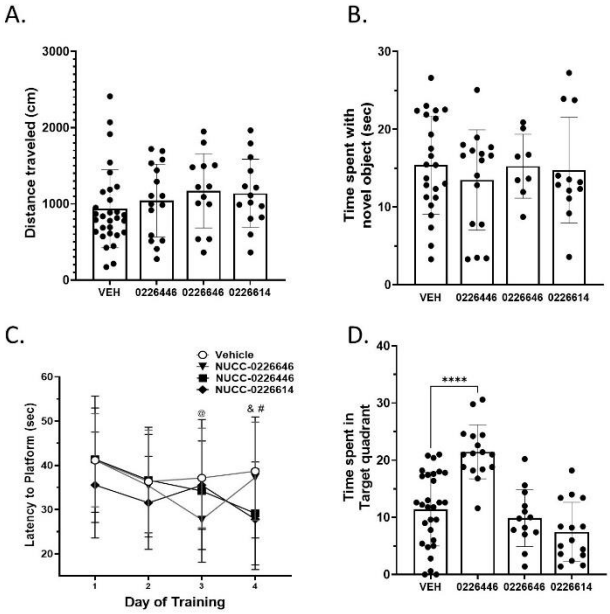


Supplementary Figure S1. The effects of SERCA PAMs on cognitive behavior of APP/PS1 mice. Administration of the compounds resulted in no differences in (A) locomotor activity as assessed in the open field (VEH ♀ $n = 13$, ♂ $n = 16$; 0226446 ♀ $n = 9$ ♂ $n = 7$; 0226614 ♀ $n = 7$; ♂ $n = 7$ and 0226646♀ $n = 4$; ♂ $n = 4$). (B) No differences were found in object memory when any of the compound-treated mice (0226446 ♀ $n = 7$ ♂ $n = 8$; 0226614 ♀ $n = 7$; ♂ $n = 7$; 0226646♀ $n = 4$; ♂ $n = 4$) were compared to vehicle-administered mice (VEH ♀ $n = 11$, ♂ n =12). In the water maze, (C) there were significant differences in specific days of water maze training. Mice treated with compound NUCC-0226646 (VEH ♀ $n = 7$, ♂ $n = 6$) performed better on day 3 and mice treated with NUCC-0226446 (VEH ♀ $n = 9$, ♂ $n = 9$) or NUCC-0226614 (VEH ♀ $n = 7$, ♂ $n = 7$) had less of a deficit on day 4 when compared to the vehicle-treated mice (VEH ♀ $n = 14$, ♂ $n = 15$). In the (D) probe trial, only mice treated with compound NUCC-0226446 spent more time in the target quadrant. Data represented as mean ± SD. ****P<0.0001, @P<0.01 NUCC-0226646 vs. vehicle, &P<0.05 NUCC-0226446 vs. vehicle, #P<0.05 NUCC-0226614 vs. vehicle.