Supplementary Method

Wortmannin (Wm) and bafilomycin (Baf) treatment *in vivo*

For wortmannin (Wm) treatment *in vivo*, Wm (0.5 mg/kg, HY-10197, MedChem Express, MCE) was dissolved in PBS and administered intraperitoneally for 3 consecutive days simultaneously after BCAS. For bafilomycin (Baf) treatment *in vivo*, Baf (10nm, HY-100558, MedChem Express, MCE) was dissolved in PBS and administered intraventricularly with ALZET osmotic mini-pumps (Cupertino, CA, model 1007D, pumping rate 0.11 μl/h, continuous application for 3 days) simultaneously after BCAS. The dose and duration was selected according to our preliminary experiments.

Primary Cell Culture with IFN-γ stimulation

Primary microglia were isolated from the brain of neonatal wild-type and TLR4 knockout mice at P1–P2 as described previously. IFN-γ (100 ng/mL Sigma–Aldrich, USA) was added to the microglial cultures for 24 hours for proinflammatory induction. The dose of IFN-γ was selected according to our preliminary experiments.

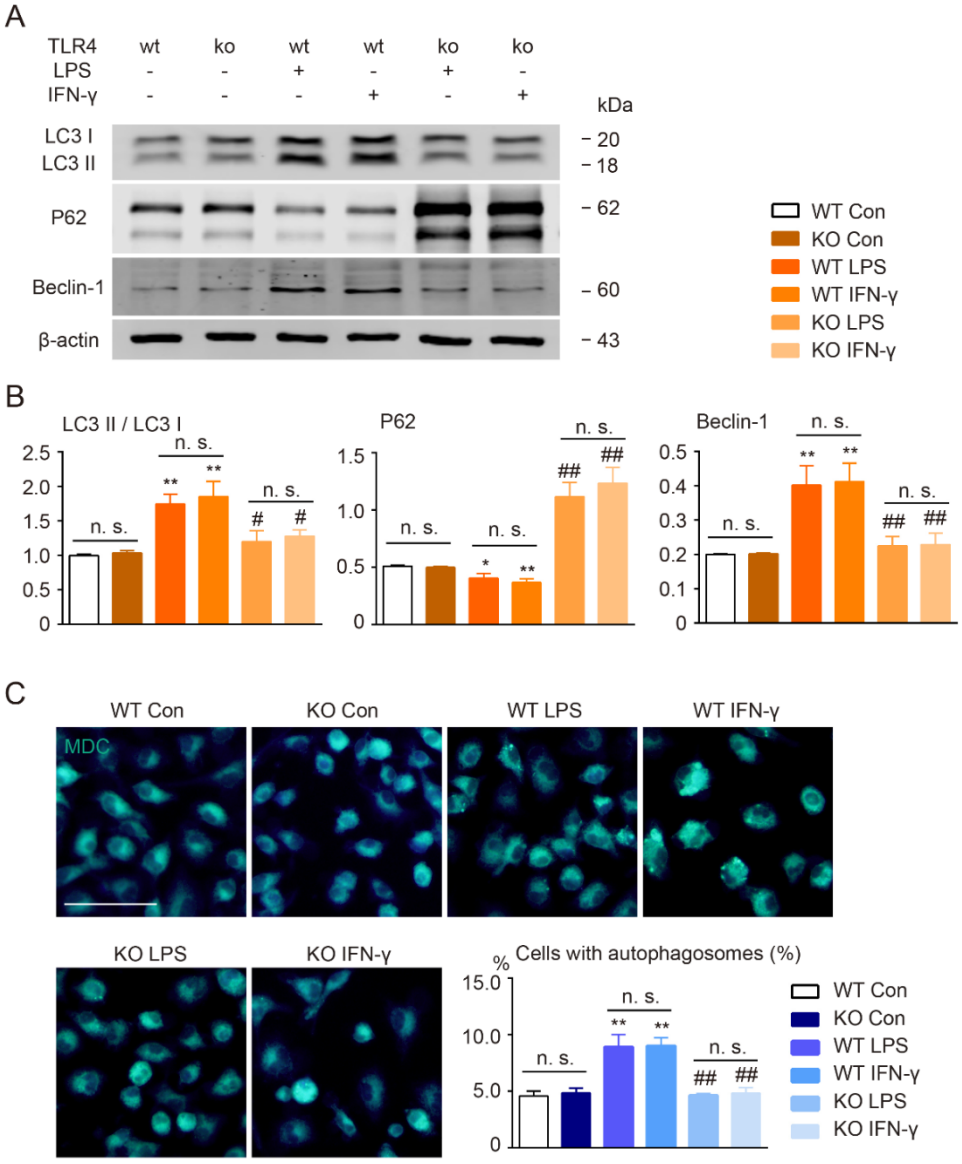

Figure S1. LPS and IFN-γ stimulated autophagy activation in cultured microglia

(**A**) The expression of autophagy related proteins (LC3, P62 and Beclin-1) in cultured microglia were detected by Western blot.

(**B**) Quantitative analysis was performed. Two-way ANOVA with Dunnett's post-hoc test, **P<0.01 versus WT Control, #P<0.05 ##P<0.01 *versus* WT LPS, n.s. no significant changes between different groups. n=8 per group.

(**C**) Representative images of MDC staining for autophagosomes in cultured microglia. Scale bar, 50 μm. Quantitative analysis of cells with autophagosomes was performed. Two-way ANOVA with Dunnett's post-hoc test, **P<0.01 *versus* WT Control, ##P<0.01 *versus* WT LPS, n.s. no significant changes between different groups. n=6 per group.

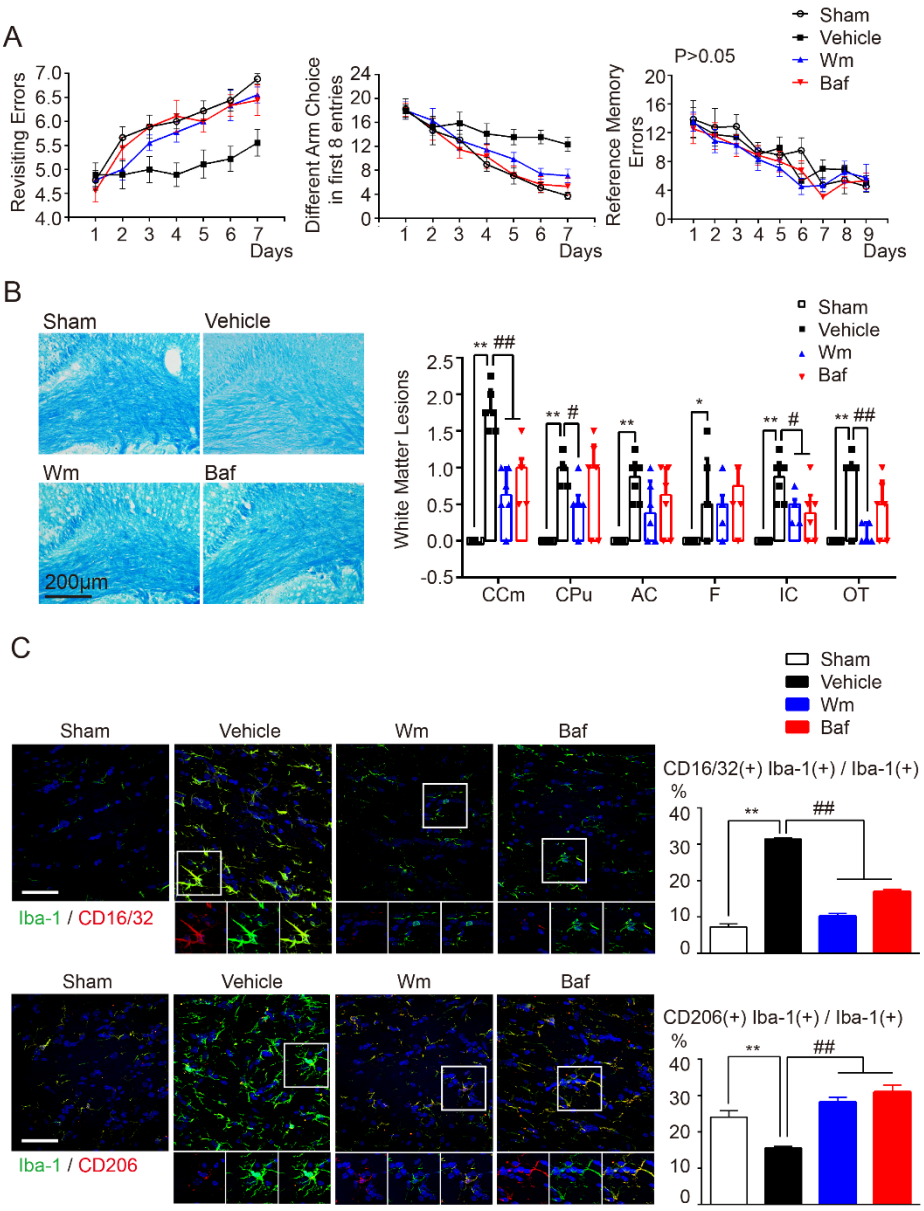

Figure S2. TLR4 deficiency attenuated cognitive impairment and white matter lesions induced by BCAS

(**A**) The working memory and reference memory of mice were assessed by the 8-arm maze test at 1-month post injury. Mice suffered from BCAS made much more revisiting errors ($P<0.001$) and less different arm choices ($P<0.001$) comparing to the sham-operated mice. Wm- and Baf- treated mice with BCAS made much less revisiting errors ($P<0.001$) and more different arm choices ($P<0.001$) comparing to the vehicle group. No impairment in spatial reference memory was revealed between different groups ($P>0.05$). Two-way analysis of variance (ANOVA) with repeated analysis, n=9 in each group.

(**B**) White matter lesions were detected by LFB staining in different groups. Scale bar, 200 μm. Dot-plot with median and interquartile range of the severity of white matter lesions in in CCm, CPu, AC, IC, F and OT in histogram. Two-way ANOVA with Dunnett's post-hoc test, **$P<0.01$ *versus* Sham, #$P<0.05$, ##$P<0.01$ *versus* Vehicle n=6 per group.

(**C**) Representative confocal images of coronal sections labeled with Iba-1, CD16/32 and CD206 at 1-month post BCAS. Scale bar, 50μm. Quantitative analysis of Iba-1, CD16/32 double positive cells and Iba-1, CD206 double positive cells was shown in the histogram. Two-way ANOVA with Dunnett's post-hoc test, **P<0.01 *versus* Sham, ##P<0.01 *versus* Vehicle. n=6 per group.