CCI-11

A role for inflammation-related molecules in behavioral depression induced by repeated stress in mice

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Abstract

Stress is a risk factor for major depression. However, the molecular mechanism about how stress alters brain functions remains poorly understood. We reported that prostaglandin (PG) E_2, an inflammation-related molecule, and its receptor EP1 are critical for behavioral depression induced by repeated stress through attenuating the prefrontal dopaminergic activity. To identify how repeated stress induces PGE_2 synthesis in the brain, we examined a role for cyclooxygenase (COX), an enzyme critical for PGE_2 synthesis, and found that COX-1 deficiency abolishes social avoidance and an increase in brain PGE_2 contents induced by repeated stress. COX-1 is localized in microglia before and after repeated stress. Repeated stress induces hyper-ramification of microglia and an increase in Iba-1 immunoreactivity, a marker for microglial activation. These results suggest that microglial activation by repeated stress induces PGE_2 synthesis in the brain for behavioral depression. Given a role of innate immune molecules in microglial activation, we have analyzed and found elevated expression of some, but not all, innate immune molecules in the brain after repeated stress. We are investigating a role for these molecules in behavioral depression.