Ethanol inhibits neurotransmission in the nucleus accumbens of juvenile mice through the activation of GABA receptors

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Methods

- Juvenile (22-30 days old) and adult (>5 months old) male C57Bl6 mice were decapitated under fluothane-induced anesthesia. Their brains were rapidly removed and coronal slices (400 µm thick) containing the NAc were prepared with a microslicer. Slices were incubated for at least 1 h at 32°C in oxygenated artificial cerebro-spinal fluid (aCSF), before they were transferred to a recording chamber where they were continuously perfused with aCSF at 28°C.
- Glutamatergic synaptic transmission in the core region of the NAc was assessed by measuring the amplitude of AMPA-mediated field excitatory postsynaptic potentials/population spikes (fEPSP/PSs) evoked by stimulation of glutamatergic inputs present in the slice.
- Ethanol and GABA receptor antagonists and agonists were applied in the perfusion solution in known concentrations.

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Introduction and aim of the study

Adolescents are more sensitive than adults to the reinforcement properties of alcohol and are particularly vulnerable to harmful effects of this addictive substance. The precise cellular mechanisms that underlie age-related alterations in brain functions produced by alcohol have not been extensively studied.

Our aim was to examine and compare the effect of acute ethanol in juvenile vs. adult mice on glutamatergic synaptic transmission in the nucleus accumbens (NAc), a brain region importantly involved in reward-motivated behaviors.

Results

I – Basic properties of synaptic transmission in NAc

Graph shows Input/Output curves in the NAc of juvenile (open squares) and adult (filled squares) mice. fEPSP/PS amplitude is plotted against stimulation intensity, which was increased by increments of 10 µA.

II – Effect of ethanol on synaptic transmission

Time course of the effect of ethanol (50 mM) on the amplitude of the fEPSP/PS (mean ± SEM) in the NAc of juvenile (n=13, a) and adult (n=10, b) mice. Representative records of fEPSP/PSs measured in different slices, at the time points indicated on the graphs, are illustrated above the graphs. In the presence of the GABA<sub>B</sub> receptor antagonist bicuculline (5 µM, n=6, c) and the GABA<sub>A</sub> receptor antagonist CGP 55845 (1 µM, n=6, d), ethanol did not depress the amplitude of the fEPSP/PS in juvenile mice.

Conclusions

1- Ethanol inhibits glutamatergic neurotransmission in the nucleus accumbens of juvenile but not adult mice.
2- This effect involves GABA<sub>A</sub> and GABA<sub>B</sub> receptors.
3- Activation of GABA<sub>A</sub> and GABA<sub>B</sub> receptors depresses neurotransmission more strongly in juvenile than in adult mice.
4- An increased GABA receptor function might thus underlie enhanced sensitivity to alcohol in adolescents.

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