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Impaired Decision-Making and Skin Conductance Responses Are Associated with Reward and Punishment Sensitivity in Individuals with Severe Alcohol Use Disorder

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Abstract

Introduction: Individuals with alcohol use disorder (AUD) have difficulties regulating alcohol consumption, despite adverse drinking-related consequences. This may be due to incapacity incorporating previous negative feedback from drinking, resulting in impaired decision-making. ***Methods:*** We assessed whether decision-making is impaired in participants with AUD related to severity of AUD, indexed by severe negative drinking consequences using the Drinkers Inventory of Consequences (DrInC) and reward and punishment sensitivity with the Behavioural Inhibition System Behavioural Activation System (BIS BAS) scales. 36 treatment-seeking alcohol-dependent participants completed the Iowa gambling task (IGT) with skin conductance responses (SCRs) measured continuously as an index of somatic autonomic arousal to evaluate impaired expectancy of negative outcomes. ***Results:*** Two-thirds of the sample showed behavioural impairment during the IGT, with greater AUD severity related to worse performance. BIS moderated IGT performance according to severity of AUD, with increased anticipatory SCRs for those with fewer reported DrInC severe consequences. Participants with more DrInC severe consequences showed IGT deficits and reduced SCRs regardless of BIS scores. BAS-Reward was associated with increased anticipatory SCRs to disadvantageous deck choices among those with lower AUD severity, while SCRs did not differ related to AUD severity for reward outcomes. ***Discussion:*** Effective decision-making in the IGT and adaptive somatic responses were moderated by punishment sensitivity contingent on severity of AUD in these drinkers, with impairments in expectancy to negative outcomes from risky choices, including reduced somatic responses, resulting in poor decision-making processes that may help explain impaired drinking and worse drinking-related consequences.

Introduction

Some individuals with alcohol use disorder (AUD) continue to drink despite possible harmful consequences [1], potentially reflecting poor or dysfunctional

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decision-making regarding drinking choices. Research has identified that people dependent on substances demonstrate preference for immediate short-term gratification rather than avoid negative consequences in the long term, suggesting deficits in decision-making [2]. People with severe AUD fail to regulate their drinking, even after often experiencing salient health, personal, and financial negative consequences. This may be due to erroneous or impaired decision-making processes that lead to disadvantageous drinking choices and subsequent negative drinking-related consequences.

The Iowa gambling task (IGT [3]) is a simulated card game which models real-life decision-making processes for short-term and delayed reward, thus indicating decision-making deficits related to difficulties learning from negative consequences. Participants make choices between higher short-term rewards leading to larger punishments that in the long-term are disadvantageous versus lower short-term rewards with smaller punishments that are more advantageous over time, thus emulating real-world decision-making situations [4]. Two recent meta-analyses further established that AUDs are associated with decision-making deficits in the IGT [5, 6]. However, the decision-making deficit for IGT in severe AUD may be specific to that under risk only (towards the task end) rather than learning through physiological somatic feedback (during the beginning of task) [7]. Additionally, this specific deficit was not associated with relapse prediction power in recently detoxified patients, potentially limiting the clinical applicability of IGT.

Measurement of psychophysiological indices of autonomic nervous system activity such as skin conductance response (SCR) during the IGT, both before the onset (anticipatory responses) and after the reinforcers are presented, allows for examination of participants' expectation of potential consequences. Bechara and Damasio [8] examined the behavioural IGT performance of participants with substance use disorders, patients with ventromedial prefrontal cortex (VMPFC) lesions, and healthy controls. A subgroup of substance use disorder individuals who demonstrated behavioural impairment on the IGT also exhibited reduced anticipatory SCRs for these risky choices only compared to healthy controls but were not as significantly impaired as VMPFC-lesioned patients [8]. This suggests an absence of arousal signalling expectancy of a negative reinforcer for "risky" decisions with potentially severe negative outcomes [8], particularly relevant to reinforcement learning via physiological somatic feedback during the initial exploratory strategy phase where decision-making is conducted under uncertainty [9]. Anticipatory SCRs indicate affective evaluation processes involved in different choice options [10], and this response can even occur prior to understanding potential choice consequences [11]. Therefore, reduction in SCRs may reflect decision-making deficits in individuals with severe AUD in a real-world context, such as appropriate regulation of alcohol consumption.

Impulsivity is a multi-dimensional construct and another important factor that is implicated in both effective decision-making during the IGT as well as an established risk factor in AUD. Self-report instruments such as the Behavioural Activation System and Behavioural Inhibition System (BIS BAS) scales assess reward and punishment sensitivity, which has also been associated with neurophysiological correlates [12]. The BIS BAS reflects Gray's reinforcement sensitivity theory (RST, [13]) which posits two systems guiding behaviour regulation mediated by motivated behaviours and emotional traits: the BIS, related to sensitivity, the aversive stimuli or punishment that invokes subsequent avoidant behaviour; and the BAS, encapsulating impulsivity and reward sensitivity, characterised by the BAS subscales (motivational drive, reward sensitivity, and fun-seeking). The BIS was originally proposed to reflect sensitivity to aversive stimuli or punishment, leading to avoidant behaviour, although revisions to the RST revises BIS as a goal-conflict resolution system that can be both positively (leading to approach) and negatively (leading to avoidance) activated in response to reward [14]. Studies have demonstrated associations with BIS and BAS subscales and increased substance use behaviours [15]. BAS is an established risk factor in problematic alcohol use [16], and hypersensitivity to reward has been shown by hazardous drinkers during IGT [17]. BAS has been shown to mediate approach behaviour related to drives or urges to consume substances such as alcohol [18] (for review, see [19]), and BAS positively correlated with reward bias in the IGT along with corresponding brain activation in those with substance use disorder [12]. Thus, individuals with AUD that exhibit greater reward dependence, coupled with greater insensitivity to punishment, may manifest disadvantageous decision-making patterns that can be evaluated using sensitive instruments such as the BIS BAS, coupled with neuropsychological correlates such as the IGT.

We aimed to assess whether people with AUD demonstrate greater decision-making impairment in the IGT as a function of greater severity of AUD, indexed by more

reported severe consequences measured using the Drinkers Inventory of Consequences [20]. Further, we evaluated whether there were differences in psychophysiological SCRs in anticipation of reinforcers, as a potential indicator of impaired expectation of negative outcomes. We hypothesise that (1) AUD participants with greater AUD severity demonstrate lower IGT net scores than those with lesser AUD severity, indicating a deficit in decision-making processes. As impaired anticipation of reinforcers may relate to dysfunctional learning after negative outcomes, we also hypothesise (2) those AUD participants with greater AUD severity will demonstrate reduced anticipatory SCRs to disadvantageous deck choices during the IGT. Lastly, as reward and punishment sensitivity is associated with problematic alcohol use and may influence detrimental decision-making in individuals with AUD, we employed the BIS BAS scales to evaluate approach and avoidance behaviours in this sample and hypothesised (3) that participants with greater reward sensitivity (higher BAS scores) would demonstrate risky decision-making through more disadvantageous deck choices in the IGT, whereas those with greater punishment sensitivity (higher BIS scores) would show adaptive SCR responses across the IGT, such as increased SCRs to disadvantageous deck choices.

Methods

Participants

Participants were recruited as outpatients identified by treating clinicians at an outpatient drug and alcohol unit or responded to online advertising of a pharmacotherapy trial [21] at Drug Health Services, Royal Prince Alfred Hospital. Assessments were conducted by researchers to identify alcohol dependence in participants with and without ALD. Consenting participants required alcohol dependence according to the ICD-10 criteria [22], age between 18 and 75 years, and adequate cognition and English language skills to give valid consent and perform cognitive tasks. Participants with any clinically evident alcohol withdrawal symptoms using the revised Clinical Institute Withdrawal Assessment for Alcohol scale (CIWA-Ar; [23] score of >10) were referred to detoxification treatment according to local detoxification guidelines and were able to be enrolled in the parent study once detoxification was sufficiently achieved. Participants had no major mental disorder associated with psychosis or significant suicide risk, no other usual substance use other than nicotine, and no clinical evidence of persisting hepatic encephalopathy (drowsiness, sleep inversion, or asterixis).

Testing took place within the first week of treatment to reduce any protracted abstinence effect, and participants were not required to cessate drinking during this time. Participants gave informed consent and were remunerated $40 AUD. The study was approved by the Human Ethic Review Committee of the Sydney Local Health District (X11-0154).

Measures

Measures of Dysregulated Alcohol Consumption

Timeline follow-back interview (TLFB [24]) was used to measure the number of standard drinks per drinking day in the preceding 30 days of drinking, with a standard drink defined as an Australian standard unit (10 g ethanol). Participants were actively prompted to recall number of drinks. The TLFB has demonstrated reliability and validity [25].

Alcohol Dependence Scale (ADS [26]) is a 25-item self-report measure of alcohol dependence. The total score was used as an index of the severity of alcohol dependence, with higher scores indicating greater severity.

Drinkers Inventory of Consequences (DrInC) Lifetime [20] is a 50-item questionnaire measuring physical, emotional, and social consequences related to alcohol use that have ever been experienced and is a reliable and valid measure of experienced adverse consequences [27]. A recent psychometric evaluation of the original factor structure of the DrInC demonstrated the five subscale structures commonly used had poor construct validity and were invariant across time [28] and sensitivity/specificity testing on large multisite trials revealed a three-factor structure for DrInC. This structure better reflected the continuum of severity of AUD characteristics and aligned with diagnostic criteria of AUD, comprising mild, moderate, and severe consequences. We therefore applied the frequency item score for these severe consequences "ever experienced" as an index of greater AUD severity, henceforth referred to as DrInC severe consequences. The items (3, 7, 10, 11, 20, 23, 26, 28, 31, 32, 31, 42, 43, 44, 46, 47, 48, 49, 50) consisted of relatively rare, severe drinking consequences, such as physical injury to oneself or others from drinking, significant financial and relationship problems, and detrimental health behaviours.

Behavioural Inhibition/Behavioural Activation Scales (BIS/BAS) [29] contain 20 items assessing reward drive and responsiveness. The internal consistency for the scales for this study was acceptable or higher (BIS: $\alpha = 0.78$; BAS-$\alpha = 0.90$), but BAS subscales demonstrated slightly reduced reliability (Drive: $\alpha = 0.77$; Fun-seeking $\alpha = 0.81$; Reward Responsiveness $\alpha = 0.76$).

Iowa Gambling Task

A computerised IGT [3] was used in this study, and the task is briefly described here with further detail in the online supplementary materials (for all online suppl. material, see www.karger.com/doi/10.1159/000529156). Participants are presented with four decks of cards on screen (decks A', B', C', and D'); they begin with a hypothetical balance of $2,000 and instructed to win as much money as possible. Decks C' and D' are disadvantageous: rewarding participants with high money gain ($100) while also unpredictably with higher penalties, so that the difference between rewards and losses in these decks will be negative over the long term (i.e., –$250 net loss per block of 10 cards). Decks A' and B' are advantageous over the long term: a smaller immediate $50, but future losses are also smaller over the long run, so the long-term reward/loss difference is positive (i.e., $250 net gain per block of 10 cards). Deck selections were followed by presentation of the money won and lost. Participants completed 100 trials, with deck positions counterbalanced across participants. Punishment trials were randomised within each deck per 10 selections according to specific rules (see online suppl. materials). A net score was calculated by subtracting the total advantageous deck trial selections from the

disadvantageous decks: for all trials ([A' + B'] – [C' + D']; total net score) and per block of 20 trials (block net score), with scores above 0 reflecting better overall decision-making performance.

Trial Components

Trial components were implemented for assessing SCR changes during the IGT, with inter-component intervals where participants were unable to respond: (1) *trial start*, the beginning of a new trial signalled by participants clicking a "continue" button; (2) *trial selection*, when participants selected a deck and followed by a 5-s inter-component interval; and (3) *trial outcome*, the moment when information was presented of wins and losses associated with the selected card, also followed by 5-s inter-component interval (shown in online suppl. Fig. 1). The trial components were scored online by the experimenter to demarcate quantification of SCR periods of interest using LabChart Pro 7.3.7 software [30], with scoring synchronisation confirmed post-task using video recordings.

SCR Acquisition

Skin conductance data were acquired using MLT117F GSR Electrodes (ADInstruments, Sydney, Australia) fixed to the second and third middle phalanges of the participants' non-dominant hand, with the signal amplified via the FE116 GSR Amplifier (ADInstruments, Sydney, Australia) via the PowerLab 8/25 System (ADInstruments, Sydney, Australia) to a PC operating LabChart Pro software. Sampling rate was 1,000/sec. Skin conductance was manually inspected for movement artefacts and automatically processed using LabChart Pro software.

There were 2 main time periods of interest for SCR per trial (shown in online suppl. Fig. 1): (1) outcome SCR, the 5-s period immediately following trial outcome to examine responses to both reward and punishment cards; (2) anticipatory SCR, which measures the period from trial start where a participant is free to choose which deck to select up to beginning of trial outcome presentation. We aimed to provide a clear separation of outcome SCR from the previous trial, and the period of deck selection (i.e., $trial_b$ start to $trial_b$ selection) coupled with an enforced period, whereby participants could not respond and contemplated the impending outcome ($trial_b$ selection to $trial_b$ outcome). Therefore, the anticipatory SCR period varied according to the time taken by participants to select a deck after the beginning of a trial (i.e., *n* sec). SCR data transformation methods are presented in the online supplementary material.

Procedure

Enrolment

Participants underwent a structured interview and medical consultation to assess eligibility for the trial and for medical markers of liver disease to assess and exclude any participants with severe alcoholic liver disease but none were. Baseline questionnaires ADS, DrInC, and TLFB for consumption in the previous month were also administered.

IGT Session

Testing was conducted an average of 11 days (±5 days) after enrolment, with the IGT completed at a consistent time of day (10:30 a.m.–3 p.m.). Participants were instructed to avoid drinking alcohol the night preceding test session and session day and to avoid caffeine and nicotine 4 h prior to the test session. Participants were breathalysed prior to session, with a BrAC above 0.05 excluding them from testing. Participants were seated in an armchair in front of a 58-cm monitor used for IGT presentation. All questionnaires were completed with pen and paper. A face-to-face interview was first conducted to obtain drinking over the past week with a TLFB. Table 1 reports patient demographic and clinical characteristics. The IGT was completed on a PC using Inquisit 3.0.5.0 software [31], followed by the BIS BAS. Participants were then debriefed.

Statistical Analysis

Analyses were conducted in R software (version 4.0.3). As fewer risky-deck choices occur across the task, adequate between-subject reliability of SCR scores for the risky-deck task condition was assessed through split half-reliability (odd numbered trials, even number trials) per subject and mean scores correlated between subjects corrected with the Spearman-Brown prophecy formula [32]. A high correlation was observed ($r = 0.92$), indicating excellent between-subject reliability for SCR scores. Correlational analyses were also conducted using Spearman's correlation coefficient tests examining relationships between demographics, dysregulated drinking measures, BIS BAS and DrInC subscales, and IGT total net score variables (shown in online suppl. Fig. 2).

SCR data were analysed using linear mixed-effects models (LMMs) using lme4 package [33], which allows participants' data to remain in the model if a data point from a level of the repeated measure (i.e., ≥1 card blocks) is missing. This is relevant for both outcome and anticipatory SCRs, as participants performing well during the IGT should select more cards from the advantageous decks as the task progresses, resulting in fewer (and potentially zero) disadvantageous deck choices. Correspondingly, these models incorporate these values with no loss of participants from the overall analysis. Four SCR blocks were calculated, comprising the first two blocks of 10 selections (i.e., trials 1–10, 11–20) and last two blocks of 40 selections (trials 21–60, 61–100). This accounted for the expected reductions in disadvantageous deck choices across the IGT [8].

A random-intercept model was fitted to compare the anticipatory and outcome SCRs across repeated within-subjects fixed factor of the four SCR blocks. To assess whether participants' previous history of dysregulated drinking behaviour was associated with impaired anticipatory responses, DrInC severe consequences scores were further added as a variable of interest, and two-way interactions for SCR blocks. The BIS BAS scale (BAS-Reward, BAS-Drive, BAS-Funseeking, BIS) scores were further added to assess the role of impulsivity during the IGT, along with respective two-way interactions with SCR blocks. Lastly, three-way interactions of anticipatory blocks, DrInC, and separate BIS BAS scales were added to evaluate whether differences in approach and inhibition related to history of dysregulated drinking severity moderated SCR responses during the IGT. Bonferroni corrections were applied within two SCR types (anticipation, outcome SCRs) to account for multiple comparisons, resulting in a corrected value threshold of $p = 0.025$. Only the pertinent higher order interactions associated with BIS BAS scales are reported within the results section, with full model tables presented.

Behavioural performance in the IGT was assessed using the same model structure for parsimony, assessing block net score by applying a within-subjects repeated factor of five IGT blocks, with 20 trials per IGT block. The models were similarly fitted with fixed-factor DrInC severe consequences, an IGT block and DrInC severe consequences, and three-way interactions with BIS BAS scales.

Table 1. Sample demographics, clinical characteristics, and IGT performance

Variable	M ± SD (range: min–max)
Age, years	49.67±9.64 (29–68)
Sex, *n* (%) male	27 (75)
TLFB mean units per drinking day	14.14±6.53 (6–34.5)
Alcohol Dependence Scale (ADS)	19.94±10.91 (4–47)
Drinkers Inventory of Negative Consequences (DrInC)	29.74±7.5
Mild	5.19±1.56 (0–6)
Moderate	15.39±4.7 (2–20)
Severe	10.31±4.64 (2–19)
BIS BAS scales	22.05±3.85
BIS	20.89±3.62 (13–28)
BAS-Reward	15.53±2.91 (6–20)
BAS-Drive	9.64±3.13 (4–16)
BAS-Funseeking	10.56±3.07 (4–16)
IGT net scores	
Card block 1–20	−2.67±7.93
Card block 21–40	−2.41±10.93
Card block 41–60	−2.67±10.84
Card block 61–80	1.08±11.58
Card block 81–100	1.54±12.79
Total net score	−1.72±40.27 (−72–94)

Means with SDs shown in brackets unless specified otherwise. TLFB, timeline follow-back; BIS, Behavioural Inhibition Scale; BAS, Behavioural Activation Scale; IGT, Iowa gambling task.

Results

Sample Demographics and Clinical Characteristics

Table 1 presents the overall sample data. Forty-two participants recruited to a pharmacotherapy trial in the placebo arm were initially tested but some were excluded from following analyses for the following: reported frontal lobe damage (n = 1); significant performance anxiety during IGT (n = 1); 0.05 breath alcohol concentration (BrAC) (n = 1); SCR data variance through poor electrode contact (n = 3). The final sample thus comprised 36 participants. Participants were older (age M = 49.67, SD = 9.64) and mostly male (75%), with a range of mean units of alcohol drinks per drinking day (TLFB: M = 14.14, SD = 6.53). Participants had moderate to severe average ADS scores (M = 19.94, SD = 10.91), with 33 participants categorised as alcohol-dependent participants using the ADS when applying a cut-off score of 9 [34]. There was a range of DrInC: Severe scores seen (M = 10.31, SD = 4.64, range 2–19), indicating that these participants experienced a variety of severe negative consequences from drinking. BIS BAS scale scores also showed a broad range, indicating varying levels of behavioural avoidance and approach tendencies among this drinking sample.

IGT Behavioural Performance

The net block scores for five blocks of 20 trials and total net score for the IGT are shown in Table 1. The LMM of net block scores (shown in Table 2) showed that net block scores did not differ across the task overall (p = 0.53), indicating no improvement across the task. When applying total net score cut-off of 10 – the highest score observed in VMPFC-impaired patients in the study by Bechara and Damasio [8] and used to delineate impaired (≤10 total net score) performance – only 11 participants were considered non-impaired in this study, while 17 participants were considered impaired. No main effect of DrInC: Severe was seen (p = 0.592).

Three-way interactions for block, DrInC: Severe, and BIS BAS scales showed a significant block*DrInC: Severe*BIS scale p = 0.042, where BIS had a moderating effect on performance across IGT according to DrInC severe consequences reported as seen in Figure 1. For participants reporting lower DrInC severe consequences, those with higher BIS scores (which indicate tendency for avoidance of punishment) demonstrated improvement across the IGT task with scores above 0 across the blocks, indicating progressively fewer risky deck selections. Among participants reporting higher DrInC severe consequences, however, higher BIS scores were associated

Table 2. Linear mixed models of IGT net block scores across participants

Predictors	Estimates	CI	*p* value
Blocks	−4.11	−16.92 to 8.71	0.53
DrInC: Severe	−0.19	−0.90 to 0.51	0.592
Blocks* DrInC: Severe	0.86	−0.33 to 2.06	0.155
Blocks* BAS-Reward	−0.04	−1.34 to 1.26	0.95
Blocks * BAS-Drive	0.01	−0.71 to 0.73	0.98
Blocks* BAS-Funseeking	−0.31	−1.43 to 0.81	0.59
Blocks* BIS	0.48	0.05–0.91	**0.03**
Blocks* DrInC: Severe * BAS-Reward	−0.03	−0.15 to 0.09	0.609
Blocks* DrInC: Severe * BAS-Drive	0.01	−0.06 to 0.08	0.78
Blocks* DrInC: Severe* BAS-Funseeking	0.04	−0.08 to 0.15	0.529
Blocks* DrInC: Severe * BIS	−0.05	−0.09 to −0.00	**0.042**
Random effects			
σ2	0.48		
τ00	1.53 (ID)		
ICC	0.76		
N	36 (ID)		
Observations	144		
Marginal R2/conditional R2	0.049/0.775		

DrInC, Drinkers Inventory of Consequences questionnaire; BAS, Behavioural activation scale; BIS, Behavioural Inhibition Scale.

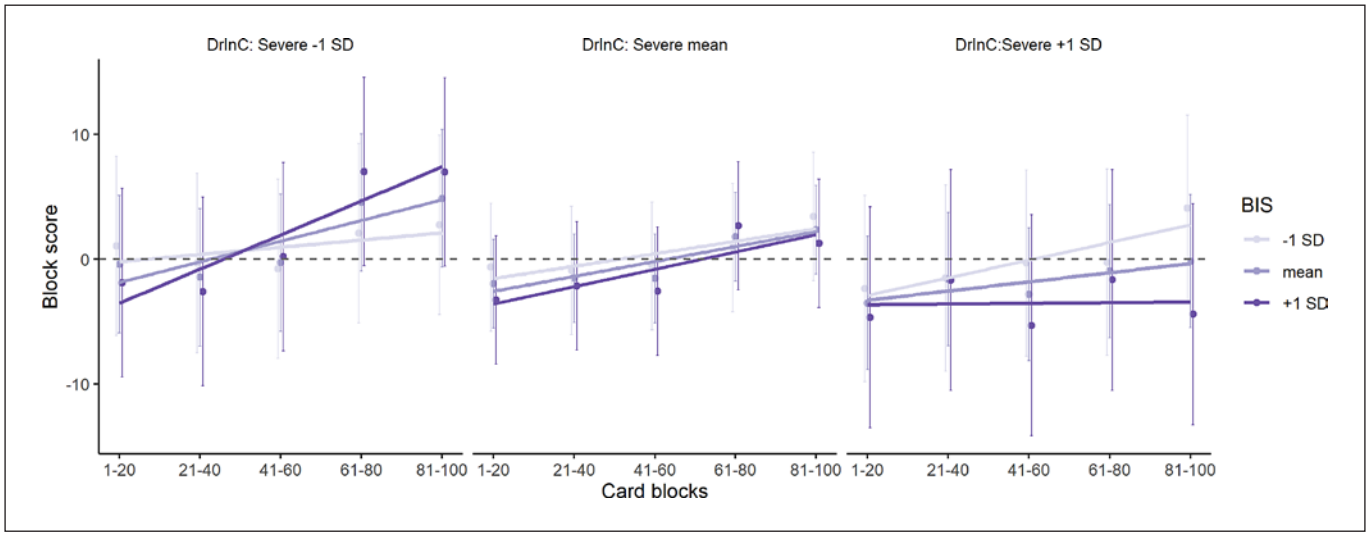

Fig. 1. Estimated marginal means of net scores across blocks for IGT task performance for AUD participants across card blocks, according to lower/mean/higher (−1/mean/+1 SD) DrInC scores and lower/mean/higher (−1/mean/+1 SD) reported BIS scores. A higher score indicates better task performance through more advantageous deck choices. Error bars represent 95% confidence interval, with linear-fitted trend lines shown for BIS. Points are offset horizontally so that error bars are visible.

with overall worse performance. Moreover, those participants reporting lower BIS scores showed little improvement across the IGT task regardless of DrInC severe consequences. No other significant three-way interactions for BAS scales were seen ($p > 0.529$).

Anticipatory SCRs

Advantageous Deck Choice SCRs

The LMM for advantageous anticipatory SCR deck choices (shown in Table 3) showed no main effect of SCR block, DrInC Severe, or SCR block by DrInC interaction

Table 3. Linear mixed models of IGT anticipation SCRs for advantageous and disadvantageous deck choices across participants

Predictors	Advantageous deck SCRs			Disadvantageous deck SCRs		
	estimates	CI	*p* value	estimates	CI	*p* value
Blocks	−0.44	−2.46 to 1.59	0.672	2.65	0.39–4.91	**0.021**
DrInC: Severe	0.01	−0.08 to 0.11	0.779	0.01	−0.09 to 0.10	0.903
Blocks* DrInC: Severe	0.06	−0.13 to 0.24	0.563	−0.23	−0.43 to −0.03	**0.022**
Blocks * BAS-Reward	−0.17	−0.38 to 0.03	0.1	−0.39	−0.64 to −0.15	**0.002**
Blocks * BAS-Drive	0.01	−0.10 to 0.13	0.811	0.1	−0.02 to 0.22	0.109
Blocks * BAS-Funseeking	0.14	−0.04 to 0.31	0.133	0.13	−0.11 to 0.37	0.297
Blocks * BIS	0.09	0.02–0.15	**0.014**	0.07	−0.00 to 0.14	0.062
Blocks * DrInC: Severe * BAS-Reward	0.02	−0.00 to 0.04	0.094	0.03	0.01–0.06	**0.002**
Blocks* DrInC: Severe * BAS-Drive	0	−0.01 to 0.01	0.735	−0.01	−0.02 to 0.00	0.086
Blocks * DrInC: Severe * BAS-Funseeking	−0.01	−0.03 to 0.01	0.179	−0.01	−0.03 to 0.01	0.374
Blocks* DrInC: Severe *BIS	−0.01	−0.02 to −0.00	**0.012**	−0.01	−0.01 to 0.00	0.059
Random effects						
σ2	0.58			0.42		
τ00	1.40 (ID)			1.49 (ID)		
ICC	0.71			0.78		
N	36 (ID)			36 (ID)		
Observations	142			131		
Marginal R2/conditional R2	0.059/0.723			0.083/0.799		

Bonferroni correction for multiple comparisons, *p* value threshold = 0.025 with significance denoted in bold. DrInC, Drinkers Inventory of Consequences questionnaire; BAS, Behavioural activation scale; BIS, Behavioural Inhibition Scale.

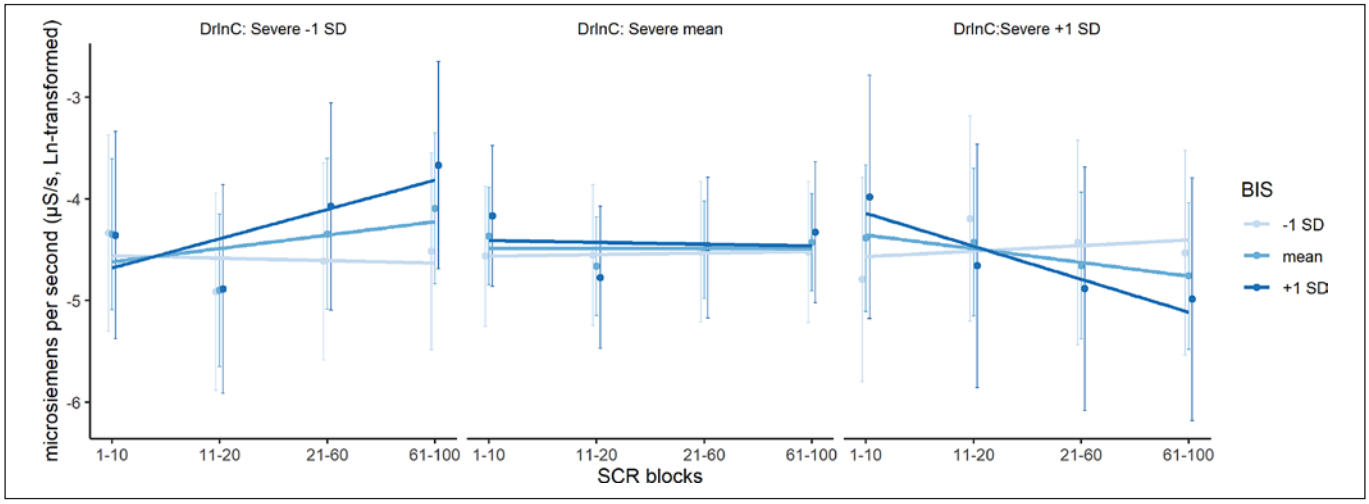

Fig. 2. Estimated marginal means of anticipatory responses to advantageous deck choices for AUD participants across SCR blocks, according to lower/mean/higher (−1/mean/+1 SD) DrInC scores and lower/mean/higher (−1/mean/+1 SD) reported BIS scores. Error bars represent 95% confidence interval, with linear-fitted trend lines shown for BIS. Points are offset horizontally so that error bars are visible.

($p > 0.051$), indicating no significant changes in anticipatory SCR for advantageous deck choices across the IGT overall or related to DrInC severe consequences. Three-way interactions for block, DrInC: Severe, and BIS BAS scales showed a significant block*DrInC: Severe*BIS scale interaction ($p = 0.012$) where BIS had a moderating effect on performance across IGT according to DrInC severe consequences reported (shown in Fig. 2). For participants

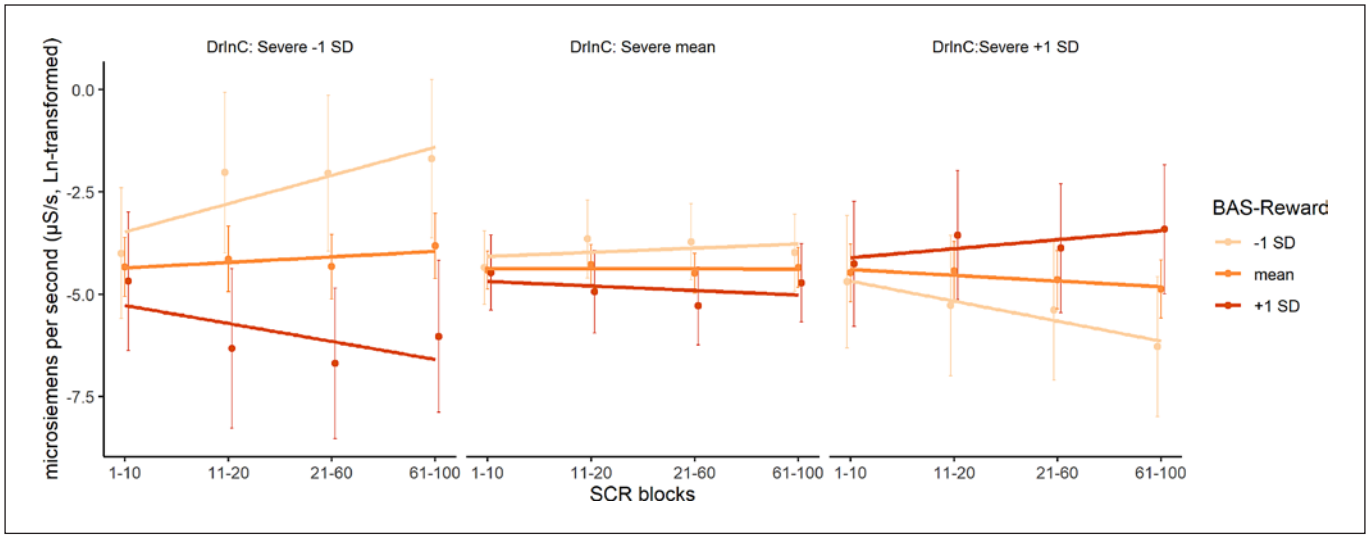

Fig. 3. Estimated marginal means of anticipatory responses to disadvantageous deck choices for AUD participants across SCR blocks, according to lower/mean/higher (−1/mean/+1 SD) DrInC scores and lower/mean/higher (−1/mean/+1 SD) reported BAS-Reward scores. Error bars represent 95% confidence interval, with linear-fitted trend lines shown for BAS-Reward. Points are offset horizontally so that error bars are visible.

reporting lower DrInC severe consequences, those with higher BIS scores exhibited increased anticipatory SCRs progressing through the IGT. Among participants reporting higher DrInC severe consequences, higher BIS scores conversely demonstrated decreased SCRs across the IGT. Participants reporting lower BIS scores showed negligible changes in SCRs across the IGT task regardless of DrInC severe consequences. No other significant three-way interactions for BAS scales were seen (p >0.094).

Disadvantageous Deck Choice SCRs

The LMM for anticipatory SCRs during disadvantageous deck choices (shown in Table 3) demonstrated a significant main effect of SCR block (p = 0.021), with a modest increase in SCRs overall across the IGT but no main effect of DrInC severe consequences, (p = 0.903). A significant two-way interaction of SCR blocks and DrInC Severe was seen (p = 0.022), whereby participants with lower reported DrInC severe consequences exhibited increasing SCRs to risky deck choices across the IGT, while those reporting higher consequences showed decreasing SCRs.

Three-way interactions for SCR block, DrInC severe consequences, and BIS BAS scales showed a significant SCR block * DrInC: Severe * BAS-Reward interaction (p =0.002) (shown in Fig. 3). For participants with lower DrInC severe consequences reported, those reporting higher BAS-Reward scores exhibited increasing SCR responses across the IGT during risky disadvantageous deck choices. However, those with lower BAS-Reward scores showed decreasing SCRs for risky deck choices across the IGT. For participants reporting higher DrInC severe consequences, these patterns were no longer seen, with no changes to SCRs across the task, or even decreasing SCRs for participants with higher BAS-Reward scores, indicating that higher reward sensitivity was associated with expected increased SCRs to risky decks only for participants who experienced fewer severe negative drinking consequences. There were no other significant three-way interactions (p > 0.059).

Reward and Punishment Outcome SCRs

The LMM for SCRs during reward outcomes across the IGT (online suppl Table 1) revealed no overall sample main effects (p > 0.41), no two-way interactions between SCR blocks and DrInC consequences or BIS BAS scales (p > 0.053), and no three-way interactions (p > 0.076). Similarly, for the LMM for SCRs during punishment, outcomes across the IGT (online suppl. Table 1) showed no overall sample main effects (p > 0.372) and no two- or three-way interactions for BAS scales were seen (p >0.039).

Discussion

This study aimed to evaluate whether AUD participants showed decision-making deficits and psychophysiological SCRs during the IGT, associated with their severity of AUD

(indexed by the DrInC) and their reward and punishment sensitivity as measured by the BIS BAS scales. We observed similar patterns of significant three-way interactions associated with DrInC severe consequences, and BIS scale for both IGT net block score performance, and anticipatory SCR responses to advantageous decks. Increased anticipatory SCRs for advantageous deck choices were associated with lower DrInC severe consequences and higher BIS scores relating to greater avoidance of punishment. Damasio [35] initially proposed with the somatic marker hypothesis that anticipatory responses to disadvantageous choices generally shift preference from the disadvantageous to advantageous decks, which we have also observed. Yet associations between anticipatory SCRs to advantageous decks related to successful IGT performance have been evidenced in healthy samples [36, 37]. Our study correspondingly revealed better IGT performance in those participants with lower DrInC severe consequences and higher BIS scores in our study, suggesting these participants may demonstrate increased anticipatory responses to advantageous decks as an index of better performance.

There have been mixed findings of associations of the BIS and problematic drinking behaviours. Studies in college/university students showed higher BIS scores were negatively associated with alcohol quantity and frequency and patterns such as bingeing [38, 39], which accord with our findings. Conversely, other research found mixed or no evidence [16, 40, 41], although this may be explained by conflation in measures of RST and flight/fight/freeze system models within the BIS (see [42]). These studies also examined emerging adult, mainly college samples, whereas our sample comprised older, severe AUD participants with demonstrated dysfunctional drinking behaviours. Fewer studies have examined the BIS and associations of IGT performance in drinker or AUD samples, with equivocal findings. Tomassini et al. [43] found some negative correlations with the Barratt Impulsiveness Scale (BIS-11, [44]) and later IGT net block scores in abstinent alcohol-dependent participants, suggesting greater impulsivity may mostly influence decision-making under risk. In polysubstance users, no relationship between IGT performance and personality factors including the BIS BAS in severe substance use disorder [45] was seen, though only IGT total score was assessed which lacks sensitivity to changes across the task. Evaluating BIS BAS subscales across the IGT net blocks in our study revealed differences in both IGT performance and SCR responses that suggests superior utility, as the BIS BAS provides involves reward and punishment sensitivity personality factors and is not limited to evaluating impulsivity to negative events only [14], which may also better reflect approach and avoidance strategies related to drinking behaviour.

We observed opposing patterns of SCR responses to risky deck choices progressing through the IGT contingent on severity of drinker consequences. Among participants who experienced fewer DrInC severe consequences, those who also had higher BAS-Reward Responsiveness – reflecting higher reward responsivity – showed increasing SCRs to risky deck choices progressing through the IGT. The BAS has established links as a risk factor in drinking problems in AUD [16, 46]. Reward sensitivity increased during a reward-incentive card-sorting task following exposure to alcohol cues in heavy social drinkers [47]. Higher BAS-Reward was associated with IGT deficits in substance use disorder participants compared to healthy controls, coupled with increased mean left hemispheric brain activation to disadvantageous decks, supportive of cognitive bias towards immediate reward [12]. The patterns of SCR activations we observed have also been demonstrated comparing individuals with substance use disorder to healthy control participants [8], with a reduced magnitude of disadvantageous deck anticipatory SCRs, while other SCRs were comparable to the performance of the healthy control group. An explanation is provided by the somatic marker hypothesis [35, 48], which posits decision-making is largely affected by emotional signals that inform decision-making processes, shifting choices towards advantageous outcomes. However, the development of disadvantageous decks anticipatory SCRs seen in our study was not matched by behavioural IGT performance and associations with BAS-Reward, which would strengthen assumptions that these emotional indicators signal risky choices that may have negative consequences [48]. These indicators are integral for decision-making conducted under uncertainty, particularly during the early blocks of the IGT [9].

While BAS-Reward generally is associated with problematic and high-risk drinking in AUD samples, BAS-Reward has been positively associated with IGT performance in healthy controls, with high reward responsiveness related to better IGT performance [49]. Considering the patterns associated with low DrInC severe consequences and BAS-Reward, anticipatory SCRs to disadvantageous decks may suggest recognition of risky decision-making in this study, particularly during later card blocks when IGT task strategies are often resolved. Relatedly, the lack of concordance of BIS and BAS-Reward and associations with SCRs may be due to the psychometric

properties of BIS and BAS scales in Gray's definition of RST, which posits BIS as a punishment sensitivity system, whereas the revised RST approach [14] defines the flight-fight-freeze system that controls responses to aversive stimuli. Moreover, the revised RST redresses BIS as a goal-conflict resolution system that can be both positively (leading to approach) and negatively (leading to avoidance) activated in response to reward, concurrent with high BAS personality factors. Little research has investigated the revised RST in AUD, but preliminary findings reveal the interactive role of both BIS and BAS as simultaneous risk factors in alcohol misuse and associated with neuropsychological performance in the motivational flanker task [50]. Notably, while we observed moderate correlations between BAS subscales, no correlations with BIS were seen. Profiling a larger sample of participants with high BIS and high BAS-Reward using cluster analyses may identify whether these participants characterise these SCR patterns and behavioural IGT performance seen in our study.

Regarding IGT behavioural performance, the majority of this sample would be considered within an impaired performance range of less than 50 cards, <50% from advantageous decks using cut-offs from normative data [51, 52]. Further, two-thirds of the sample (69%) were categorised as significantly impaired, scoring below a total net score cut-off of 10 as defined using VMPFC-impaired performance [11]. This reflects the general trend in the literature observing worse IGT performance in severe AUD [5, 53], suggesting participants with severe AUD exhibit decision-making deficits that may be reflected in real-world situations through deleterious drinking choices. Coupled with the observed patterns of anticipatory SCR to advantageous and disadvantageous deck choices, participants with severe AUD therefore may not adequately identify or learn from negative drinking consequences that may inform future choices towards advantageous options regarding drinking, resulting in worse drinking choices and thus continued deleterious outcomes. For these participants with more experienced DrInC severe consequences, inability to retain information of previous deleterious drinking-related outcomes may lead to suboptimal complex decision-making choices [2] when faced with future drinking situations. Considering that severe AUD participants display dysregulated autonomic nervous system responses to alcohol-related cues [54], the inherent strength of the alcohol-related cues present during drinking situations may further increase the temptation towards immediate gratification and dysregulated drinking [55, 56] rather than opting to restrict intake which would in turn be more advantageous in the long term (e.g., lead to better health outcomes, avoidance of negative drinking consequences).

Relatedly, SCR has been demonstrated to be functionally linked to the above regions, with activity in the medial prefrontal cortex related to generation of SCR [57]. Bechara et al. [58] demonstrated bilateral VMPFC-lesioned patients exhibited reduced anticipatory SCRs but comparable outcome SCRs to reward and punishment to those of normal participants, whereas amygdala-lesioned patients demonstrated global impairment [58]. In our study, the reduction in anticipatory SCRs demonstrated by the disadvantageous deck choices in AUD participants who experienced more negative drinking consequences suggests they do not react to potentially risky choices, potentially due to VMPFC dysfunction. This VMPFC dysfunction may impair generation of anticipatory SCR that signal risky choices in the IGT, which again may manifest in real-world decision-making during drinking situations.

There were some limitations to this study. The DrInC version (−2L) used here does not capture the frequency of consequences as it is a dichotomous item measure. We therefore could not determine whether participants experience the same negative consequences several times, which would indicate inability to learn from previous negative outcomes to inform future decisions. Implementing a frequency measure (e.g., DrInC-2R [20]) would elucidate whether these impaired anticipatory and outcome SCRs affect and maintain impaired decision-making. We used items from a three-factor structure of the DrInC as identified through the study by Kirouac and Witkiewitz [28] that better categorised rarer, more severe drinking consequences of the DrInC, which may better reflect more deleterious negative consequences within participants with severe AUD. However, the item loadings of the three-factor structure – though derived from large multisite trials [59, 60] which increase the structure's generalisability – may not correspond to our sample here, though the moderate to strong correlations with greater consumption and higher ADS scores suggest the DrInC severe consequences items characterise severe AUD relatively well. The study sample size was very limited, and prospective studies examining IGT and SCR responses should employ a larger sample. We did not employ a healthy control sample as we aimed to evaluate how severity of AUD was associated with behavioural and somatic IGT responses. We therefore cannot compare performance compared to

healthy controls, which may limit our conclusions, but ample evidence of behavioural and SCRs in healthy controls has been published as normative data (e.g., see [53] for review) and meta-analyses generally demonstrating deficits in IGT in severe AUD samples [5, 6]. Relatedly, prefrontal brain regions are vulnerable to alcohol-related brain damage through chronic alcohol consumption (see [61]), and our sample comprises some significantly dysfunctional individuals with severe AUD. Implementing a sample of participants with previous severe AUD that have successfully regulated and reduced alcohol consumption, or similarly a group of abstinent alcohol dependent participants, would be a valuable control group and better reveal whether our study findings stem from a specific somatic SCR impairment in severe AUD or an overall negative consequence from significant chronic alcohol consumption.

In conclusion, this study identified decision-making deficits and reduced physiological responses during key periods of the IGT in individuals with severe AUD individuals, potentially reflecting impairment in learning from negative events and anticipation of reward reinforcement. Individuals with AUD and a significant history of previous drinking problems demonstrated worse IGT performance, coupled with reduced anticipatory responses for risky choices and anticipatory SCRs to advantageous decks. Greater reward sensitivity was associated with anticipatory SCRs to disadvantageous decks contingent on severity of AUD, which may be protective for those with fewer negative drinking consequences. Overall, these reduced SCRs to risky choices may manifest in poorer future outcomes inherent in these samples with severe AUD, particularly those who experienced more negative drinking consequences and demonstrated reduced overall SCR regardless of reward or punishment sensitivity. Evaluating these psychophysiological responses in people with severe AUD associated with personality factors such as reward and punishment sensitivity could identify high-risk drinkers who have difficulties in learning from negative outcomes and understanding potentially risky choices, which may also reflect real-life impaired decision-making regarding drinking choices in these individuals.

Statement of Ethics

This published research complies with the guidelines for human studies and was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. This included written informed consent, and approval of the study protocol was provided by the Human Ethic Review Committee of the Sydney Local Health District, Sydney, Australia (approval number X11-0154).

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Warren Logge was involved in the conception and design of the study, the acquisition and analysis of data, drafting and preparation of the manuscript, and drafting of the resubmission. Kirsten Morley was involved in the conception and design of the study and provided feedback for the manuscript. Paul Haber provided interpretation and feedback for the study. Andrew Baillie was involved in the conception and design of the study, consultation on the analysis of data, and provided feedback for the manuscript.

Data Availability Statement

The data that support the findings of this study are not publicly available due to ethical requirements regarding pertinent clinical data but are available from Warren Logge upon reasonable request.

References

1 Schuckit MA. Biological, psychological and environmental predictors of the alcoholism risk: a longitudinal study. J Stud Alcohol. 1998;59(5):485–94.
2 Clark L, Robbins TW. Decision-making deficits in drug addiction. Trends Cogn Sci. 2002;6(9):361–3.
3 Bechara A, Damasio AR, Damasio H, Anderson SW. Insensitivity to future consequences following damage to human prefrontal cortex. Cognition. 1994;50(1–3):7–15.
4 Buelow MT, Suhr JA. Construct validity of the Iowa gambling task. Neuropsychol Rev. 2009;19(1):102–14.
5 Kovács I, Richman MJ, Janka Z, Maraz A, Andó B. Decision making measured by the Iowa Gambling Task in alcohol use disorder and gambling disorder: a systematic review and meta-analysis. Drug Alcohol Depend. 2017;181:152–61.

6 Stephan RA, Alhassoon OM, Allen KE, Wollman SC, Hall M, Thomas WJ, et al. Meta-analyses of clinical neuropsychological tests of executive dysfunction and impulsivity in alcohol use disorder. Am J Drug Alcohol Abuse. 2017;43(1):24–43.
7 Maurage P, Lannoy S, Dormal V, Blanco M, Trabut JB. Clinical usefulness of the Iowa gambling task in severe alcohol use disorders: link with relapse and cognitive-physiological deficits. Alcohol Clin Exp Res. 2018;42(11):2266–73.
8 Bechara A, Damasio H. Decision-making and addiction (part I): impaired activation of somatic states in substance dependent individuals when pondering decisions with negative future consequences. Neuropsychologia. 2002;40(10):1675–89.
9 Brevers D, Bechara A, Cleeremans A, Kornreich C, Verbanck P, Noël X. Impaired decision-making under risk in individuals with alcohol dependence. Alcohol Clin Exp Res. 2014;38(7):1924–31.
10 Figner B, Murphy R, Schulte-Mecklenburg M, Kuehberger A, Ranyard R. A handbook of process tracing methods for decision research: A critical review and user's guide. Using skin conductance in judgment and decision making research. New York, NY: Psychology Press; 2012.
11 Bechara A, Damasio H, Tranel D, Damasio AR. Deciding advantageously before knowing the advantageous strategy. Science. 1997;275(5304):1293–5.
12 Balconi M, Finocchiaro R, Canavesio Y. Reward-system effect (BAS rating), left hemispheric "unbalance" (alpha band oscillations) and decisional impairments in drug addiction. Addict Behav. 2014;39(6):1026–32.
13 Gray JA. A critique of Eysenck's theory of personality. In: Eysenck HJ, editor. A Model for Personality. Berlin, Heidelberg: Springer Berlin Heidelberg; 1981. p. 246–76.
14 Corr PJ. The Reinforcement Sensitivity Theory of Personality. Cambridge: Cambridge University Press; 2008.
15 Colder CR, O'Connor R. Attention bias and disinhibited behavior as predictors of alcohol use and enhancement reasons for drinking. Psychol Addict Behav. 2002;16(4):325–32.
16 Jonker NC, Ostafin BD, Glashouwer KA, van Hemel-Ruiter ME, de Jong PJ. Reward and punishment sensitivity and alcohol use: The moderating role of executive control. Addict Behav. 2014;39(5):945–8.
17 Gullo MJ, Stieger AA. Anticipatory stress restores decision-making deficits in heavy drinkers by increasing sensitivity to losses. Drug Alcohol Depend. 2011;117(2-3):204–10.
18 Blum K, Braverman ER, Holder JM, Lubar JF, Monastra VJ, Miller D, et al. The reward deficiency syndrome: a biogenetic model for the diagnosis and treatment of impulsive, addictive and compulsive behaviors. J Psychoactive Drugs. 2000;32(sup1):1–112.
19 Bijttebier P, Beck I, Claes L, Vandereycken W. Gray's reinforcement sensitivity theory as a framework for research on personality–psychopathology associations. Clin Psychol Rev. 2009;29(5):421–30.
20 Miller WR, Tonigan JS, Longabaugh R. The Drinker Inventory of Consequences (DrInC): An instrument for assessing adverse consequences of alcohol abuse. Rockville, MD: NIAAA; 1995.
21 Morley KC, Leung S, Baillie A, Haber PS. The efficacy and biobehavioural basis of baclofen in the treatment of Alcoholic Liver Disease (BacALD): study protocol for a randomised controlled trial. Contemp Clin Trials. 2013;36(2):348–55.
22 World Health Organization. Alcohol dependence Syndrome; 1990. Available from: http://apps.who.int/classifications/icd10/browse/2010/en#/F10.2.
23 Sullivan JT, Sykora K, Schneiderman J, Naranjo CA, Sellers EM. Assessment of alcohol withdrawal: the revised Clinical Institute Withdrawal Assessment for alcohol scale (CIWA-Ar). Br J Addict. 1989;84(11):1353–7.
24 Sobell LC, Sobell MB. Timeline Follow-Back. In: Litten RZ, Allen JP, editors. Measuring alcohol consumption: psychosocial and biochemical methods. Totowa, NJ: Humana Press; 1992. p. 41–72.
25 Sobell LC, Brown J, Leo GI, Sobell MB. The reliability of the Alcohol Timeline Followback when administered by telephone and by computer. Drug Alcohol Depend. 1996;42(1):49–54.
26 Skinner HA, Allen BA. Alcohol dependence syndrome: measurement and validation. J Abnorm Psychol. 1982;91(3):199–209.
27 Forcehimes AA, Tonigan JS, Miller WR, Kenna GA, Baer JS. Psychometrics of the Drinker Inventory of Consequences (DrInC). Addict Behav. 2007;32(8):1699–704.
28 Kirouac M, Witkiewitz K. Revisiting the drinker inventory of consequences: an extensive evaluation of psychometric properties in two alcohol clinical trials. Psychol Addict Behav. 2018;32(1):52–63.
29 Carver CS, White TL. Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: The BIS/BAS Scales. J Pers Soc Psychol. 1994;67(2):319–33.
30 ADInstruments. Labchart 7.3.7. Bella Vista, Australia: ADInstruments; 2012.
31 Millisecond Software LLC. Inquisit 3.0.5.0. Seattle, USA: Millisecond Software LLC; 2009.
32 Guilford JP. Psychometric methods. New York: McGraw-Hill; 1954.
33 Bates D, Mächler M, Bolker B, Walker S. Fitting linear mixed-effects models using lme4. J Stat Soft. 2015;67(1):1–48.
34 Ross HE, Gavin DR, Skinner HA. Diagnostic validity of the MAST and the alcohol dependence scale in the assessment of DSM-III alcohol disorders. J Stud Alcohol. 1990;51(6):506–13.
35 Damasio AR. Descartes' error: Emotion, reason and the human brain. New York: Houghton Mifflin Harcourt; 1994.
36 Denburg NL, Recknor EC, Bechara A, Tranel D. Psychophysiological anticipation of positive outcomes promotes advantageous decision-making in normal older persons. Int J Psychophysiol. 2006;61(1):19–25.
37 Hinson JM, Whitney P, Holben H, Wirick AK. Affective biasing of choices in gambling task decision making. Cogn Affect Behav Neurosci. 2006;6(3):190–200.
38 Franken IHA, Muris P. BIS/BAS personality characteristics and college students' substance use. Pers Individ Differ. 2006;40(7):1497–503.
39 Pardo Y, Aguilar R, Molinuevo B, Torrubia R. Alcohol use as a behavioural sign of disinhibition: Evidence from J.A. Gray's model of personality. Addict Behav. 2007;32(10):2398–403.
40 Haas AL, Smith SK, Kagan K. Getting "game": pregaming changes during the first weeks of college. J Am Coll Health. 2013;61(2):95–105.
41 Knyazev GG. Behavioural activation as predictor of substance use: mediating and moderating role of attitudes and social relationships. Drug Alcohol Depend. 2004;75(3):309–21.
42 Pocuca N, Hides L, Quinn CA, White MJ, Mewton L, Loxton NJ. An exploratory study of the relationship between neuroticism and problematic drinking in emerging adulthood, and the moderating effect of social anxiety. Pers Individ Differ. 2019;145:132–44.
43 Tomassini A, Struglia F, Spaziani D, Pacifico R, Stratta P, Rossi A. Decision making, impulsivity, and personality traits in alcohol-dependent subjects. Am J Addict. 2012;21(3):263–7.
44 Patton JH, Stanford MS, Barratt ES. Factor structure of the barratt impulsiveness scale. J Clin Psychol. 1995;51(6):768–74.
45 De Wilde B, Verdejo-García A, Sabbe B, Hulstijn W, Dom G. Affective decision-making is predictive of three-month relapse in polysubstance-dependent alcoholics. Eur Addict Res. 2013;19(1):21–8.
46 Franken IHA. Behavioral Approach System (BAS) sensitivity predicts alcohol craving. Pers Individ Differ. 2002;32(2):349–55.
47 Kambouropoulos N, Staiger PK. Reactivity to alcohol-related cues: Relationship among cue type, motivational processes, and personality. Psychol Addict Behav. 2004;18(3):275–83.
48 Bechara A, Damasio AR. The somatic marker hypothesis: a neural theory of economic decision. Games Econ Behav. 2005;52(2):336–372.
49 Suhr JA, Tsanadis J. Affect and personality correlates of the Iowa gambling task. Pers Individ Differ. 2007;43(1):27–36.
50 Keough MT, O'Connor RM. Clarifying the measurement and the role of the behavioral inhibition system in alcohol misuse. Alcohol Clin Exp Res. 2014;38(5):1470–9.

51 Bechara A. IGT: Iowa gambling task: professional manual. PAR Psychological Assessment Resources, Inc.; 2007.
52 Bechara A, Damasio H, Tranel D, Anderson SW. Dissociation of working memory from decision making within the human prefrontal cortex. J Neurosci. 1998;18(1):428–37.
53 Simonovic B, Stupple E, Gale M, Sheffield D. Sweating the small stuff: a meta-analysis of skin conductance on the Iowa gambling task. Cogn Affect Behav Neurosci. 2019;19(5):1097–112.
54 Logge WB, Morley KC, Haber PS, Baillie AJ. Executive functioning moderates responses to appetitive cues: a study in severe alcohol use disorder and alcoholic liver disease. Alcohol Alcohol. 2019;54(1):38–46.
55 Le Berre A-P, Fama R, Sullivan EV. Executive functions, memory, and social cognitive deficits and recovery in chronic alcoholism: a critical review to inform future research. Alcohol Clin Exp Res. 2017;41(8):1432–43.
56 Camchong J, Endres M, Fein G. Decision making, risky behavior, and alcoholism. In: Sullivan EV, Pfefferbaum A, editors. Handbook of Clinical Neurology. Elsevier; 2014. 125. p. 227–36.
57 Critchley HD, Elliott R, Mathias CJ, Dolan RJ. Neural activity relating to generation and representation of galvanic skin conductance responses: a functional magnetic resonance imaging study. J Neurosci. 2000;20(8):3033–40.
58 Bechara A, Damasio H, Damasio AR, Lee GP. Different contributions of the human amygdala and ventromedial prefrontal cortex to decision-making. J Neurosci. 1999;19(13):5473–81.
59 Group PMR. Matching Alcoholism Treatments to Client Heterogeneity: Project MATCH posttreatment drinking outcomes. J Stud Alcohol. 1997;58(1):7–29.
60 Anton RF, O'Malley SS, Ciraulo DA, Cisler RA, Couper D, Donovan DM, et al. Combined pharmacotherapies and behavioral interventions for alcohol dependence the combine study: a randomized controlled trial. JAMA. 2006;295(17):2003–17.
61 Xiao P, Dai Z, Zhong J, Zhu Y, Shi H, Pan P. Regional gray matter deficits in alcohol dependence: a meta-analysis of voxel-based morphometry studies. Drug Alcohol Depend. 2015;153:22–8.