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Fear learning deficits after acute ethanol or MK-801 treatment in adolescent and adult C57BL/6J and DBA/2J inbred mice

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Ethanol and other drugs can disrupt learning and memory processes, creating problems associated with drug use and addiction. Understanding individual factors that determine susceptibility to these effects, such as genetic background, age, and sex, is important for prevention and treatment. Comparison of inbred mouse strains can reveal genetic contributions to such phenotypes. We treated adolescent and adult, male and female, C57BL/6J and DBA/2J inbred mice with ethanol (1 g/kg or 1.5 g/kg) or MK-801 (0.05 mg/kg or 0.1 mg/kg), an NMDA receptor antagonist, prior to fear conditioning training. Contextual and cued fear retention were tested one day and eight or nine days after training. Adult DBA/2J mice were less susceptible to ethanol-and MK-801-induced contextual learning impairments than adult C57BL/6J mice. Contextual deficits were expressed one week after initial contextual testing in ethanol-treated, C57BL/6J adults. Adolescents of both strains were less susceptible to ethanol impairments than adults within the same strain. However, adolescent DBA/2J mice showed strain-specific greater contextual deficits after MK-801 than adult DBA/2J mice. Adult and adolescent C57BL/6J mice were similarly susceptible to MK-801-induced contextual deficits, and MK-801 did not affect cued learning. Sex was found to interact with strain and drug treatment to impact performance in retests and cued learning. Collectively, we demonstrate that genetic background contributes to contextual learning after ethanol or MK-801 exposure. Further, we report age-dependent drug sensitivities that are strain-and drug-specific, suggesting that age and genetic background interact to determine drug-induced contextual learning impairments.

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