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The effects of stress on alcohol consumption: mild acute and sub-chronic stressors differentially affect apomorphine susceptible and unsusceptible rats

E.L. van der Kam*, J.C.M. Coolen, B.A. Ellenbroek, A.R. Cools

Department of Psychoneuropharmacology (234), Nijmegen Institute of Neuroscience, UMC St Radboud, PO BOX 9101, 6500 HB Nijmegen, the Netherlands

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Abstract

The aim of this study was to investigate the effects of mild acute and mild sub-chronic challenges on alcohol intake and preference in the genetically selected ratlines of apomorphine susceptible (APO-SUS) and apomorphine unsusceptible (APO-UNSUS) animals. Animals from both lines were subjected to the 24 hr continuous alcohol vs. water paradigm under baseline conditions, after a single stressor and after multiple stressors. The intake of alcohol in ml was measured and converted to two values, namely intake in g/kg/24 hour of, and preference for, alcohol. This study shows that under baseline conditions the APO-UNSUS animals consume/prefer more alcohol than the APO-SUS animals. After an acute challenge the APO-SUS animals show a large increase in consumption, whereas the APO-UNSUS animals display only a small increase. Furthermore, sub-chronic challenges can further increase the consumption of the APO-UNSUS rat, but not that of the APO-SUS rat. The APO-SUS/ APO-UNSUS rats represent a good model to study the interaction between genetic factors and stress on directing alcohol consumption.

Keywords: Alcohol consumption; Individual differences; Stress; Reward; Wistar rats

* Corresponding author. Tel.: +31 243613698; fax: +31 243540044.
E-mail address: e.vanderkam@pnf.umcn.nl (E.L. van der Kam).

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Introduction

Individual susceptibility to the use and misuse of drugs of abuse, like alcohol, is a well-known phenomenon in animals (Pohorecky, 1981). Studies have shown that different strains of an animal species can be selectively bred using their differential preference for alcohol (Goodwin et al., 2000; Sinclair et al., 1992). These strains have subsequently been used to study the role of genetic and environmental factors in directing alcohol consumption (Sluyter et al., 2000; Piazza et al., 1989; Todte et al., 2001).

For instance, studies with the genetically selected alcohol-preferring rats have shown that lower dopamine levels in the striatum, a reduced number of TH-immunoreactive fibers in the ventral striatum, and lower levels of D2 receptors in the basal ganglia circuitry are correlated to high alcohol consumption (Stefanini et al., 1992; Gongwer et al., 1989; Gongwer et al., 1989; Murphy et al., 1982; Casu et al., 2002; Mcbride and Li, 1998). Furthermore, Taylor et al have shown that rats, selectively bred for high plasma (nor)adrenaline levels, have a higher preference for alcohol than their counterparts (Taylor et al., 1990). Since several studies have suggested an interaction or even a direct link between peripheral and central adrenergic systems (Maas, 1984; Matsumoto et al., 1991; Dietl, 1985), it is not unlikely that a high brain noradrenergic activity is also associated with high alcohol consumption.

Another factor that has been shown to be important in (re)directing the vulnerability to drugs of abuse is the amount of stress during or preceding use (Dellu et al., 1996; Piazza and Le Moal, 1996; Piazza and Le Moal, 1998; Fahlke and Eriksson, 2000; Fahlke et al., 1994a; Fahlke et al., 1994b; Pohorecky, 1981). However, knowledge on the specific effects of stress on alcohol addiction is contradictory as both in- or decreases of intake after stress have been described (Fahlke et al., 1994a; Pohorecky, 1981). Research, however, has revealed that plasma corticosterone levels are positively correlated with alcohol intake (Lindley et al., 2002; Fahlke et al., 1994a; Fahlke et al., 1996).

From these data an association is suggested between alcohol consumption and the genetically determined function of the striatal dopaminergic and central noradrenergic system as well as the reactivity of the stress system.

However, the currently available studies on the influence of stress have used extreme stressors like for instance cold-water immobilization prior to alcohol consumption (Rockman et al., 1987), and the effects of daily mild stressors on alcohol consumption remain undisclosed.

This study will therefore investigate the role of mild acute and mild sub-chronic challenges on alcohol intake and preference in the genetically selected ratlines of apomorphine susceptible (APO-SUS) and apomorphine unsusceptible (APO-UNSUS) animals to further elucidate the impact of both genetic as well as environmental factors in directing alcohol consumption. The APO-SUS/APO-UNSUS rat model is based on the characteristic behavior response to a single injection of the selective dopaminergic D1/D2 agonist apomorphine (Cools et al., 1990). Subsequent selective breeding has resulted in two distinct rat types that are divergent in the structure and function of, amongst others, the dopaminergic and noradrenergic system and the stress sensitivity. Under non challenged conditions, the APO-SUS rats are characterized by higher levels of TH immunoreactivity in the ventral striatum (Van der Elst et al., in press a), and a higher amount of dopaminergic D2 receptors in the striatum in comparison to the APO-UNSUS rats (Rots et al., 1996). Furthermore, the APO-SUS rats have a functionally lower noradrenergic activity in the ventral striatum than the APO-UNSUS rats as determined by (α-)adrenergic agents induced locomotor activity by accumbal infusions (Ellenbroek and Cools, 1993; Cools et al., 1990), and