Nucleus accumbens MC4-R stimulation reduces food and ethanol intake in adult rats regardless of binge-like ethanol exposure during adolescence

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The melanocortin (MC) system regulates feeding and ethanol consumption. Recent evidence shows that melanocortin 4 receptor (MC4-R) stimulation within the nucleus accumbens (NAc) elicits anorectic responses and reduces ethanol consumption and ethanol palatability in adult rats. Ethanol exposure during adolescence causes long-lasting changes in neural pathways critically involved in neurobehavioral responses to ethanol. In this regard, binge-like ethanol exposure during adolescence reduces basal alpha-melanocyte-stimulating hormone (?-MSH) and alters the levels of agouti-related peptide (AgRP) in hypothalamic and limbic areas. Given the protective role of MC against excessive ethanol consumption, disturbances in the MC system induced by binge-like ethanol exposure during adolescence might contribute to excessive ethanol consumption during adulthood. In the present study, we evaluated whether binge-like ethanol exposure during adolescence leads to elevated ethanol intake and/or eating disturbance during adulthood. Toward that aim, Sprague-Dawley rats were treated with ethanol (3 g/kg i.p.; BEP group) or saline (SP group) for 14 days (PND 25 to PND 38). On PND73, all the groups were given access to 20% ethanol on an intermittent schedule. Our results showed that adult rats given intermittent access (IAE) to 20% ethanol achieved high spontaneous ethanol intake that was not significantly enhanced by binge-like ethanol pretreatment during adolescence. However, BEP group exhibited an increase in food intake without a parallel increase in body weight (BW) relative to SP group suggesting caloric efficiency disturbance. Additionally, we evaluated whether binge-like ethanol exposure during

adolescence alters the expected reduction in feeding and ethanol consumption following NAc shell administration of a selective MC4-R agonist in adult rats showing high rates of ethanol consumption. For that, animals in each pretreatment condition (SP and BEP) were divided into three subgroups and given bilateral NAc infusions of the selective MC4-R agonist cyclo(NH-CH2 -CH2 -CO-His-D-Phe-Arg-Trp-Glu)-NH2 (0, 0.75 or 1.5 μg). Results revealed that MC4-R stimulation within the NAc reduced feeding and ethanol intake in high ethanol-drinking adult rats, regardless of previous binge-like ethanol exposure during adolescence, which adds new evidence regarding the dual ability of MC compounds to control excessive ethanol and food intake.

Adolescence

Binge-like ethanol exposure

Intermittent-access ethanol paradigm

MC4-R

Melanocortin

Nucleus accumbens

alcohol

melanocortin 4 receptor

melanocortin receptor agonist

adolescent

adult

alcohol consumption

animal experiment

Article

blood level

body weight gain

caloric intake

controlled study

eating disorder

exposure

food intake

male

nonhuman

nucleus accumbens

nucleus accumbens shell

protein function

rat