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Recognition memory is selectively impaired in adult rats exposed to binge-like doses of ethanol during early postnatal life

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ABSTRACT

Exposure to alcohol *in utero* can induce a variety of physical and mental impairments, collectively known as fetal alcohol spectrum disorders (FASD). This study explores the persistent cognitive consequences of ethanol administration in rat pups over postnatal days (PD) 4–9, modeling human third trimester consumption. Between PD65-70, ethanol-exposed (5E) and control rats were evaluated in two variants of recognition memory, the spontaneous novel object recognition (NOR) task, using 20 and 240 min sample-to-test delays, and the associative object-in-context (OIC) task, using a 20 min delay. No treatment group differences were observed in object exploration during the sample session for any task. In the 20 min NOR test session the 5E rats explored the novel object significantly less than controls, relative to the total time exploring both objects. Postnatal ethanol exposure is hypothesized to impede object memory consolidation in the perirhinal cortex of 5E rats, hindering their ability to discriminate between familiar and novel objects at short delays. The 5E rats performed as well or better than control rats in the 240 min NOR and the 20 min OIC tasks, indicating developmental ethanol exposure selectively impairs the retention and expression of recognition memories in young adult rats.

1. Introduction

Fetal alcohol spectrum disorders (FASD) represent a range of long-lasting somatic and cognitive impairments in children and adults exposed to alcohol in the womb (Mattson, Crocker, & Nguyen, 2011; Schaefer & Deere, 2011; Streissguth, 2007). Worldwide, FASD remains a major public health issue (Roozen et al., 2016) and one of the leading preventable causes of mental retardation (May et al., 2009; Senturias & Asamoah, 2014). Neuroimaging studies of the central nervous system (CNS) in individuals with FASD have shown decreases in white matter and overall brain volume (Archibald et al., 2001), including reductions in the hippocampus (HC) and prefrontal cortex (Bookstein, Sampson, Streissguth, & Connor, 2001; Spadoni, McGee, Fryer, & Riley, 2007). Binge drinking is particularly detrimental to fetal development (Maier & West, 2001) and, during the third trimester, induces persistent impairments in higher-order cognition (Brown et al., 1991; Korkman, Kettunen, & Autti-Ramo, 2003), including executive function, learning, and memory (Kodituwakku, Handmaker, Cutler, Weathersby, & Handmaker, 1995; Lee, Mattson, & Riley, 2004; Nanson & Hiscock, 1990).

Similar to humans, FASD model rodents demonstrate altered neurodevelopment following perinatal (pre- and/or postnatal) ethanol exposure (Driscoll, Streissguth, & Riley, 1990; Patten, Fontaine, & Christie, 2014). The extent of ethanol's neurotoxic effects is principally determined by the timing of exposure and the resulting peak blood alcohol concentration (BAC). Modeling FASD, our lab administers binge-like doses of ethanol to rat pups over postnatal days (PD) 4–9, a period comparable to the human third trimester (Bayer, Altman, Russo, & Zhang, 1993). The developing HC and medial prefrontal cortex (mPFC) are particularly vulnerable to postnatal ethanol, which induces cell death, aberrant cell migration and survival, and reductions in synaptic density and complexity (Gil-Mohapel, Boehme, Kainer, & Christie, 2010; Hamilton, Whitcher, & Klintsova, 2010; Livy, Miller, Maier, & West, 2003; Whitcher & Klintsova, 2008). Postnatal ethanol has also been dose-dependently linked to forebrain-dependent learning and memory deficits in juvenile and adult rodents, including spatial

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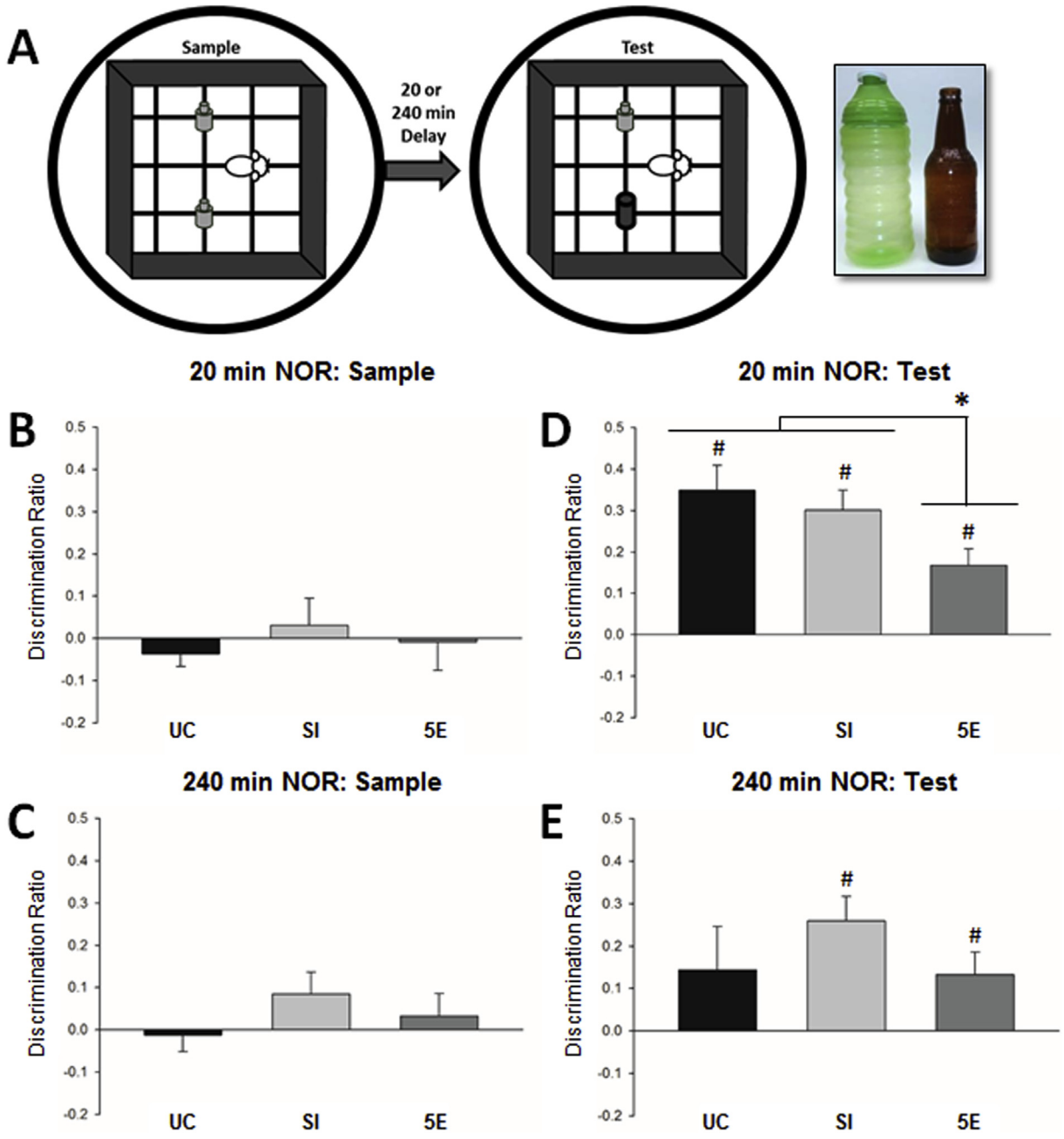

Fig. 1. Novel object recognition (NOR) memory task. (**A**) Subjects were exposed to context A, surrounded by a 180 cm high black curtain, containing one pair of identical objects (counter-balanced) during the sample session (5 min). Novel object recognition memory was tested 20 or 240 min later during the test session (3 min), with subjects exposed to one familiar and one novel object (counter-balanced across left-right position). The photograph shows the two objects used in the NOR and OIC (see Fig. 2) tasks. Discrimination ratios (mean ± SE) reflect the time exploring one object (as a proportion of total exploration). No treatment group differences were seen for the (**B**) 20 min or (**C**) 240 min NOR sample sessions. (**D**) Novel object exploration, with the 20 min delay, was significantly impaired in the 5E rats relative to UC and SI rats during the test session (asterisk). All treatment groups explored the novel object at rates greater than chance (pound sign). (**E**) Novel object exploration, with the 240 min delay, was not significantly affected by postnatal treatment during the test session. The SI and 5E, but not UC, treatment rats explored the novel object at rates greater than chance (pound sign).

learning (Goodlett & Peterson, 1995; Idrus, McGough, Riley, & Thomas, 2014), one-trial context fear conditioning (Goodfellow & Lindquist, 2014; Murawski & Stanton, 2010), and trace fear conditioning (DuPont, Coppola, Kaercher, & Lindquist, 2014; Goodfellow, Abdulla, & Lindquist, 2016; Hunt & Barnet, 2014).

In the FASD population, learning and memory deficits are selectively compromised rather than global in nature. For example, abnormal declarative (or explicit) memory but not procedural (or implicit) memory has been reported following prenatal alcohol exposure in both children and adults (Mattson et al., 2011; Olson, Feldman, Streissguth, Sampson, & Bookstein, 1998). One of the most widely studied forms of declarative memory is recognition memory (Manns, Hopkins, Reed, Kitchener, & Squire, 2003), which relies on a subject's sense of familiarity for previously encountered objects or environments and/or the recollection of specific details about the experience, such as what was encountered and where (Brown & Aggleton, 2001; Mandler, 1980). In rodents, attention and a preference for novelty leads to the incidental acquisition of