**Supplementary materials**

**Additional file 1.**

**Morris water maze**

The Morris water maze test was conducted to measure mouse long-term spatial cognitive function, as described previously [19]. Four Training was performed over 7 consecutive days, with 4 trials per day. During the first two days, mice were trained to find a dark-colored cylindrical platform with a diameter of 10 cm, sitting 0.5 cm above the water surface. Mice did not receive the next hidden platform tests if they had apparent motor and/or visual deficits indicated by low swimming speed (< 75 mm/s) or long escape latency (> 50 s). On the 3rd day, the platform was submerged 1 cm below the surface of the water and moved to the opposite quadrant. Escape latency, swimming distance and swimming speed were calculated. On day 8, the hidden platform was removed, allowing mice to swim freely in the pool for 60 s. The percentage of time spent in the target quadrant and the number of crossing where the platform had been previously located were analyzed.

**Y-maze test**

The Y-maze test was performed to evaluate mouse short-term spatial working memory, as previously described [19]. One arm, termed the novel arm, was blocked by a black baffle, allowing the mice to only move in the other two arms for 5 min. Two hours later, the novel arm was opened, allowing mice to freely move throughout the three arms. The percentage of time traveled in, number of entries into the novel arm, as well as travelling speed during the test, was calculated.

Mouse activity in the aforementioned behavioral apparatuses was collected by a digital video camera connected to a computer-controlled system (Beijing Sunny Instruments Co. Ltd, China). All tests were performed by two independent experimenters, who were each blind to the treatment schedule.

**Additional file 2.**

**Figure S1.** No obvious effects of AQP4 deletion on spatial cognitive function of 3-month-old APP/PS1 mice. **a, b** The mean escape latency and swimming speed during the hidden platform training period of the Morris water maze test. **c** The number of crossing the platform area. **d** The percentage of time spent in the target quadrant. **e** The number of entries into the novel arm. **f** The percentage of time spent in the novel arm in the Y-maze. Data in **S1a**, **b** were analyzed by repeated-measures ANOVA with post hoc Student-Newman-Keuls test. Other Data were analyzed by ANOVA with post hoc Student Newman-Keuls test. Data are means ± SEM. n = 12 per group.

**Figure S2.** AQP4 deletion did not affect astrocyte activation in 3-month-old APP/PS1 mice. **a** Double immunofluorescence for GFAP and total-Aβ. **b** Quantification of GFAP positive area in the cerebral cortex. **c** Immunofluorescence for GS positive astrocytes in the cortex. **d** Quantification of GS positive area in the cerebral cortex. GS or GFAP positive astrocytes were mildly activated in the cerebral cortex of APP/PS1 mice and AQP4-/-/APP/PS1 mice. Data are means ± SEM. n = 4 per group, two-way ANOVA with Newman-Keuls post-hoc test.

**Figure S3.** AQP4 polarization was impaired in the cerebral cortex of 3-month-old APP/PS1 mice. **a** Double immunofluorescence for AQP4 and GFAP. In WT mice, AQP4 was specifically expressed abutting the microvessels (arrow) and pia surface (arrowhead). By contrast, AQP4 immunoreactivity was abnormally increased in the adjacent parenchyma (indicated by stars) in APP/PS1 mice. There was no immunoreactive signal for AQP4 in the cortex of AQP4-/- mice and AQP4-/-/APP/PS1 mice. **b** Quantitative analyses of the AQP4 polarization abutting pia mater and microvessels. Data are means ± SEM. n = 4 per group, Student’s t-test. \*\**p* < 0.01; \*\*\**p* < 0.001.

**Figure S4.** Increased astrocyte activation in the frontal cortex in 3-month-old APP/PS1 mice and AQP4-/-/APP/PS1 mice receiving local injection of clodronate liposomes. **a** Double immunofluorescence for total-Aβ and GFAP. GFAP positive astrocytes further underwent activation both in APP/PS1 mice and AQP4-/-/APP/PS1 received clodronate liposome treatment. **b** Quantification of GFAP positive area fraction in the cerebral cortex. Data are means ± SEM. n = 4 per group, two-way ANOVA with Newman-Keuls post-hoc test.

**Figure S5.** An image shows GFP expression in the frontal cortex one month after injection of AAV encoding apoE siRNAs. **a** GFP positive area represented where the AAVs was injected and apoE siRNAs were expressed. **b-d** Double immunofluorescence for GFP and GFAP. Note that apoE siRNAs were expressed in GFAP positive astrocytes (arrowheads).