

PRENATAL ETHANOL EXPOSURE EFFECTS ON MAP-KINASES PATHWAY IN A GENETIC MODEL OF ABSENCE EPILEPSY: THE WAG/RIJ RAT

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Ethanol exposure during pregnancy and the first post-natal period interferes with neuronal proliferation, migration, differentiation, neurochemical development and can lead, in humans, to a condition known as the fetal alcohol syndrome (FAS), characterized by a wide array of neuropathologies and concomitant cognitive and behavioral dysfunctions. Little is known about the molecular mechanism by which ethanol produces developmental abnormalities. The intracellular signal transduction pathway of “mitogen activated protein kinases” (MAPK), is a major link between events at the level of the plasma membrane and both cytoplasmic and nuclear events. The present study was designed to investigate the molecular bases of ethanol-induced effects in two group of rat strains the Wistar and the WAG/Rij, a genetic model of non-convulsive epilepsy, with particular attention towards the signal transduction-pathways activated by stress-activated protein kinases (total and phosphorylated ERK 1/2, JNK and p-38) after ethanol chronic exposure (during pregnancy until 12 days after the birth). Female rats of the two rat strains drank since the last 10 days of pregnancy to 12 days after delivery a liquid diet consisting of 20% absolute ethanol; the control group received a sucrose replaced isocaloric diet. The newborns (10 ethanol-treated and 10 control rats) at the end of treatment (12 days) were sacrificed and different brain areas (cerebral cortex, hippocampus, diencephalon and cerebellum) were quickly dissected on dry ice and prepared for western blotting analysis. Wistar-ethanol rats showed an activation of the stress-related kinases signaling pathway, not homogeneous for all kinases. A 3-4 fold increase of the phosphorylated form of ERK1/2 MAPKs can be demonstrated only in the hippocampus and diencephalon. A lower and not significant activation of ERK1/2 was found in the diencephalon of sucrose-treated newborns. JKN expression seems to follow ERK1/2 pattern, even though a much higher degree of activation was detected in the hippocampus of ethanol-treated rats while the expression of p-p38 does not seem to be affected by ethanol administration. On the other hand, WAG/Rij-ethanol rats showed a reduction of the expression of the three major stress-activated kinases without differences among the cerebral areas investigated, with a particular emphasis for phosphorylated-ERK 1/2 expression. These data suggest that ethanol influences in a different way the two rat strains probably for their different genetic background and put in evidence an important role played by phosphorylated-ERK 1/2 kinases in the genesis of this kind of epilepsy.