EFFECTS OF THE ENVIRONMENTAL TOXICANT, PARAQUAT, ON BINGE-LIKE ALCOHOL DRINKING AND ALCOHOL-INDUCED LOCOMOTOR SENSITIZATION IN HIGH AND LOW-ALCOHOL-PREFERRING MICE

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Introduction

Aim: To explore motivation and reward-related disturbances in PD and excessive alcohol consumption using an environmental toxicant exposure model and mice susceptible for high alcohol preference.

Parkinson's Disease (PD): • Characterized by significant dopaminergic (DA) neuron loss in the substantia nigra and motor impairments. • Non-motor symptoms range from autonomic disturbances to neuropsychiatric comorbidities (e.g. motivational dysregulations).

Alcohol Use Disorder (AUD): • Dysregulations in striatal dopaminergic systems underlie motivation and reward-related changes.

PQ: A common herbicide toxic to DA and is an environmental risk factor for PD.

High (HAP) & Low (LAP) alcohol-prefering mice: A genetic animal model for inherited propensity toward risk for AUD. Neurobiological processes related to excessive alcohol consumption may interact with PD-related changes.

Hypothesis: Paraquat exposed mice will show greater binge-like alcohol drinking and alcohol-induced locomotor sensitization compared to non-exposed mice.

Methods

Exp. 1: Binge-like Alcohol Drinking In HAP Mice

Fig 1. 2-hour ETOH intake across 4 days

Fig 2. DA and turnover in Dorsal (DS) and Ventral (VS) striatum

Mixed ANOVA (Sex x PQ x Time)
• PQ x Sex, p = 0.032; PQ-exposed HAP males had significantly lower ETOH intake than non-PQ HAP males, p = 0.002. This effect was absent in females.
• In a subset of animals there was a trend of higher DA turnover in VS of PQ-exposed mice, and a lower 5-HT turnover in DS of PQ-exposed males (not shown).

Discussion

• PQ reduced binge-like alcohol drinking in male mice genetically susceptible for high alcohol preference, but not females.
• Motivation vs. Hedonic changes?
• Higher DA turnover in VS suggest a possible compensatory DA activity in response to PQ-induced damage.
• PQ-treated mice had greater variability in their alcohol-induced locomotor activity. Increase PQ exposure?

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References