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Purines are essential molecules for the synthesis of DNA, RNA, and energy metabolism, and implicated in various cellular functions. There are two pathways for purine synthesis in mammals: de novo pathway and salvage pathway. The balance between these pathways is critical for normal brain development. Impairment in purine metabolism leads to various neurological diseases such as Lesch-Nyhan syndrome. At pesent, it remains to be elucidated how the deficiency in purine metabolism elicits the pathogenesis of these diseases. In addition, the spatiotemporal regulation of these purine synthesis pathways in the central nervous system remains unknown. Here, we investigated the expression profile and the functional significance of purine synthesis enzymes during mammalian brain development. Developmental immunoblot analysis of mice brain revealed that phosphoribosylaminoimidazole carboxylase phosphoribosylaminoimidazole succinocarboxamide synthetase (Paics) and formylglycin-amidine ribonucleotide synthase (Fgams), both of which catalyze de novo purine synthesis, are abundant in the embryonic stage and the expression level of these enzymes were downregulated toward the postnatal and adult stage. Conversely, the expression level of the salvage pathway enzyme, hypoxanthine-guanine phosphoribosyltransferase (Hgprt) is low in the embryonic brain and gradually increases in postnatal and adult stages. During the embryonic and early postnatal period, Paics, Fgams, and Hgprt immunoreactivities were broadly observed in the different brain regions. Noticeably, Hgprt was abundantly expressed in external germinal layer of neonatal cerebellum and blood vessels. In the adult brain, Paics and Fgams were strongly expressed in the brain stem nuclei including red nucleus, cerebellar nuclei, and facial nucleus, while the high level of expression of Hgprt was observed in forebrain and diencephalon, including arcuate hypothalamic nucleus, posterior intralaminar thalamic. Based on these observations, we speculate that the regulated driving balance of de novo and salvage pathways is essential for the proper function of distinct brain regions or developmental stages. To elucidate the functional significance of two pathways, we are currently estimating the effects of the selective inhibitors for de novo or salvage pathways on the embryonic brain neurogenesis. Our findings will contribute to better understanding of neurological diseases caused by abnormalities in purine metabolism.
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