Effect of different thyroid states on mitochondrial porin synthesis and hexokinase activity in developing rabbit brain.
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Abstract
Voltage-dependent anion-selective channel proteins (VDACs) are pore-forming proteins found in the outer mitochondrial membrane of all eukaryotes and in brain postsynaptic membranes. VDACs regulate anion fluxes of a series of metabolites including ATP, thus regulating mitochondrial metabolic functions. Hexokinase binds to porin. The mitochondrially bound hexokinase can greatly increase the rate of aerobic glycolysis. The activities of hexokinase and protein levels of mitochondrial porin were determined in brains of hypothyroid rabbits and in hypothyroid rabbits administered with thyroxine. Proteins were separated by electrophoresis, and the proteins of interest were quantified. Western blotting analysis revealed a significant decrease (approximately 50%) in the relative amount of porin in the hypothyroid compared with euthyroid rabbits. The changes in the developmental pattern of hexokinase activity in the brain of hypothyroid rabbits and the effect of T(4) on this enzyme activity have been investigated. Hypothyroid rabbits showed lower activity than their corresponding age-matched normal neonates. Administration of thyroxine to the hypothyroid neonates at birth abolished the effects of methimazole [1-methyl-2-mercaptoimidazole (MMI)]. These findings apparently indicate that the synthesis of the pore-forming protein and the hexokinase enzymes are under thyroid control during the fetal and the early postnatal period.