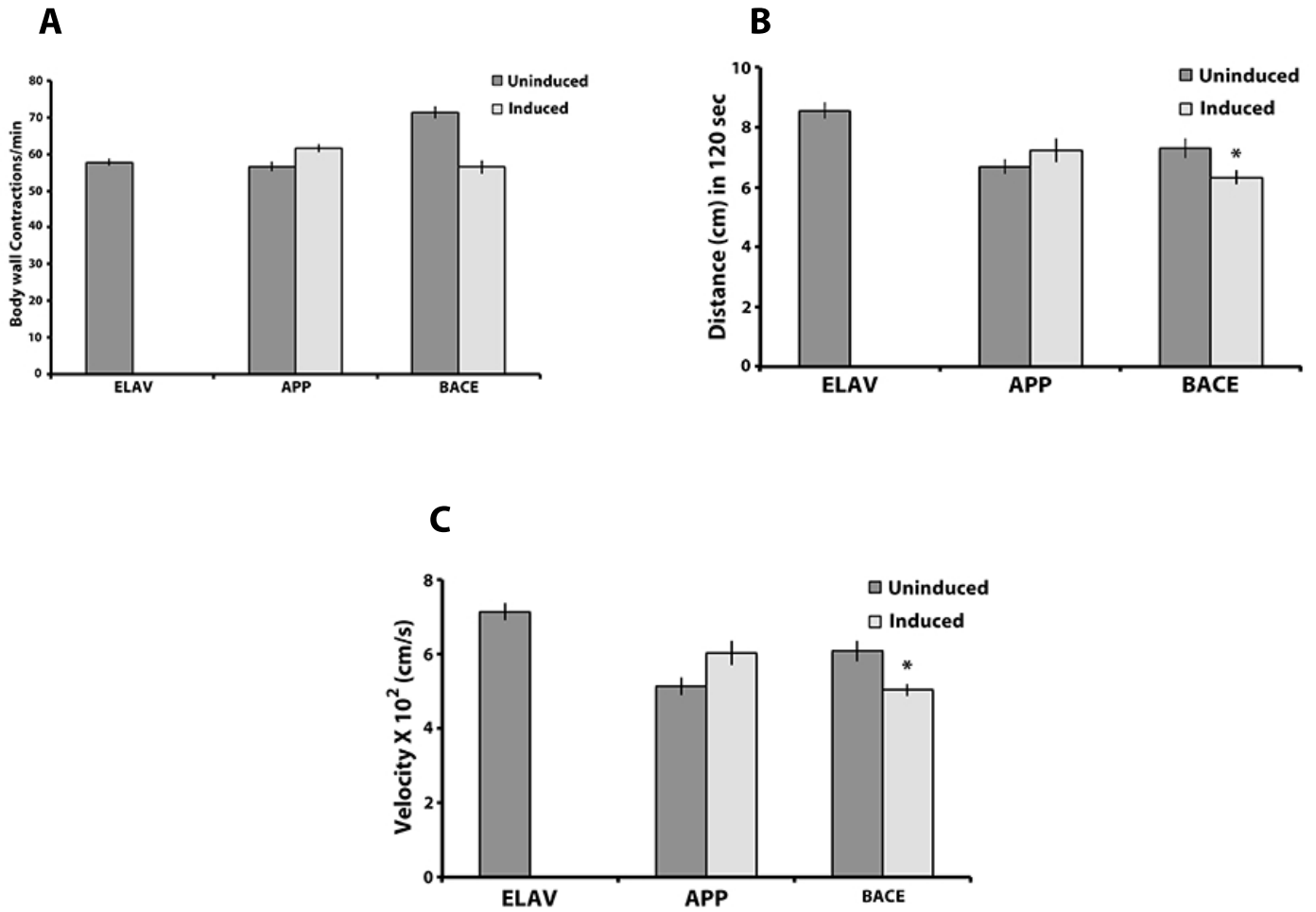


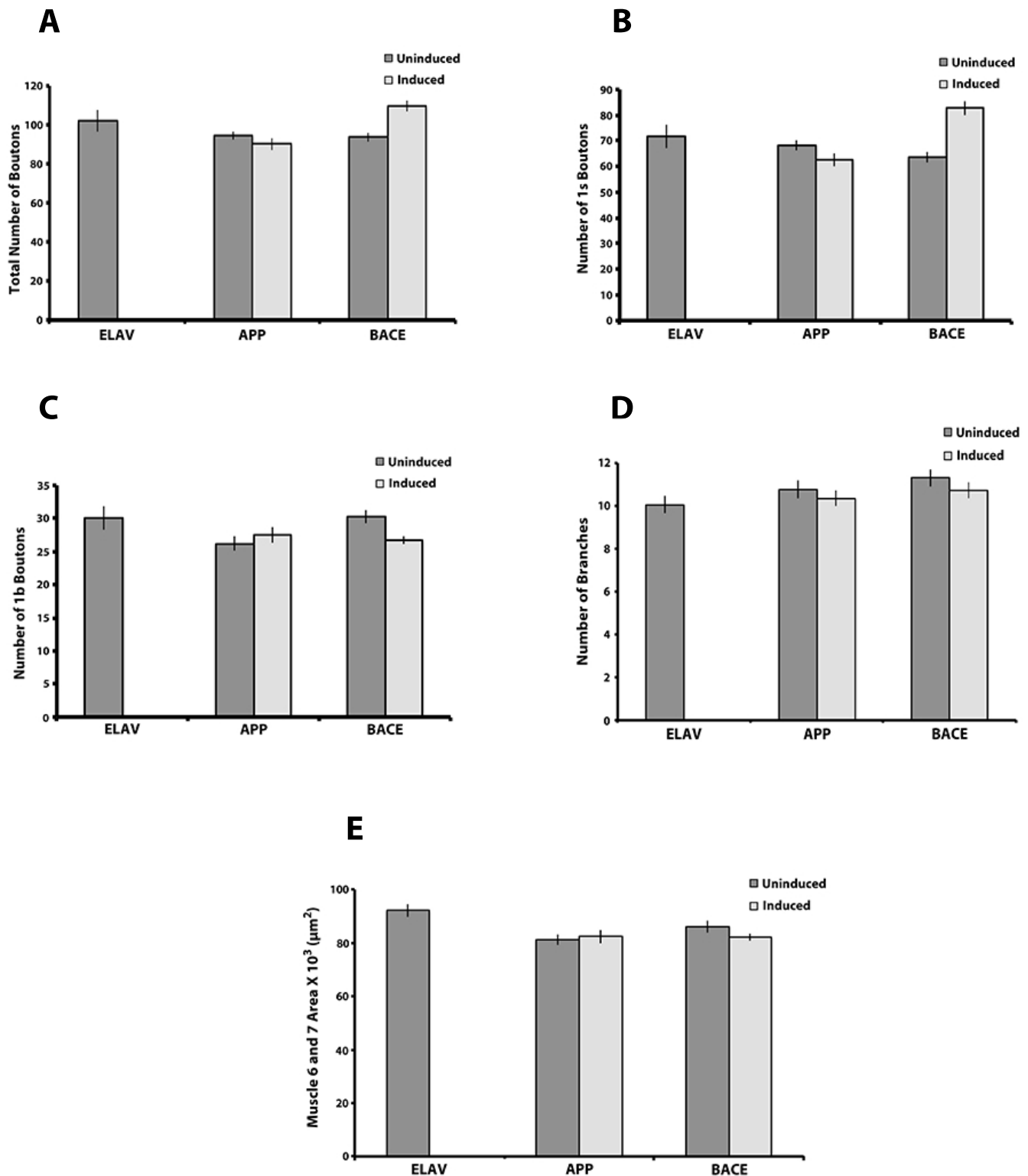
Supplemental Figure 1: Western Blot demonstrating presence of endogenous Appl-CFTs

Western blot analysis of human APP, human BACE, fly Appl and β -actin is detected in fly head lysates. Fly lines over-expressing endogenous Appl and Appl null mutant lines are tested to verify the presence of Appl-CFTs. Lane 1; *elav*; +; + heterozygous flies. Lane 2: *elav*; *APP*; *BACE* (low) heterozygous flies. Lane 3: *elav*; *APP*; *BACE* (high) heterozygous flies. Lane 4: *App1* null mutant flies. Lane 5: *elav*; *App1*; + heterozygous flies. Lane 6: *elav*; +; *BACE*/+ heterozygous flies. Lane 7: +; +; *BACE*/+ heterozygous flies. FL-APP (full length APP, ~110kD), APP-CTFs (C-terminal fragments, ~10-12 kD) and Appl-CFTs (~15 kD) were detected by C1/6.1. BACE (~70kD) was detected by 3D5 antibody. Arrow indicates β -CTFs in lanes 2 and 3. Arrowhead indicates Appl-CFTs in lanes 1-3, 4-6. β -actin antibody was utilized for loading controls.



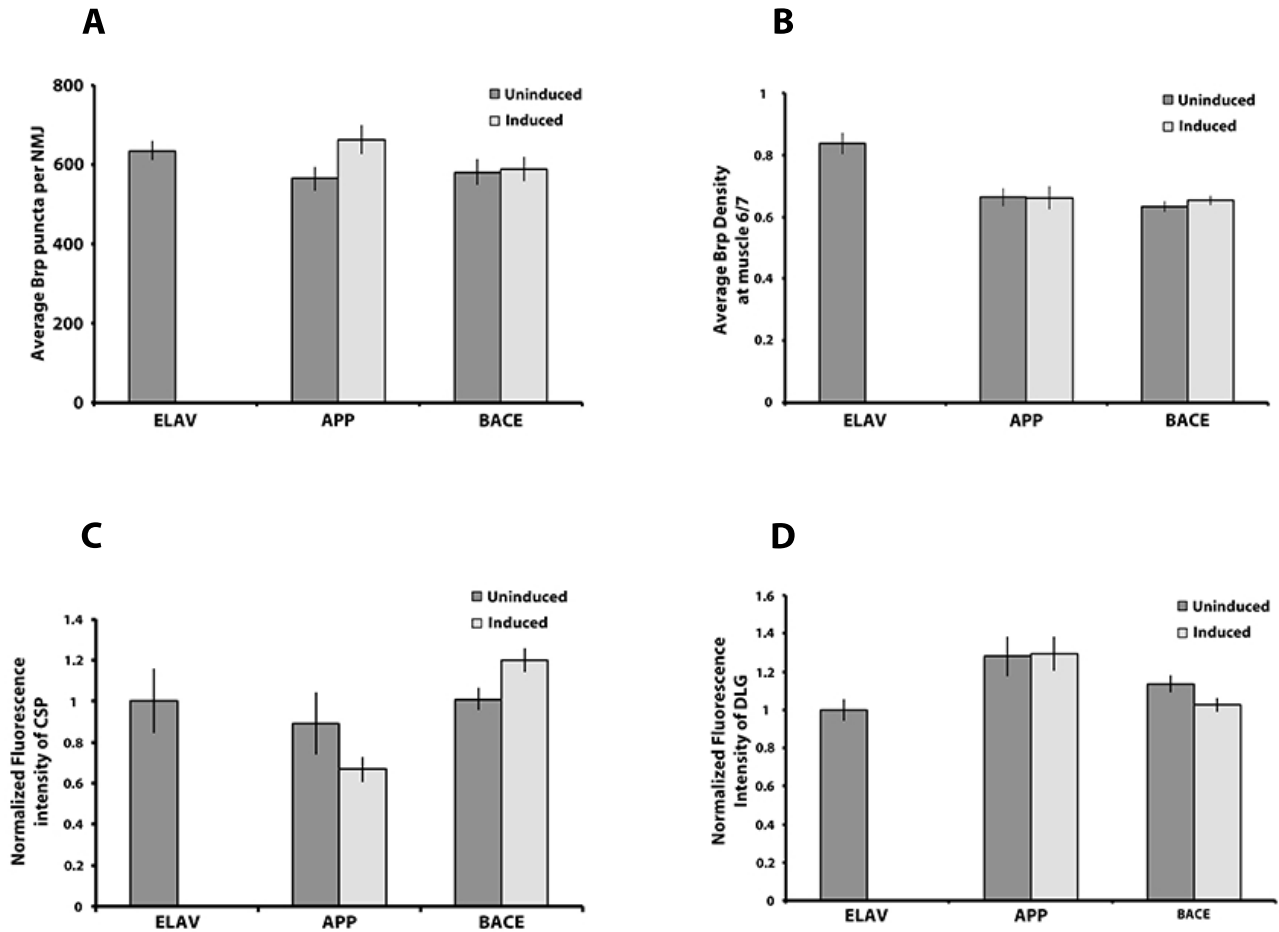
Supplemental Figure 2: Effect of expressing APP alone and BACE alone on behavioral phenotypes of *Drosophila* 3rd instar larvae.

A) Number of body wall contraction per minute of third instar larvae under induced (*Gal4* with *UAS*) and uninduced (*Gal4* or *UAS* alone) conditions ($n > 30$). **B)** Distance crawled by larvae in 120 sec ($n > 30$). **C)** Crawling velocity in cm/sec for the third instar larvae under examination ($n > 30$). Treatments are indicated. * indicates p -value < 0.05 . Error bar represents standard error in each case.



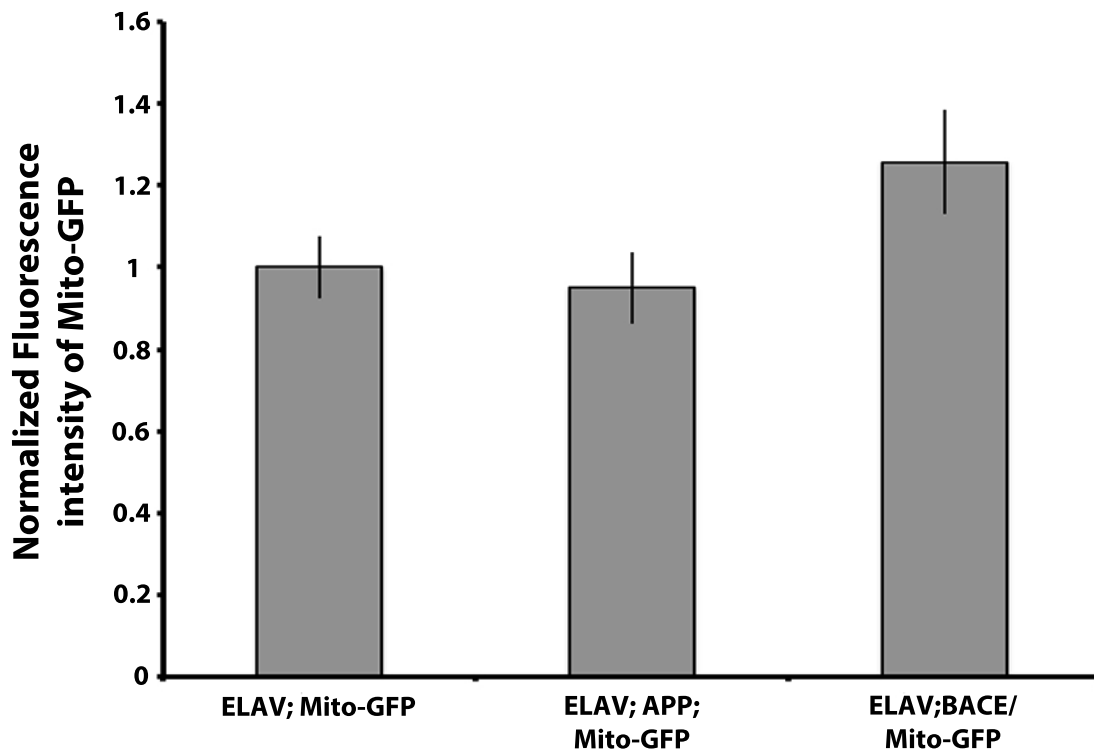
Supplemental Figure 3: Expressing APP alone and BACE alone does not alter synapse formation.

Histogram depicts quantitative analysis of bouton and branch number on muscles 6 and 7 at abdominal segment 3 of larvae expressing APP alone or BACE alone under induced (*Gal4* with *UAS*) and uninduced (*Gal4* or *UAS* alone), where **A**) Total number of boutons, **B**) Number of 1s type boutons, **C**) Number of 1b type boutons, **D**) Total number of branches, **E**) Average muscle 6 and 7 area. Treatments are indicated. Analysis represents $n > 15$. * indicates p -value < 0.05 . Error bar represents standard error in each case.



Supplemental Figure 4: Expressing APP alone and BACE alone has no effect on pre- and post-synaptic proteins.

Histogram depicts quantitative analysis pre- and post-synaptic proteins present at the synapse formed on muscles 6 and 7 at abdominal segment 3 of larvae expressing APP alone or BACE alone under induced (*Gal4* with *UAS*) and uninduced (*Gal4* or *UAS* alone), where **A**) Average number of active zones per synapse, **B**) Average Brp density, **C**) Normalized Fluorescence intensity of CSP, and **D**) Normalized Fluorescence intensity of DLG. Treatments are indicated. Analysis represents n = 10-14. * indicates p-value < 0.05. Error bar represents standard error in each case.



Supplemental Figure 5: Expressing APP alone and BACE alone has no effect on mitochondrial localization in the motor neurons.

Histogram depicts quantitative analysis of normalized fluorescence intensity of Mito-GFP upon expressing APP alone or BACE alone under induced (*Gal4* with *UAS*) and uninduced (*Gal4* or *UAS* alone). Treatment indicated. Analysis represent n= 10-14. * indicates p-value< 0.05. Error bar represents standard error in each case.