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Zinc-aggravated M1 microglia suppress astrocytic engulfing activity via P2X7 receptors

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[AIM] M1 microglia influence astrocytic neuroprotective functions, including engulfment of cell debris. Recently, extracellular zinc has been shown to aggravate M1 phenotype in microglia through intracellular zinc accumulation and reactive oxygen species (ROS) generation. Here, we investigated whether zinc-enhanced M1 microglia affects the astrocytic engulfing activity.

[METHODS] Mouse primary astrocytes were preincubated with microglial-conditioned medium (MCM) collected from M1 microglia induced by lipopolysaccharide (LPS) after $ZnCl_2$ treatment in the presence of TPEN, a membrane permeable zinc chelator, or Trolox, a ROS scavenger, and then incubated with fluorescent latex beads. P2X7 receptors (P2X7R) mRNA level in astrocytes was measured by real-time PCR.

[RESULTS] MCM from M1 microglia increased the astrocytes bead uptake. This increased uptake activity was suppressed when MCM from LPS-induced M1 microglia pretreated with $ZnCl_2$ was applied to astrocytes, which was further abolished by TPEN and Trolox. In addition, P2X7R mRNA level was increased in astrocytes treated with MCM from M1 microglia, but not in the M1 microglia pretreated with $ZnCl_2$.

[CONCLUSION] These results suggest zinc pretreatment abolishes the ability of M1 microglia to increase the engulfing activity in astrocytes via alteration of astrocytic P2X7R.