

## Supplementary Material

Figure. S1 Detection of physiological indexes between WT mice and *Chd8*<sup>+/-</sup> mice.

There was no difference in somatic growth among experimental and control mice both in male and female offspring.

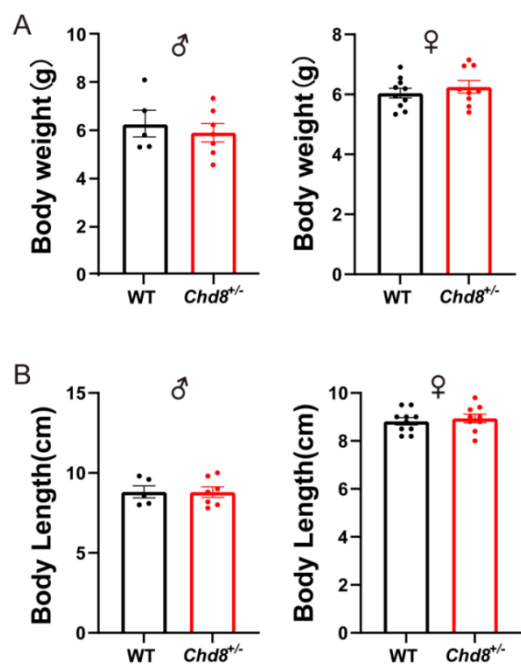


Figure. S1 Detection of physiological indexes between WT mice and *Chd8*<sup>+/-</sup> mice. (A) Body weight of two groups in male and female mice. (B) Body length of two groups in male and female mice.

Figure. S2 Basic athletic behaviors among the three groups of mice.

There was no difference in action capacity and anxiety-like behavior directed by marble burying test in three groups of mice.

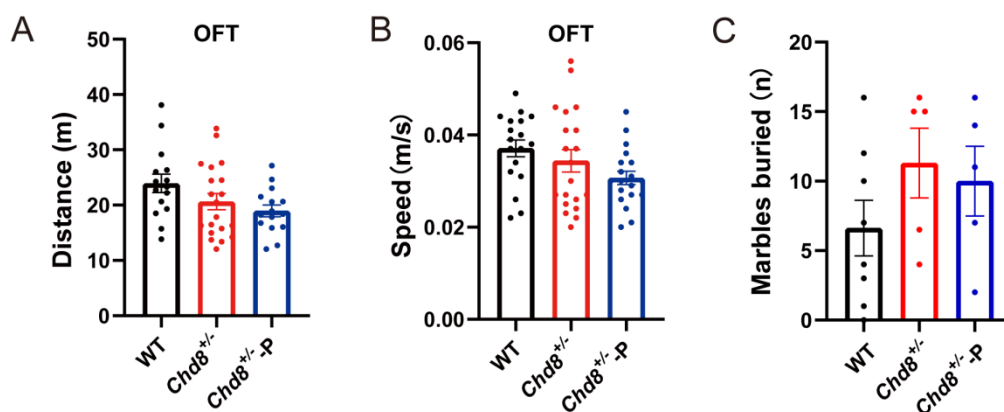


Figure. S2 Basic athletic behaviors tests among the three groups of mice. (A) Distance and average speed (B) in OFT. (C) Marbles buried in cages.

Figure. S3 Comparison of different genera and gut microbiota composition.

Several gut bacteria genera were differentially expressed in WT group and experimental group or experimental group and intervention group, and there were significant differences in microbiota composition among the three groups at family level. Besides, there was no difference in short-chain fatty acids like isoacetic acid among the groups.

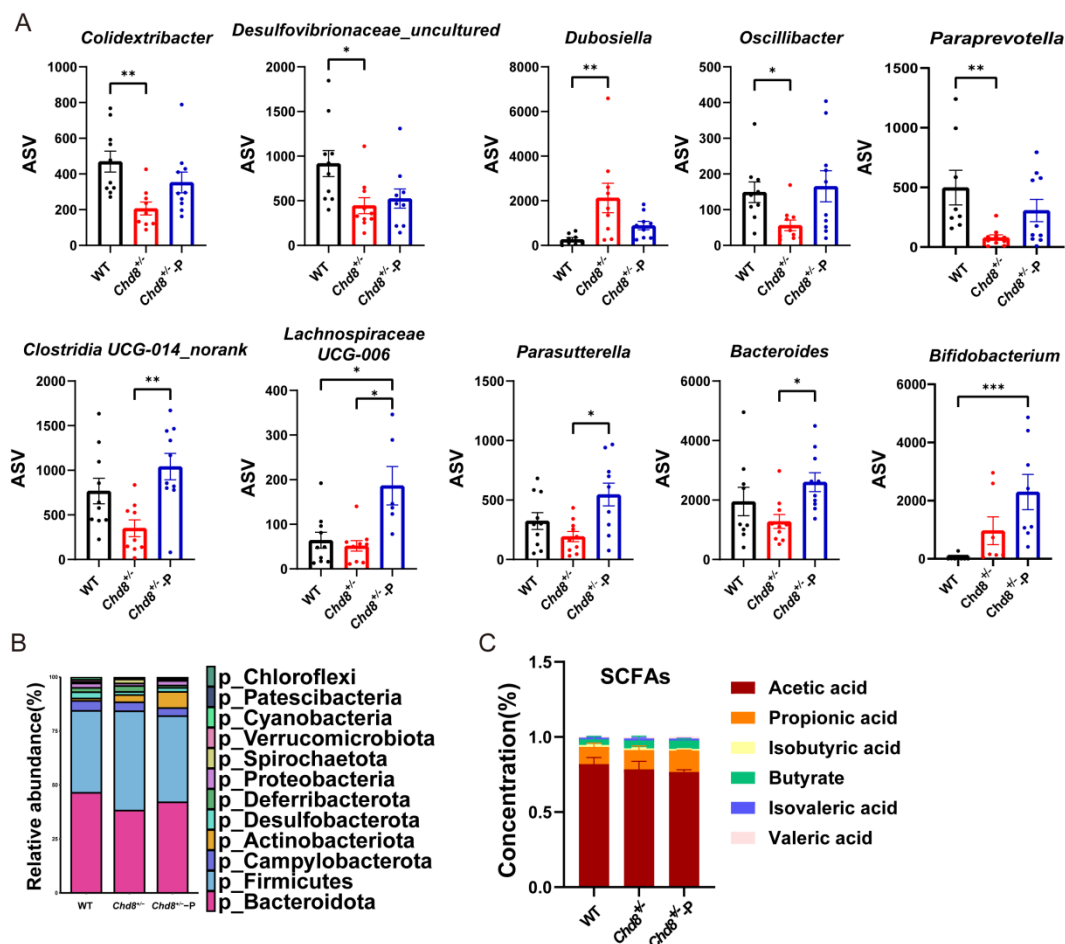


Figure. S3 Comparison of different genera and gut microbiota composition. (A) Relative abundance of bacterial genera such as *Colidextribacter*. (B) Community composition bar plot at the phylum level. (C) Histogram of the expression of 6 short-chain fatty acids, acetic acid, propionic acid, isobutyric acid, butyric acid, isovaleric acid and valeric acid in the three groups. Data are presented as mean  $\pm$  SEM. \* $p \leq 0.05$ , \*\* $p \leq 0.01$ , one-way ANOVA was used for multiple-group comparisons.

Figure. S4 Expression of 42 neurotransmitters in hippocampus and plasma of three groups of mice.

The data show a comparison of all 42 neurotransmitter concentrations among the three groups, including not differentially expressed ones.

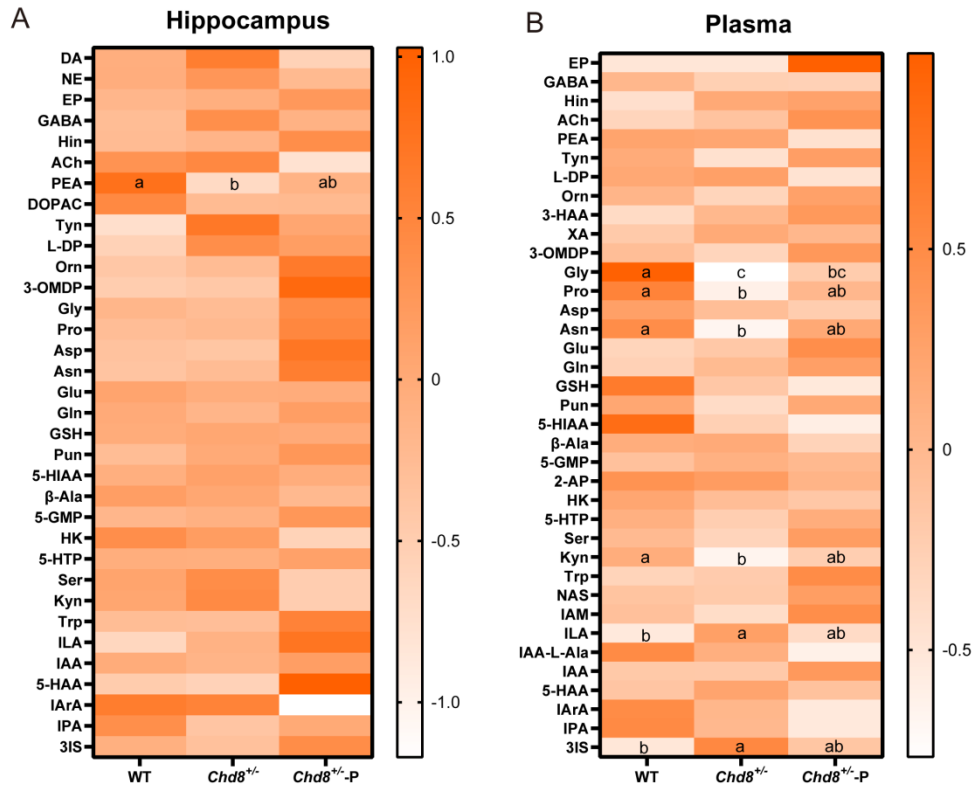


Figure. S4 Expression of 42 neurotransmitters in hippocampus and plasma of three groups of mice. (A) Heatmap showing neurotransmitter expression levels in hippocampus and plasma (B). Data was converted to Z-score and one-way ANOVA was used for multiple-group comparisons. Letters a, b, and c indicate a descending order of abundance; different letters indicate significant differences between groups, while shared letters indicate no significant difference.

Figure. S5 c-Fos detection in regions of hippocampus and mPFC with no significant differences.

c-Fos expression in IL region of mPFC and CA2, CA3 and DG regions of hippocampus showed no significant difference among three groups of mice.

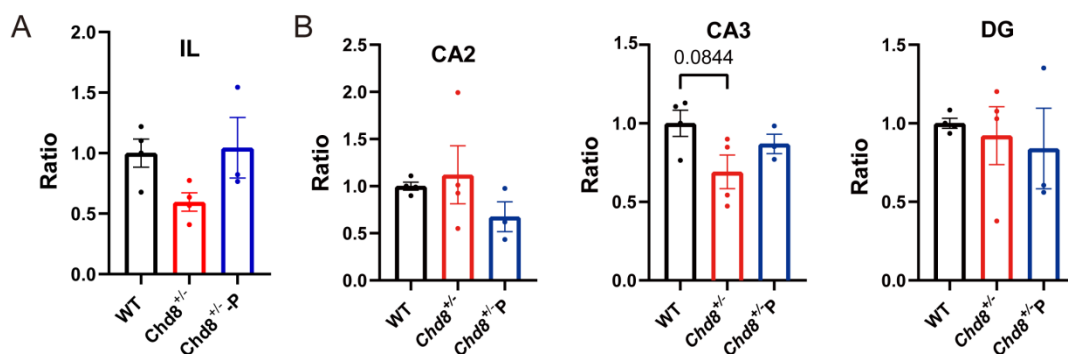


Figure. S5 c-Fos detection in regions of hippocampus and mPFC with no significant differences. Quantification of c-Fos<sup>+</sup> neurons in mPFC(A) and hippocampal subregions (B). Data are presented as mean ± SEM, one-way ANOVA was used for multiple-group comparisons.