



**Fig. S2.** CNO-induced activity results in *cfos* expression in both hM<sub>3</sub>D<sub>q</sub>-expressing and hM<sub>3</sub>D<sub>q</sub>-non-expressing cells. In CA1, where hM<sub>3</sub>D<sub>q</sub>R expression can be observed somatically,  $91.4 \pm 2\%$  of hM<sub>3</sub>D<sub>q</sub>R expressing cells also show *cfos* expression ( $n = 4$ ) indicating the effectiveness of CNO to induce activity in hM<sub>3</sub>D<sub>q</sub>R cells.  $43.5 \pm 5\%$  ( $n = 4$ ) of GFP expressing cells do not also express hM<sub>3</sub>D<sub>q</sub>R indicating activation of additional cells that do not express the receptor.