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Alcohol metabolism in hangover sensitive versus hangover resistant social drinkers

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ABSTRACT

Background: Previous research demonstrated that urinary ethanol concentrations were significantly lower in hangover resistant individuals compared to drinkers who reported having a hangover. This finding suggests that the rate of ethanol metabolism is faster in drinkers who do not experience an alcohol hangover. This study aimed to directly compare alcohol metabolism after administering a low dose of ethanol to hangover sensitive drinkers and hangover resistant drinkers.

Methods: Social drinkers who previously participated in hangover trials at Utrecht University were invited to participate. It was aimed to include 12 hangover resistant drinkers and 12 hangover sensitive drinkers. Participants consumed alcohol to reach a breath alcohol concentration (BrAC) of 0.05%. Every 5 min BrAC was determined, until BrAC reached zero. Every 15 min, the Karolinska Sleeping Scale (KSS) was administered to assess subjective sleepiness, and subjective intoxication was measured.

Results: Data of N = 23 participants with a mean age of 22.4 (± 1.9) years was included in the analyses. No significant difference in BrAC over time was found between the hangover resistant group and the hangover sensitive group. In line, subjective sleepiness scores and subjective intoxication ratings did not significantly differ between the groups at any point in time after alcohol consumption.

Conclusion: Hangover resistant individuals and hangover sensitive drinkers did not significantly differ on BrAC, subjective sleepiness, and subjective intoxication after consuming a moderate amount of alcohol. These findings suggest that drinkers who usually experience hangovers after a heavy drinking occasion do not experience alcohol intoxication differently than hangover resistant drinkers.

1. Introduction

The alcohol hangover refers to the combination of mental and physical symptoms, experienced the day after a single episode of heavy drinking, starting when blood alcohol concentration (BAC) approaches zero (Van Schrojenstein Lantman et al., 2016).

Currently, there is no effective hangover treatment available (Verster and Penning, 2010). The main reason for this is the limited of knowledge on the pathology of the alcohol hangover. Although several theories exist (Penning et al., 2010), these originate from research conducted in the 1980s, of which most studies have not been replicated since then. However, since the founding of the Alcohol Hangover Research Group (Verster et al., 2010), more research has been devoted to elucidate the pathology of the alcohol hangover. Currently, two hypotheses are examined that may explain the development of alcohol hangovers (Mackus et al., 2016). One line of thinking views the alcohol hangover as an immune response caused by heavy drinking. Other researchers argue that differences in alcohol metabolism may be the cause that some drinkers experiences (more severe) hangovers, while other drinkers claim to be hangover resistant. Future research should investigate both possibilities.

In this context, directly comparing hangover sensitive versus hangover resistant drinkers may help increase our understanding of the alcohol hangover. Recent studies revealed that, despite consuming large amounts of alcohol, about 10% of all social drinkers with an estimated peak BAC > 0.18% report being hangover resistant (Verster

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et al., 2013, Kruisselbrink et al., 2017). The key question is in what respect these groups differ from each other. A recent naturalistic study, examining various biobehavioral correlates of the alcohol hangover state, compared both groups (Hogewoning et al., 2016, Van de Loo et al., 2017, Mackus et al., 2017). They found that the concentration of ethanol in urine, collected during the hangover state, was significantly higher among drinkers who experienced a hangover when compared to hangover resistant drinkers (Van de Loo et al., 2017). The observed difference suggests a difference in the metabolizing rate of ethanol in both groups, in that drinkers who do not experience hangovers may have a faster alcohol metabolism (Lee et al., 2014; Quertemont, 2004; Edenberg, 2007). In the study by Van de Loo et al. (2017), urine ethanol concentration correlated significantly to overall hangover severity, and the severity of various individual hangover symptoms such as headache and nausea. These findings support the hypothesis that the presence and severity of the alcohol hangover may be related to alcohol metabolism rate. The fact that differences in alcohol metabolism can be profound amongst healthy young social drinkers has been observed in clinical studies (Van de Loo et al., 2016; Benson and Scholey, 2014; Crabb et al., 2004).

The aim of the current study was to directly compare the alcohol metabolism of drinkers who experience hangovers with those who claim to be hangover resistant.

2. Methods

2.1. Study population

Dutch young adults, aged 18–30 years old, were asked to participate in the study. To ensure that subjects could be correctly allocated to the hangover group or hangover resistant group, only subjects that participated in previous hangover studies conducted at our institute were invited to participate (Hogewoning et al., 2016, Van de Loo et al., 2017). Together, the pool of potential participants comprised of N = 48 healthy social drinkers who participated in our studies over the past 3 years. However, as expected several original participants were lost to follow up, while others were not interested in participating in a second study. In line with previous research (Jones et al., 2006), and given the limited subject pool, it was aimed to include at least 12 hangover resistant drinkers and 12 drinkers who have hangovers after a heavy drinking session. Participants were allocated to one of the two groups according to the results of the hangover study they participated in (screening assessments and an actual alcohol challenge). Using this approach, we could be pretty confident that participants were allocated to the correct group. From previous screening it was clear that the estimated peak BAC on a regular drinking occasion of these drinkers was higher than 0.08%, ensuring that the allocation to the hangover resistant group was meaningful (Hogewoning et al., 2016). During the screening for the current status it was verified whether the hangover sensitive or resistant status was changed since their previous study participation. Also, their drinking behaviour was re-assessed.

Participants were included if they were healthy social drinkers, implying the absence of treated or untreated physical or mental disease, and being non-alcoholic and nondependent drinkers. Participants were excluded from participation in case of smoking, and if a positive urine drug or pregnancy screen was obtained, and in case of using medicinal drugs (including over-the-counter pain killers), caffeine consumption on the test day, or alcohol consumption within 24 h before the start of the test day. The University of Groningen Psychology Ethics Committee approved the study, and written informed consent was obtained from each subject before the start of the study.

2.2. Design

The study comprised one test day. Participants were required to abstain from eating for at least 3 h before the start of the study. After informed consent was obtained, subjects received a standardized meal, consisting of a glass of water and a currant bun, which they had to consume within 10 min. After finishing the meal, a breathalyzer test was conducted to confirm that breath alcohol concentration (BrAC) was zero (Dräger Alcotest® 7410^{Plus} COM), and a urine sample was collected to test for pregnancy and recent drug use (InstantView; testing for the recent use of amphetamines (including MDMA), barbiturates, cannabinoids, benzodiazepines, cocaine, and opiates). Subjects' weight was determined, and the amount of alcohol (mL) to be consumed to achieve a peak BrAC of 0.05% was calculated for each subject, applying a modified Friel formula (Friel et al., 1999):

[Friel's factor * subjects body weight (kg)]/[Alcohol density of ethanol]

Alcohol density = 0.79 g/cm^3.

2.2.1. Friel's factor:

Males: 1.068 g/kg × ((100 × % BrAC needed)/12) = 0.445

Females: 0.915 g/kg × ((100 * % BrAC needed)/12) = 0.381

Orange juice was added to the calculated amount of alcohol to a volume of 250 ml. One hour after consuming the standardized meal, subjects had to consume the beverage within 5–10 min. Thereafter, every 5 min a Breathalyzer test was conducted. Every 15 min after alcohol consumption, subjects completed the Karolinska Sleepiness Scale (KSS) and a subjective intoxication scale. Before alcohol consumption, participants were asked to visit the toilet if necessary. Voiding during the experiment was allowed, but participants were asked to postpone voiding if possible. Time of voiding after alcohol consumption was recorded, but no information was gathered on the amount of voiding. Fluid and food intake were not allowed during the experiment.

The KSS was administered to assess subjective sleepiness. Subjects had to choose one of nine statements about their current state of sleepiness ranging from 1 (extremely alert) to 9 (extremely sleepy, fighting sleep) (Åkerstedt and Gillberg, 1990). Subjective intoxication was measured using a scale ranging from 0 (sober) to 10 (highly intoxicated), with increments of 0.5 point (Van de Loo et al., 2016). The test day was completed after two subsequent measurements of BrAC zero.

2.3. Data analysis

Statistical analyses were conducted with SPSS, version 24. Data from the hangover sensitive group and the hangover resistant group was compared, regarding peak BrAC, time to reach peak BrAC, time from peak BrAC to a BrAC of zero, the Area Under the Curve (AUC), elimination rate, and clearance. Also, for each time point, sleepiness and subjective intoxication was compared between the groups. Data was analyzed using Independent Samples Paired T-Tests or the Independent Samples Mann-Whitney U Test in case the data was not normally distributed. Differences between the groups were considered significant if $p < 0.05$.

3. Results

Of the N = 48 subjects that were invited, N = 23 subjects participated in the study. Their mean (SD) age was 22.4 (1.9) years old. The hangover sensitive group consisted of 12 subjects (41.7% men), and N = 11 subjects were part of the hangover resistant group (54.5% men). Demographic data and alcohol consumption of both groups are summarized in Table 1.

The average time needed to consume the beverage was 5 min and 22 s. The BrAC distribution over time for both groups is presented in Fig. 1. Table 2 summarizes the alcohol metabolism parameters of both groups.

Table 1
Alcohol metabolism of drinkers who experience hangovers and hangover resistant drinkers.

	Hangover sensitive group (N = 12)	Hangover resistant group (N = 11)	Overall
Age	22.8 (2.0)	22.0 (1.8)	22.4 (1.9)
Height (m)	1.76 (0.1)	1.80 (0.1)	1.78 (0.1)
Weight (kg)	66.3 (10.4)	74.1 (13.9)	70.0 (12.6)
BMI	21.4 (2.4)	22.7 (2.8)	22.0 (2.6)
Number of alcoholic drinks/week	10.2 (5.5)	11.3 (7.3)	10.7 (6.3)
SRE[a] – total score	24.5 (7.8)	23.7 (8.6)	24.1 (8.0)
SRE – early life	3.8 (1.8)	3.2 (1.8)	3.5 (1.8)

[a] Self-Rating of the Effects of Alcohol.

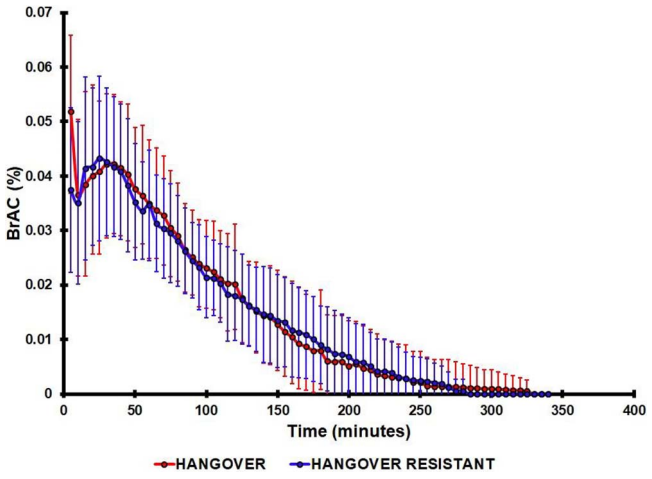

Fig. 1. Breath Alcohol Concentration (BrAC) of hangover sensitive and hangover resistant drinkers.

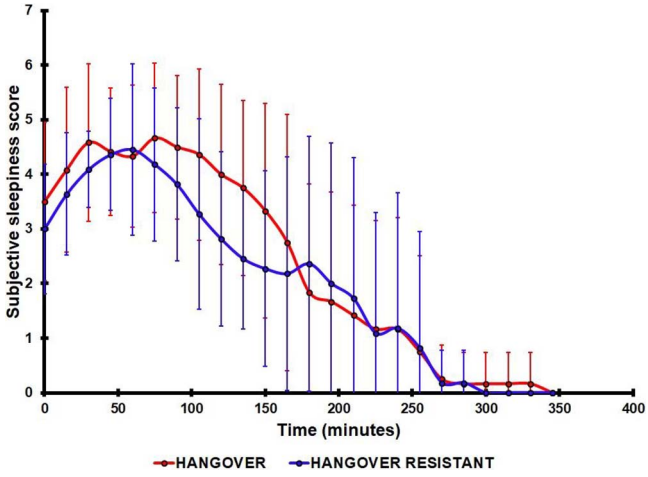

Fig. 2. Sleepiness of hangover sensitive and hangover resistant drinkers.

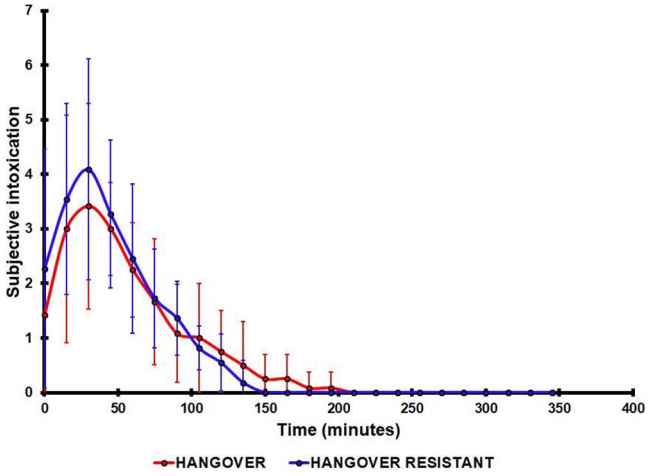

Fig. 3. Subjective intoxication of hangover sensitive and hangover resistant drinkers.

It is evident from Fig. 1 that BrAC measurements over time did not differ between the hangover sensitive group and the hangover resistant group. Table 1 shows that the groups did not significantly differ on any of the metabolism related parameters that were assessed.

In line, subjective sleepiness (Fig. 2) and subjective intoxication (Fig. 3) did not significantly differ between the two groups at any time point.

3.1. Water consumption, voiding and toilet time

N = 15 of 23 participants visited the toilet after alcohol consumption, on average after 110 min (range 50–195 min), corresponding to an average BrAC of 0.021%. Time of first voiding was significantly earlier (p = .003) in hangover sensitive drinkers (N = 7; 81 min) when compared to hangover resistant drinkers (N = 8;134 min). Accordingly, the average BrAC at the time of voiding of hangover sensitive drinkers was significantly higher (p = .028) compared to the BrAC of the hangover resistant drinkers (0.033% versus 0.020%, respectively).

Table 2
Alcohol metabolism of drinkers who experience hangovers and hangover resistant drinkers.

	Hangover sensitive group (N = 12)	Hangover resistant group (N = 11)	Overall
Volume ethanol (ml)	30.9 (10.3)	36.3 (12.2)	33.5 (11.3)
Dose (ml/kg)	0.457 (0.094)	0.481 (0.094)	0.469 (0.093)
Drinking time (m:s)	05:11 (03:19)	05:34 (02:53)	05:22 (03:03)
Peak BrAC (%)	0.0453 (0.0137)	0.0471 (0.0151)	0.0461 (0.0141)
Time to peak BrAC (m:s)	26:56 (10:47)	31:51 (12:10)	29:17 (11:28)
Elimination time (from start drinking (h:m:s)	3:19:36 (0:56:41)	3:27:34 (0:56:04)	3:23:25 (55:15)
Elimination time (from peak BrAC (h:m:s)	2:52:40 (0:57:13)	2:55:43 (0:57:57)	2:54:07 (0:56:16)
Elimination rate (BrAC reduction/hour)	0.0159 (0.0017)	0.0165 (0.0039)	0.0162 (0.0029)
AUC (mg/100 ml per hr)	0.0810 (0.041)	0.0811 (0.33)	0.0811 (0.036)
Clearance (100 ml/hr)	448.9 (47.5)	421.3 (112.6)	435.7 (84.2)

Abbreviations: BrAC = breath alcohol concentration, AUC = area under the curve.

4. Discussion

The aim of this study was to compare alcohol metabolism of hangover sensitive drinkers with those who claim to be hangover resistant. The results showed no apparent difference between those two groups, according to their BrAC values over time, subjective sleepiness and subjective intoxication. Thus, in contrast to differences in symptom severity observed in the hangover state (Hogewoning et al., 2016), the current findings suggest that hangover resistant drinkers are equally sensitive to acute alcohol effects as drinkers who usually experience hangovers.

As the demographic data of both groups were similar, the absence of the expected discrepancy in alcohol metabolism should be explained otherwise. A possible explanation for why there was no observed difference in the metabolic rate of the two groups might be within the study design. Participants were administered alcohol to reach an estimated BAC value of 0.05%. This was equivalent to 1–3 drinks for females, and 3–5 drinks for males. This is less than half of the amount one would normally consume during a night out. For example, the average number of alcoholic drinks consumed during their last drinking occasion was equivalent to 10.7 drinks (Hogewoning et al., 2016). Thus, the administered dosage of alcohol might have been too low to see an actual difference in metabolic rate between the groups.

In addition, it should be taken into account that BrAC measurements are a proxy of the rate of alcohol metabolism. Also, a recent study showed that when BrAC values are equivalent to zero, ethanol still may be present in blood or urine (Verster et al., 2017). Therefore, BAC determination in blood samples would perhaps have given a more accurate representation of alcohol metabolism than assessments via breath (Kriikku et al., 2014). However, the observed correlations between alcohol content assessed in blood, breath and urine were high (Peleg et al., 2010; Verster et al., 2017) making it unlikely that using other assays than breath would yield a different study outcome.

The sample size of this study was relatively low. This is in part due to the fact that the total sample of potentially available subjects was relatively small (N = 48 eligible participants from previous studies of which about half was hangover resistant). We invited all of them to participate in the current study. Eventually, N = 23 subjects participated in the current study. Although N = 12 per group may be regarded a small sample size, other research into blood alcohol curves (e.g., Jones et al., 2006) or biomarkers of recent alcohol consumption (e.g., Hagan and Helander 1997) successfully used samples of similar sizes to demonstrate significant differences.

The current findings do not rule out that there are differences in metabolites of alcohol between the groups. For example, in one group the breakdown of acetaldehyde may be faster than in the other group. Differences in metabolites could then explain why although breath ethanol concentration does not differ between the two groups, some drinkers claim hangover resistance while others are hangover sensitive. Future research should examine the possible differences in alcohol metabolites between hangover sensitive and hangover resistant drinkers. Interestingly, there was a significant difference between hangover sensitive and resistant drinkers in the first time of voiding after alcohol consumption. Unfortunately, no information was gathered on the volume of voiding. Although hangover sensitive drinkers voided significantly earlier, the BrAC of both groups at that time did not significantly differ, nor did the beverage volume consumed to achieve this BrAC (see Table 2). Thus, although the moment of voiding was significantly different between the two groups this did not affect any outcome measure.

Taken together, this study revealed no significant differences in BrAC levels over time between hangover sensitive and hangover resistant drinkers. Further research is required to elucidate the unique characteristics of hangover resistant drinkers.

Contributors

AK, JG, KB, and JV, designed the study, data was collected by MM, MvSL, and AvdL. MvSL conducted the statistical analyses, MM and MvSL drafted the manuscript. All authors were involved in data interpretation, and approved the final manuscript.

Conflict of interest

Joris Verster has received grants/research support from the Dutch Ministry of Infrastructure and the Environment, Janssen Research and Development, Nutricia, Red Bull, Sequential, and Takeda, and has acted as a consultant for the Canadian Beverage Association, Centraal Bureau Drogisterijbedrijven, Coleman Frost, Danone, Deenox, Eisai, Janssen, Jazz, Purdue, Red Bull, Sanofi-Aventis, Sen-Jam Pharmaceutical, Sepracor, Takeda, Transcept, Trimbos Institute, and Vital Beverages. Aletta Kraneveld has received grants/research support from Top Institute Pharma, NWO, Janssen, GSK, Nutricia Research, and Friesland Campina. Karel Brookhuis has received grants/research support from NWO, the Dutch Ministry of Infrastructure and the Environment, European Commission, Wyeth, Sanofi, Schering, Nissan, JARI, Mercedes Benz, and Verbond van Verzekeraars. Johan Garssen is part-time employee of Nutricia Research and received research grants from Nutricia research foundation, Top Institute Pharma, Top Institute Food and Nutrition, GSK, STW, NWO, Friesland Campina, CCC, Raak-Pro, and EU. The other authors have no potential conflicts of interest to disclose.

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