Institutionen för Fysiologi och Farmakologi

Effects of acute alcohol exposure on glutamate neurotransmission in adolescents and adults: a preclinical study

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ABSTRACT

The age at which an individual first uses alcohol is a powerful predictor of alcohol dependence later in life. Brain development and maturation continues during adolescence until adulthood in humans. There are continuous morphological and functional alterations within the brain areas involved in emotions, learning, decision-making and reward-motivated behaviors and alcohol exposure during this period may modify the development of these regions, increasing the sensitivity of adolescents to some of alcohol's effects. Thus, adolescents might be or may become more sensitive to the rewarding properties of alcohol than adults. Despite the important role of glutamate neurotransmission for brain development and many other brain functions and despite the fact that ethanol consumption during adolescence may have a detrimental impact on these functions, we know surprisingly little about glutamatergic transmission in the adolescent brain and its modulation by alcohol. Here the acute effects of ethanol on glutamatergic neurotransmission in nucleus accumbens (NAc) were studied using brain slice electrophysiology and glutamate release and dynamics in the prefrontal cortex (PFC) were studied using enzyme-based microelectrode amperometry.

The results of the present thesis reveal several age-dependent differences in glutamatergic neurotransmission in these brain regions. Using extracellular electrophysiology, I found that the inhibitory effect of acute ethanol on glutamatergic transmission (fEPSP/PS) in the NAc was higher in brain slices from adolescent animals compared to brain slices from adults. As previously reported, the mechanism by which acute ethanol inhibits glutamate neurotransmission was found to be presynaptic inhibition of glutamate release and this effect was blocked by GABA receptor antagonists. Moreover, acute ethanol was found to inhibit the induction on long-term potentiation (LTP) in the NAc. In the PFC, glutamate levels in freely moving animals were measured and it was found that basal levels of glutamate were more than three times higher in adolescent animals than in adults. Spontaneous release of glutamate in terms of glutamate transients was higher in the PFC of adolescent rats than in the PFC of adult rats. The transients were inhibited by ethanol in the adolescent animals but they were unaffected in the adults. The data in my thesis thereby confirms previous studies suggesting age-dependent differences in glutamatergic neurotransmission in response to ethanol and extend our knowledge about effects of ethanol on adolescent brain. These age-related differences and differential effects of alcohol on glutamate neurotransmission in adolescent animals may be a contributing factor underlying the increased susceptibility of a young individuals' brain to develop alcoholism or other addictions later in life.

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