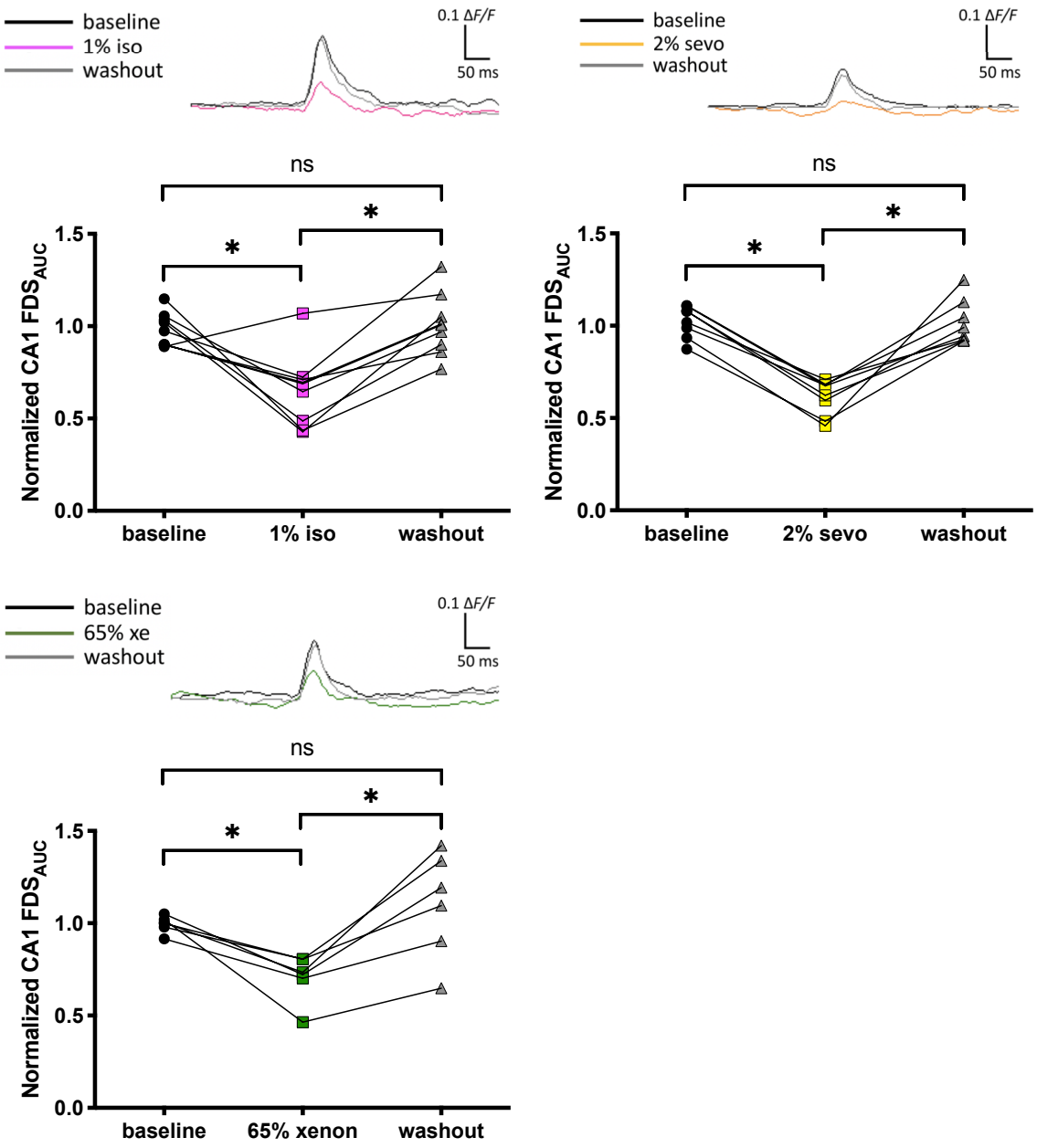
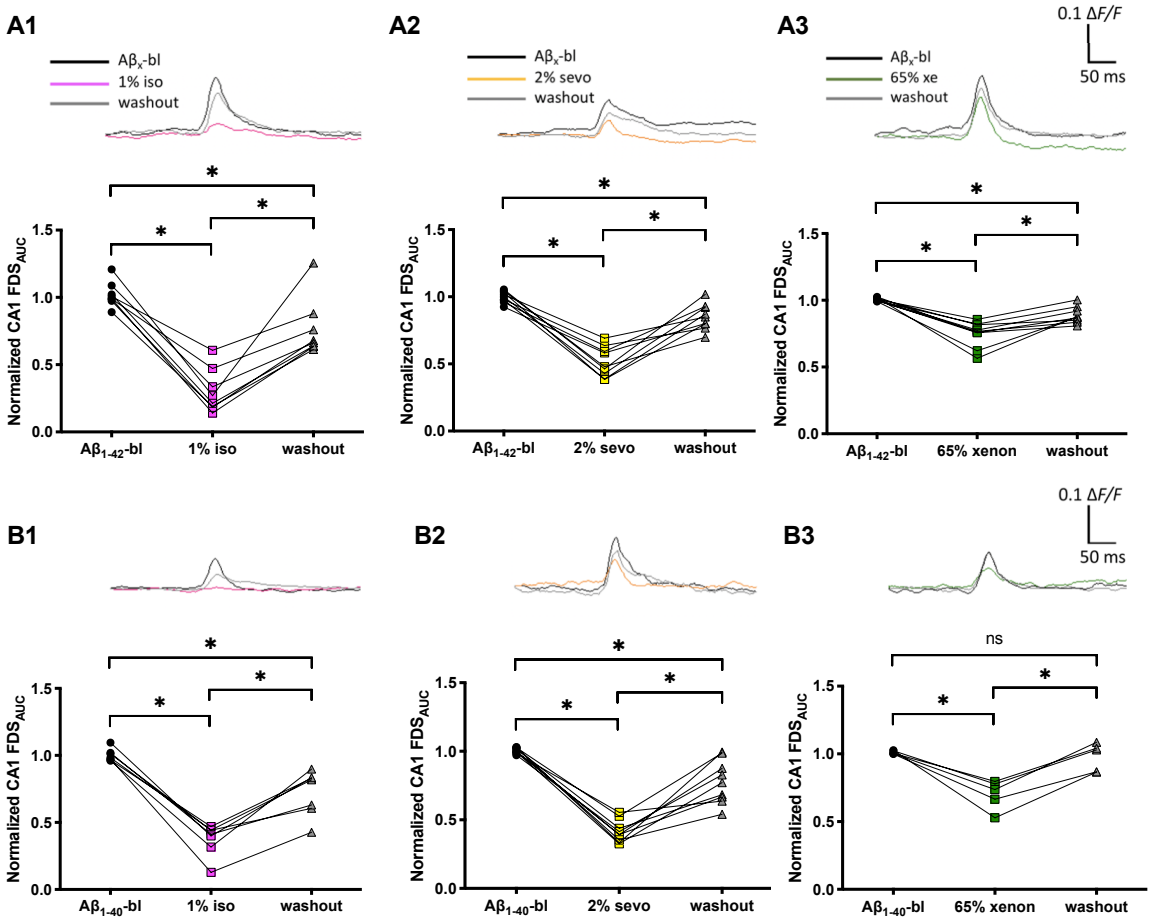
Supplementary Material

Inhalational Anesthetics Do Not Deteriorate Amyloid-β-Derived Pathophysiology in Alzheimer's Disease: Investigations on the Molecular, Neuronal, and Behavioral Level

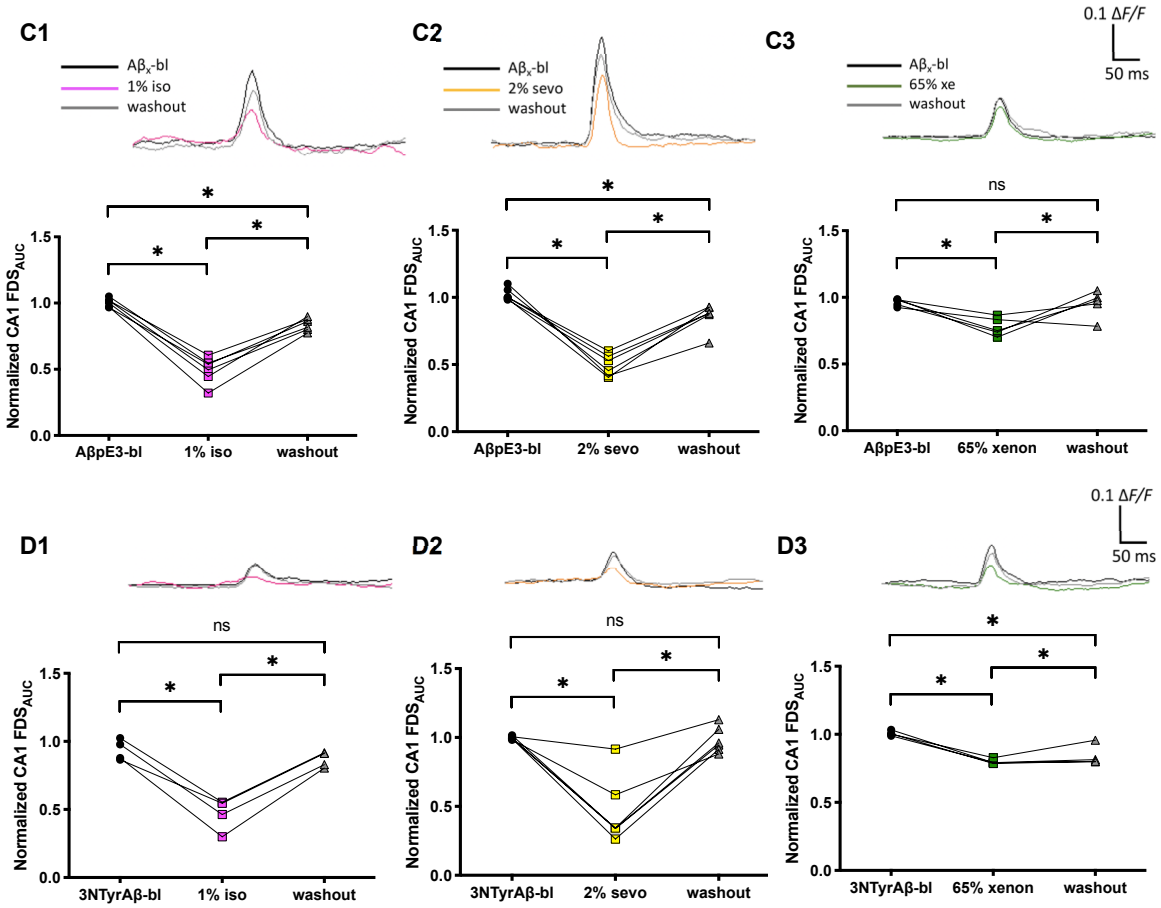


Supplementary Figure 1. Effects of anesthetics on neuronal activity in the hippocampus. 1% isoflurane (iso) decreased neuronal activity represented here as the normalized FDS_{AUC} ($\Delta F/F$) of the VSDI signal in the CA1 region significantly (baseline (bl): 0.97 ± 0.03, 1% iso: 0.69 ± 0.06,

p=0.0006; n=8). The activity recovered back to bl-levels after a washout (wo) of 60 min (wo: 1.01 ± 0.05; p≥0.9999, n=8). 2% sevoflurane (sevo) decreased neuronal activity significantly (bl: 1.05 ± 0.03, 2% sevo: 0.65 ± 0.03; p≤0.0001, n=8). The activity recovered back to bl-levels after a washout of 60 min (wo: 0.97 ± 0.04; p≥0.9999, n=8). 65% xenon decreased neuronal activity significantly (bl: 1.00 ± 0.02, 65% xenon: 0.73 ± 0.05; p=0.0382, n=6). The activity recovered back to bl-levels after a washout of 60 min (wo: 1.14 ± 0.12; p=0.5879, n=6). Representative VSDI recording traces represent the time courses of the average of $\Delta F/F$ values within the CA1 region at baseline conditions, after treatment with anesthetics and after washout.



Supplementary Figure 2.1. After removal of anesthetics, neuronal activity tends not to fully recover in the presence of Aβ isoforms. A1-A3) 1% isoflurane (iso), 2% sevoflurane (sevo), and 65% xenon (xe) decreased neuronal activity in the presence of $A\beta_{1\text{-}42}$ significantly (A1: $A\beta_{1\text{-}42}$-baseline (-bl): 1.00 ± 0.03, 1% iso: 0.24 ± 0.06; p≤0.0001, n=8; A2: $A\beta_{1\text{-}42}$-bl: 1.00 ± 0.01, 2% sevo: 0.48 ± 0.04; p≤0.0001, n=9; A3: $A\beta_{1\text{-}42}$-bl: 1.00 ± 0.004, 65% xe: 0.77 ± 0.03; p≤0.0001, n=9). The activity did not recover to $A\beta_{1\text{-}42}$ bl-levels after a washout (wo) of 60 min (A1: wo: 0.67 ± 0.08; p=0.0165, n=8; A2: wo: 0.85 ± 0.03; p=0.0054, n=9; A3: wo: 0.87 ± 0.02; p=0.0025, n=9). B1-B3) 1% iso, 2% sevo, and 65% xe decreased neuronal activity in the presence of $A\beta_{1\text{-}40}$ significantly (B1: $A\beta_{1\text{-}40}$-bl: 0.98 ± 0.02, 1% iso: 0.41 ± 0.04; p≤0.0001, n=7; B2: $A\beta_{1\text{-}40}$-bl: 1.00 ± 0.007, 2% sevo: 0.39 ± 0.03; p≤0.0001, n=9; B3: $A\beta_{1\text{-}40}$-bl: 1.00 ± 0.006, 65% xenon: 0.74 ± 0.05; p=0.0003, n=5). Activity of B1 and B2 did not recover to $A\beta_{1\text{-}40}$-bl-levels after a wo of 60 min (B1: wo: 0.82 ± 0.06; p=0.0014, n=7; B2: wo: 0.77 ± 0.05; p=0.0003, n=9; B3: wo: 1.03 ± 0.05; p=0.0330, n=5). Representative VSDI recording traces represent the time courses of the average of Δ*F*/*F* values within the CA1 region at Aβ conditions, after treatment with anesthetics and after washout.



Supplementary Figure 2.2. After removal of anesthetics, neuronal activity tends not to fully recover in the presence of Aβ isoforms. C1-C3) 1% isoflurane (iso), 2% sevoflurane (sevo), and 65% xenon (xe) decreased neuronal activity in the presence of AβpE3 significantly (C1: AβpE3-baseline (-bl): 1.00 ± 0.01, 1% iso: 052 ± 0.04; p≤0.0001, n=6; C2: AβpE3-bl: 1.00 ± 0.02, 2% sevo: 0.49 ± 0.03; p≤0.0001, n=6; C3: AβpE3-bl: 0.98 ± 0.01, 65% xenon: 0.75 ± 0.03; p=0.0048, n=5). Here, only the activity of group C3 recovered back to AβpE3-bl-levels after a wo of 60 min (C1: WO: 0.84 ± 0.02; p=0.0017, n=6; C2: wo: 0.88 ± 0.04; p=0.0079, n=6; C3: wo: 0.97 ± 0.045; p≥0.9999, n=5). D1-D3) 1% iso, 2% sevo and 65% xe decreased neuronal activity in the presence of 3NTyrAβ significantly (D1: 3NTyrAβ-bl: 0.93 ± 0.04, 1% iso: 0.5 ± 0.06; p=0.0400, n=4; D2: 3NTyrAβ-bl: 0.99 ± 0.005, 2% sevo: 0.34 ± 0.10; p≤0.0001, n=6; D3: 3NTyrAβ-bl: 1.00 ± 0.009, 65% xenon: 0.79 ± 0.01; p=0.0004, n=4). The activity of D3 did not recover back to 3NTyrAβ-bl-levels after a wo of 60 min, D1 and D2 recovered (D1: wo: 0.87 ± 0.03; p≥0.9999, n=4; D2: wo: 0.95 ± 0.04; p≥0.9999, n=6; D3: wo: 0.81 ± 0.04; p=0.0023, n=4). Representative VSDI recording traces represent the time courses of the average of Δ*F/F* values within the CA1 region at Aβ conditions, after treatment with anesthetics and after washout.