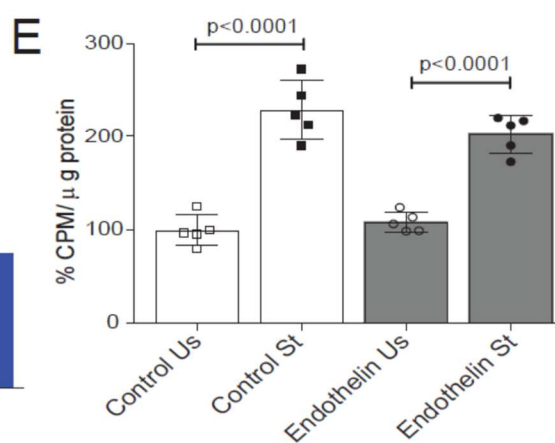
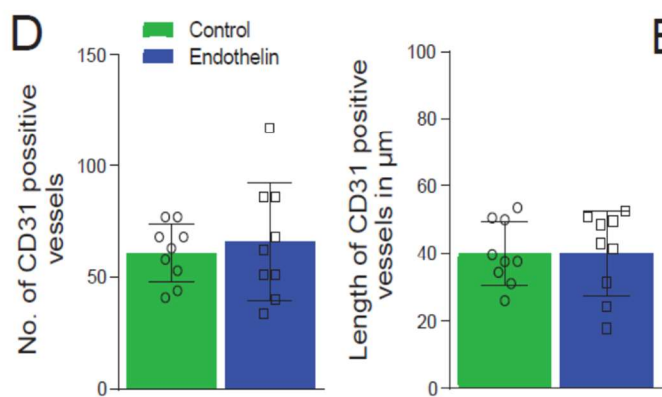
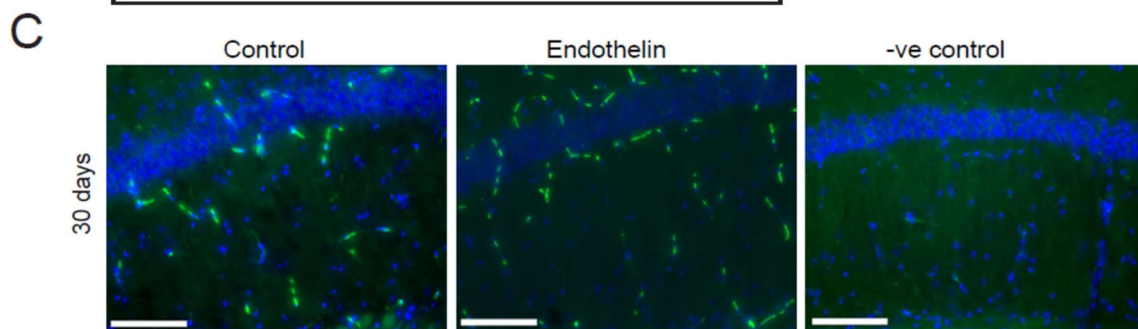
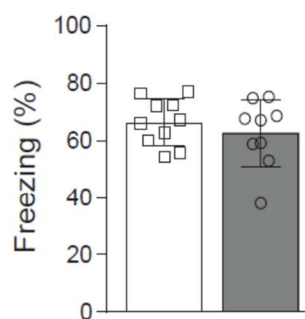
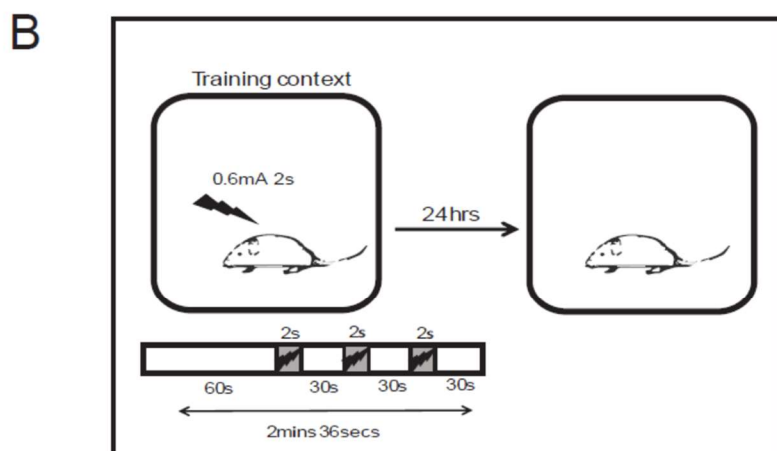
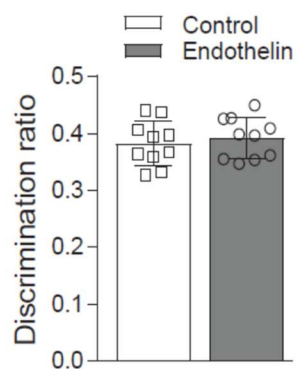
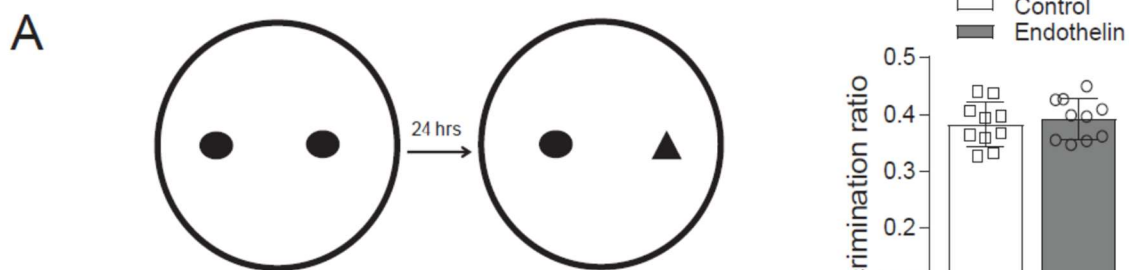
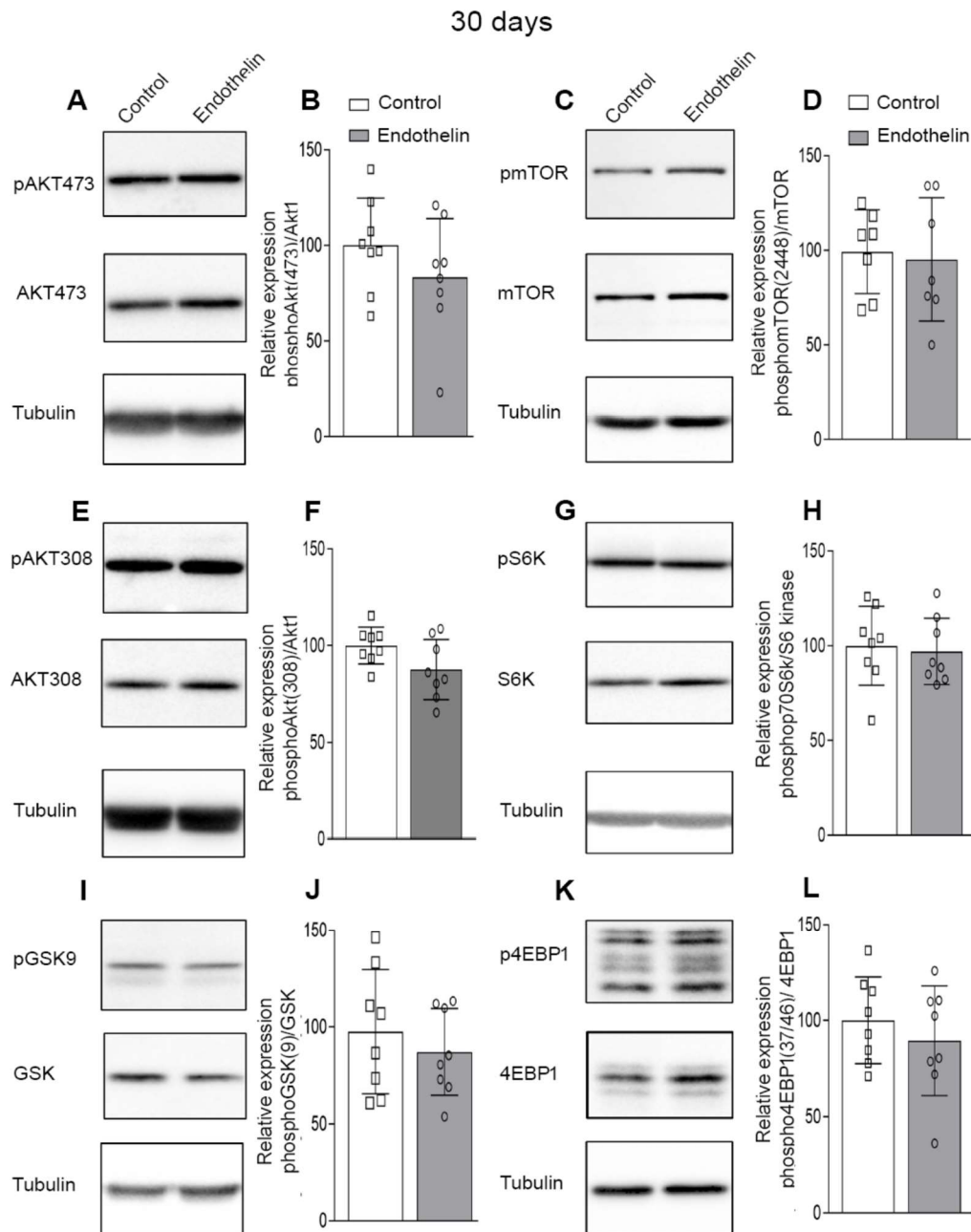


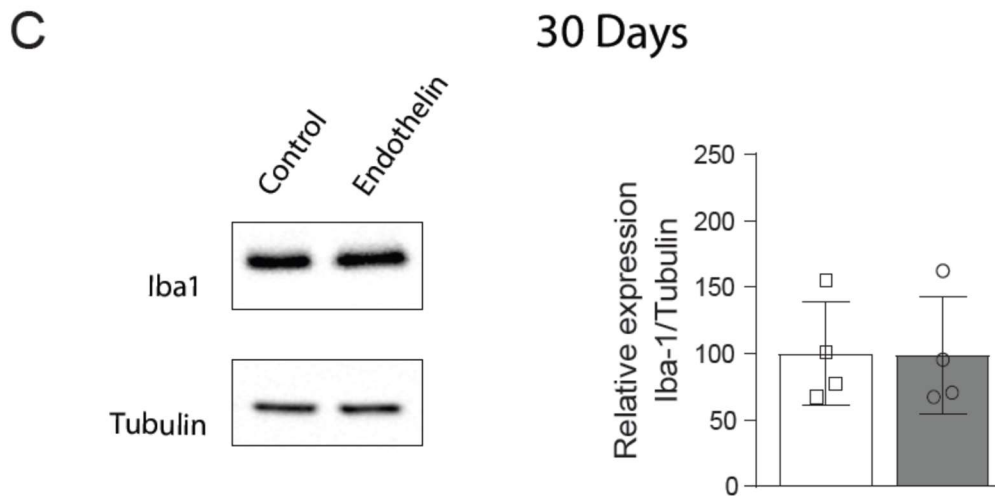
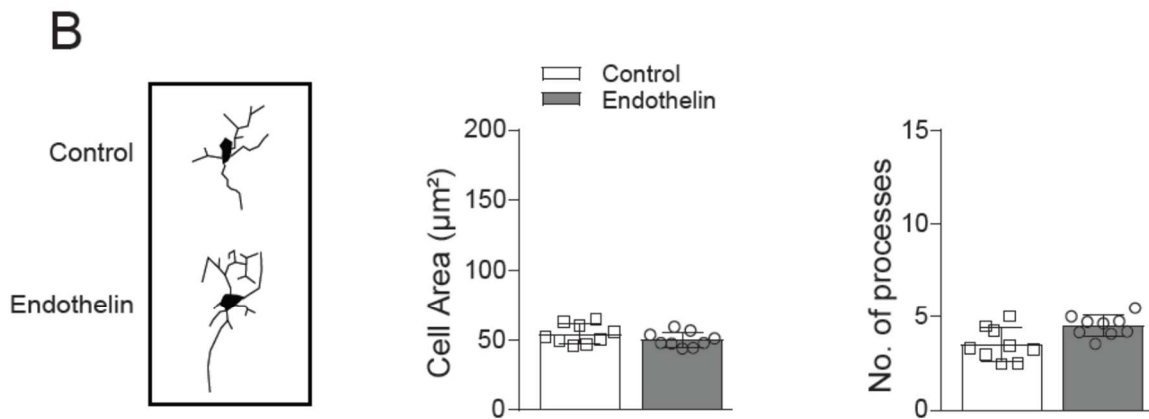
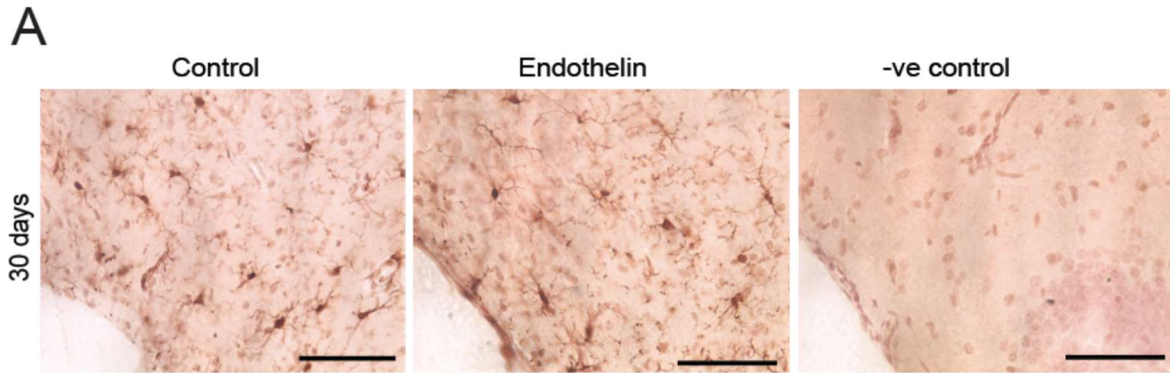
**Supplementary Figure.1. Analysis of footprints and Rotarod balancing for 15 days after ET-1 injection in C57 mice.** **A.** Graph shows the stride and stance length measured in centimeters for 15 days of endothelin treatment. The dashed box depicts the transient increase in stance length (Day3-7) in the mice upon endothelin treatment. The values are mean length of n=8 animals however it was statistically not significant. **B.** Representative footprints to show the measurement of stride and stance length. **C.** Image of rotarod and representative graph to show the measurement of time in seconds the mice able to balance on the rotarod. The values are Mean  $\pm$  SD of n=8 animals.



**Supplementary Figure.2. Reversal in memory deficit and CD31 expression by 30 days of ET-1 treatment.** **A.** Shows graphical representation of novel object paradigm and graph showed no difference in discrimination ratio in ET-1 injected mice after 30 days. The graph shows Mean  $\pm$  SD of n=10 animals p=0.566. **B.** The percentage of freezing did not decrease when mice were given shock on 29th day and recall was after 30 days of ET-1 injection. p=0.4068. Values are expressed as Mean  $\pm$  SD in seconds for n=10 animals. **C.** Representative images shows CD31 expression was reversed by 30 days of ET-1 treatment. **D.** The graphical representation of number and length of CD31 positive vessels from three sections of hippocampus of control and ET-1 injected mice expressed as Mean  $\pm$  SD of n=3 animals. Statistically there was no difference in number and length of CD31 positive vessels between saline and ET- injected animals after 30 days (p=6536, p=4415). **E.** S<sup>35</sup>-methionine incorporation was unaffected in synaptoneurosomes prepared from 30 days of ET-1 treatment after KCl stimulation. We saw stimulation both in control and ET-1 injected mice (p<0.0001). Data are represented as Mean  $\pm$  SD (n = 5 mice).



**Supplementary Figure.3. Akt-mTOR phosphorylation after 30 days of ET-1 treatment. A, B, E, F, I and J.** The levels of both phosphorylated forms of Akt1 Ser473 and Thr308 as well as GSK did not show any difference after 30 days of ET-1 treatment. Values are Mean  $\pm$  SD, n=8 animals. **C, D, G, H, K and L.** There was no change in levels of phosphorylated mTOR and its downstream molecules p4EBP at Thr46/47 and pS6K at Thr389 in hippocampal lysate of bilateral ET-1 injected mice compared to controls after 30 days. Values are Mean  $\pm$  SD, n=8 animals.



**Supplementary Figure.4. Expression of Iba-1 showing microglia near the ventricles after 30 days of ET-1 treatment. A. ET-1 treatment did not stimulate microglial activation after 30 days**

around the ventricles. **B.** The graph shows no difference in cell area and number of process in microglia of ET-1 treated mice compared to vehicle controls (n=3). **C.** The immunoblot for Iba-1 expression in hippocampal lysate did not show any change after 30 days of ET-1 treatment. Data are represented as Mean  $\pm$  SD (n = 4 mice).