

**Microglia-mediated neurogenesis is linked to cognitive deficits in a two-hit
model of maternal immune activation and juvenile stress**

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Background: The mechanisms by which microglia mediate cognitive impairments in individuals exposed to dual stress remains poorly understood. Therefore, the author designed a two-hit model that consists of maternal immune activation (first hit) and subsequent juvenile stress (second hit) to induce the neurodevelopment disorder in the offspring. The author then used Minocycline (MINO) to reduce the inflammation and Temozolomide (TMZ) to inhibit neurogenesis, thereby exploring the role of microglia in the two-hit model.

Objective: To clarify the underlying mechanism involving microglial regulation of neurogenesis that contributes to the observed neurodevelopmental disorder.

Results: Microglia in the MIA-Stress group shift into a neuropathological state and enhance the inflammation response. This shift is associated with decreased hippocampal neurogenesis and subsequent impairments of hippocampus-dependent spatial learning and memory. However, Minocycline may help to reverse these pathological effects.

Conclusion: The neuroprotective effect of Minocycline was abolished by TMZ, suggesting that microglial-mediated cognitive improvement depends on neurogenesis. This study highlights a neurogenesis-related neuroprotective role of microglial cells in cognitive function within the two-hit model.