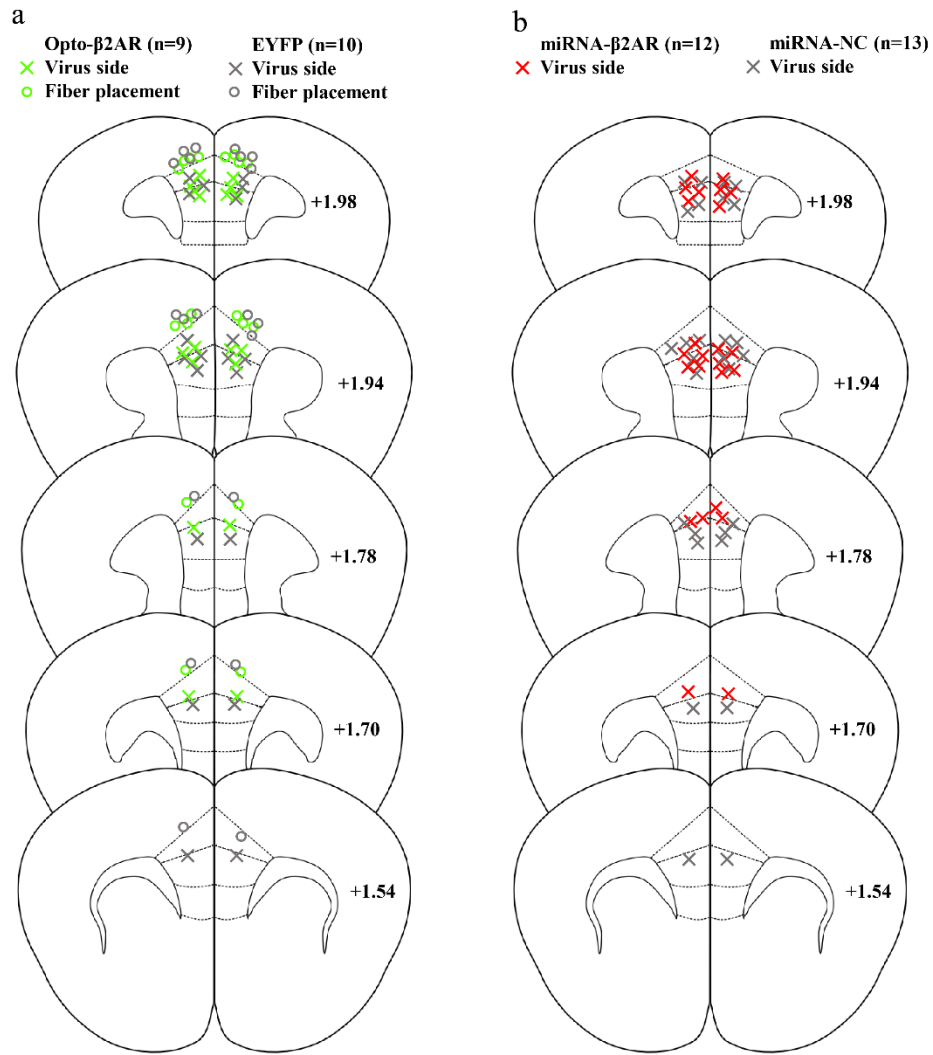


**Supplemental Figure S1.  $\beta$ 2-AR is abundantly present in CaMKII $\alpha$  positive neurons in the mPFC, and opto- $\beta$ 2-AR are highly co-expressed with CaMKII $\alpha$  and cFos.**

**(a)** Immunofluorescence images showed that  $\beta$ 2-AR (red, Alomone Labs, #AAR-016) is abundantly present in CaMKII $\alpha$  positive neurons (green) in the mPFC. Up panel is low magnification images, down panel is high magnification images.

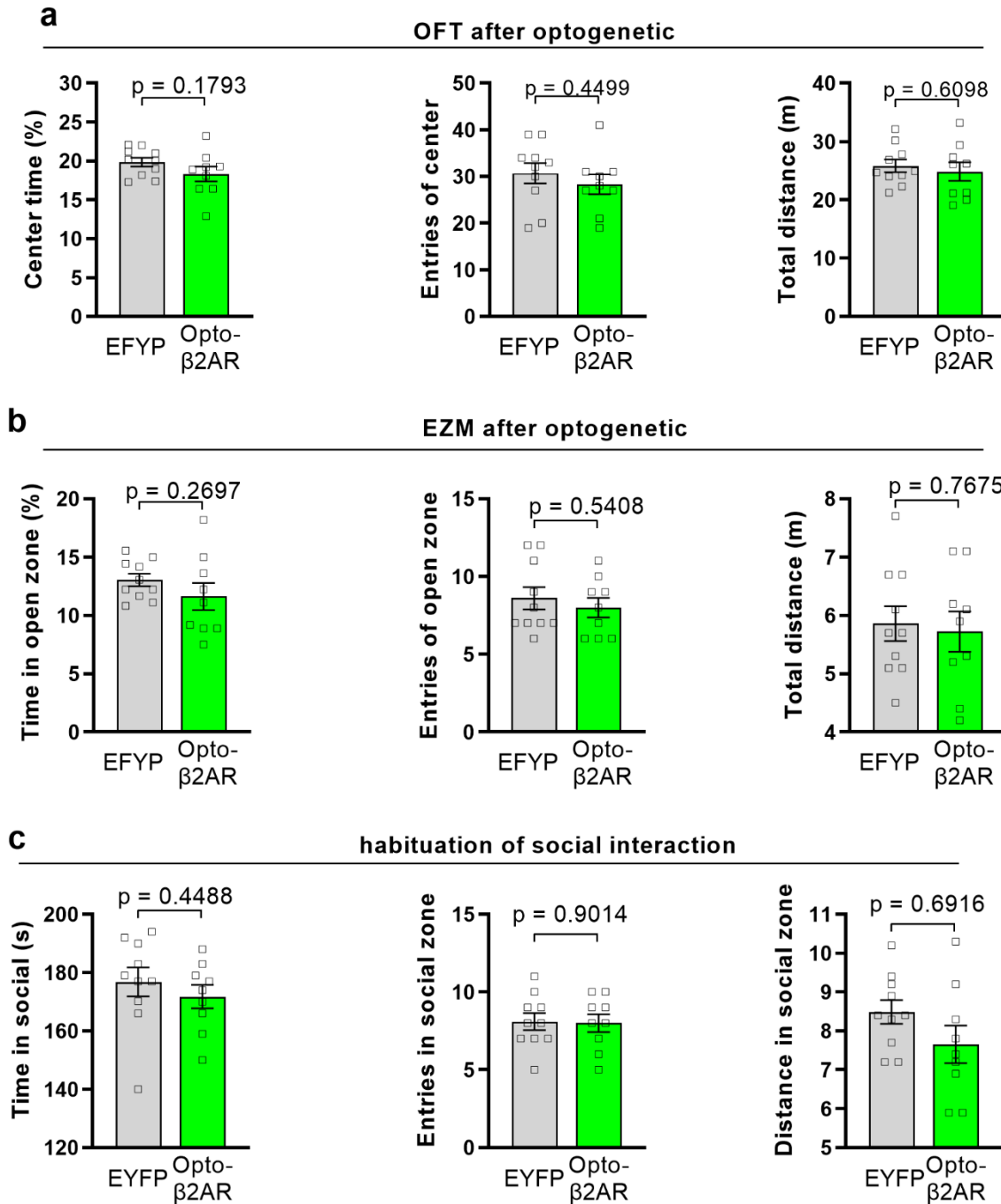
**(b)** Immunofluorescence images showed that opto- $\beta$ 2-AR (green) or EYFP (green) and CaMKII $\alpha$  (red) are highly co-expressed in the mPFC. Up panel is opto- $\beta$ 2AR group, down panel is EYFP control group.

**(c)** Quantification of percentage of total opto- $\beta$ 2AR positive cells co-expressed with CaMKII $\alpha$  (n = 4, 2 slices for each mouse).



**Supplemental Figure S2. Graphical summary of the site of injection of AAVs for the individual animals for each experiment.**

- (a)** Virus injection side (crosses) and optic fiber placement (circles) of opto- $\beta$ 2AR (green, n = 9) and EYFP (gray, n = 10) in mPFC (the graphical figure is adapted to (Felix-Ortiz et al., 2016)).
- (b)** Virus injection side (crosses) miRNA- $\beta$ 2AR (red, n = 12) and miRNA-NC (gray, n = 13).

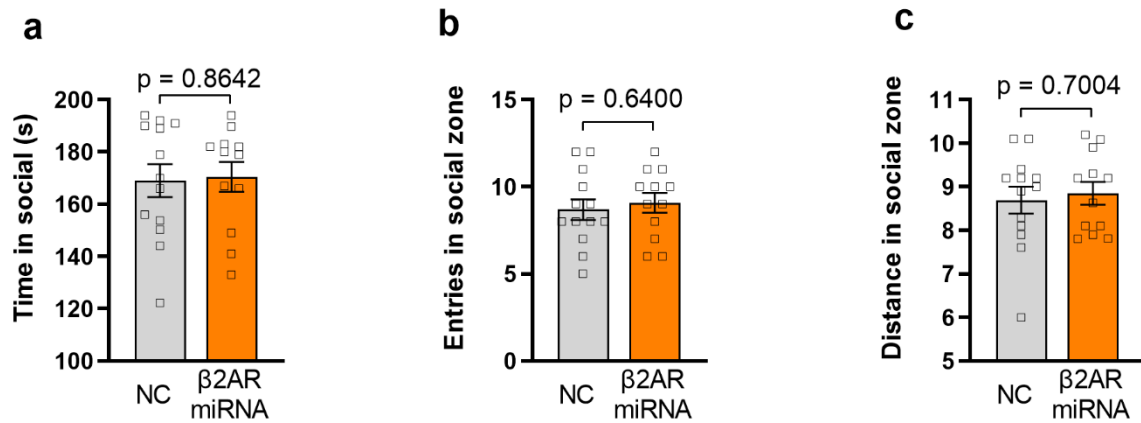


**Supplemental Figure S3. Opto-β2AR mice and control mice have no significant difference in anxiety level after optogenetic and place preference during habituation of social interaction.**

**(a)** Opto-β2AR<sup>PFC/CaMKii</sup> mice (green) showed no significant difference in time in center, entries in center, and total activity after optogenetic in OFT, compared with control (grey) (unpaired-T test).

**(b)** Opto-β2AR<sup>PFC/CaMKii</sup> mice (green) showed no significant difference in time, entries in open zone, and total activity after optogenetic in EZM, compared with control (grey) (unpaired-T test).

**(c)** Opto-β2AR<sup>PFC/CaMKii</sup> mice (green) showed no significant difference in time in social zone, entries in social zone, and distance in social zone during habituation of social interaction test, compared with control (grey) (unpaired-T test) (Opto-β2AR group, n = 9; control group, n = 10).



**Supplemental Figure S4. miRNA-β2AR mice and control mice have no significant difference in the place preference during habituation of social interaction.**

- (a) β2AR-miRNA<sup>PFC/CaMKii</sup> mice (orange) spent no significant different time in habituation social (no mouse) zone as compared with control (grey) (unpaired-T test,  $p = 0.8642$ ).
- (b) β2AR-miRNA<sup>PFC/CaMKii</sup> mice (orange) had no significant different entries in habituation social zone as compared with control (grey) (unpaired-T test,  $p = 0.6400$ ).
- (c) β2AR-miRNA<sup>PFC/CaMKii</sup> mice (orange) had no significant different travel distance in habituation social zone as compared with control (grey) (unpaired-T test,  $P = 0.7004$ ).
- (miRNA-β2AR group,  $n = 12$ ; control group,  $n = 13$ ).