ELSEVIER

Alcohol 41 (2007) 253–261

ALCOHOL

Early postnatal alcohol exposure reduced the size of vibrissal barrel field in rat somatosensory cortex (SI) but did not disrupt barrel field organization

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Received 2 January 2007; received in revised form 13 April 2007; accepted 13 April 2007

Abstract

Prenatal alcohol exposure (PAE) has been shown to alter the somatosensory cortex in both human and animal studies. In rodents, PAE reduced the size, but not the pattern of the posteromedial barrel subfield (PMBSF) associated with the representation of the whiskers, in newborn, juvenile, and adult rats. However, the PMBSF is not present at birth, but rather first appears in the middle of the first postnatal week during the brain-growth spurt period. These findings raise questions whether early postnatal alcohol exposure might disrupt both barrel field pattern and size, questions that were investigated in the present study. Newborn Sprague-Dawley rats were assigned into alcohol (Alc), nutritional gastric control (GC), and suckle control (SC) groups on postnatal day 4 (P4). Rat pups in Alc and GC were artificially fed with alcohol and maltose-dextrin dissolved in milk, respectively, via an implant gastrostomy tube, from P4 to P9. Pups in the Alc group received alcohol (6.0 g/kg) in milk, while the GC controls received isocaloric equivalent maltose-dextrin dissolved in milk. Pups in the SC group remained with their mothers and breast fed throughout the experimental period. On P10, pups in each group were weighed, sacrificed, and their brains removed and weighed. Cortical hemispheres were separated, weighed, flattened, sectioned tangentially, stained with cytochrome oxidase, and PMBSF measured. The sizes of barrels and the interbarrel septal region within PMBSF, as well as body and brain weights were compared between the three groups. The sizes of PMSBF barrel and septal areas were significantly smaller ($P < .01$) in Alc group compared to controls, while the PMBSF barrel pattern remained unaltered. Body, whole-brain, forebrain, and hemisphere weights were significantly reduced ($P < .01$) in Alc pups compared to control groups. GC and SC groups did not differ significantly in all dependent variables, except body weight at P9 and P10 ($P < .01$). These results suggest that postnatal alcohol exposure, like prenatal exposure, significantly influenced the size of the barrel field, but not barrel field pattern formation, indicating that barrel field pattern formation consolidated prior to P4. These results are important for understanding sensorimotor deficits reported in children suffering from fetal alcohol spectrum disorder (FASD).

Keywords: Fetal Alcohol Syndrome; FAS; Somatosensory cortex; Barrel cortex; Whisker barrels; Sensorimotor deficits; Somatotopy

Introduction

Exposure to alcohol during prenatal development has been shown to lead to growth retardation, facial dysmorphology, and brain anomalies in humans (Jones and Smith, 1973, 1975), collectively referred to as fetal alcohol syndrome (FAS) (Clarren and Smith, 1978; Connor et al., 2006; Streissguth et al., 1984, 1991). These anomalies have also been reported in rodents exposed to alcohol during gestation and/or during the early postnatal period (Lopez-Tejero et al., 1986; Mattson et al., 2001; Tran et al., 2000). The behavioral deficits seen in offspring of mothers that abuse alcohol during pregnancy and in rodents exposed to alcohol during gestation and early postnatal periods indicate that the sensorimotor system is particularly susceptible to alcohol during brain development. Children with FAS have delayed motor development and somatosensory impairments necessary for performance of fine and gross

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0741-8329/07/$ – see front matter © 2007 Elsevier Inc. All rights reserved.
doi: 10.1016/j.alcohol.2007.04.005

motor skills (Burd et al., 2003; Connor et al., 2006; Lopez-Tejero et al., 1986). Exposure to alcohol during brain development has been shown to affect reaction time, attention, and response latency in children with FAS (Streissguth et al., 1984). In rodents, prenatal exposure to alcohol disrupted the distribution of callosal projection neurons in first somatosensory cortex (SI) (Miller, 1997), significantly decreased somatosensory cortical volume, total neuron and glial cell numbers (Miller and Potempa, 1990), and resulted in significant structural and metabolic alterations in rat cerebral cortex (Miller and Dow-Edwards, 1988, 1993). Similarly, early postnatal alcohol exposure decreased brain weight (Bonthius and West, 1991; Maier et al., 1999), reduced neocortical volume (Mooney and Napper, 2005), and reduced the size of neocortex (Miller, 1996) in rats.

The stages of brain development are similar in both humans and rodents, except for their timing with respect to birth. The full gestation period (prenatal life) in rodents is equivalent to the first and second trimesters, while postnatal day 1 (P1) to P10 corresponds roughly to the third trimester in humans (Bayer et al., 1993). Thus, exposure of rodents to alcohol during pre- and postnatal periods is expected to produce similar deficits as seen in offspring of human mothers who abuse alcohol during pregnancy. Since the brain undergoes regional differences in growth, genesis, migration, and proliferation of various neuronal cell types during development, the nature of anatomical anomalies and functional deficits seen in animals and humans exposed to alcohol early in life is dependent on the period of the exposure. Rats exposed to alcohol during either the latter half of gestation, throughout gestation, or the early postnatal period had significant reductions in body and brain weights compared to those exposed to alcohol during the early gestational period (Tran et al., 2000). These findings show that the latter half of gestation and the early postnatal period, which are analogous to the second and third trimesters of pregnancy in humans, constitute critical periods of vulnerability of brain to the deleterious effects of alcohol.

The rodent barrel field in layer IV of SI consists of clusters of cells, called barrels, that are organized into larger subfields associated with the representation of the body surface (Welker and Woolsey, 1974). One subfield, the posteromedial barrel subfield (PMBSF) is associated with the representation of large mystacial vibrissae on the contralateral face (Welker and Woolsey, 1974). The presence of barrels in PMBSF is dependent on thalamocortical afferents from the ventral posterior medial nucleus (VPM) of the thalamus. VPM receives input from the principal trigeminal nucleus that in turn receives input from deep vibrissal nerves (Rice, 1995). The first postnatal week is a critical period for barrel field development since the barrel field is not present until P3 (McCandlish et al., 1989) and requires an intact periphery for development of a normal barrel field pattern (Dawson and Killackey, 1987; Waters et al., 1990).

The PMBSF has recently been used as a model system to study the effects of prenatal alcohol exposure (PAE) on barrel field organization and development. PAE has been reported to delay the development of PMBSF and limb barrel subfields by 1–2 days (Margret et al., 2006), reduce total PMBSF area and sizes of individual barrels within the PMBSF in rats (Margret et al., 2005b) and mice (Powrozek and Zhou, 2005), and delay thalamocortical afferents from reaching presumptive barrel field cortex (Margret et al., 2005a). Since the first postnatal week also constitutes a critical period for brain vulnerability to alcohol exposure (Tran et al., 2000) and a critical period of development of the PMBSF barrel field in rodents (Killackey and Belford, 1979; Margret et al., 2006; McCandlish et al., 1989; Rice, 1995; Rice and Van der Loos, 1977; Wu and Gonzalez, 1997), it was unknown whether early postnatal alcohol exposure would alter barrel field pattern formation and/or barrel field size. In the present study, we extended our previous PAE findings (Margret et al., 2005b) to an examination of effects of postnatal alcohol exposure on barrel field size and pattern in rat PMBSF.

Methods

The Texas A&M University Laboratory Animal Care Committee approved all procedures prior to the start of the experiment. All animal care procedures were performed under the minimal standards set forth by the NIH Guide for the Care and Use of Laboratory Animals (NIH Publication No. 80-23).

Animals

Twenty-eight male and female rat pups derived from 8 timed pregnant adult female Sprague-Dawley rats were used in this study. Pregnant female rats were generated on-site (The Texas A&M University) and housed individually for the duration of pregnancy. On the day following birth, litters were culled to 10 (equal gender when possible) and fostering methods were used to maintain litters between eight to ten pups from P1 to P4 (the day of surgery).

Treatment groups

There were three treatment groups: alcohol (Alc, 6.0 g/kg/day; $n = 10$), nutritional gastrostomy control (GC; $n = 10$), and suckle control (SC; $n = 8$). Whenever possible, all three treatment groups were represented within one litter and no more than two pups (one of each gender) from the same litter were placed into the same treatment group. All pups remained with their untreated, lactating dams until they were randomly assigned into the three treatment groups at P4; fostering methods were used to maintain the litter size at a minimum of eight pups. The pups in Alc and GC groups were artificially reared. Those in Alc group received two, 20-min infusions of milk diet containing