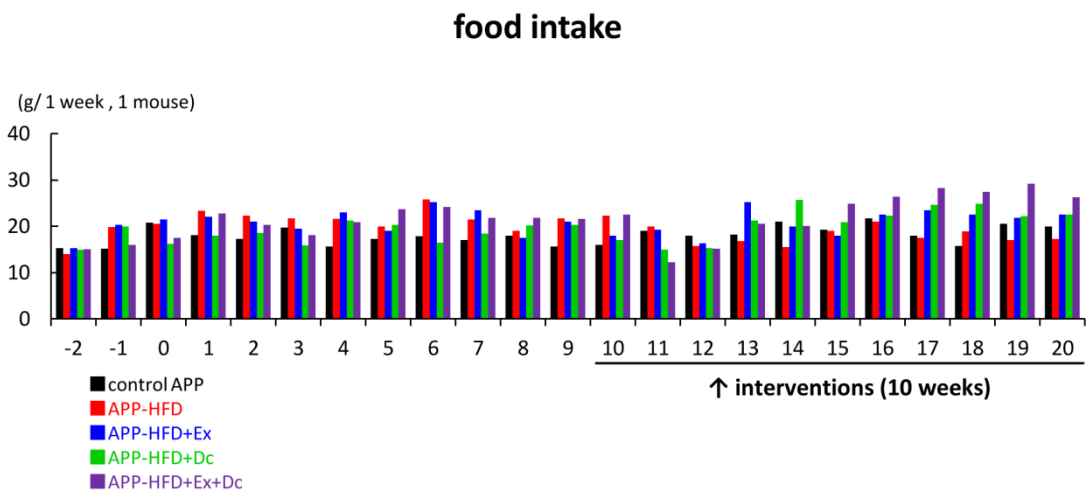
Maesako et al., Supplemental Figure

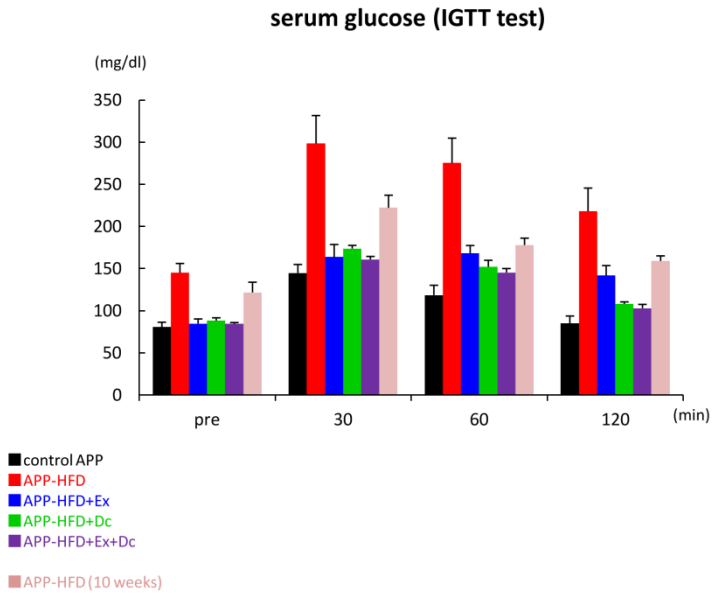
Supplemental Fig. 1. **Every week monitoring of the amount of food intake.**

The amount of food intake in APP-HFD+Dc and APP-HFD+Ex+Dc mice were monitored every week. After the induction of exercise or diet control, APP-HFD+Dc and APP-HFD+Ex+Dc mice tended to have more food than APP-HFD mice did.



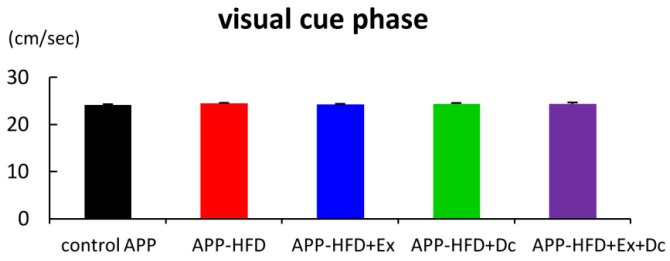
Supplemental Fig. 2. **Comparison of glucose tolerance activities of APP-HFD+Dc and APP-HFD+Ex +Dc mice with 10 weeks HFD-induced APP mice by IGTT.**

After 10 weeks induction of HFD (at the time of the switch from the poor environment to the EE), the mice were given a single dose of intra-peritoneal injection of glucose (2 g/kg body weight) after 14 hours fasting, and blood was collected from the tail-vein periodically over 2 hours. Blood glucose content was measured by using LabAssay Glucose (Wako, Japan). The glucose tolerance of the mice at the time of the switch from the normal to the exercise condition was worse than that of APP-HFD+Dc and APP-HFD+Ex+Dc mice.



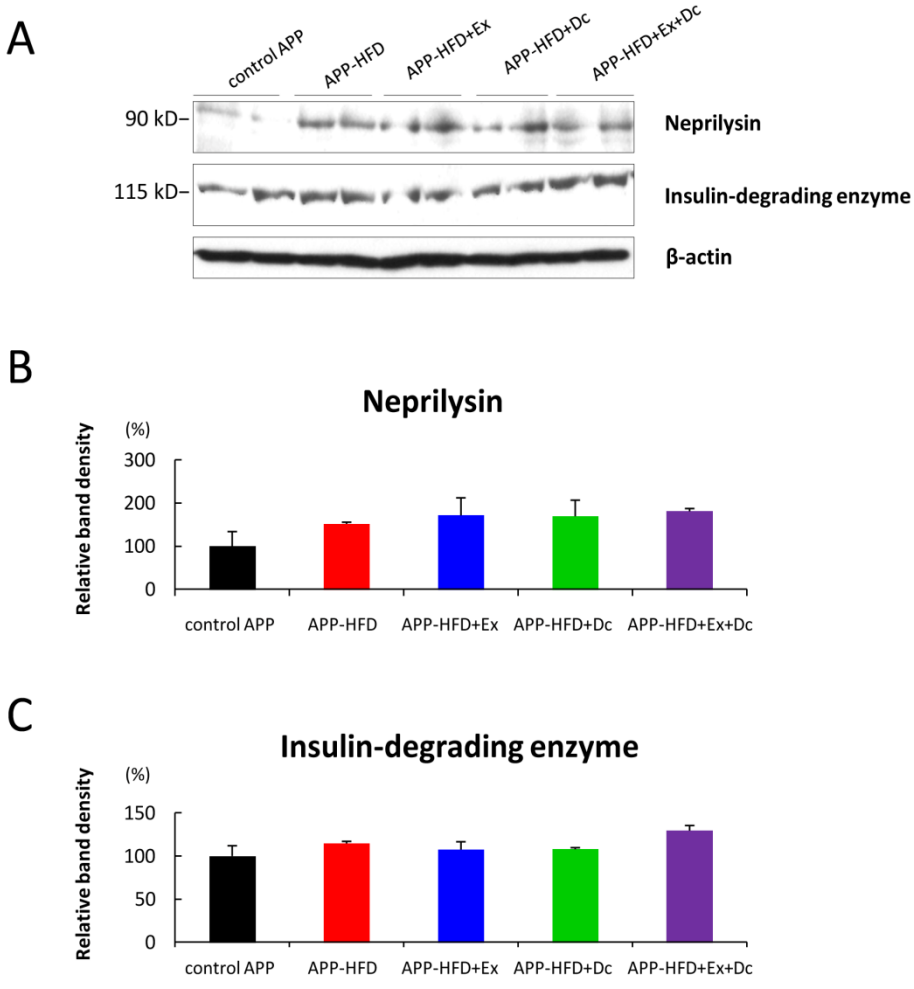
Supplemental Fig. 3. **Locomotor activities in Morris water maze test.**

Locomotor activity in the visual cue phase of Morris water maze test. There was no statistical significance among control APP, APP-HFD, APP-HFD+Ex, APP-HFD+Dc and APP-HFD+Ex+Dc induced mice.



Supplemental Fig. 4. **The expression levels of neprilysin and insulin-degrading enzyme.**

Immunoblotting analysis for the contents of neprilysin and insulin-degrading enzyme. The expression levels of neprilysin and insulin-degrading enzyme were not different between APP-HFD+Ex and APP-HFD+Dc mice.



Supplemental Fig. 5. **Correlation analysis between memory function and metabolic conditions in control APP and APP-HFD mice.**

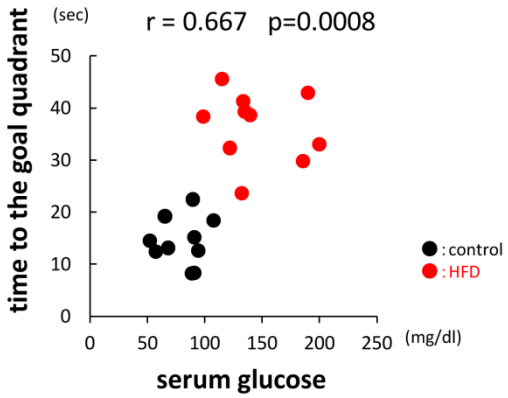
Memory function was assessed by the score of the probe trial phase of Morris water maze test (time to the goal quadrant). The longer time to the goal quadrant indicates that the memory function of mice is disrupted.

A. Significant correlation was established by comparing the scores of the probe trial phase of Morris water maze test (time to the goal quadrant) and the blood glucose levels, using Pearson's correlation coefficients. The time to the goal quadrant was positively correlated with the blood glucose level ($r = 0.667$, $p = 0.0008$).

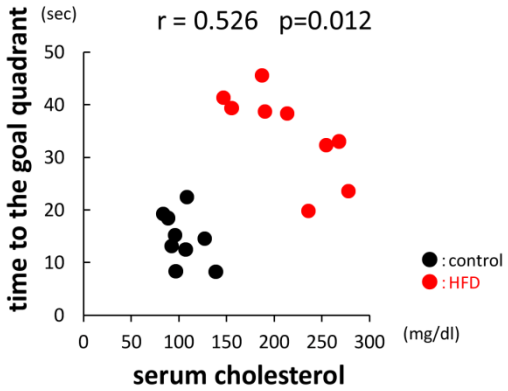
B. Significant correlation was established by comparing the scores of the probe trial phase of Morris water maze test (time to the goal quadrant) and the blood cholesterol levels, using Pearson's correlation coefficients. The time to the goal quadrant was positively correlated with the blood cholesterol level ($r = 0.526$, $p = 0.012$).

C. Significant correlation was established by comparing the scores of the probe trial phase of Morris water maze test (time to the goal quadrant) and the blood insulin levels, using Pearson's correlation coefficients. The time to the goal quadrant was positively correlated with the blood insulin level ($r = 0.433$, $p = 0.045$).

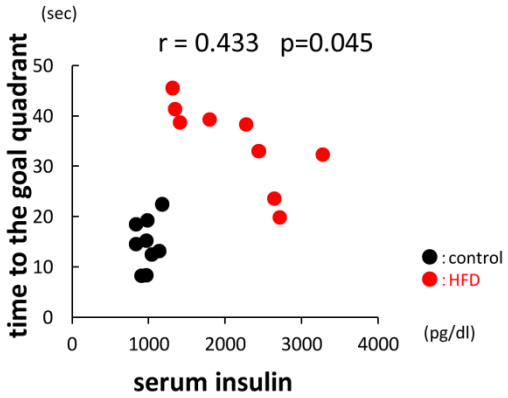
A


r = 0.667 p=0.0008
(sec)
time to the goal quadrant
50
40
30
20
10
0
0 50 100 150 200 250
(mg/dl)
serum glucose
: control
: HFD

B


r = 0.526 p=0.012
(sec)
time to the goal quadrant
50
40
30
20
10
0
0 50 100 150 200 250 300
(mg/dl)
serum cholesterol
: control
: HFD

C


r = 0.433 p=0.045
(sec)
time to the goal quadrant
50
40
30
20
10
0
0 1000 2000 3000 4000
(pg/dl)
serum insulin
: control
: HFD