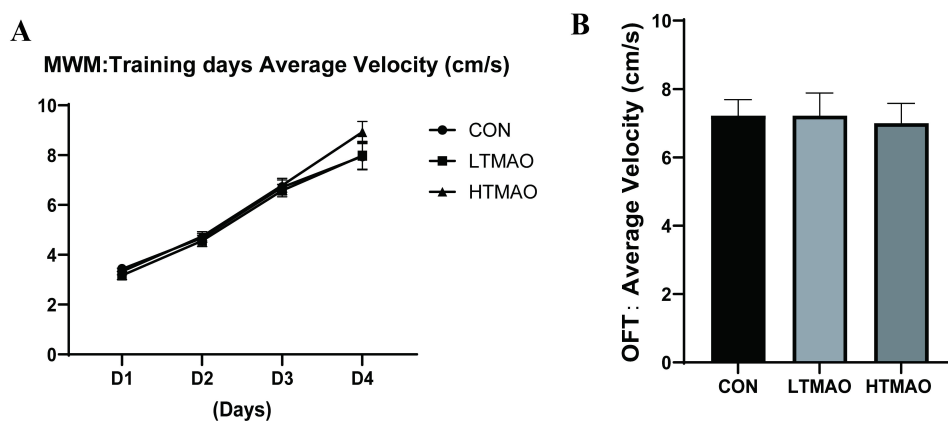


Supplementary materials

TMAO intervention shows no effect to the Mobility of mice

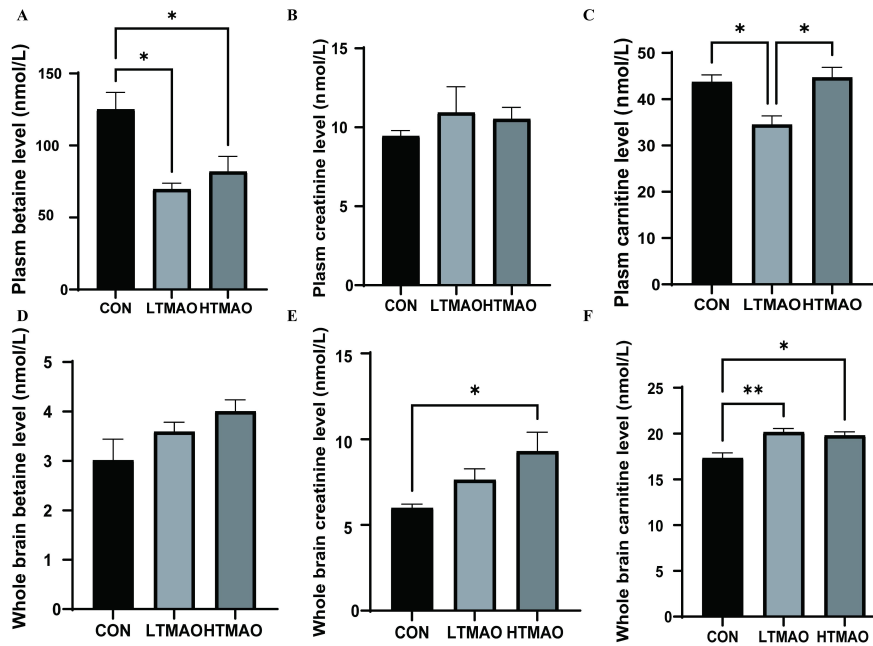
As indicated in the S.1, the average velocity of the MWM and OFT show little changes after TMAO treatment. It is suggested that TMAO intervention does not affect mice Mobility.



S.1 TMAO intervention have no effect on the mice mobility. (A) The average velocity in the training days of MWM; (B) The average velocity in OFT. Data are shown as the mean \pm SEM. Data versus by one-way ANOVA and comparisons between two groups were performed using posthoc Tukey multiple comparison tests ($n = 3$ each group, $*p < 0.05$, $**p < 0.01$).

TMAO and its precursor metabolites concentration in serum and whole brain after TMAO intervention

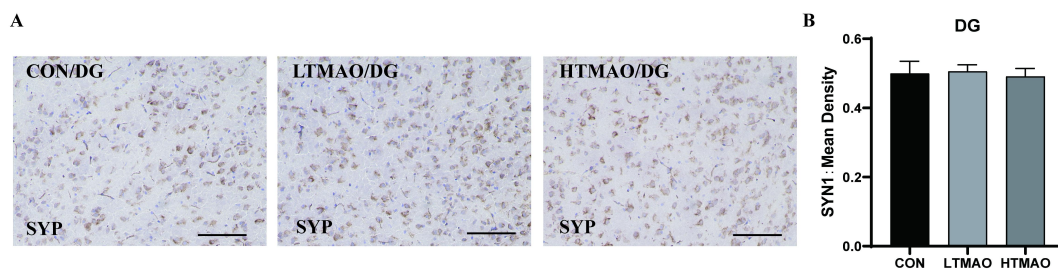
TMAO supplement altered the plasm and brain levels of its precursor metabolites. As shown in the S.2. The plasm level of betaine decreased. In addition, the brain level of creatinine and carnitine increased after TMAO treatment.



S.2 TMAO precursor metabolites concentration in plasma and whole brain. (A-C) Plasma level of carnitine, creatinine, betaine; (D-F) Whole brain level of carnitine, creatinine, betaine. Data are shown as the mean \pm SEM. Data versus by one-way ANOVA and comparisons between two groups were performed using posthoc Tukey multiple comparison tests (n = 3 each group, *p < 0.05, **p < 0.01).

TMAO intervention did not reduce the synaptic plasticity-related proteins in the DG.

As illustrated in the S.3, there were no statistic differences among three groups for the SYP IHC results in DG.



S.3 TMAO intervention resulted in the reduction of synaptic plasticity-related proteins in the hippocampus. (A) Representative IHC images of SYP in DG; (B) Quantitative comparison of IHC; All data were analyzed using one-way ANOVA, and comparisons between two groups were performed using Tukey's multiple comparison test (n =3 for each group, *p < 0.05, **p < 0.01, ***p < 0.001).

