**Appendix S1.** Protocol for the experiment performed to generate Fig. 2. A total of 10 male C57BL/6J mice (body weight, 21-23 g; age, 8 weeks) were obtained from the Experimental Animal Center of Zhejiang Academy of Medical Science and divided into a Sham (n=5) and a traumatic brain injury (TBI) (n=5) group. Mice were housed under a 12-h light/dark cycle at a constant temperature of 22-25˚C and humidity of 50±10%, and had free access to food and water throughout the study. All procedures involved in this study were performed with the approval of the Institutional (Zhejiang Normal University) Animal Care and Use Committee and in accordance with the laws and regulations: Care and Use Standard of the Laboratory Animal (China Ministry of Health publication) and the National Institute of Health (NIH) Guide for the Care and Use of Laboratory Animals (2011 edition).

Based on the protocol in previous studies by our group (1,2), anesthesia was induced with sodium pentobarbital (45 mg/kg i.p.). A 3.0-mm craniectomy was performed on the right frontal motorsensory cortex, 1.5 mm anterior to the bregma and 1.5-2.0 mm lateral to the midline. An adjusted Luer lock (3 mm inside diameter, made from a 19 G needle hub) was glued to the craniectomy site and fixate with dental cement. After return of the paw withdrawal reflex was observed, TBI was induced using an adapted fluid percussion (FP) device (1). With a closed-form pad (with the hardness values of 50, Huizhou Fanzhongbao Plastic Foam Co. Ltd.) attached to the strike face of the piston pole, the pendulum fell from 17˚ and generated an 2.5-2.6 atm percussion force according to previously established protocols (3). Sham-injured animals received identical anesthesia and craniotomy but were not exposed to lateral FP brain injury. Following TBI or sham injury, mice were disconnected from the device, the incision was sutured and antibiotic ointment was applied to the wounds.

Mice were perfused with chilled PBS (pH 7.4), followed by chilled 4% paraformaldehyde under anesthesia with sodium pentobarbital (45 mg/kg i.p.) at day 8 post-TBI. Brains were removed and fixed in 4% paraformaldehyde for 24 h. The whole brain was trimmed (3 mm before and after the impacted somatosensory cortex) and then the brain blocks were placed in 75, 85, 95 and 100% alcohols for gradient dehydration, cleared with xylene and embedded in wax blocks. Six-micrometer sections were cut through the impacted cortex using a microtome (HistoCore BIOCUT; Leica Microsystems).

The slices were placed in an oven at 50˚C for 2 h and made transparent with xylene I and II for 5 min each. The slices were sequentially transferred into 100% alcohol (5 min), 95% alcohol (5 min), 85% alcohol (3 min), 75% alcohol (3 min) and immersed in PBS for 10 min at room temperature. The slices were then placed in preheated 0.01 M citric acid sodium buffer and containers were maintained in a water bath at 100˚C for 10 min. After cooling down completely, the sections were removed and incubated in 5% bovine serum albumin blocking solution (Wuhan Boster Bio-Engineering Co., Ltd.) for 1 h at room temperature. The slices were taken from the solution, the serum was shaken off, 30 $\mu$l of primary antibody (rabbit anti-Caprin1; polyclonal; 1:500 dilution; cat. no. 15112-1-AP; Proteintech) was added to each brain slice, and samples were sealed with parafilm at 4˚C overnight.

The next day, the slices were allowed to rewarm to room temperature for 1 h, put in PBS, washed 3 times in a shaker (5 min at 23 g). The moisture was shaken off from the slices, they were blow-dried and 30 $\mu$l of diluted secondary antibody (goat anti-rabbit IgG, Alexa Fluor 488, 1:500; cat. no. A-11034; Thermo Fisher Scientific, Inc.) was added to each brain slice, followed by incubation for 1 h at room temperature. The slices were then placed into a shaker and washed 6 times using PBS, and then sealed with a coverslip. The x100 and x200 images were acquired using a fluorescence microscope (Discovery V12; Zeiss AG). Image J software (version 1.8.0_172, NIH) was used to analyze the cortical neurons in the images at x200 magnification.

## References


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