aggregation. However, further extensive studies are required to elucidate the underlying mechanism.

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Prenatal nicotine exposure impairs the proliferation of neuronal progenitors, leading to fewer glutamatergic neurons in the medial prefrontal cortex

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Abstract

Cigarette smoking during pregnancy is associated with various disabilities in the offspring such as attention deficit/hyperactivity disorder, learning disabilities, and persistent anxiety. We have reported that nicotine exposure in female mice during pregnancy, in particular from embryonic day 14 (E14) to postnatal day 0 (P0), induces long-lasting behavioral deficits in offspring. However, the mechanism by which prenatal nicotine exposure (PNE) affects neurodevelopment, resulting in behavioral deficits, has remained unclear. Here, we report that PNE disrupted the proliferation of neuronal progenitors, leading to a decrease in the progenitor pool in the ventricular and subventricular zones. In addition, using a cumulative 5-bromo-2'-deoxyuridine labeling assay, we evaluated the rate of cell cycle progression causing the impairment of neuronal progenitor proliferation, and uncovered anomalous cell cycle kinetics in mice with PNE. Accordingly, the density of glutamatergic neurons in the medial prefrontal cortex (medial PFC) was reduced, implying glutamatergic dysregulation. Mice with PNE exhibited behavioral impairments in attentional function and behavioral flexibility in adulthood, and the deficits were ameliorated by microinjection of D-cycloserine into the PFC. Collectively, our findings suggest that PNE affects the proliferation and maturation of progenitor cells to glutamatergic neuron during neurodevelopment in the medial PFC, which may be associated with cognitive deficits in the offspring.

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Involvement of astrocyte-neuron lactate shuttle dysfunction in the cognitive impairment in diabetic mice

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Abstract

Diabetes mellitus is a risk factor for cognitive dysfunction. Several investigations have pointed that hippocampus is the key brain region in diabetic cognitive impairment. However, there are no effective curatives for diabetic cognitive impairment. Since recent reports suggested that the hippocampal astrocyte-neuron-lactate-shuttle (ANLS) is essential for the memory formation, the present study was then designed to investigate the role of ANLS in the cognitive impairment of streptozotocin-induced diabetic mice. Diabetic mice exhibit cognitive impairment in the novel object recognition test and reduced long-term potentiation (LTP) of synaptic transmission in hippocampus. These behavioral and electrophysiological changes are improved by L-lactate. We observed that inhibition of l-lactate synthesis by lactate dehydrogenase (LDH) inhibitor isosafrole caused cognitive dysfunction and reduced hippocampal LTP formation in non-diabetic, but not diabetic mice. Therefore, it is possible that diabetic cognitive dysfunction might be due to the reduced l-lactate supply in the hippocampus. We also observed that the expression of LDH5 was decreased in the hippocampus of diabetic mice as compared with non-diabetic mice. The expression of monocarboxylate transporter (MCT) that transport l-lactate, especially MCT1 and MCT4 isoform, was also decreased in the hippocampus of diabetic mice. These results indicated that the production and supply of l-lactate is attenuated in the hippocampus of diabetic mice. Since l-lactate is synthesized and released from the astrocytes, the expression of glial fibriary acidic protein (GFAP) in the hippocampus was examined. GFAP-immunoreactivity was increased in diabetic mice than non-diabetic mice, indicating that the function of hippocampal astrocytes might be changed. Inhibition of astroglial l-lactate production by pharmacological inhibition of MCT or glycogen phosphorylase caused the cognitive dysfunction in non-diabetic, but not diabetic mice. Therefore, it is possible that the cognitive impairment in diabetic mice is due to the dysfunction of the ANLS in the hippocampus.

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Prenatal nicotine exposure impairs adolescent mouse hippocampal function

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Abstract

It is not clear how prenatal nicotine exposure (PNE) may cause cognitive impairment in offspring. In this study, we investigated whether the exposure to nicotine (0.2 mg/mL in drinking water with 2 % sucrose) during E14-P0 impaired hippocampus-dependent learning and memory in adolescence. In the hippocampal CA1 region, the induction and maintenance of *N*-methyl-D-aspartate (NMDA) receptor dependent long-term potentiation (LTP) was diminished by PNE, whereas the paired-pulse facilitation was not affected. Behaviorally, PNE impaired contextual- but not tone-dependent fear memory in 7- to 8-week-old mice. Both impairments were attenuated by the repeated co-treatment with methyllycaconitine (5 mg/kg s.c.), a nicotinic alpha 7 receptor antagonist. The results suggest that the nicotinic alpha 7 receptor dependent plasticity during embryonic period may be required for NMDA receptor-related long-term memory formation, and that PNE may disrupt this form of plasticity.