Early microglia inhibition preemptively alleviates the depression development of adolescence mice suffered maternal separation

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Abstract: Objective Exposure to early adversity increase vulnerability to psychiatric disorders in later development. Current addressed therapies for this long-lasting risk in physiology and behavior are still insufficient due to the high rates of complexity, recurrence and unpredictability. A novel therapeutic strategy should be capable of preventing and mitigating for the psychopathology.

Methods It has been shown generally that activated microglia link to individual abnormal behavior. Using maternal separation (MS) (3 h/day, PD1–PD14), a mouse model of early-life stress, we investigated the alterations in passive stress coping and the activation phenotype of microglia under basal conditions or suffered simple restraint stress (SS) in adolescence. Depressive-like behaviors were evaluated by sucrose preference (SP), tail suspension test (TST). Open field test (OFT) was used to evaluate anxiety behavior and locomotor activity. Minocycline was administered intraperitoneally 30 mg per kilogram per day for 2 weeks. The expression of cytokines was determined by real time-PCR (RT-PCR). The activated microglial phenotype was confirmed by immunohistochemistry

Results The results of our study showed that the simple restraint stress during adolescence enhanced the subject response in sucrose preference test, tail suspension test, open field test accompanied by unbalanced expression of pro- and anti-inflammatory cytokines and deficiency of neurogenesis. Addressing with minocycline, a specific inhibitor of microglia, can attenuate susceptibility to adverse
events of MS mice. Simultaneously, we found a decrease in the expression of inflammatory factors and increase of neurogenesis in the hippocampus.

**Conclusion** These results suggest that activated microglia contribute to development of depression and anxiety because its effects on the central microenvironment and neurons. Our study presents potential capacity of the regulation of microglia phenotype in prevention of early psychopathology.

**Keywords:** Maternal separation, Depressive-like behavior, Neuroinflammatory, Microglia, Neurogenesis