Binge drinking differentially impairs decision making and dopamine transmission in the core of the nucleus accumbens depending on sex

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Introduction: Binge drinking (BD) is a harmful behavior for health and is a predictive factor for the development of alcohol addiction (AUD). Weak decision-making (DM) capacities could play a role in vulnerability to BD which in turn would lead to DM impairments and thus perpetuate BD. Differences in BD vulnerability have been reported according to sex. Few longitudinal studies have attempted to understand the mechanisms underlying the interaction between decision-making and BD. We used two procedures to mimic binge-like alcohol intake in male and female rats, one passive exposure and one voluntary ingestion, and assessed DM capacity before binge exposure onset and after the end of the BD period. Dopaminergic transmission is well known to underlie both the DM mechanisms and the rewarding effects of alcohol. Dopamine (DA) release in the core of the nucleus accumbens (NAc) is a mechanism involved in both DM and rewarding effect of alcohol; and is regulated by dopamine D2/3 autoreceptors. Ex vivo DA transmission was assessed short term after the end of the binge exposure in the core of the NAc using the fast-scan cyclic voltammetry (FSCV) technique.

We assessed DM abilities of male and female rats before and after an exposure to ethanol mimicking BD, either a voluntary or forced procedure, using the Rat Gambling Task (RGT). Anxiolytic and learning abilities were also assessed using the light-dark box (LDB) and Novel Object Recognition (NOR) procedures. We studied modifications of the dopaminergic phasic transmission in the NAc core at the end of the experiment, using the fast-scan cyclic voltammetry (FSCV) technique in brain slices.

Materials and Methods

Decision-making: Rat gambling task

Rats were trained daily to nose poking in response to red lights in response to earn sugar pellets. Each hole was associated with a fixed probability of reward (sugar pellets) and punishment (time-out period) allowing to discriminate betweenaversive options (P1 and P2, where P1 being more profitable) and disadvantageous ones (P3 and P4, with P4 being least profitable).

Results: behavior

Decision-making before ethanol

(Right) Male and female rats had a different choice strategy in the RGT before ethanol exposure. The male rats preferred the optimal P2 option, while the female rats preferred both P1 and P2 without distinction. The P1 option can be seen as a risk-averse as it is associated with low reward and punishment. The male group had significantly more individuals with a poor decision-making level (≤53% advantageous choices) than the female group, who were devoid of those.

Results: neurobiology

Baseline DA phasic transmission

(B, C) Extracellular dopamine was recorded in the nucleus accumbens core (NAc) by applying a triangular waveform (0.4 to 1.2, 40V) to a carbon-fiber working electrode. Phasic release of DA was elicited every 30 s using monophasic stimulation (54 pulses, 2ms width) for 5.3 ms with a 100 μA intensity and a 60Hz frequency. Pharmacology was performed using ethanol and quinpirole.

BD history, whether forced or voluntary, did not affect baseline DA phasic transmission. [D] BD did modify DAPα3 (maximal extracellular concentration of DA released), DAPα2 (DA concentration released per pulse) and Vmax (velocity of the dopaminergic transporter).

Baseline DA phasic transmission wasn't different depending on sex.

Conclusion: This preclinical longitudinal study examined the impact of BD on DM capacities taking into account for sex and BD-exposure paradigm and assessing changes in DA signaling in the core of the NAc. Choice processes were impaired specifically in males, after either passive or active BD history, however, decrease in impulse control was highlighted in both sexes. Thus, the binge history differentially affected two of the main factors known to underly DM behavior in both sexes. Behavioral changes were associated with changes in the DA signaling in the core of the NAc with a blunting or reversal of the enhancing effect of acute alcohol in males, and an increase in the sensitivity of quinpirole-mediated inhibition of dopamine release in females but not in males. The observed changes in DA signaling after the binge history may involve adaptations of the D2/D3 autoreceptors in both sexes. Overall, our study demonstrated that binge exposure affected both DM processes and DA signaling in the core of the NAc in a sex-related manner, further suggesting that these effects may play a role in the vicious cycle leading to BD perpetuation and the early onset of AUD and dependence.