

Microglial activation contributes to the aberrant migration of newborn neurons induced by severe seizures in adult rats

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Background and Objective: Our previous studies have shown that different seizure severity has different effects on neurogenesis in the dentate gyrus of adult rats.¹ Mild epileptic seizures promoted the most of newborn neurons migrating into the granule cell layer from subgranule zone in the dentate gyrus.² In contrast, severe seizures resulted in the large majority of newborn neurons migrating into the hilus, but not the granule cell layer. These newborn neurons developed into hilar ectopic granule cells with cell bodies oriented in different planes and processes projecting in varying directions, which likely contribute to network abnormalities in the epileptic hippocampal formation. Thus, further investigation needs to be done for the detailed understanding of the mechanisms responsible for the newborn neuron aberrant migration, which might provide a new strategy for epilepsy treatment. We strove to examine the role of microglia in the aberrant migration of newborn neurons induced by severe seizures in the dentate gyrus.

Methods: Using ED7 to label activated microglia and Doublecortin (DCX) to label the migrating neurons, we observed the spatio-temporal profile of microglial activation and the neuronal migration in the hippocampus in the lithium-pilocarpine model. Minocycline was injected intraperitoneally to inhibit microglial activation after severe seizures. Activation of microglia was induced by stereotactic injection of LPS into the dentate hilus.

Results: Activated microglia was observed from 1 day to 15 days after severe seizures. The peak of ED7 positive cells appeared at 7 days. The minocycline treatment inhibited the seizure-induced microglial activation and partially prevented the aberrant migration of newborn neurons in the hippocampus. Furthermore, we found that the LPS local injection induced the expression of ED7 positive cells in the dentate hilus, and produced many ectopic newborn neurons in the dentate gyrus.

Conclusion: Activated microglia might contribute to the aberrant migration of newborn neurons induced by severe seizures in the hippocampus.

References

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