



Short Communication

The breathtaking truth about breath alcohol readings of zero

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HIGHLIGHTS

- It has been postulated that the hangover state starts when breath alcohol concentration is zero.
- Ethanol may still be present in the blood and urine during the hangover state, despite breath analyser readings of zero.
- The consensus to postpone cognitive testing in hangover studies until breath alcohol levels are zero should be reconsidered.

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ABSTRACT

Introduction: It has been postulated that the hangover state starts when breath alcohol concentration is zero.**Methods:** Data from 2 studies that assessed ethanol in breath, blood and urine were compared.**Results:** The data revealed that ethanol may still be present in the blood and urine during the hangover state, despite breath analyser readings of zero.**Discussion:** As ethanol is still present in the body despite zero breath alcohol readings, the current consensus to postpone cognitive testing in hangover studies until breath alcohol concentration is zero should be reconsidered.

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1. Introduction

The alcohol hangover is loosely defined as a combination of the next day negative effects of alcohol consumption. There is consensus that hangover symptoms present when the parent molecule, ethanol, is fully metabolized and no longer present (Stephens, Grange, Jones, & Owen, 2014; Stephens, Ling, Heffernan, Heather, & Jones, 2008; Verster, 2008; Wiese, Shlipak, & Browner, 2000). This concept was adopted by the Alcohol Hangover Research Group who recommend commencing cognitive testing on hangover days only when blood alcohol concentration have returned to zero (Verster, et al., 2010). The rationale for this definition is that if Blood Alcohol Concentration (BAC) has not yet reached zero, residual alcohol may affect performance and mood. Indeed, research has shown that low BACs (e.g., BAC 0.02% to

0.05%) can have a negative impact on cognitive and psychomotor performance (Holloway, 1994).

Although previous research has shown very high correlations ($r > 0.9$) between ethanol concentrations determined in blood and urine (Jones, 1998; Papierz, Berent, Markuszewski, & Szram, 2004), the usual way to confirm a BAC of zero is by applying a breath alcohol analyser (“breathalyser”) test (Stephens et al., 2014).

Several studies have reported a dissociation between breath and blood alcohol levels. Specifically, although the correlation between breath and blood alcohol content may be high, for individual drinkers the breath alcohol test provides a poor estimate of actual blood ethanol content (Nanau & Neuman, 2015). Additionally, the sensitivity of different breathalysers varies considerably and may underestimate blood ethanol levels (Ashdown, Fleming, Spencer, Thompson, & Stevens, 2014). Thus, breath readings may falsely indicate that it is safe to drive while in fact the driver is intoxicated (Kriikku et al., 2014). In another study, breath test results also correlated poorly with blood ethanol readings in bar patrons, with individual breath measures reflecting both overestimates and underestimates of blood ethanol levels (Clapp et al., 2009). The general differences in alcohol concentrations in blood,

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breath and urine are related to ethanol's metabolism - i.e. absorption into the blood stream, break down into metabolites by the liver, and excretion via urine - and the differential timing of these processes. The observed individual differences may be explained by variations in drinking pattern of the bar patrons including such factors as pre-loading, total drinking time, and number of drinks consumed per hour (Clapp et al., 2009; Quigg, Hughes, & Bellis, 2013).

The above literature illustrates that alcohol may not be fully absent from the body when it is no longer detectable in breath. In the current paper, data from two studies were considered (Verster, Van Duin, Volkerts, Schreuder, & Verbaten, 2003; Van de Loo et al., 2017), to directly compare breath, urine and blood ethanol concentrations.

2. Methods & Results

The first study (Verster et al., 2003) was a controlled, single-blind laboratory study in healthy young volunteers. Subjects completed an evening drinking session. Starting around 10.30 pm, within half an hour they consumed 500 mL orange juice either mixed with ethanol (1.4 g/kg body weight) or without ethanol (placebo). After achieving peak BAC (0.155%), subjects had a normal night of sleep, lasting approximately 7 h. The following morning, around 9 am, i.e. 10 h after alcohol consumption, $N = 12$ subjects conducted a breath alcohol test, and a blood sample was taken to determine ethanol concentration. The results are summarized in Table 1.

On the hangover day, ethanol was detectable in 6 of the 12 subjects (50%) only using the breath analyser, while ethanol was present in 9 of 12 (75%) corresponding blood samples. A Wilcoxon Signed Ranks Test revealed that the ethanol concentration in blood was significantly higher than in breath measurements ($Z = -2.67, p = 0.008$). Table 1 further shows a great variability in observed BAC values with ethanol concentration in blood varying from 0 to 458.3 mg/L (0 to 0.05%), and a range of 0 to 300 mg/L (0 to 0.03%) in breath measures. This suggests that there are slow and fast metabolisers of ethanol among the participants. The correlation between breath and blood ethanol concentration was highly significant (Spearman's rho = 0.895, $p = 0.0001$). In a second investigation, $N = 36$ social drinkers participated in a naturalistic study (Van de Loo et al., 2017). Study 2 comprised of a hangover day (alcohol consumed the day before) and a control day (no alcohol consumed). The cohort was selected such that half of the participants reported having regular hangovers ($N = 18$, the hangover group), while the other half claimed never to have hangovers despite drinking similar large quantities of alcohol. The naturalistic design meant that subjects consumed alcohol (or not) without restrictions regarding pace or quantity, in a setting of their own choice and without the presence of the investigators (for a detailed description of the study

Table 1

Breath and blood ethanol determinations. Mean, standard deviation (SD) and range are presented.

| Subject | Breath ethanol (mg/L) | Blood ethanol (mg/L) |
|---------|-----------------------|----------------------|
| S01 | 290 | 402.9 |
| S02 | 190 | 323.4 |
| S03 | 0 | 0 |
| S04 | 0 | 25.5 |
| S05 | 0 | 0 |
| S06 | 0 | 88.5 |
| S07 | 110 | 354.6 |
| S08 | 0 | 0 |
| S09 | 50 | 68.2 |
| S10 | 140 | 392.1 |
| S11 | 0 | 33.7 |
| S12 | 300 | 458.3 |
| Mean | 90.0 | 178.9 |
| SD | 115.7 | 187.4 |
| Range | 0–300 | 0–458.3 |

methodology, see Hogewoning et al., 2016). During the drinking session, subjects consumed on average 11.6 standardized alcoholic drinks, corresponding to an estimated peak BAC of 0.175%. No alcohol was consumed the evening before the control day. On each test day at 9:30 am, a breathalyser test was conducted and a urine sample was obtained. Urine ethanol concentration was determined using headspace gas chromatography. The results for each participant are summarized in Table 2.

There was no significant difference in the amount of alcohol consumption reported by the two groups (11–12 standardized alcoholic drinks). On the hangover day, ethanol was measured in 7 out of 36 subjects (19.4%) only using the breath analyser, while it was present in 31 of 36 (86.1%) corresponding urine samples. On the control day, breath ethanol concentration was zero in all subjects, whereas very small (clinically irrelevant) traces of ethanol were detected in 33 out of 36 subjects (up to 0.001%). A Wilcoxon Signed Ranks Test revealed no significant differences between breath and urine ethanol concentration on the

Table 2

Breath and urine ethanol determinations. Mean, standard deviation (SD) and range are presented. Significant differences ($p < 0.05$) between the hangover group and hangover-immune group are indicated by *.

| Subject | Hangover Group | | | |
|---------|-----------------------|--------------|----------------------|--------------|
| | Breath ethanol (mg/L) | | Urine ethanol (mg/L) | |
| | Control day | Hangover day | Control day | Hangover day |
| S101 | 0 | 0 | 11.9 | 48.4 |
| S102 | 0 | 0 | 0.5 | 3.6 |
| S103 | 0 | 258.0 | 0 | 476.0 |
| S104 | 0 | 0 | 1.3 | 338.3 |
| S105 | 0 | 0 | 0.5 | 366.1 |
| S106 | 0 | 0 | 0.2 | 2.3 |
| S107 | 0 | 0 | 1.7 | 1.2 |
| S108 | 0 | 330.0 | 2.2 | 438.8 |
| S109 | 0 | 0 | 8.0 | 0.9 |
| S110 | 0 | 328.0 | 1.9 | 800.2 |
| S111 | 0 | 0 | 1.9 | 2.6 |
| S112 | 0 | 194.0 | 0.3 | 307.9 |
| S113 | 0 | 0 | 0.3 | 1.0 |
| S114 | 0 | 0 | 0.2 | 0.9 |
| S115 | 0 | 0 | 11.3 | 1.6 |
| S116 | 0 | 642.0 | 5.0 | 431.9 |
| S117 | 0 | 0 | 1.9 | 77.2 |
| S118 | 0 | 0 | 0.4 | 35.8 |
| Mean | 0 | 97.3 | 2.8 | 185.3 * |
| SD | 0 | 181.9 | 3.8 | 240.2 |
| Range | 0 | 0–642 | 0–11.9 | 0.87–800.2 |
| Subject | Hangover-immune Group | | | |
| | Breath ethanol (mg/L) | | Urine ethanol (mg/L) | |
| | Control day | Hangover day | Control day | Hangover day |
| S201 | 0 | 0 | 1.2 | 6.3 |
| S202 | 0 | 0 | 1.9 | 6.2 |
| S203 | 0 | 0 | 1.4 | 0.6 |
| S204 | 0 | 0 | 2.0 | 2.7 |
| S205 | 0 | 0 | 0 | 2.4 |
| S206 | 0 | 0 | 1.3 | 42.3 |
| S207 | 0 | 90.0 | 3.9 | 1.5 |
| S208 | 0 | 144.0 | 0 | 436.7 |
| S209 | 0 | 0 | 2.0 | 3.2 |
| S210 | 0 | 0 | 2.2 | 2.0 |
| S211 | 0 | 0 | 0.6 | 2.5 |
| S212 | 0 | 0 | 0.9 | 26.4 |
| S213 | 0 | 0 | 0.2 | 0 |
| S214 | 0 | 0 | 0.3 | 9.3 |
| S215 | 0 | 0 | 0.4 | 0.6 |
| S216 | 0 | 0 | 0.5 | 3.4 |
| S217 | 0 | 0 | 0.5 | 1.1 |
| S218 | 0 | 0 | 1.1 | 61.7 |
| Mean | 0 | 13.0 | 1.1 | 33.8 |
| SD | 0 | 39.0 | 1 | 101.9 |
| Range | 0 | 0–144 | 0–3.9 | 0–436.7 |

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