Prenatal Ethanol Effects on NGF Level, NPY and ChAT Immunoreactivity in Mouse Entorhinal Cortex: A Preliminary Study

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ANGELUCCI, F., M. FIORE, C. COZZARI AND L. ALOE. Prenatal ethanol effects on NGF level, NPY and ChAT immunoreactivity in mouse entorhinal cortex: A preliminary study. NEUROTOXICOL TERATOL 21(4) 415–425, 1999.—It has been reported that maternal ethanol consumption leads to deficits in the limbic areas involved in cognitive functions and interferes with synthesis and utilization of neurotrophins. In the present study, it was hypothesized that prenatal alcohol intake might induce neuroanatomical alterations in the entorhinal cortex (EC). We also investigated the possible EC involvement of brain nerve growth factor (NGF), the first neurotrophin to be isolated, during such pathological events. To test this hypothesis, we used pregnant mice exposed to ethanol during EC neurogenesis (starting about gestational day 8). Our data show that prenatal alcohol intake in male mice alters the EC neuronal growth and differentiation. These morphological alterations are accompanied by an altered NGF level in the EC of prenatal alcohol-treated mice. We also found a decrease in choline acetyltransferase- and neuropeptide Y-immunopositive neurons in the EC of alcohol-exposed mice. However, the relationship between neuronal damage induced in the EC by ethanol, low presence of NGF, and the possible functional and behavioral consequences remains to be elucidated. © 1999 Elsevier Science Inc. All rights reserved.

NGF Entorhinal cortex Ethanol ChAT NPY Schizophrenia

MATERNAL ethanol abuse is considered to be one of the most prominent causes of neurobiological malformations in the postnatal and adult life of the offspring (44,46,48). Considerable experimental and clinical evidence indicates that alcohol intake during pregnancy can cause growth retardation and impairment in the proliferating and differentiating activity of neurons (4), leading to deficits in the limbic areas involved in cognitive functions (23). A reduction in the neuronal number and dendritic branches in the hippocampus of the offspring has also been observed (8,22,38).

The entorhinal cortex (EC) constitutes the main source of afferents to the hippocampus and receives cholinergic innervation from the septum (45,58). EC also acts as a relay station between cortical association areas and the hippocampus (58). This brain region is divided into six cortical layers (two of which are poor in cells), containing cholinergic, GABAergic, and glutamatergic neurons (5). During prenatal life, disruptions of migration and neuronal generation in the cortical layers of the EC are associated with pathological states in adult life, including psychiatric disorders (25,36,52).

Recent studies published by our group indicate that alcohol consumption, in both adult rodents and humans, can interfere with the synthesis and utilization of neurotrophins (1–3). If the exposure occurs during prenatal life, ethanol alters the synthesis and uptake of brain nerve growth factor (NGF), the first isolated and best characterized member of a neurotrophin family (35). The major target sites of this alcohol injury are the basal forebrain cholinergic neurons (BFCN). They demand NGF produced in the hippocampus and cortex, for their normal survival and maintenance (4,29,40,41). Our data indicate that maternal alcohol consumption reduces NGF levels in the hippocampus and NGF receptor expression in the BFCN (6). NGF is involved in regulating trophism and innervation of EC (19,49). It has been hypothesized that deficits in synthesis and/or release of NGF during a critical period of EC neurogenesis might result in damage in this brain region. Lesions and neu...