The perinatal mice administered prostaglandin E₂ develop psychobehavioral and neuronal impairments in adults

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Background: Preclinical and clinical evidence suggest that exposure to perinatal inflammatory mediators such as pro-inflammatory cytokines and prostaglandins is known as risk factors for development of psychiatric disorders. Our previous study revealed that various inflammatory mediators were induced by perinatal exposure to environmental factors; viral infection [injection of polyinosinic-polycytidylic acid (PolyI:C)], hypoxia (exposure to CO₂), and neglect (separation from the dams), and further the prostaglandin E₂ (PGE₂) may be one of common inflammatory mediators induced by environmental factors. However, the roles of PGE₂ in the development of psychiatric disorders are not yet clear. The present study was designed to examine effects of a perinatal PGE₂ administration on the psychobehaviors in adults and effects of PGE₂ on neurite outgrowth in the primary culture.

Methods: The PGE₂ administered at the dose of 10mg/kg/day to C57BL/6N mice during PD 2-6. Emotional and cognitive behavioral analysis were performed in PD35 and PD70. We investigated the effect of PGE₂-EP1 receptor antagonist, indomethacin (cyclooxygenase inhibitor), and EP1 KO mice on behavioral impairment in mice administered of PGE₂. Hippocampal cultures were prepared from gestational day 13-15 old mice, and affects of exposure to PGE₂ on neurite growth were examined.

Results: The mice administered PGE₂ during PD2-6 exhibited impairment of social behaviors, object recognition memory, and pre-pulse inhibition (PPI) in PD70 (adults), but not PD35 (adolescents). These behavioral impairments were attenuated by blockade of PGE₂-EP1 receptor, indomethacin, and genetic deletion of PGE₂-EP1 receptor. In the primary culture, the PGE₂ induced the decrease in neurite growth. Such neuronal change was also prevented by PGE₂-EP1 receptor antagonist.

Conclusion: Our findings suggest that PGE₂ is one of potential common inflammatory mediators induced by environmental factors, and PGE₂ plays a crucial role in the development of behavioral and neuronal impairments, which are associated with activation of PGE₂-EP1 receptor.