Consistency of hangover experiences after a night of drinking: a controlled laboratory

study.

Running header: Reliability hangover laboratory study

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ABSTRACT

Objective: Research into cognitive performance during a hangover has produced equivocal findings. This study investigated the reliability of inducing hangover symptoms and effects on cognitive performance (including applied tasks) under standardised conditions. Method: Twenty-one participants (13M; 24±3 years) completed two identical trials, involving alcohol consumption and an overnight laboratory stay. Outcome measures included: hangover severity (a single-item 'Hangover' rating, and a sum of hangover symptoms [OSS]), cognitive function (trail making test), simulated driving (standard deviation of lateral position; lane crossings), and typing performance. Spearman's correlations were used to assess reliability between trials for all participants, and when ratings of 'Hangover' were consistent. Results: Participants demonstrated reliable 'Hangover' rating change from baseline (Trial A: 2.0 (2.0); Trial B: 2.0 (2.0), rho=0.680, p=0.001), but not for OSS (Trial A: 8.0 (12.0); Trial B: 5.0 (9.0), rho=0.309, p=0.173). Performance in cognitive/applied tasks (range rho=0.447-0771) was consistent, except simulated driving (range rho=0.035–0.272), however the impairment was trivial. The subgroup analysis did not reveal substantial changes in reliability. Conclusion: A single 'Hangover' rating was a reliable way of determining 'mild' to 'moderate' hangover severity. The present data could be used to assist the methodological design of future hangover research.

INTRODUCTION

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2 Alcohol hangover has been defined as the combination of negative mental and physical symptoms associated with a single episode of alcohol consumption; when blood alcohol 3 concentration (BrAC) has returned to zero (Verster, Scholey, van de Loo, Benson, & Stock, 4 2020). Besides inducing a variety of unpleasant symptoms (e.g. headache, nausea, discomfort, 5 6 tiredness), alcohol-induced hangovers have the potential to impair cognitive function (Gunn, 7 Mackus, Griffin, Munafò, & Adams, 2018). This may have serious implications for individuals performing applied cognitive tasks such as driving a motor vehicle (Cameron & French, 2015; 8 9 Hoiseth, Fosen, Liane, Bogstrand, & Morland, 2015; Verster, Bervoets, et al., 2014) or 10 undertaking occupational duties (e.g. operating machinery (Van Dyken, Szlabick, & Sticca, 11 2013)). However, studies that have examined the cognitive effects of alcohol hangover have produced equivocal findings (Gunn et al., 2018), possibly as a result of methodological 12 limitations. 13 The methodological approach employed for this type of research is an important consideration. 14 15 When participants self-report alcohol consumption and when between-subject designs are 16 employed outcomes are subject to potential confounding variables (e.g. inaccuracies in alcohol reporting, age, gender, cognitive capacity, alcohol pharmacokinetics, etc.) (Hopkins, 2000). To 17 date, 15 laboratory studies have employed what are considered to be more rigorous procedures 18 19 (i.e. prescribed alcohol and within-subject study designs) to investigate the effects of alcohol 20 hangover on discrete cognitive tasks (Chait & Perry, 1994; Finnigan, Hammersley, & Cooper, 1998; Howland, Rohsenow, Bliss, et al., 2010; Howland, Rohsenow, Greece, et al., 2010; 21 Kruisselbrink, Martin, Megeney, Fowles, & Murphy, 2006; Lemon, Chesher, Fox, Greeley, & 22 Nabke, 1993; Roehrs, Roehrs, Yoon, & Roth, 1991; Rohsenow et al., 2010; Verster, Van Duin, 23 Volkerts, Schreuder, & Verbaten, 2003) and/or performance during applied workplace 24 25 scenarios (Collins, 1980; Collins & Chiles, 1980; Morrow, Leirer, Yesavage, & Tinklenberg,

1991; Streufert et al., 1995; Yesavage, Dolhert, & Taylor, 1994; Yesavage & Leirer, 1986). 26 Despite this, results from these studies indicate varied cognitive responses. Unfortunately, not 27 28 all of these studies confirmed participants' breath alcohol concentration (BrAC) had returned to zero at the time of testing (Chait & Perry, 1994; Collins, 1980; Collins & Chiles, 1980; 29 Howland, Rohsenow, Bliss, et al., 2010; Morrow et al., 1991; Rohsenow et al., 2010; 30 Rohsenow, Howland, Minsky, & Arnedt, 2006). Hence, these results could be confounded by 31 32 residual alcohol intoxication. In addition, other factors known to independently affect cognitive function (e.g. insufficient sleep (Lim & Dinges, 2010), hydration status (Masento, Golightly, 33 34 Field, Butler, & van Reekum, 2014), or awareness of exposure to alcohol (Christiansen, Townsend, Knibb, & Field, 2017; Verster, Bervoets, et al., 2014)), have rarely been considered 35 within standardisation procedures. These methodological limitations may, in part, explain 36 37 some of the varied responses observed. 38 It is also possible that the "true" effect of alcohol hangover on cognitive function may be inconsistent. Indeed, subjective responses to a fixed dose of alcohol may vary between 39 40 occasions due to a number of physiological and behavioural factors (Viken, Rose, Morzorati, Christian, & Li, 2003), which could potentially influence cognitive performance. In the absence 41 42 of objective indicators of alcohol hangover (e.g. biomarkers (Mackus et al., 2017)), individuals' 43 perceptions are the only available predictors of hangover severity. However, it is unclear whether an individuals' perception of hangover severity influences the level of cognitive 44 impairment observed. To date, no study has investigated the reliability of subjective symptoms 45 46 and cognitive performance in response to a fixed dose of alcohol intended to elicit a hangover. Understanding the consistency of hangover symptoms (and subsequent effects) experienced by 47 individuals would help with interpretation of results from investigations into the impact of 48 alcohol-induced hangovers. In addition, reliability data could be used to assist methodological 49 design of future hangover research, by identifying cognitive tasks least likely to produce 50 51 spurious outcomes.

The present study investigated the consistency of alcohol-induced hangover symptoms and cognitive performance (including two applied tasks; typing and simulated driving) across two separate occasions (using a within-subject design) and under standardised laboratory conditions. We hypothesised that subjective hangover responses would be comparable, and a similar degree of cognitive impairment would be observed between repeated trials.

METHODS

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58 **Study design.** Participants (n=21) visited the laboratory on three separate occasions. The initial visit involved task familiarisation and baseline measures of cognitive function and applied task 59 performance. Participants then undertook two identical experimental trials (Trial A and B), 60 61 which involved consuming a fixed dose of alcohol designed to induce a morning hangover. Trials also involved standardised food, water and alcohol consumption in the evening, followed 62 by an overnight stay in the laboratory. The following morning, participants completed a discrete 63 cognitive test of processing speed and executive functioning (Trail Making Tasks (TMT)) and 64 applied (i.e. simulated driving and typing) tasks. Experimental trials were separated by at least 65 66 14 days. **Screening and Recruitment.** Prior to the initial visit, participants were screened for eligibility. 67 Participants were required to: be over 18 years of age, self-report having experienced a 68 hangover in the last 12 months, and be generally healthy. Participant exclusion criteria 69 included: being pregnant, taking medications that could interact with alcohol, regular tobacco 70 71 use, a possibility of alcohol or drug abuse (i.e. a score of 4 or more on the Short Michigan Alcohol Screening Test, (Selzer, Vinokur, & van Rooijen, 1975)), and having a possible 72 genetic alcohol intolerance (Yokoyama et al., 2005). Recruitment was conducted via email and 73 convenience snowball sampling. The investigation was approved by the University's Human 74 Research Ethics Committee (XXXXXX; blinded for peer review). Prior to undertaking 75 experimental trials, eligible participants were required to provide informed consent. 76 77 **Initial visit.** Participants attended the initial visit in the morning (between 0600 hrs and 1100 hrs) to ensure familiarisation and baseline values for the cognitive function and applied tasks 78 79 (described below) were collected at approximately the same time of day as experimental trials. Given the experimental trials involved a standardised evening meal and overnight sleep within 80 the laboratory, for the familiarisation/baseline measures participants were encouraged to stay 81

hydrated (i.e. consume at least 500 mL of water within 2 hrs of retiring to bed the night before), obtain ≥7 hrs of quality sleep, and to avoid caffeine on the morning of the visit. All other food and activity/lifestyle standardisation procedures were consistent with the subsequent experimental trials (detailed below).

Experimental Trials

Prior Standardisation. Prior to experimental trials, participants were advised to abstain from illicit drugs/tobacco smoking for 48 hrs; avoid alcohol and vigorous physical activity for 24 hrs; abstain from consuming caffeinated foods, beverages, and supplements after 1200 hrs on the trial day; and refrain from consuming calorie-containing foods and beverages from 1500 hrs. To monitor compliance and promote similar nutritional intake, participants were required to keep a 24-hr food diary leading up to the first laboratory visit; a copy of which was provided to participants, for replication prior to the subsequent trial.

Procedure. Experimental procedures are illustrated in Figure 1. On arrival to the laboratory (1830 hrs), verbal confirmation of compliance to all pre-trial standardisation procedures was obtained, prior to a urine sample being collected for determination of hydration status (Urine Specific Gravity [U_{SG}]; Refractometer UG- α^{\odot} ; Atago Co., Ltd., Tokyo, Japan). If deemed dehydrated (U_{SG}>1.020) (Casa et al., 2000), participants were asked to consume a 500 mL bolus of plain water, with a second urine sample collected to verify euhydration 30 mins later. If U_{SG}>1.020, the trial was rescheduled. For participants requiring the additional water on their initial trial (n=5), this was replicated in the subsequent trial irrespective of initial hydration status. Other measures collected upon arrival included an initial BrAC (Alcolizer LE4; Alcolizer Technology, Cleveland, QLD, Australia) (to confirm abstinence from alcohol), baseline hangover severity ratings (described below), height and nude body weight (platform scales HW-PT200; A&D Company Ltd, Tokyo, Japan).

Following these initial procedures, participants were provided with 4 alcoholic beverages (see Alcohol Administration), with a standardised meal (consumed over 30 mins) provided following the second alcoholic beverage. The standardised meal consisted of: Lean Cuisine® Frozen Rich Beef Lasagne 400g, and Smiths® Original Potato Chips 2x19g packets, which provided in total: energy = 2498 kJ, carbohydrates = 68.4 g, fat = 22.4 g, protein = 25.4 g. Participants' BrAC was recorded every 15 mins following administration of the first alcoholic beverage; with none of the readings revealed to participants. To minimise any hangover effects associated with changes in hydration status, during the first trial participants were encouraged to consume a minimum of 1 L of water between the commencement of the first alcoholic beverage and retiring to sleep. The actual amount and rate of consumption was recorded every 30 mins for replication in the second trial. Following the standardised drinking and evening meal protocol, participants remained supervised in the laboratory and could participate in sedentary-based activities (e.g. playing board games, watching movies). To minimise the impact of sleep variation, participants were sent to the laboratory sleeping quarters at 2200 hrs with no access to technologies (e.g. smart phones). Within the sleeping quarters, participants were able to be observed without interruption until the pre-determined waking time of 0600 hrs. Upon waking, participants provided a urine sample for UsG determination and BrAC was measured. If BrAC = 0.000%, a 30 min period was allocated prior to measuring hangover severity and asking two additional questions regarding sleep quality (overall sleep quality rating (1:poor to, 10:best), and the number of sleep interruptions experienced during the night). Alternatively, if waking BrAC>0.000% these tasks were delayed until no detectable breath alcohol was recorded (maximum 90 mins later). Participants then completed the battery of cognitive function and applied tasks.

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Alcohol Administration. The aim of the alcohol administration protocol was to provide a sufficient dose of alcohol likely to induce a hangover without emesis. Participants consumed the same type and volume of alcoholic beverage on both trials, and were initially able to select either bourbon, whisky or dark rum as their trial beverage. These beverage options were available because of the higher congener content, which may increase hangover severity (Verster, Schrurs, & Owen, 2014). Beverages were provided without dilution in 4 aliquots with participants encouraged to consume each serve within 3 mins. It has been previously suggested that a BrAC of ~0.100% can induce a hangover (Verster et al., 2010). To achieve this BrAC, the first three alcoholic beverages provided were fixed doses consisting of: 0.4 g (1900 hrs); 0.4 g (1915 hrs) and 0.2 g (2000 hrs) of ethanol/kg body weight (BW). The final beverage (2045 hrs) was titrated depending on the BrAC reading at 2030 hrs according to the following schedule (i.e. 0.2 g/kg BW for BrAC > 0.070%; 0.3 g/kg BW for BrAC between 0.060-0.070%; 0.4 g/kg BW for BrAC <0.060%). The same dose of alcohol was provided to participants in their subsequent trial, irrespective of their BrAC responses. BrAC_{max} was considered the highest BrAC recorded from assessments taken between 1900-2200 hrs. Measuring Hangover. The Acute Hangover Scale (AHS) (Rohsenow et al., 2007) was adapted to measure subjective hangover severity. The scale consists of nine items: 'Hangover', 'Thirst', 'Tiredness', 'Headache', 'Dizziness', 'Loss of Appetite', 'Stomach Ache', 'Nausea', and 'Heart Racing' with participants rating each symptom between 0-7 guided by the following anchors: None (0), Mild (1), Moderate (4) and Incapacitating (7). Outcome measures included the change from baseline for individual 'Hangover' rating, all remaining AHS symptoms ratings, as well as the sum of the remaining symptoms (Overall Symptoms Score [OSS]). Trail Making Test (TMT). The TMT was used to assess processing speed and executive functioning. This cognitive tasks were selected on the basis of previous studies demonstrating

hangover-induced impairments employing this task (Scholey et al., 2019). The TMT (Inquisit

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5 Lab, Millisecond Software) was ~3 mins in duration and administered on a laptop computer. The test consisted of two elements. The first component (TMT 1) examined cognitive processing speed and involved participants connecting numbered targets in a sequential order (up to 25 targets). The second component (TMT 2) examined executive functioning and required participants to connect targets, with the labels alternating between numbers and letters (1, A, 2, B, etc.). The participant was instructed to connect the targets as quickly as possible while maintaining accuracy. Outcome measures included the change in completion time and the number of errors from baseline.

Applied Tasks. On completion of the discrete cognitive function testing, participants undertook two applied tasks: a simulated drive and a typing task. The simulated drive has previously demonstrated sensitivity in detecting alcohol-induced changes (Irwin, Iudakhina, Desbrow, & McCartney, 2017). The typing task was selected as a relatively common occupational assignment, in contrast to highly specialised workplace simulations used in previous hangover research (e.g. ship power plant operation) (Rohsenow et al., 2006; Streufert et al., 1995).

Simulated Drive. A computerised driving simulation task was used to measure driving performance (SCANeR studio simulation engine, v1.6, OKTAL, Paris, France). The driving simulator hardware is described in detail elsewhere (Irwin, Leveritt, Shum, & Desbrow, 2014; McCartney, Desbrow, & Irwin, 2017). Participants drove a 16 km course (~10 mins), which consisted of a bi-directional single-lane road with gentle hills and curves requiring minor speed adjustments. The drive incorporated 7 curves, with curvature radii of: 3.3 km; 1.0 km; 3.3 km; 0.7 km; 0.5 km; 0.7 km; and 0.5 km. Oncoming traffic (e.g. cars, trucks, cyclists) programmed to exhibit non-conflicting behaviour was present in the scenario. Individuals were instructed to stay in the middle of the left-hand lane (Australian road rules) and follow the target car in front of them without overtaking it. Unknown to participants, the target car moved at a pre-

determined speed of 80 km/h. Outcome measures included the change in standard deviation of lateral position (SDLP, "weaving" of the car) and lane crossing (e.g. contact with or crossed lane markings) from baseline. During the initial visit, participants completed the driving task three times. The first two drives were familiarisation, which has been considered suitable to minimise learning effects based on the same driving scenario (McCartney et al., 2017). The final drive was used to obtain baseline outcome measures and was separated from the familiarisation drives by at least 10 mins to minimise fatigue. For each experimental trial, participants completed the simulated drive once.

Typing Task. A typing task lasting ~5 mins was administered using a standard QWERTY keyboard and a typing application (Mavis Beacon Teaches Typing, Version 20, Software: Broaderbund®). At the initial visit, participants completed two short familiarisation text passages (70-80 words long), followed by a baseline typing test (1 of 4 text passages, 240-260 words long). The order that participants received each text passage was randomised and the remaining texts were used for the experimental trials. The outcome measure was the change in adjusted typing speed (ATS) from baseline, calculated using the following formula:

ATS = average speed (words per min) x percentage of error free characters typed.

Randomisation and Statistical Analysis. At screening participants had their first trial allocated trial code A or B, such that analysis could be performed as a traditional trial order (trial 1 vs trial 2) and a randomised trial order (trial A vs trial B). This approach facilitated a trial order analysis of BrAC and 'Hangover' ratings on the basis that prior alcohol hangover exposure (trial 1) may have influenced subsequent trial outcomes (trial 2). Data were analysed using SPSS for Windows version 23.0 (SPSS, Chicago, Illinois, USA). All data were examined for normality and sphericity using the Shapiro-Wilk test and Mauchly's test, respectively. Paired t-tests were used to compare normally distributed data (i.e. TMT Time and typing). When sphericity assumptions were violated, the Greenhouse-Geisser correction was applied.

Where data was identified as being non-normally distributed, Wilcoxon signed-rank tests were used for statistical comparisons (i.e. all hangover ratings, TMT errors and all driving parameters). All outcomes were assessed for reliability between randomised trials using the change score from baseline. In addition, reliability of outcomes were examined in a subgroup of individuals who had consistent 'Hangover' ratings between the two randomised trials. A hangover was deemed consistent when the individual 'Hangover' rating fell within the same symptom interval ("0" = none, "1-3" = 'mild'; "4-6" = 'moderate'; "7" = 'severe'). Spearman's rank order correlations were used to assess reliability of measures with correlations (rho values) described according to Evans, 1996 (e.g. 0.00-0.19 regarded as 'very weak', 0.20-0.39 as 'weak', 0.40-0.59 as 'moderate', 0.60-0.79 as 'strong' and 0.80-1.00 as 'very strong'). Values are described as mean \pm SD for normally distributed data and median (IQR) for non-normally distributed data. Statistical significance considered at p<0.05.

RESULTS

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- 219 Participants, Trial Order and Standardisation. Twenty-three participants initially enrolled in the study; two could not attend their second trial due to conflicting commitments. Thus, 21 220 participants (13 male, 8 female; age 24±3 years; baseline BMI 23.5±2.6 kg/m²) completed both 221 trials. Trial order analysis revealed no differences for BrAC_{max} (Trial 1: 0.093±0.016, Trial 2: 222 0.091 ± 0.012 , p=0.490) or 'Hangover' ratings (Trial 1: 2.0 ± 1.6 , Trial 2: 2.0 ± 1.4 , p=0.754). 223 224 Baseline individual 'Hangover' rating was 0 for all participants. There was no difference between the starting U_{SG} values between randomised trials (Trial A: 1.014±0.008, Trial B: 225 1.013 ± 0.009 , p=0.509). The mean amount of ethanol consumed was: 90 ± 15 g (n=19 consumed 226 227 1.2g ethanol/kg BW, n=1 consumed 1.3g ethanol/kg BW and n=1 consumed 1.4g ethanol/kg 228 BW). There was no difference between mean BrAC_{max} achieved: Trial A: 0.090±0.013%; Trial B: $0.094\pm0.016\%$ (range = 0.070-0.145%, p=0.245). No differences were observed between 229 trials for subjective sleep quality rating (Trial A: 5.7 ± 2.3 , Trial B: 6.4 ± 1.4 , p=0.167) or self-230 reported awakenings (Trial A: 3.0 ± 1.8 , Trial B: 3.0 ± 1.8 , p=0.916). 231 232 **Reliability between Trial A and B.** Table 1 presents the change between baseline and trial A 233 and B values for subjective hangover symptom ratings, cognitive function and applied task performance. Spearman's correlation coefficients between the two change scores are also 234 shown. (Supplementary Table 1 present the baseline and trial data for all participants (n=21), 235 236 including hangover symptom ratings, cognitive function and applied tasks). 237 [Insert Table 1 here]

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Baseline subjective hangover ratings were not significantly different between Trial A and B (all p's>0.05). The change from baseline for subjective ratings of 'Hangover' and 'Loss of Appetite' was consistent for both trials (p's<0.05). TMT performance was compromised during alcohol hangover (i.e. time and errors increased on both trials). All changes in discrete cognitive function from baseline performance demonstrated moderate to strong reliability

between trials (*p*'s<0.05). For driving performance, no effect of alcohol hangover was observed for SDLP or total number of lane crossing's (*p*'s>0.05). In addition, changes observed from baseline for these outcomes were not found to be reliable between trials. ATS improved during alcohol hangover (only statistically different for Trial B) and demonstrated moderate reliability between trials (*p*'s<0.05).

Table 2 provides a subgroup analysis (*n*=12 participants with consistent 'Hangover' ratings between trials) of change from baseline data and reliability between trials for subjective hangover symptom ratings, cognitive function and applied task performance. The subgroup analysis revealed similar outcomes to those of the whole group analysis, with the exception of 'Tiredness', which was identified as having significant reliability between trials and 'TMT 1', which was no longer reliable between trials. No other substantial changes in reliability were noted.

[Insert Table 2 here]

DISCUSSION

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This within-subjects study investigated the consistency of morning hangover symptoms and cognitive/applied task performance in response to a fixed dose of alcohol (intended to elicit a hangover) provided the evening prior. In agreement with our hypothesis, participants' subjective rating of 'Hangover' was consistent between trials. However, when assessed individually or as a sum of individual hangover symptoms (i.e. overall symptoms score), reliability was typically not demonstrated. While performance in cognitive/applied tasks (except simulated driving) was consistent across both trials, in most cases impairment was either not observed, or if it was (i.e. ATS Trial B), the magnitude was trivial in the context of 'mild' to 'moderate' hangovers. Repeated alcohol administration (i.e. same type and dose, under standardised conditions) produced similar general subjective ratings of 'Hangover', which was not evident when hangover was assessed as the sum of individual symptoms. Previous studies have attempted to develop and validate hangover scales by correlating hangover symptoms with reported alcohol intakes (Penning et al., 2013; Rohsenow et al., 2007; Slutske, Piasecki, & Hunt-Carter, 2003). The most recent of these, suggested strong correlations between multiple-item hangover scales and the quantity of alcohol consumed, while the authors concluded that a single-item hangover rating should not be used to assess hangover severity (Penning et al., 2013). In contrast, a recent review recommended using a 1-item overall hangover rating as primary endpoint in hangover studies (Verster, van de Loo, Benson, Scholey, & Stock, 2020). The present results indicate that when hangover severity was assessed according to the sum of individual symptoms (e.g. those from the AHS scale (Rohsenow et al., 2007)), this was found to be unreliable. This is surprising, given that our standardisation procedures (e.g. pre-trial hydration check and prescribed water intake) were expected to reduce variability in some symptoms (i.e. "thirst", "headache") and suggests that many of these specific indicators change in relation to factors

independent of alcohol consumption. The current study confirms that a single-item hangover rating is a more reliable way of determining hangover severity during repeated measures hangover studies.

The results of the current study are in contrast with a recent meta-analysis demonstrating that hangovers may impair cognitive function (Gunn et al., 2018). The present results indicate no impairments from baseline for discrete cognitive processing speed and executive functioning, while the meta-analysis indicated a moderate negative effect on psychomotor speed (hedges' g=0.66). Two potential explanations for the disparity in findings relate to task complexity and hangover severity. The meta-analysis determined the effect of hangover on psychomotor speed exclusively through investigations employing simple and choice reaction time tasks, whereas the TMT incorporates speed and function. In addition, the severity of hangovers induced in the current study were subjectively rated as 'mild' to 'moderate' by the majority of participants (with only one hangover across both trials described as being 'severe'). This may have influenced our outcomes given that TMT impairment has previously been demonstrated as having a significant, albeit weak, correlation with hangover severity (Scholey et al., 2019). Further research is required to establish the extent to which more "severe" hangovers can reliably induce detectible impairments in cognitive function.

In terms of simulated driving, increases in SDLP have been demonstrated as being the most sensitive measure of alcohol intoxication (Irwin et al., 2017). Despite SDLP increasing in magnitude to that previously observed under BrAC = 0.05% and close to 'clinically meaningful' values (Mets et al., 2011), SDLP changes in the present study were not statistically significant; nor were results found to be reliable between repeated trials. Two previous studies (from one research group) have demonstrated equivocal findings of a hangover on SDLP using simulated driving (Alford et al., 2020; Verster, Bervoets, et al., 2014). In the most recent of these, no difference in SDLP was observed with a hangover +/- residual alcohol (Alford et al.,

2020). The driving task employed was 20 minutes and more engaging (urban/environmental stimuli) (Alford et al., 2020), than the previous 1-hr simulated highway drive (requiring greater levels of sustained attention) (Verster, Bervoets, et al., 2014). The previous studies have employed naturalistic designs where participants consumed ad libitum amounts of alcohol (Alford et al., 2020; Verster, Bervoets, et al., 2014). Typically, this has resulted in larger quantities of alcohol being consumed and reports of more severe hangovers (i.e. severity rated ~50% of maximum) (Alford et al., 2020; Verster, Bervoets, et al., 2014). In addition, data from participants who reported no hangover symptoms in Verster et al. (2014) were excluded from the analysis (Verster, Bervoets, et al., 2014), potentially biasing the outcome. Collectively, the results from the three studies suggest reliable decrements in simulated driving performance are only likely to be detectible when associated with moderate to severe hangovers in monotonous scenarios requiring sustained attention. The second applied task (typing test), was selected as a relatively common occupational undertaking, in contrast to highly specialised simulations used in previous hangover research (Kocher, Warwick, Al-Ghnaniem, & Patel, 2006; Rohsenow et al., 2006; Streufert et al., 1995). Although the task demonstrated high reliability, the practicality for further use in hangover

undertaking, in contrast to highly specialised simulations used in previous hangover research (Kocher, Warwick, Al-Ghnaniem, & Patel, 2006; Rohsenow et al., 2006; Streufert et al., 1995). Although the task demonstrated high reliability, the practicality for further use in hangover research is debatable, since observed changes were not significant in both trials and adjusted typing speed is unlikely to have a meaningful impact on overall workplace productivity. While not directly comparable with the task used in the present study, Howland et al (2010) found that college students academic test performance was not impacted by a mild hangover (AHS severity rating 1.4 ± 0.8). Likewise, outcomes from two of the three studies (Collins & Chiles, 1980; Rohsenow et al., 2006) employing specialised simulation tasks failed to observe effects of alcohol hangover on performance. Only one study that examined simulated surgical dexterity (n=5) has identified performance impairment following a night of drinking (when BrAC = 0.000% the next morning) (Kocher et al., 2006). However, subjective perceptions of hangover severity and symptoms were not measured directly in this study; thus, impairments

cannot be attributed to alcohol hangover per se. Collectively, results from this body of work 332 suggest that alcohol hangover is unlikely to impair performance on applied tasks of this nature. 333 However, we cannot generalise the impact of alcohol hangover based on this collection of 334 studies to performance on all occupational-type tasks. 335 The subgroup analysis of individuals who had consistent 'Hangover' ratings between the two 336 randomised trials produced similar outcomes to the whole group analysis. It is possible that 337 subjective symptoms shift cognitive performance by expectancy effects based on one's 338 estimates of how "drunk" they got the night before (i.e. greater symptoms = more "drunk") 339 (Testa et al., 2006). In the present study, participants were aware that they had received the 340 341 same alcohol dose and type, potentially moderating expectancy effects. Further research is 342 required to determine the reliability of cognitive effects when symptoms and belief in alcohol consumed are moderated. 343 While the study was primarily focussed on assessing consistency of effects resulting from a 344 hangover, it is important to acknowledge the consequences of not incorporating a placebo trial 345 346 within the current investigation. Without a placebo trial, we are unable to determine the extent to which perturbations in sleep (as a result of staying overnight in a laboratory environment 347 rather than the participants home) may have contributed to the changes observed in cognitive 348 function. 349 350 In conclusion, the present investigation determined the reliability of subjective symptoms and 351 measures of cognitive function/applied task performance in response to receiving a fixed dose of alcohol (intended to induce a hangover). A general rating (single-item) of 'Hangover' was 352 observed to be consistent between trials. In response to an alcohol hangover, the performance 353

in cognitive/applied tasks (except simulated driving) was consistent, however the impairment

was trivial in the context of 'mild' to 'moderate' hangovers.

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REFERENCES

363	Alford, C., Broom, C., Carver, H., Johnson, S. J., Lands, S., Reece, R., & Verster, J. C.
364	(2020). The Impact of Alcohol Hangover on Simulated Driving Performance During a
365	'Commute to Work'—Zero and Residual Alcohol Effects Compared. Journal of
366	clinical medicine, 9(5), 1435. doi: 10.3390/jcm9051435
367	Cameron, E., & French, D. P. (2015). Predicting perceived safety to drive the morning after
368	drinking: The importance of hangover symptoms. Drug Alcohol Review.
369	doi:10.1111/dar.12311
370	Casa, D. J., Armstrong, L. E., Hillman, S. K., Montain, S. J., Reiff, R. V., Rich, B. S.,
371	Roberts, W. O., & Stone, J. A. (2000). National athletic trainers' association position
372	statement: fluid replacement for athletes. <i>Journal of athletic training</i> , 35(2), 212-224.
373	Chait, L., & Perry, J. (1994). Acute and residual effects of alcohol and marijuana, alone and
374	in combination, on mood and performance. Psychopharmacology, 115(3), 340-349.
375	doi: 10.1007/BF02245075
376	Christiansen, P., Townsend, G., Knibb, G., & Field, M. (2017). Bibi ergo sum: the effects of
377	a placebo and contextual alcohol cues on motivation to drink alcohol.
378	Psychopharmacology (Berl), 234(5), 827-835. doi:10.1007/s00213-016-4518-0
379	Collins, W. E. (1980). Performance effects of alcohol intoxication and hangover at ground
380	level and at simulated altitude. Aviation, Space, and Environmental Medicine, 51,
381	327-335.
382	Collins, W. E., & Chiles, W. D. (1980). Laboratory performance during acute alcohol
383	intoxication and hangover. Human Factors, 22(4), 445-462.
384	doi:10.1177/001872088002200406

385	Finnigan, F., Hammersley, R., & Cooper, T. (1998). An examination of next-day hangover
386	effects after a 100 mg/100 ml dose of alcohol in heavy social drinkers. Addiction,
387	93(12), 1829-1838. doi: 10.1046/j.1360-0443.1998.931218298.x
388	Gunn, C., Mackus, M., Griffin, C., Munafò, M. R., & Adams, S. (2018). A systematic review
389	of the next-day effects of heavy alcohol consumption on cognitive performance.
390	Addiction, 113(12), 2182-2193. doi:10.1111/add.14404
391	Hoiseth, G., Fosen, J. T., Liane, V., Bogstrand, S. T., & Morland, J. (2015). Alcohol
392	hangover as a cause of impairment in apprehended drivers. Traffic Injury Prevention,
393	16(4), 323-328. doi:10.1080/15389588.2014.938324
394	Hopkins, W. G. (2000). Measures of Reliability in Sports Medicine and Science. Sports
395	Medicine, 30(1), 1-15. doi:10.2165/00007256-200030010-00001
396	Howland, J., Rohsenow, D. J., Bliss, C. A., Almeida, A. B., Calise, T. V., Heeren, T., &
397	Winter, M. (2010). Hangover Predicts Residual Alcohol Effects on Psychomotor
398	Vigilance the Morning After Intoxication. Journal of addiction research & therapy,
399	<i>I</i> (101), 1000101. doi:10.4172/2155-6105.1000101
400	Howland, J., Rohsenow, D. J., Greece, J. A., Littlefield, C. A., Almeida, A., Heeren, T.,
401	Winter, M., Bliss, C. A., Hunt, S., & Hermos, J. (2010). The Effects of Binge
402	Drinking on College Students' Next-Day Academic Test-Taking Performance and
403	Mood State. Addiction, 105(4), 655-665. doi:10.1111/j.1360-0443.2009.02880.x
404	Irwin, C., Iudakhina, E., Desbrow, B., & McCartney, D. (2017). Effects of acute alcohol
405	consumption on measures of simulated driving: a systematic review and meta-
406	analysis. Accident Analysis & Prevention, 102, 248-266. doi:
407	10.1016/j.aap.2017.03.001

Irwin, C., Leveritt, M., Shum, D. H., & Desbrow, B. (2014). Mild to moderate dehydration 408 combined with moderate alcohol consumption has no influence on simulated driving 409 410 performance. Traffic Injury Prevention, 15(6), 652-662. doi:10.1080/15389588.2013.810335 411 Kocher, H., Warwick, J., Al-Ghnaniem, R., & Patel, A. (2006). Surgical dexterity after a 412 'night out on the town'. ANZ Journal of Surgery, 76(3), 110-112. doi:10.1111/j.1445-413 2197.2006.03664.x 414 Kruisselbrink, L. D., Martin, K. L., Megeney, M., Fowles, J. R., & Murphy, R. J. L. (2006). 415 Physical and psychomotor functioning of females the morning after consuming low to 416 moderate quantities of beer. Journal of Studies on Alcohol, 67(3), 416. doi: 417 10.15288/jsa.2006.67.416 418 419 Lemon, J., Chesher, G., Fox, A., Greeley, J., & Nabke, C. (1993). Investigation of the "hangover" effects of an acute dose of alcohol on psychomotor performance. 420 Alcoholism: Clinical and Experimental Research, 17(3), 665-668. doi: 421 10.1111/j.1530-0277.1993.tb00816.x422 Lim, J., & Dinges, D. F. (2010). A meta-analysis of the impact of short-term sleep 423 deprivation on cognitive variables. *Psychological bulletin*, 136(3), 375-389. 424 doi:10.1037/a0018883 425 Mackus, M., van de Loo, A., Raasveld, S. J., Hogewoning, A., Sastre Torano, J., Flesch, F. 426 M., Korte-Bouws, G., van Neer, R., Wang, X., Nguyen, T., Brookhuis, K., Kraneveld, 427 A., Garssen, J., & Verster, J. C. (2017). Biomarkers of the alcohol hangover state: 428 Ethyl glucuronide (EtG) and ethyl sulfate (EtS). Human Psychopharmacology: 429 Clinical and Experimental, 32(5). doi:10.1002/hup.2624 430

- 431 Masento, N. A., Golightly, M., Field, D. T., Butler, L. T., & van Reekum, C. M. (2014).
- Effects of hydration status on cognitive performance and mood. *British Journal of*
- *Nutrition*, 111(10), 1841-1852. doi:10.1017/s0007114513004455
- 434 McCartney, D., Desbrow, B., & Irwin, C. (2017). Using alcohol intoxication goggles (Fatal
- Vision(R) goggles) to detect alcohol related impairment in simulated driving. *Traffic*
- 436 *Injury Prevention*, 18(1), 19-27. doi:10.1080/15389588.2016.1190015
- 437 Mets, M. A., Kuipers, E., de Senerpont Domis, L. M., Leenders, M., Olivier, B., & Verster, J.
- 438 C. (2011). Effects of alcohol on highway driving in the STISIM driving simulator.
- 439 *Human Psychopharmacology: Clinical and Experimental*, 26(6), 434-439. doi:
- 440 10.1002/hup.1226
- Morrow, D., Leirer, V., Yesavage, J., & Tinklenberg, J. (1991). Alcohol, age, and piloting:
- judgment, mood, and actual performance. *International journal of the addictions*,
- 443 26(6), 669-683. doi: 10.3109/10826089109058912
- 444 Penning, R., McKinney, A., Bus, L. D., Olivier, B., Slot, K., & Verster, J. C. (2013).
- Measurement of alcohol hangover severity: development of the Alcohol Hangover
- Severity Scale (AHSS). *Psychopharmacology*, 225(4), 803-810. doi: 10.1007/s00213-
- 447 012-2866-y
- Roehrs, T., Roehrs, T., Yoon, J., & Roth, T. (1991). Nocturnal and next-day effects of
- ethanol and basal level of sleepiness. *Human psychopharmacology: Clinical and*
- 450 Experimental, 6(4), 307-311. doi: 10.1002/hup.470060407
- Rohsenow, D. J., Howland, J., Arnedt, J. T., Almeida, A. B., Greece, J., Minsky, S. J.,
- Kempler, C. S., & Sales, S. (2010). Intoxication with bourbon versus vodka: effects
- on hangover, sleep, and next-day neurocognitive performance in young adults.

Alcoholism: Clinical and Experimental Research, 34(3), 509-518. doi: 454 10.1111/j.1530-0277.2009.01116.x 455 Rohsenow, D. J., Howland, J., Minsky, S. J., & Arnedt, J. T. (2006). Effects of heavy 456 drinking by maritime academy cadets on hangover, perceived sleep, and next-day ship 457 power plant operation. Journal of Studies on Alcohol, 67(3), 406-415. doi: 458 10.15288/jsa.2006.67.406 459 Rohsenow, D. J., Howland, J., Minsky, S. J., Greece, J., Almeida, A., & Roehrs, T. A. 460 461 (2007). The Acute Hangover Scale: A new measure of immediate hangover symptoms. Addictive Behaviour, 32(6), 1314-1320. doi:10.1016/j.addbeh.2006.10.001 462 Scholey, A., Benson, S., Kaufman, J., Terpstra, C., Ayre, E., Verster, J. C., Allen, C., & 463 Devilly, G. J. (2019). Effects of alcohol hangover on cognitive performance: Findings 464 from a field/internet mixed methodology study. Journal of clinical medicine, 8(4), 465 440. doi: 10.3390/jcm8040440 466 Selzer, M. L., Vinokur, A., & van Rooijen, L. (1975). A self-administered Short Michigan 467 Alcoholism Screening Test (SMAST). Journal of Studies on Alcohol, 36(1), 117-126. 468 doi: 10.15288/jsa.1975.36.117 469 Slutske, W. S., Piasecki, T. M., & Hunt-Carter, E. E. (2003). Development and initial 470 validation of the Hangover Symptoms Scale: Prevalence and correlates of hangover 471 symptoms in college students. Alcoholism: Clinical and Experimental Research, 472 27(9), 1442-1450. doi: 10.1097/01.ALC.0000085585.81711.AE 473 Streufert, S., Pogash, R., Braig, D., Gingrich, D., Kantner, A., Landis, R., Lonardi, L., 474 Roache, J., & Severs, W. (1995). Alcohol hangover and managerial effectiveness. 475 Alcoholism: Clinical and Experimental Research, 19(5), 1141-1146. doi: 476 10.1111/j.1530-0277.1995.tb01592.x 477

- 478 Testa, M., Fillmore, M. T., Norris, J., Abbey, A., Curtin, J. J., Leonard, K. E., Mariano, K.
- A., Thomas, M. C., Nomensen, K. J., George, W. H., Vanzile-Tamsen, C., Livingston,
- J. A., Saenz, C., Buck, P. O., Zawacki, T., Parkhill, M. R., Jacques, A. J., & Hayman,
- 481 L. W., Jr. (2006). Understanding alcohol expectancy effects: revisiting the placebo
- 482 condition. *Alcoholism: Clinical and Experimental Research*, 30(2), 339-348.
- 483 doi:10.1111/j.1530-0277.2006.00039.x
- Van Dyken, I., Szlabick, R. E., & Sticca, R. P. (2013). Effect of alcohol on surgical dexterity
- after a night of moderate alcohol intake. American Journal of Surgery, 206(6), 964-
- 486 968. doi:10.1016/j.amjsurg.2013.08.006
- Verster, J. C., Bervoets, A., Klerk, S., Vreman, R., Olivier, B., Roth, T., & Brookhuis, K.
- 488 (2014). Effects of alcohol hangover on simulated highway driving performance.
- 489 *Psychopharmacology*, 231(15), 2999-3008. doi:10.1007/s00213-014-3474-9
- 490 Verster, J. C., Scholey, A., van de Loo, A., Benson, S., & Stock, A. (2020). Updating the
- definition of the alcohol hangover. *Journal of clinical medicine*, 9(3), 823. doi:
- 492 10.3390/jcm9030823
- Verster, J. C., Schrurs, E. M. C., & Owen, L. (2014). Alcohol Congeners and Their Impact on
- 494 Hangover Severity. Alcoholism: Clinical & Experimental Research, 38.
- Verster, J. C., Stephens, R., Penning, R., Rohsenow, D. J., McGeary, J., Levy, D., McKinney,
- 496 A. Finnigan, F., Piasecki, T. M., Adan, A., Batty, G. D., Fliervoet, L. A. L.,
- Heffernan, T., Howland, J., Kim, D., Kruisselbrink, L. D., Ling, J., McGregor, N.,
- Murphy, R. J. L., van Nuland, M., Oudelaar, M., Parkes, A., Prat, G., Reed, N.,
- 499 Slutske, W. S., Smith, G., & Young, M. (2010). The Alcohol Hangover Research
- Group Consensus Statement on Best Practice in Alcohol Hangover Research. *Current*
- 501 *Drug Abuse Reviews*, *3*(2), 116-126.

Verster, J. C., van de Loo, A., Benson, S., Scholey, A., & Stock, A. (2020). The assessment 502 of overall hangover severity. Journal of clinical medicine, 9(3), 786. doi: 503 10.3390/jcm9030786 504 Verster, J. C., Van Duin, D., Volkerts, E. R., Schreuder, A. H., & Verbaten, M. N. (2003). 505 Alcohol hangover effects on memory functioning and vigilance performance after an 506 evening of binge drinking. *Neuropsychopharmacology*, 28(4), 740-746. doi: 507 10.1038/sj.npp.1300090 508 Viken, R. J., Rose, R. J., Morzorati, S. L., Christian, J. C., & Li, T.-K. (2003). Subjective 509 Intoxication in Response to Alcohol Challenge: Heritability and Covariation With 510 Personality, Breath Alcohol Level, and Drinking History. Alcoholism: Clinical and 511 Experimental Research, 27(5), 795-803. doi:10.1097/01.ALC.0000067974.41160.95 512 513 Yesavage, J. A., Dolhert, N., & Taylor, J. L. (1994). Flight simulator performance of younger and older aircraft pilots: effects of age and alcohol. *Journal of the American* 514 Geriatrics Society, 42(6), 577-582. doi: 10.1111/j.1532-5415.1994.tb06852.x 515 516 Yesavage, J. A., & Leirer, V. O. (1986). Hangover effects on aircraft pilots 14 hours after alcohol ingestion: a preliminary report. The American journal of psychiatry. 143(12), 517 1546–1550. doi: 10.1176/ajp.143.12.1546 518 Yokoyama, M., Yokoyama, A., Yokoyama, T., Funazu, K., Hamana, G., Kondo, S., 519 520 Yamashita, T., & Nakamura, H. (2005). Hangover susceptibility in relation to aldehyde dehydrogenase-2 genotype, alcohol flushing, and mean corpuscular volume 521 in Japanese workers. Alcoholism: Clinical and Experimental Research, 29(7), 1165-522

1171. doi: 10.1097/01.ALC.0000172457.62535.EE