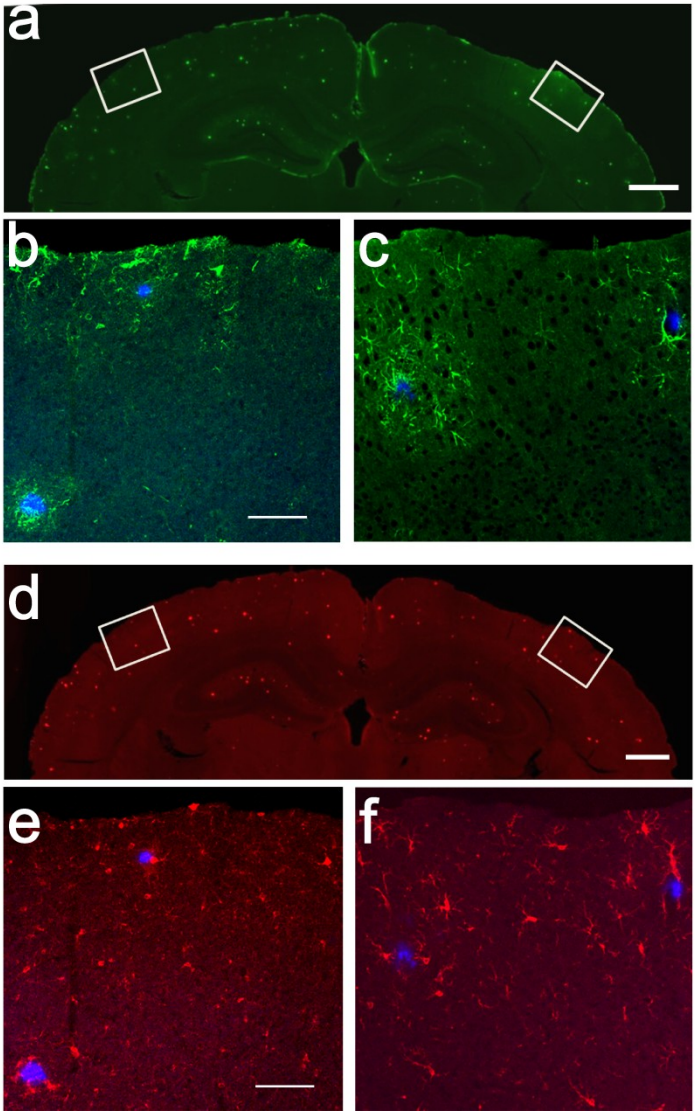
Supplementary Figure 2 Time course of picrotoxin and tetrodotoxin treatment on ISF $A\beta_{x\text{-}40}$ and lactate levels in hippocampus. (**a**,**b**) Young (3.5 ± 0.5 month-old) Tg2576 mice were treated sequentially with picrotoxin (12.5 μM; PTX) and tetrodotoxin (5 μM; TTX) via reverse microdialysis during the microdialysis sampling period. (**a**) ISF lactate and (**b**) $A\beta_{x\text{-}40}$ levels were increased during PTX treatment and decreased during TTX treatment (*n* = 4 per group). Values represent mean ± SEM.



Supplementary Figure 3 ISF $A\beta_{x\text{-}40}$ clearance rates across brain regions of young Tg2576 mouse brain. (**a**,**b**) After baseline ISF $A\beta_{x\text{-}40}$ levels were established, young (3.5 ± 0.5 month-old) Tg2576 mice were treated with a potent γ-secretase inhibitor, Compound E (CPE; 10 mg kg^{-1}), during the microdialysis sampling period to halt Aβ synthesis and permit ISF $A\beta_{x\text{-}40}$ $t_{1/2}$ determination. ISF $A\beta_{x\text{-}40}$ $t_{1/2}$ did not differ across barrel cortex (BC), hippocampus (HC) and striatum (ST; *n* = 4 per group; one-way ANOVA, Tukey's post hoc test for multiple comparisons). ○, barrel cortex; ■, hippocampus; Δ, striatum. Values represent mean ± SEM.



Supplementary Figure 4 APP expression and processing are not associated with regional ISF Aβ levels or plaque deposition. (**a**–**c**) Piriform (PC), cingulate (CC) and barrel (BC) cortices were dissected from fresh brain sections (500 μm thick) of young (3.5 ± 0.5 month-old) Tg2576 mice. Dissected tissue samples were analyzed for expression of (**a**) full-length APP, (**b**) CTF-β and CTF-α by western blot analysis. APP and CTF expression in each lane was normalized to fluorescein-conjugated bovine serum albumin (Fl-BSA) loading control. (**c**) Expression of APP, CTF-β and CTF-α did not differ across piriform, cingulate and barrel cortices (*n* = 6 per group; one-way ANOVA, Tukey's post hoc test for multiple comparisons). (**d**–**f**) Whole cortex (CTX), hippocampus (HC) and striatum (ST) were dissected from fresh brain tissue of young (3.5 ± 0.5 month-old) Tg2576 mice. Dissected tissue samples were analyzed for expression of (**d**) full-length APP, (**e**) CTF-β and CTF-α by western blot analysis. APP and CTF expression in each lane was normalized to Fl-BSA loading control. (**f**) Expression of full-length APP was significantly greater in cortex compared to hippocampus and striatum. CTF-β expression was greater in hippocampus compared to striatum. CTF-α expression did not differ significantly across brain regions (*n* = 7 per group; one-way ANOVA, Tukey's post hoc test for multiple comparisons). ■, full-length APP; ■, CTF-β; □, CTF-α. *, $P < 0.05$; **, $P < 0.01$. Panels **a**,**b**,**d**,**e** contain cropped blots. Values represent mean ± SEM.



Supplementary Figure 5 Glial activation in barrel cortex following long-term vibrissae deprivation. (**a**) Low-power image of a representative brain section from an APP/PS1 (7–7.5 months old) mouse that underwent 28-day unilateral vibrissae deprivation stained with an anti-GFAP antibody to visualize astrocytes (green) and counter-stained with X-34 to visualize amyloid plaque deposition (blue). No clear difference in GFAP staining was evident between vibrissae-deprived (left; **b**) and control (right; **c**) hemispheres (*n* = 6). (**d**) Low-power image of a representative brain section from an APP/PS1 (7–7.5 months old) mouse that underwent 28 day unilateral vibrissae deprivation stained with an anti-Iba-1 antibody to visualize microglia (red) and counter-stained with X-34 to visualize amyloid plaque deposition (blue). No clear difference in Iba-1staining was present between vibrissae-deprived (left; **e**) and control (right; **f**) hemispheres (*n* = 6). White rectangles in **a**,**d** denote barrel cortex. Scale bars in **a**,**d**, 1 mm; scale bars in **b**,**e**, 50 μM.