Supplementary Figure legends.

Fig. S1. Brain structure is not altered but phosphorylation of eIF2α is reduced in eIF2α$^{+/S51A}$ mice. Immunohistochemical analysis of the hippocampus of WT and eIF2α$^{+/S51A}$ mice. Coronal brain sections were stained with Nissl stain (**A, B**), and with antibodies against GAP43 (**C**), synaptophysin (**D**) and p-eIF2α (E). There was no visible difference in hippocampal cytoarchitecture between eIF2α$^{+/S51A}$ and WT littermates. Imunohistochemistry (**E**) and Western blots (**F**) show that eIF2α phosphorylation was reduced in the hippocampus from eIF2α$^{+/S51A}$ mice as compared to WT mice. In hippocampal extracts, expression of ATF4 (**G**) is reduced in eIF2α$^{+/S51A}$ mice.

Fig. S2. Normal basal synaptic transmission in eIF2α$^{+/S51A}$ slices.

A,B) Input-output data show similar field excitatory postsynaptic potentials (fEPSPs) over a wide range of stimulus intensities for both eIF2α$^{+/S51A}$ and control (WT) littermates. **C)** Paired-pulse facilitation also did not differ between eIF2α$^{+/S51A}$ and WT slices; normalized data are means (± SEM) of second fEPSP as % of first fEPSP, for various intervals of paired stimulation.

Fig. S3. Normal forskolin-induced L-LTP in eIF2α$^{+/S51A}$ slices.

Means (± SEM) show similar amplitude and time course of L-LTP induced by 50μM forskolin (FSK) in slices from eIF2α$^{+/S51A}$ and WT mice (at 240 min, $p < 0.05$).

Fig. S4. Short term memory is not altered in eIF2α$^{+/S51A}$ mice. Mice were subjected to contextual (**A**) and auditory (**B**) fear conditioning and tested one hour after training.

Fig S5. eIF2α$^{+/S51A}$ mice react normally to sweet and bitter tastes.

A) The preference for saccharin (aversion index < 0.5) did not differ between WT and eIF2α$^{+/S51A}$ mice (WT=4, eIF2α$^{+/S51A}$ mice=4; $p > 0.05$). **B)** On three consecutive days the strong natural aversion to quinine did not differ between WT and eIF2α$^{+/S51A}$ mice (WT: n=4, eIF2α$^{+/S51A}$: n=4; $p > 0.05$). All data are means ± SEM.

Fig. S6. In WT slices, Sal003 did not affect basal transmission, E-LTP and the maintenance of L-LTP. A) LTP elicited by a single 100 Hz train (1 s) is not altered by Sal003 (at 180 min, $p > 0.05$). **B)** Application of Sal003 did not affect base line transmission during 2.5 h of recording ($p > 0.05$). **C)** Sal003 is ineffective if applied 30 min after the end of stimulation, when L-LTP is already established (at 240 min, $p > 0.05$). All data are means ± SEM

Fig. S7. Schematic representation of the dorsal hippocampus at five different rostrocaudal planes. Numbers are posterior coordinates (mm) from bregma. Cannula tip placements in rats infused with Sal003 (filled squares) and vehicle (filled circles).

Fig. S8. Sal003 impairs spatial long-term memory consolidation. Data (means ± S.E.M.) were obtained in the conventional version of the Morris water maze (3 trials per day). **A)** Escape latency during the first trial of each training session is plotted for six

successive days. Sal003 and Vehicle were infused bilaterally into hippocampus immediately after each training session. Note that Sal003-treated rats failed to show overnight memory of the location of the platform. **B)** In the probe test performed after the completion of training, unlike vehicle-treated rats (closed columns, $p < 0.001$) Sal-infused rats (open columns) showed no preference for the target quadrant ($p > 0.05$). Dark syringes refer to either Vehicle or Sal003 infusions across groups.

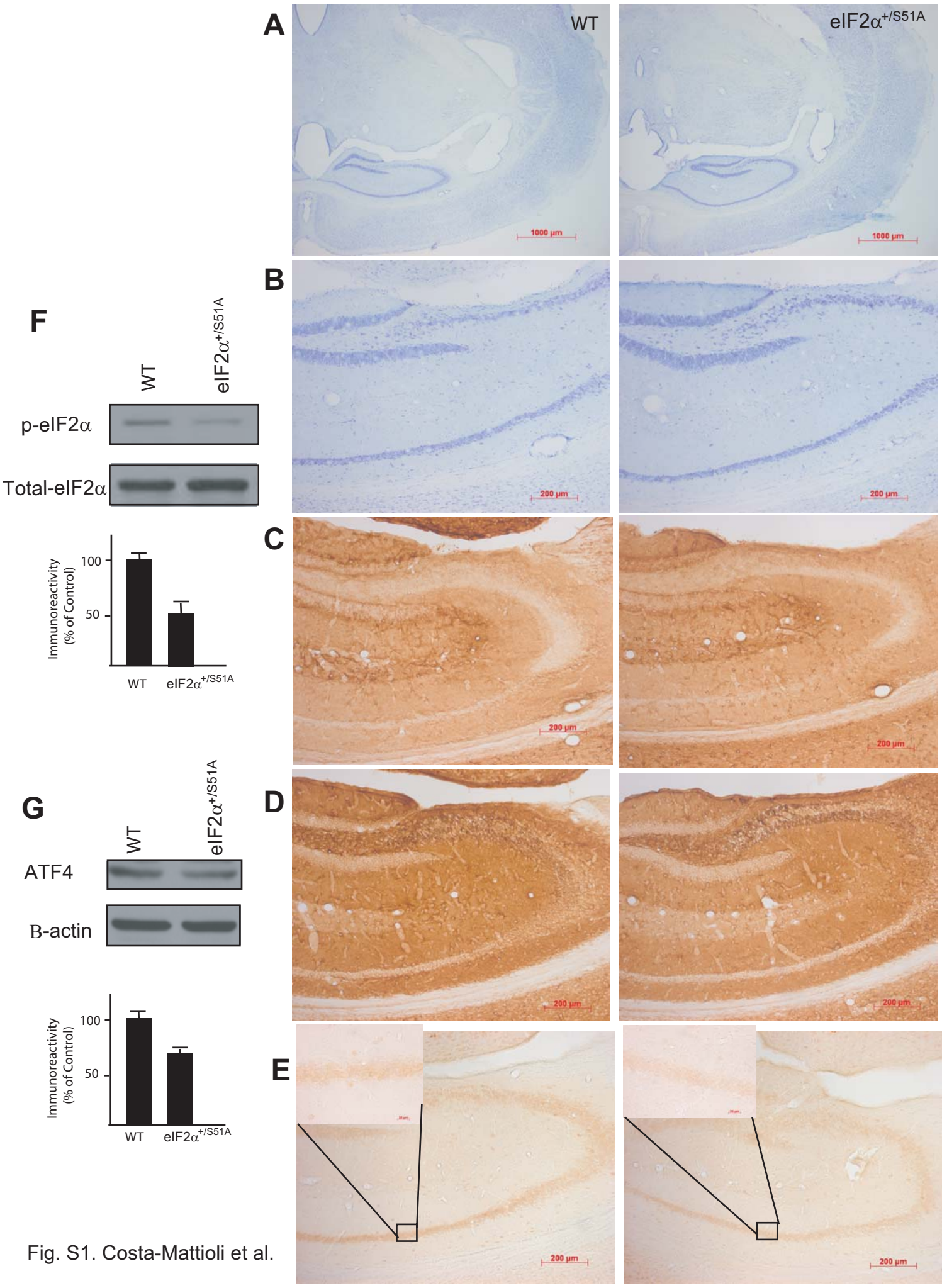


Fig. S1. Costa-Mattioli et al.

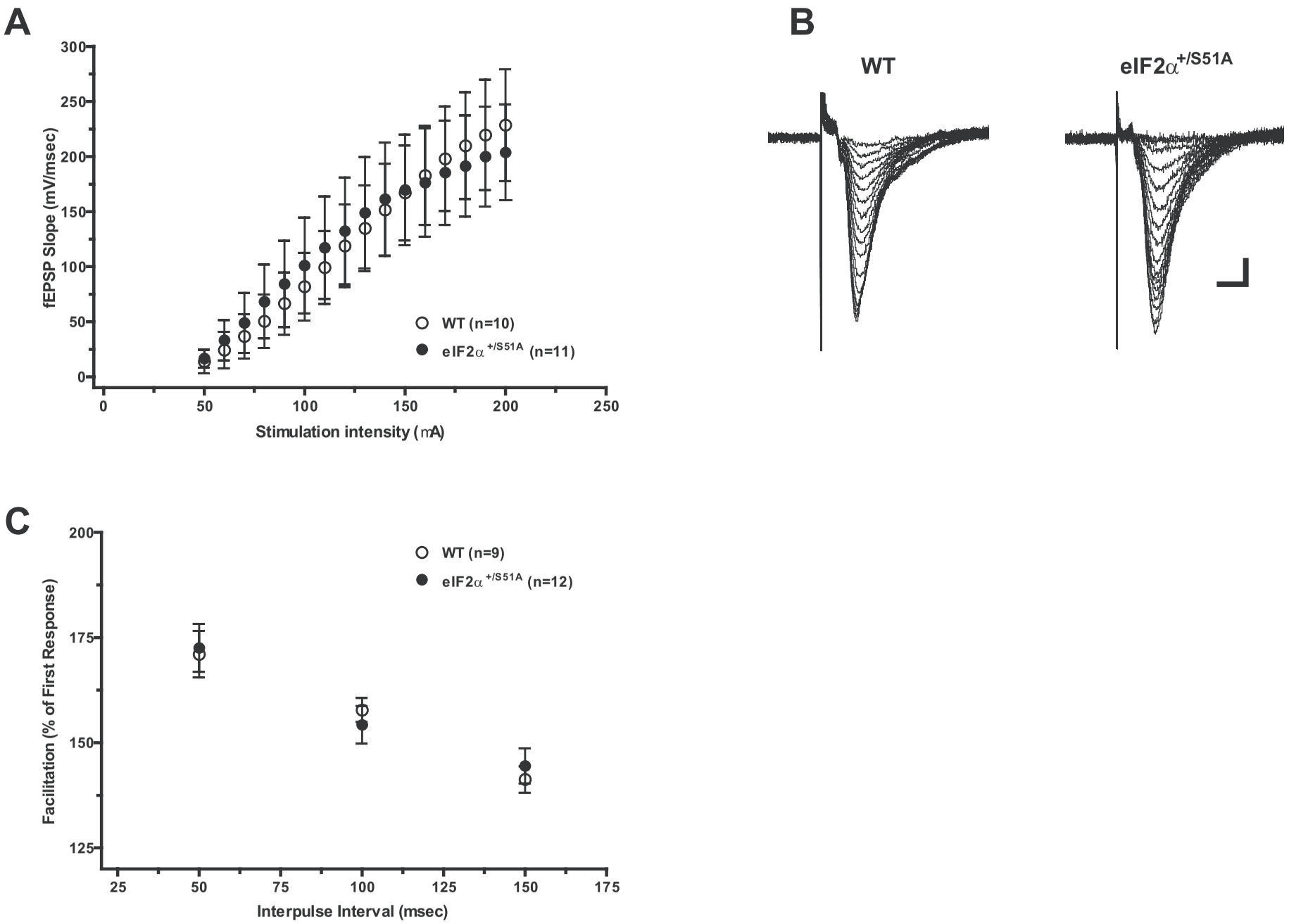
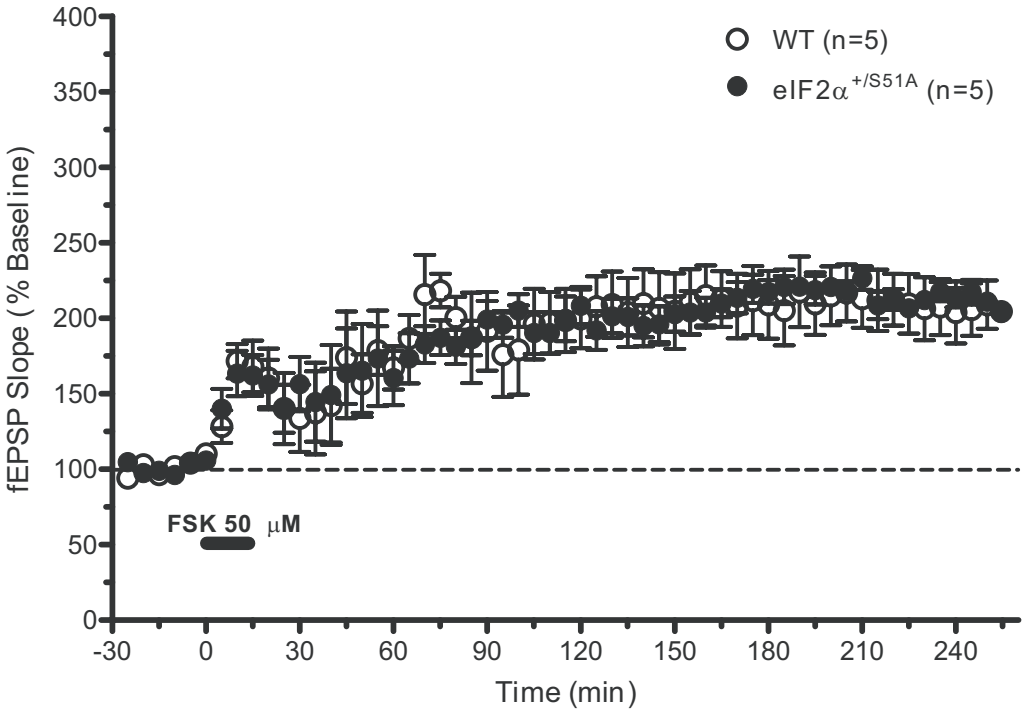


Fig. S2. Costa-Mattioli et al.



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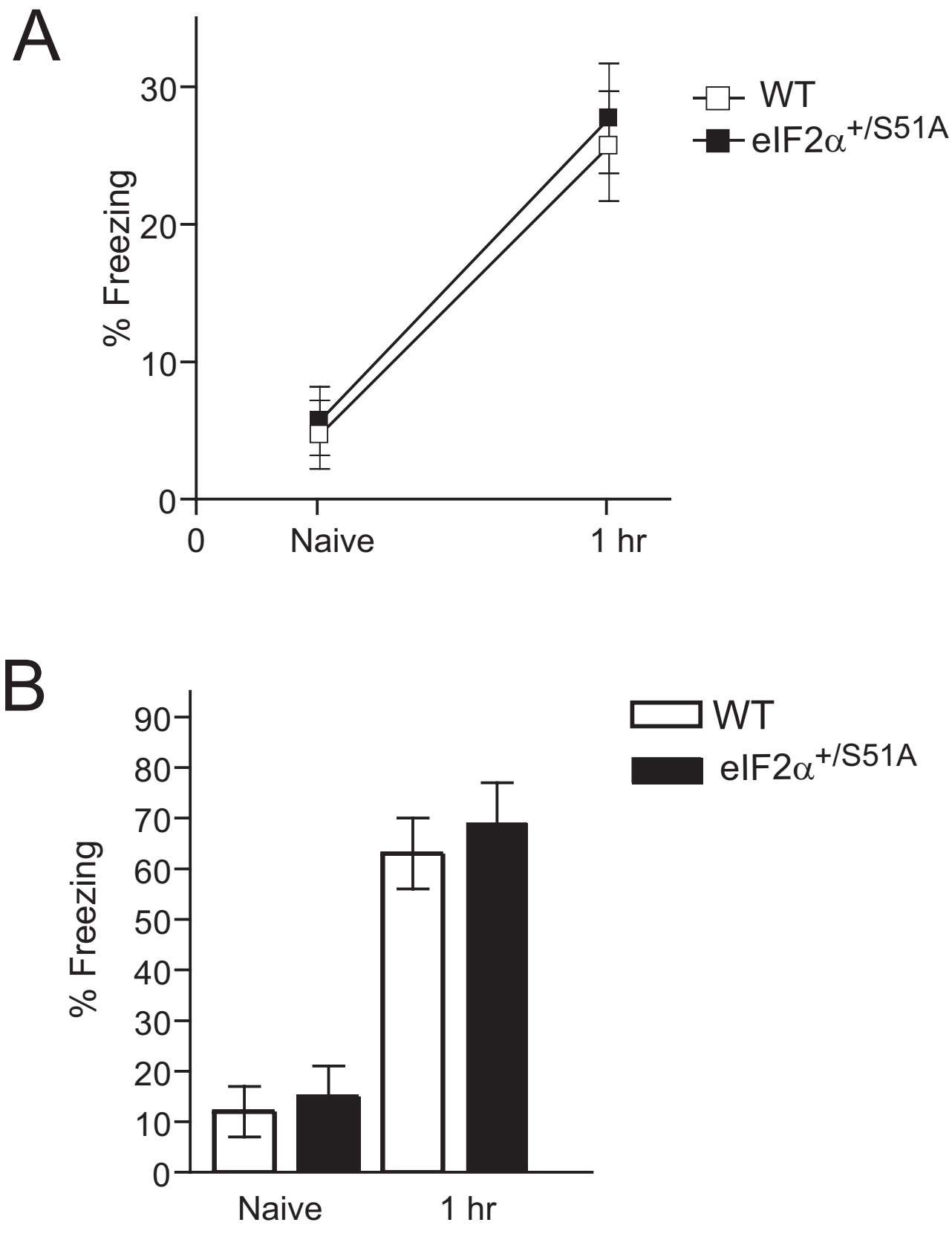


Figure S4. Costa-Mattioli et al.

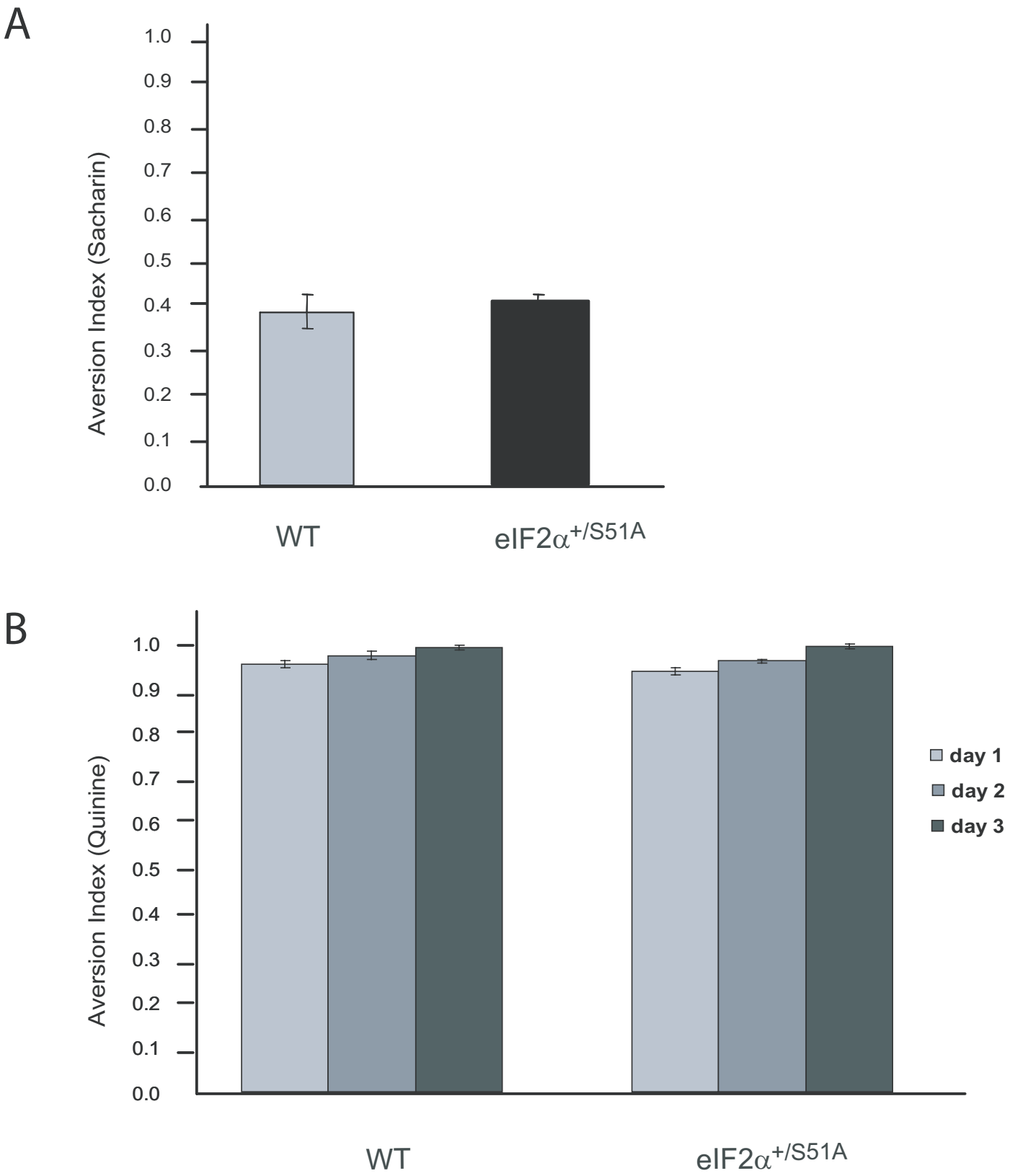
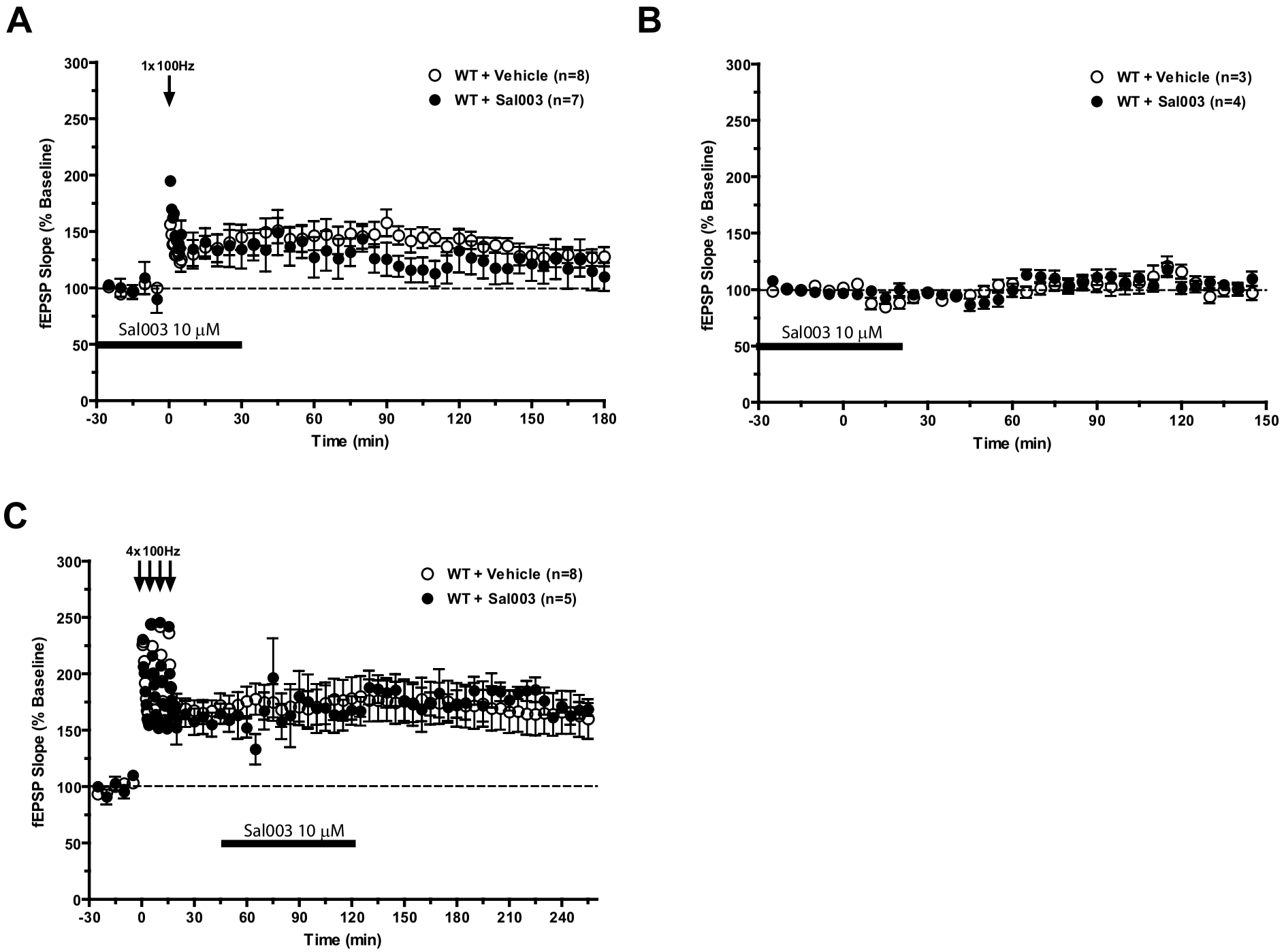


Fig. S5. Costa-Mattioli et al



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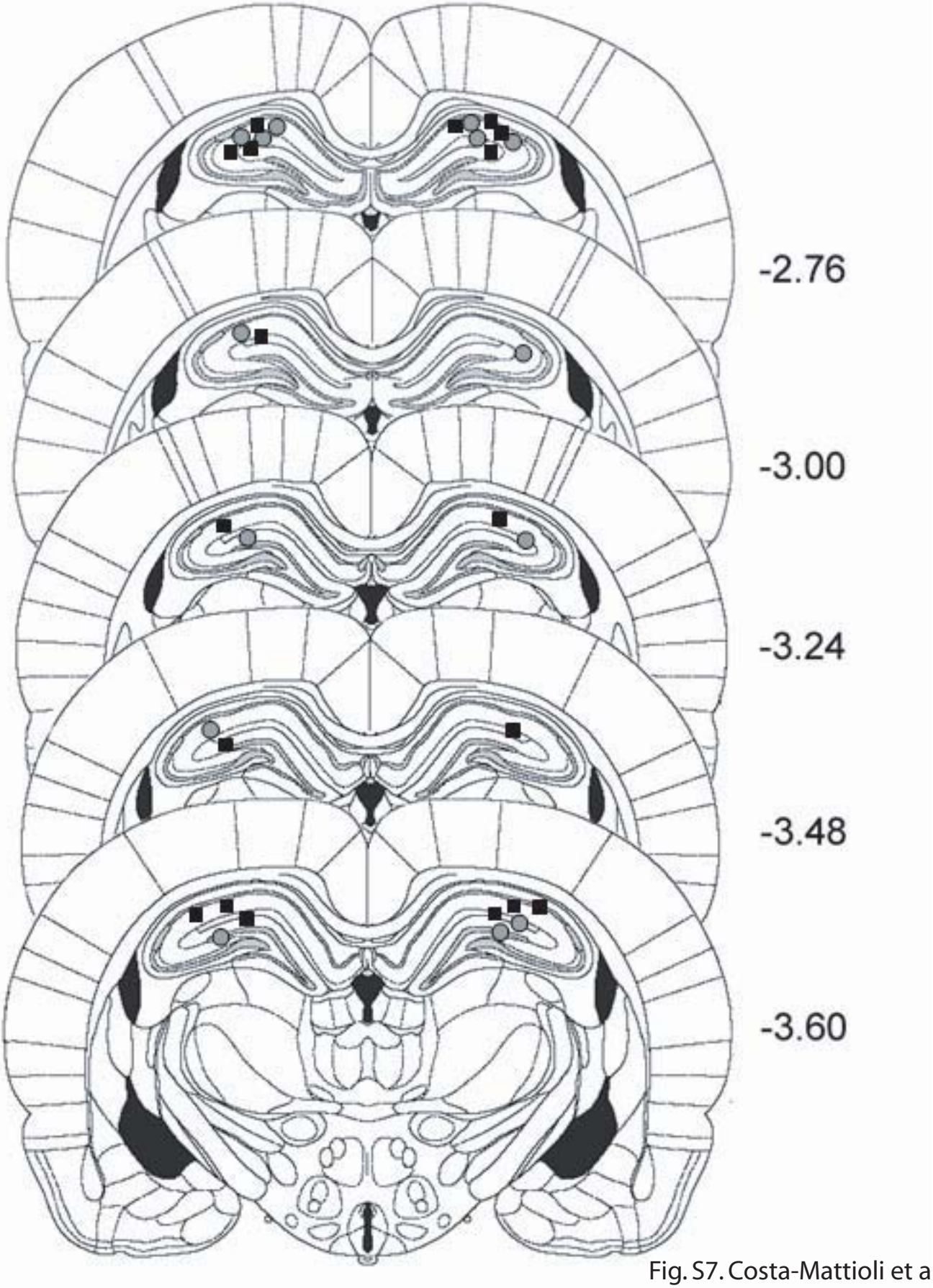

Fig. S7. Costa-Mattioli et al.

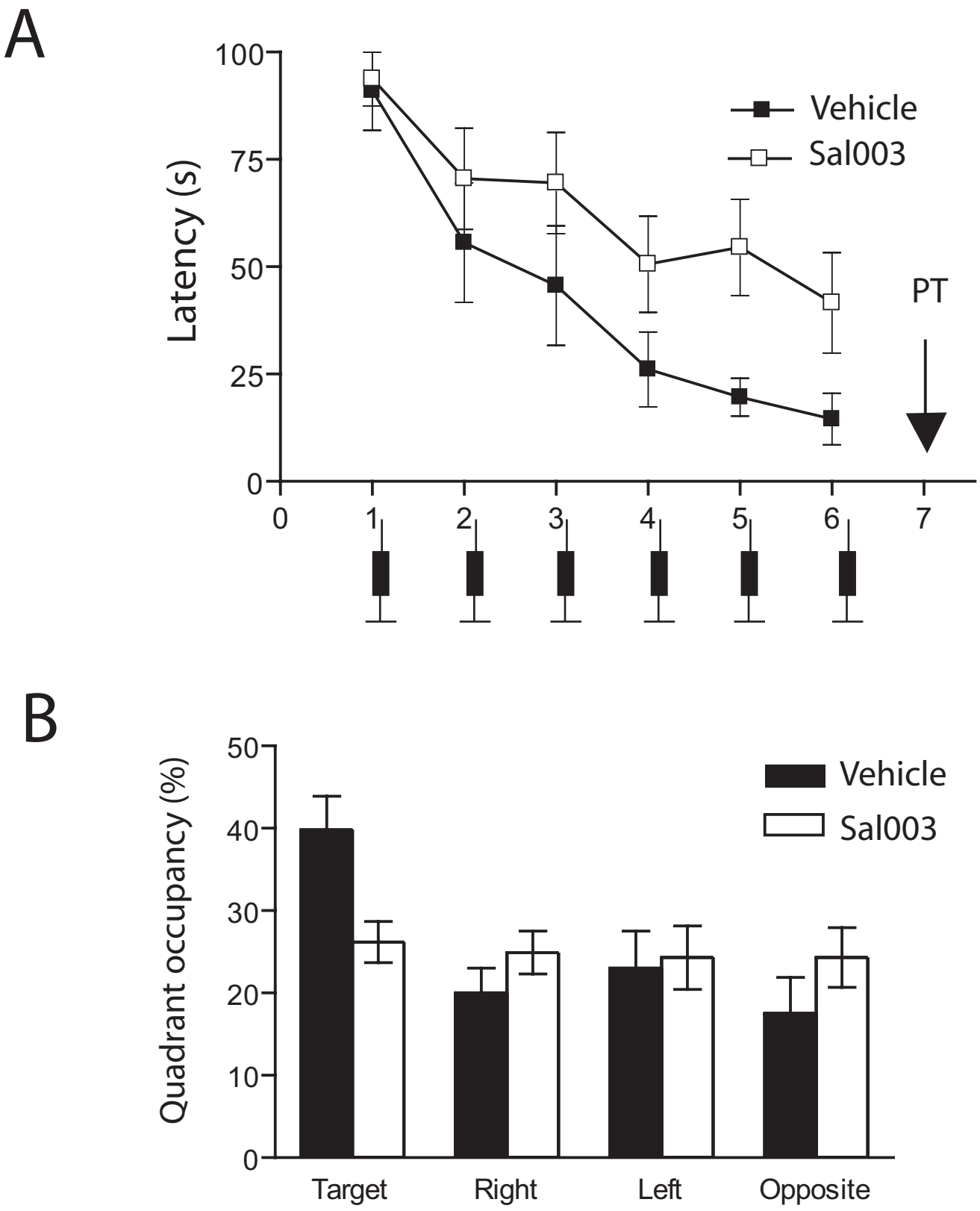

Fig. S8. Costa-Matttioli et al.