Age-related effects of restraint stress on ethanol intake

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INTRODUCTION

Adolescence is a developmental stage associated with remodeling of brain architecture, and it involves behavioral and hormonal changes (Spear, 2000). These changes may underlie the greater vulnerability to drug abuse during this stage (Spear, 2000; Andersen, 2003; Dahl, 2004). Several work has suggested that adolescents may be significantly more sensitive to stress, and to ethanol-stress interactions, than adults, which can enhance the appetitive reinforcing and decrease effects of ethanol (Bertoglio, 2002), promoting greater engagement and escalation into alcohol consumption (Sinha, 2010; Polter, 2014). The blockade of kappa opioid receptor (KOR) system can moderate aversive effects of alcohol, and even modulate the consequences of stress on alcohol intake.

It is thus important to analyze stress-reactive drinking during adolescence and potential treatments to ameliorate it. We analyzed the permissive effects of stress on alcohol intake in adolescents, possible sex-differences and effects of the blockade of KOP on alcohol intake in stressed subjects.

RESULTS

Experiment 1 showed a significative interaction between Sex and Stress exposure, on absolute intake (g/kg) and on preference (percent of ethanol consumed): $F(1,24)= 17,83$; $F(1,24)= 17,53$; $ps < 0,001$, respectively. Stressed females exhibited higher levels of alcohol intake than control females. (Fig. 2). The opposite pattern was observed on males. Experiment 2 indicated that the facilitatory effects of stress on alcohol intake in female rats was blockaded by nor-BNI (Fig. 3). Nor-BNI administered stressed females consumed significantly less alcohol than those that did not received nor-BNI: $F(1,26)= 6.60$; $F(1,26)= 5.09$, $ps < 0.05$, for g/kg and percent of preference, respectively).

DISCUSSION

Exposure to adverse events may enhance the risk of exacerbated alcohol intake in adolescents. A pronounced sex-related difference in the response stress was observed, with females consuming significantly more alcohol after stress exposure, when compared to untreated counterparts.

They also suggest a possible treatment to decrease this effects, through the blockade of kappa opioid system, on female group.

MATERIALS Y METHODS

In Experiment 1, male and female rats, 30 days-old, were subjected to five daily sessions of 120 minutes of restraint stress, using PVC tubes 20 cm long and 5-8 cm wide (Fig. 1); vs. control. The two-bottle alcohol intake test (Fig. 1) lasted 2 weeks, with intermittent, 18 hours per day, three times a week. Solutions were ethanol 4% v/v on the first week, and 5% v/v in the second; vs. vehicle (water). Experiment 2 replicated this procedure on female rats administrated with 10 mg/kg kappa antagonist, nor-Binaltorphimine (nor-BNI), 24 hours before the first stress session; vs. vehicle (saline solution). Body weight was registered before each stress session, as well g/kg alcohol consumed and percent preference, and body weight was analyzed as a percentage increase from day 1 of stress to day 5 [(day5weight – day1weight)/day1*100].

Figure 1. Left: Restraint stress tubes.Right: Two-bottles alcohol self-administration Test.

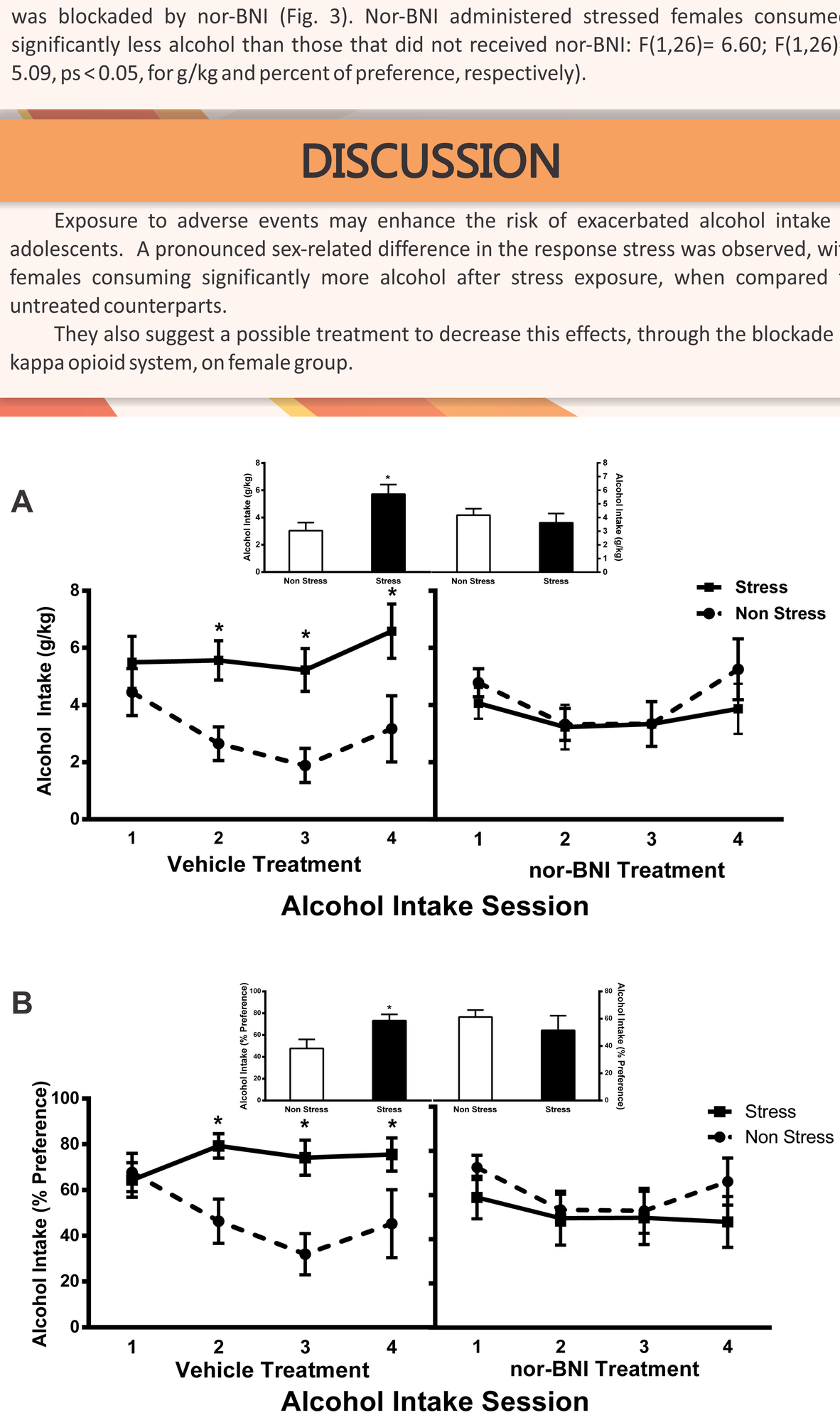

Figure 2. A- Alcohol Intake (g/kg) on Female and Male Adolescent Rats, exposed to five daily restraint stress session of 120 minutes each one. Animals were evaluated on a two bottle intake test, during six sessions. **B-** Alcohol Intake, expressed on Percentage of Preference. Asterisk (*) indicate a significant difference, with p-value ≤ 0.05.

Figure 3. A- Alcohol Intake (g/kg) on Female Adolescent Rats, exposed to vehicle or 10.0 mg/kg de nor-BNI, and twenty four hours later five daily restraint stress session of 120 minutes each one. Animals were evaluated on a two bottle intake test, during six sessions. **B-** Alcohol Intake, expressed on Percentage of Preference. Asterisk (*) indicate a significant difference, with p-value ≤ 0.05.Animals were evaluated on a two bottle intake test, during six sessions.