SUPPLEMENTAL DOCUMENT

Morris water maze test

A spatial memory test was performed. The Morris water maze is a white circular pool (diameter: 150 cm and height: 35 cm) with a featureless inner surface (XR-XM101, Shanghai Xinruan Information Technology Co. Ltd, Shanghai, China). The circular pool was filled with nontoxic water and kept at 23-25 °C. The pool was divided into four quadrants of equal area. A transparent plastic platform (4.5 cm in diameter and 14.5 cm in height) was centered in one of the four quadrants of the pool. There are four prominent visual cues on each side of four quadrants of the pool. The swimming route of mouse, from the start position to the platform, was monitored and analyzed by a video tracking system (SuperMaze software, Shanghai Xinruan Information Technology, Co. Ltd, China). Four habituation training were performed on day 3. The water in the pool was un-dyed, and the platform was visible (1.5 cm above the water surface). Test trials were conducted for 5 days (day 4-day 8). The water was white-dyed with non-toxic agents (Food grade titanium dioxide), and the platform was submerged 0.5-1.0 cm below the water surface so that it was invisible at water level. For each daily trial, the mouse was placed into the water maze at one of three randomly determined locations and released allowing the animal to find the hidden platform. After the mouse found and climbed onto the platform, the trial was stopped and the escape latency was recorded. The maximum trial length was 60 s. If animals did not locate the platform within 60 s, the experimenter guided the mouse by hand to the platform, then the mouse was kept on the escape platform for 30 s and an escape latency of 60 s was recorded. In

order to assess the spatial retention of the location of the hidden platform, a probe trial was conducted 24 h after the last acquisition session. During this trial, the platform was removed from the maze, and each mouse was allowed to search the pool for 60 s before being removed. The time spent in the target quadrant was used as a measure of consolidated spatial memory.

Cell viability assay

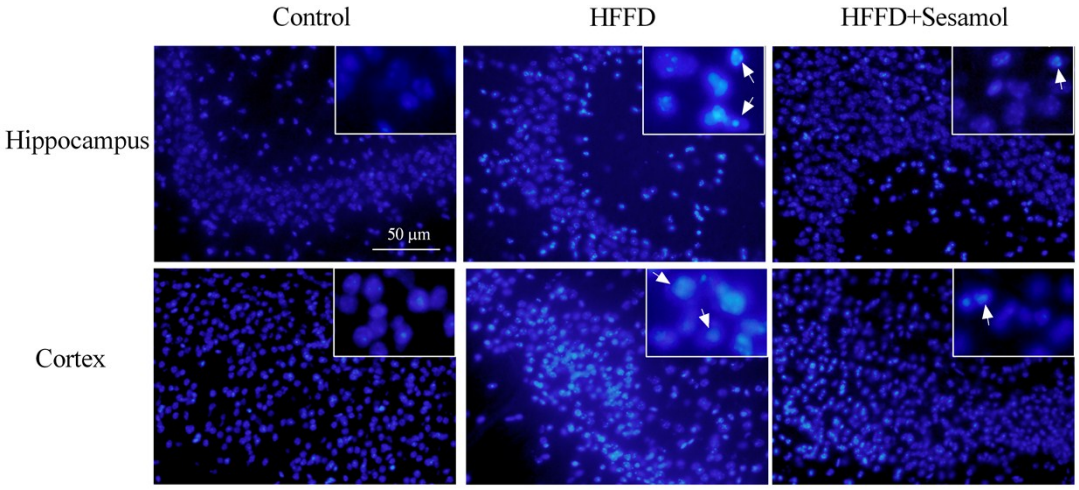
Cell viability was determined using the MTT assay. Briefly, SH-SY5Y cells were seeded in a 96-well plate at a density of 7.0×10^4 cells/well for 12 h. Different concentrations of glucose and sesamol were added to each well and the cells were cultured for 12 h, followed by incubation with 0.5 mg/mL MTT for 4 h. Finally, 100 μL of DMSO was added to each well to dissolve the formazan crystals. Absorbance at 570 nm was measured with a Model 680 microplate reader (Bio-Rad, Hercules, CA, USA). Cell viability was expressed as a percentage of the control (untreated cells). The result was shown in **Supplemental Fig.2.**

Supplemental Table 1

Table 1 Composition of experimental diets

Composition(g/kg)	Control Diet (AIN93M)	High-fat Diet (TP230100)
Casein	140	175
Corn Starch	465.7	132
Maltodextrin	155	125
Sucrose	100	202
Soybean Oil	40	30
Lard	0	196
Cellulose	50	62
Mineral Mix, M1021	35.0	61
Vitamin Mix, V1010）	10	12
L-Cystine	1.8	2
Choline Bitartrate	2.5	3
TBHQ	0.045	0.045
Total	1000	1000

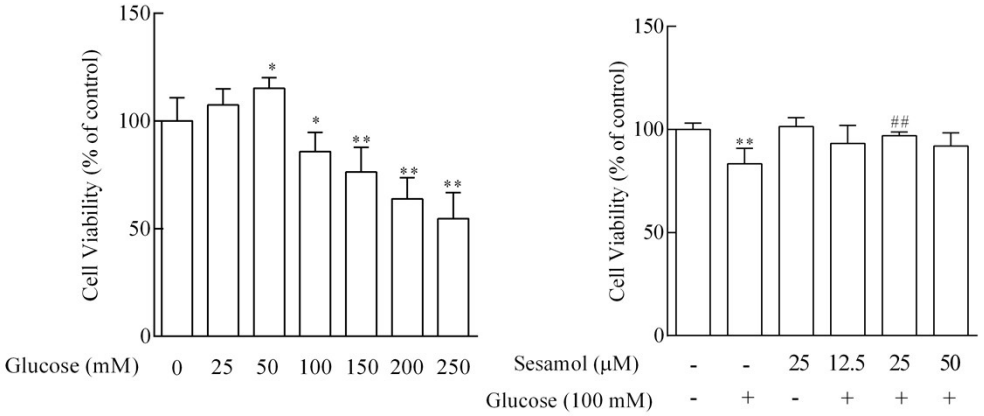
Supplemental Fig.1



S. Fig.1 *Effects of sesamol on HFFD-induced neuron damage in hippocampus and cortex*

Representative photomicrographs of DAPI fluorescence staining in hippocampus CA1, CA3, DG region, and cortex (× 200) to show nuclear pyknosis. The staining procedure was as described in Methods section.

Supplemental Fig.2



S. Fig.2 *Effects of various concentration of glucose and sesamol on SH-SY5Y cell viability*

The cell viability was determined by MTT assay as described in Materials and methods section. Data presented as mean±SD, n=10. *p < 0.05, **p < 0.01, *versus* control group, $^{\#}$p < 0.05, $^{\#\#}$p < 0.01 *versus* HFFD group.