# Supporting Information

## Supplementary Methods

**Preparation of microbubbles (MBs).** The MBs used for focused ultrasound cavitation were composed of 1,2-Distearoyl-sn-glycero-3-phosphatidylcholine (DSPC) and 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[methoxy(polyethylene glycol)-2000] (DSPE-PEG2000), and encapsulating a high-molecular-weight gas core of perfluoropropane ($C_3F_8$). Appropriate amounts of DSPC, DSPE-PEG2000 (90:10, molar ratio) were added into 1 mL chloroform, and the solvent was removed completely under nitrogen flow and then in vacuum at room temperature for ~2 h. The dried thin-film lipids were hydrated at 60 °C with 5 mL Tris buffer (100 mM Tris:glycerol:propyleneglycol at a volume ratio of 80:10:10, pH 7.4) followed by addition of $C_3F_8$. The admixture was mechanically vibrated for 30 s to obtain the MBs.

**Characterization of MBs.** A drop of MBs suspensions (about 50 μl, $1 \times 10^8$ particles/mL) was diluted and applied to the microscope slide with a coverslip and morphologically examined under a microscope (Leica DMI3000B). The measurement of MBs for the particle size, size distribution and concentration were analyzed by particle counter with a 0.5 μm in diameter lower detection limit (Accusizer 780; Particle Sizing Systems, Santa Barbara, CA, USA).

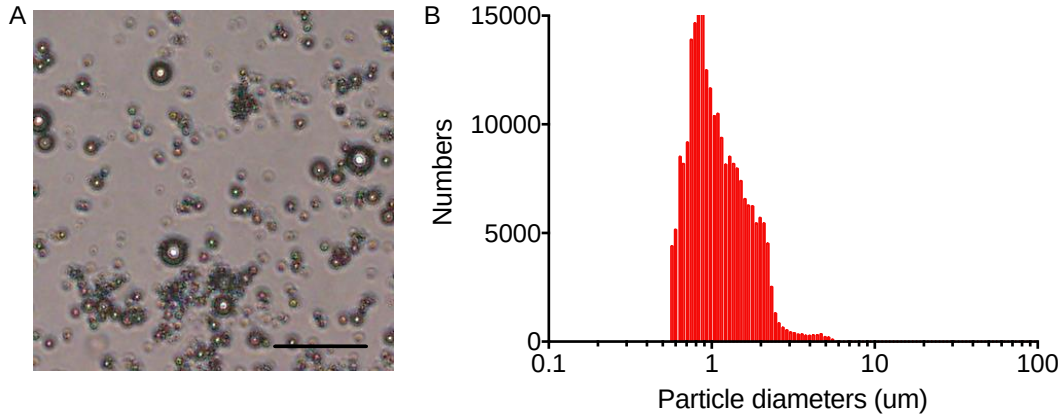
**Cell morphology and ZO1 junction staining**. B.End.3 cells were cultured on transwell membrane and used as BBB model. Pre-treated cells were fixed in 4% PFA

for 10 min, permeablized for 30 min with 2% Triton X, and washed by PBS for three times. ZO1 was visualized by using mouse anti-ZO1 (Cell Signaling Technology, 1:100 dilution) followed by secondary labelling with goat anti-mouse 488 (Abcam, 1:200 dilution), and the detection was conducted with CLSM.

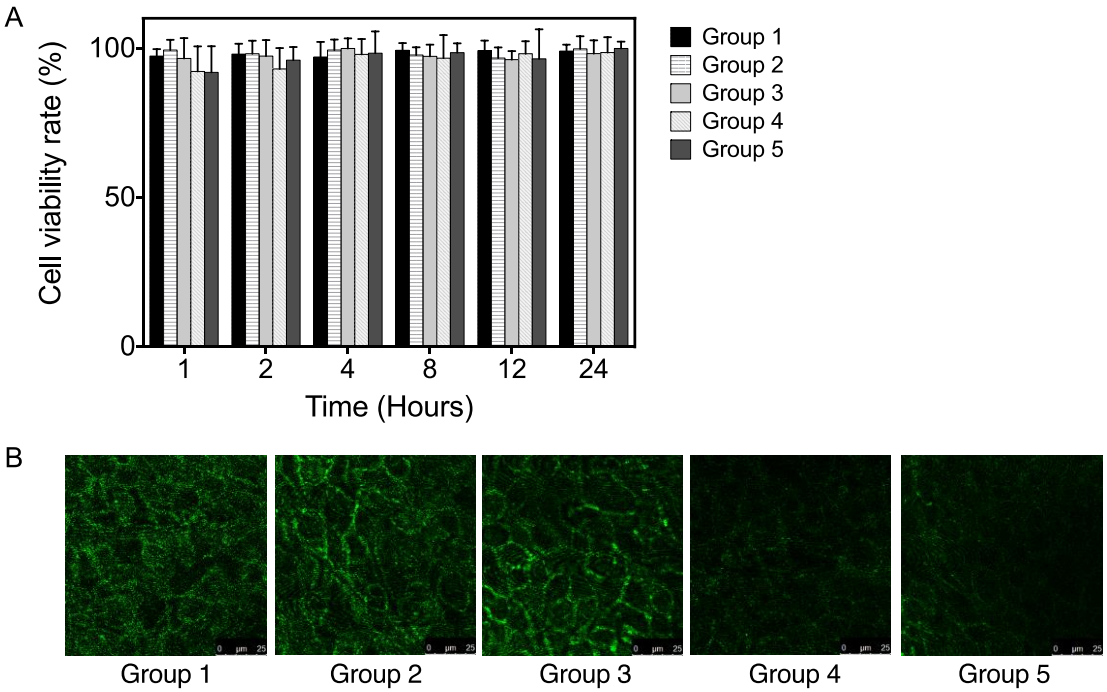
**Western blot analysis for TH and α-syn.** The basolateral SH-SY5Y cells were collected into EP tubes and washed by PBS for 3 times by centrifugation (1000 rpm for 4 min at 4 °C). Radio-immunoprecipitation assay (RIPA) buffer containing protease inhibitors was used for cell lysis about 10 min on ice, and then the mixture was centrifuged (12,000 rpm for 10 min at 4 °C) and collected the deposits as the samples. The concentration of the protein was determined by using BCA protein assay kit while the standard curve was deduced by standard protein solution and the total protein amount in each sample was adjusted equally. 10 mg of protein from each sample were separated on 10% SDS-PAGE gel using constant current (U=90 V, 30 min). Separated proteins were electrophoretically transferred to polyvinylidene difluoride (PVDF) membranes with a semi-dry blotting system (I=300 mA, 60 min). The PVDF membranes were incubated for 3 h at room temperature with 5% bull serum albumin (BSA) in tris-buffered saline containing 0.1% Tween 20 (TBST) solution. Followed by overnight incubation at 4 °C with the desired antibodies: The rabbit polyclonal antibody against TH (Abcam) and α-syn (Abcam) and the rat monoclonal antibody against the DAT were diluted in TBST (1:2000 for primary antibodies). Membranes were washed 3 times for 5 min by TBST and incubated with a horseradish peroxidase (HRP) (Abcam)

conjugated secondary antibody in TBST for 1.5 h (1:2000 for secondary antibodies) at room temperature. Immunoreactivity was detected by enhanced chemiluminescent autoradiography (ECL kit, Thermos Fisher Scientific) in accordance with the manufacturer's instructions. The densities of immunoreactive bands were analyzed by image analysis software.

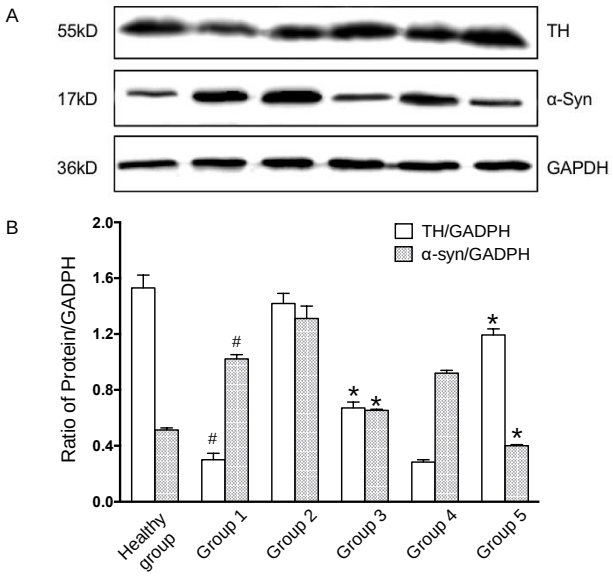
**Behavioral tests.** The suspension experiment was to observe the fatigue feature and grasp strength of the mice, and the score of each test represented the mean number of paws the mouse grasped on the string for three times after training once. The climbing pole experiment was to observe behavior disorder situation, and the run duration time that mice climbed from the top of pole in 60 cm length to the bottom was recorded at least 3 times after training once. The video and scores were recorded during the experiment for evaluating the recovery statues of the C57BL/6 mice with different treatment respectively.



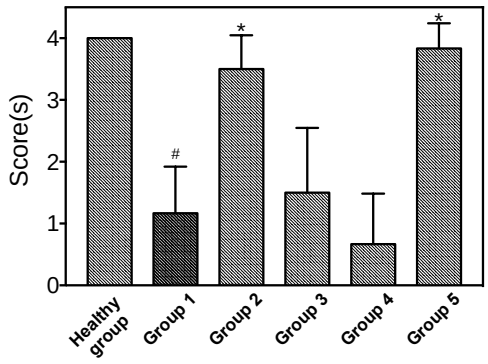

**Supplementary Figure 1.** A. The appearance and representative micrograph of the MBs used for UTMD under a microscope. Scale bar=10 μm. B. The particle size and size distributions of MBs.




**Supplementary Figure 2.** A. The cell viability rate by CCK-8 assay in B.End.3 cell line with different treatment in continual observation to reflect the non-toxicity of CPC in BBB cell model. B. the laser confocal microscopy observation of the zo-1 on B.End 3 membrane surface when differently treated for 24 h (The scale bar at right bottom of the panels represented 25 μm).




**Supplementary Figure 2.** The western blot analysis for TH and AS with respective treatment. (Significances were marked as # P<0.05 vs control group, * P<0.05 vs MPTP group.)




**Supplementary Figure 3.** The scores recorded for the suspension experiment with different treatments after 2 weeks. (Significances were marked as # $P<0.05$ vs control group, * $P<0.05$ vs MPTP group.)

**Supplementary Movie 1.** The representative capture for the suspension experiment of the mice after 2 weeks.

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