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High cortisol responders to stress show increased sedation to alcohol compared to low cortisol responders: An alcohol dose–response study

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ABSTRACT

Aims: The present study was designed to examine the relationship between high and low cortisol response to an acute stressful situation and the subjective effects after different doses of alcohol, in healthy social drinkers.
Method: Sixty-four subjects (32 men and 32 women) participated in one laboratory session. They performed a modified version of the Trier Social Stress Test (TSST) immediately before consumption of either placebo or alcohol (0.2, 0.4 or 0.8 g/kg). Subjects in each dose group were then divided into high (HCR; $n = 32$) or low (LCR; $n = 32$) cortisol responders. Primary dependent measures were self-report questionnaires of mood.
Results: The HCR reported increased ratings on Sedation on the Biphasic Alcohol Effects Scale (BAES) with increased dose in comparison with the LCR. This increase in sedation also correlated to the increase in cortisol levels.
Conclusion: We conclude that a high cortisol response to stress modulates the subjective response to alcohol, dose-dependently. HCR subjects experience increased sedative effects of alcohol after consumption of higher doses of alcohol following stress compared to LCR subjects.

1. Introduction

Most of the physiological changes after an exposure to a stressful situation are mediated by the HPA axis. Plasma concentrations of the primary glucocorticoid hormone cortisol rise and can directly influence responses to alcohol in both animals and humans (Fahlke et al., 1994a, b, 1995; Söderpalm and de Wit, 2002). According to epidemiological studies, people usually consume more alcohol during and after stressful life events such as after a divorce or having financial difficulties (Jose et al., 2000). This is supported indirectly by the observation that alcohol abusers report more stressful life events than non-abusers (O'Doherty, 1991). The effect of stress on alcohol craving and consumption has also been studied in experimental clinical studies. For example, the Trier Social Stress Test (TSST), administered prior to alcohol drinking, doubled the consumption of drinks provided to alcohol dependent subjects compared to a no stress condition (Thomas et al., 2011). Furthermore, and consistent with this finding, stressful negative mood states, negative affect imagery or a psychosocial stressor, increases the urge to drink alcohol in alcohol dependent subjects, either directly (Litt et al., 1990) or after exposure to alcohol-related cues (Litt et al., 2000; Sinha et al., 2009). The association between stress, craving and consumption has also been found in subjects addicted to other drugs than alcohol. Thus, stress has been found to increase craving for alcohol and cocaine in cocaine dependent subjects (Sinha et al., 2009), cigarette craving and nicotine intake in daily smokers (Buchmann et al., 2010) and marijuana craving in marijuana-dependent subjects (McRae-Clark et al., 2011).

Stress has also a direct effect on the subjective effects of alcohol and other substances in normal healthy volunteers. Söderpalm and de Wit (2002) found that the stressed subjects reported increased "Liking" of alcohol compared to no stress controls. They also showed that subjects exposed to the TSST not only consumed more alcohol but also more of the placebo after stress (de Wit et al., 2003). These effects are in line with previous studies investigating the effects of acute stress on alcohol (Söderpalm and de Wit, 2002; de Wit et al., 2003) but also previous research on the self-medication hypothesis, suggesting an increase in drug intake for relaxing purposes (Swendsen et al., 2000). These studies, using negative mood induction techniques, indicate that acute stress increases the urge to drink alcohol in individuals addicted to alcohol, and that stress affects both the subjective response to alcohol and alcohol consumption in normal healthy volunteers. It has also been shown that individuals with alcohol use disorder in withdrawal show three- to fourfold higher cortisol levels compared to controls (Stalder et al., 2010).

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In human stress research, there is further evidence for the existence of high vs. low cortisol responders (HCR vs. LCR) to the TSST. Approximately 30% of healthy subjects display a high cortisol level to stress and a smaller rise in cortisol is observed in the rest of the population (Kirschbaum et al., 1995). This effect seems to be independent of age or gender (Kudielka et al., 2004). However, a subpopulation of persistent high cortisol responders to repeated administration of the TSST do exist (Kirschbaum et al., 1995). A differentiation between high- and low-responders to psychosocial stress is of significant interest regarding the pituitary-adrenocortical system (Schommer et al., 2003). Whether high cortisol responders show an altered subjective response to a pharmacological challenge, e.g. to alcohol, as proposed in this study, has to our knowledge not been investigated. Previous studies in the literature provide evidence merely of how one fixed and moderate dose of alcohol enhances craving or subjective effects of alcohol after stress. We therefore aimed to evaluate and extend previous results by using a modified version of the TSST and by examining how the psychosocial stressor affects subjective responses to four different doses of alcohol in both genders. We hypothesized that high and low cortisol responses to stress modulate the subjective response to alcohol in a dose-dependent manner.

2. Materials and methods

2.1. Subject recruitment and screening

Sixty-four healthy social drinkers recruited via advertisements, were initially screened by telephone for major eligibility criteria. Participants were invited to the laboratory for further screening upon meeting the eligibility requirements of: age (18–35 years), normal BMI (18.5–25), moderate consuming of alcohol, (i.e. no more than 9 standard drinks per week for women and 12–14 for men), negative history of substance abuse and or negative history of somatic diseases. Subjects completed the Alcohol Use Disorders Identification Test (AUDIT; Babor et al., 1992) and the psychiatric symptom checklist (SCL-90; Derogatis, 1994) assessing medical and psychiatric histories. All participants underwent a physical examination to ensure good physical health. The study was approved by the regional ethics committee of the University of Gothenburg and complied with the guidelines of the Declaration of Helsinki.

2.2. Design and procedure

The study was conducted in a comfortable environment, furnished like an apartment living room. Subjects were always run in groups of three or four. Each group consisted of 16 participants with an equal number of men and women in each dose group. The session procedure was as follows: subjects arrived at the laboratory at 1300 h. Objective measures of breath alcohol levels (BAL) and salivary cortisol levels and subjective self-report measures of Stimulation and Sedation, were assessed at baseline (0 min). Subjects were then taken into a second room where a modified version of the standardized stress test, TSST, an arithmetic task, was conducted by an interviewer (Kirschbaum et al., 1993; Dickerson and Kemeny, 2004; Söderpalm Gordh et al., 2011). The stress task was administered during a period of 10 min. Subjects were guided back to the laboratory environment where they immediately rated how distressed they felt on four visual analogue scales (FVAS). During the following 15 min subjects consumed a beverage containing 0.0, 0.2, 0.4 or 0.8 g/kg alcohol. Thus there were four experimental conditions: stress + 0.0 g/kg, stress + 0.2 g/kg alcohol, stress + 0.4 g/kg alcohol and stress + 0.8 g/kg alcohol. BAL, salivary cortisol, and subjective self-report measures of Stimulation and Sedation on the Biphasic Alcohol Effects Scale (BAES), respectively, and on a Drug Effects Questionnaire (DEQ) were thereafter obtained at four more occasions (30, 45, 60, and 75 min; Fig. 1). After the last measurements were taken, subjects stayed at the laboratory until their BAL reached 0.0 promille, ‰. At the end of the study participants were debriefed by the experimenter and received a compensation for their participation.

2.3. Ethanol and placebo beverages

The beverage containing ethanol (Absolut Vodka 40%) and pulp free Tropicana orange juice was mixed in order to reach a concentration of 5, 11 or 16% ethanol depending on dose administered (e.g. 5% for 0.2 g/kg, 11% for 0.4 g/kg, and 16% for 0.8 g/kg alcohol). The beverage was based on weight. The total dose was divided into two white colored glasses to be consumed during a 15 min period. The target BAL was 0.2‰, 0.4‰, and 0.8‰ for each of the doses. The placebo beverage consisted of orange juice laced with 1 ml vodka in order to increase the effectiveness of the placebo manipulation.

2.4. Self-reported and objective measures

The Biphasic Alcohol Effects Scale (BAES) is a 14-item adjective rating scale that is sensitive to stimulant and sedative effects produced by ethanol (Martin et al., 1993). Subjects indicated the extent to which they are feeling each adjective on a 100-point scale from “not at all” (0) to “extremely” (100). The Stimulant scale score was measured by summing the scores for the adjectives “Elated”, “Energetic”, “Excited”, “Stimulated”, “Talkative”, “Up”, and “Vigorous”. The Sedation scale was measured by summing up the scores for the adjectives “Down”, “Heavy head”, “Inactive”, “Difficulty concentrating”, “Sedated”, “Slow thoughts”, and “Sluggish”.

The Drug Effects Questionnaire (DEQ) consists of four questions concerning current drug effects and drug liking (Fischman and Foltin, 1991). Subjects indicate on 100-mm lines, labeled from “not at all” to “very much”, whether they feel the “Effect”, “Liking”, “High”, and if they “Want more”.

The Four Visual Analogue Scale (FVAS) (Söderpalm and Söderpalm, 2011; Söderpalm Gordh et al., 2011) consists of four adjectives, “Uneasy”, “Anxious”, “Nervous” and “Calm”, each associated with a 100 mm line, labeled from “not at all” to “extremely”.

Blood alcohol levels were estimated from breath alcohol levels (BALs) using Alco-Sensor III breathalyzer alcometer (Alert J5, Professional Breathalyzer, Alcohol Countermeasure Systems Corp., Canada).

Salivary cortisol levels represent free cortisol, which is the end product of the HPA axis. Once in the bloodstream, most of the cortisol

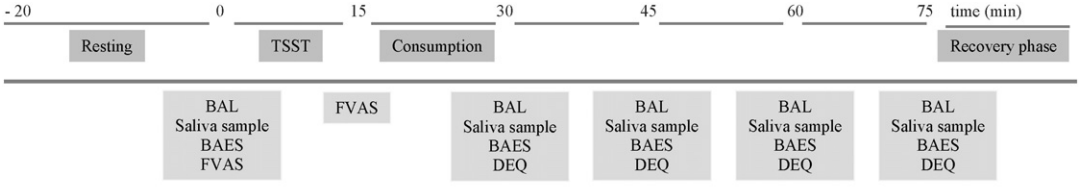

Fig. 1. Diagram represents the study procedure over time (minutes).