The influence of alcohol-specific episodic memory and cue exposure on value-based decision-making and its role in ad libitum drinking

Background

The aim of this project is to explore whether value-based decision-making (VBDM) changes when people experience heightened craving to consume alcohol, and whether parameters of VBDM are predictive of actual drinking behaviour. The central tenet of behavioural economic accounts is that the progression to addiction is characterised by persistently high valuation of substance use relative to alternative sources of reinforcement, and devaluation of outcomes that are only available after a delay (Bickel et al., 2014; Bickel & Athamneh, 2020). Research commonly uses hypothetical purchase tasks (Murphy & MacKillop, 2006) and concurrent choice tasks (Hogarth & Hardy, 2018) to measure "demand"—a behavioural economic construct that represents the reinforcing value of a substance (Martínez-Loredo et al., 2021).

Experimental manipulations reliably influence the value ascribed to alcohol (Acuff et al., 2020): for example, induction of stress increases, whereas aversive taste decreases alcohol demand. Alcohol value is also augmented by memories of past experiences with alcohol (Bornstein & Pickard, 2020), and listening back to personal memories associated with substance use increases craving (Kilts et al., 2018). What is less known, however, are the underlying mechanisms by which changes in valuation processes alter decision-making (Rose et al., 2013). Value-based decision-making (VBDM) provides a framework and set of experimental tools that can model the internal processes that determine decisions made (Berkman et al., 2017); this has been tentatively extended to the study of addiction and recovery from it (Copeland et al., 2021; Field et al., 2020). This project capitalises on these recent methodological developments and computational advances in the measurement of value-based choice (Copeland et al., 2022). In doing so, this study will provide an insight into the influence of vivid positive drinking experiences and alcohol cue exposure on VBDM and its role in ad libitum drinking. Participants will be randomised to one of two experimental conditions:

1) **Alcohol-specific episodic memory and cue exposure** – participants will listen back to their own vivid positive alcohol-related memory and will be instructed to sniff and allow their preferred alcoholic drink to touch their lips, but to refrain from drinking it.
2) **Non-alcohol episodic memory and cue exposure** – participants will listen back to their own vivid positive memory (not related to alcohol) and will be instructed to sniff and allow their preferred soft drink to touch their lips, but to refrain from drinking it.

Research aim: Attempt to experimentally increase alcohol craving by instructing participants to think about vivid positive drinking experiences before exposing them to alcohol cues in order to identify how VBDM changes during this momentary state, and to explore which specific aspects of VBDM are predictive of the volume of alcohol consumed.

Core hypotheses: Compared to the control condition, participants in whom the value of alcohol has been experimentally increased will have:

- Higher drift rates, and lower response thresholds, when making alcohol-related decisions; and lower drift rates, and higher response thresholds, when making non-alcohol (alcohol-free reinforcement) decisions (VBDM task).
- A higher % choice of alcohol over the alcohol-free alternative reward (image enlargement; concurrent choice (CC) task), and this group difference will be mediated by VBDM parameters.
- A higher volume of alcohol consumed, and this group difference in alcohol consumption will be mediated by VBDM parameters, over and above % alcohol choice from the concurrent choice task.

Secondary hypotheses:

- Compared to the control condition, people who are experimentally primed to crave alcohol will have greater self-report demand for alcohol (intensity, breakpoint, O_{max}, P_{max}, and elasticity).
- In all participants, VBDM parameters will predict a statistically significant amount of variance in % alcohol choice on the CC task.

Methodology:

Design

Pre-registered, experimental between-subject design with data collected in-person. Dependent variables will be evidence accumulation (EA) rates and response thresholds (estimated by fitting a drift-diffusion model (DDM) to reaction time and error data during the VBDM task), % of alcohol (relative to non-alcohol) choice (concurrent choice task), and volume of alcohol consumed (as a % of the total amount offered) during ad-libitum taste test. The independent variable is experimental condition (alcohol-specific episodic memory and cue exposure or non-alcohol episodic memory and cue exposure).

Participants

Based upon an *a priori* power analysis ($\alpha = .01$, 90% power), we will recruit 126 people (>21 years old) who consume 28 or more UK units of alcohol per week (1 UK unit = 8g of alcohol). This threshold represents a doubling of the UK "low-risk" weekly drinking guidelines (Department of Health, 2016) and based upon our previous work (including Copeland et al., 2022) most people who drink at this level are likely to have an AUDIT score greater than 15. Exclusion criteria are 1) currently taking any medication for which alcohol is contraindicated, such as benzodiazepines (e.g., zopiclone, valium), 2) having any underlying health condition(s) that would be affected by alcohol consumption, or 3) having ever received treatment for an alcohol use disorder (alcoholism) or advised by a GP or other health professional to seek treatment.

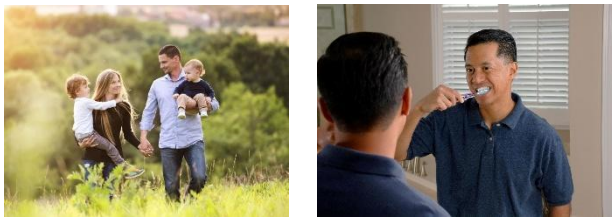
Materials

Pictorial stimuli

Alcoholic and soft drinks: These will be captured by 35 images (of each drink type) that have been used in our previous work (Copeland et al., 2022) and depict different beverages of commonly consumed UK brands on a white background.

Example of alcohol (left) and soft drink (right) images

Alcohol-free reinforcement: This will be captured by 35 images depicting family; pets; travel; sports; hobbies; mutual-aid groups; employment; volunteering / charity work; nature / wildlife. We recently consulted with a patient and public involvement (PPI) panel of people with lived experience of addiction, and they advised us against using participants' own personal images (e.g., images they have taken themselves). We showed the PPI panel images from an existing project (Manning et al., 2020) and the feedback was that these images were good and that they could be supplemented by images that depict other things that are (less) important to people as AUD worsens such as hygiene (e.g., brushing teeth, tidying the home, and showering) and "growing old".



Example of alcohol-free images

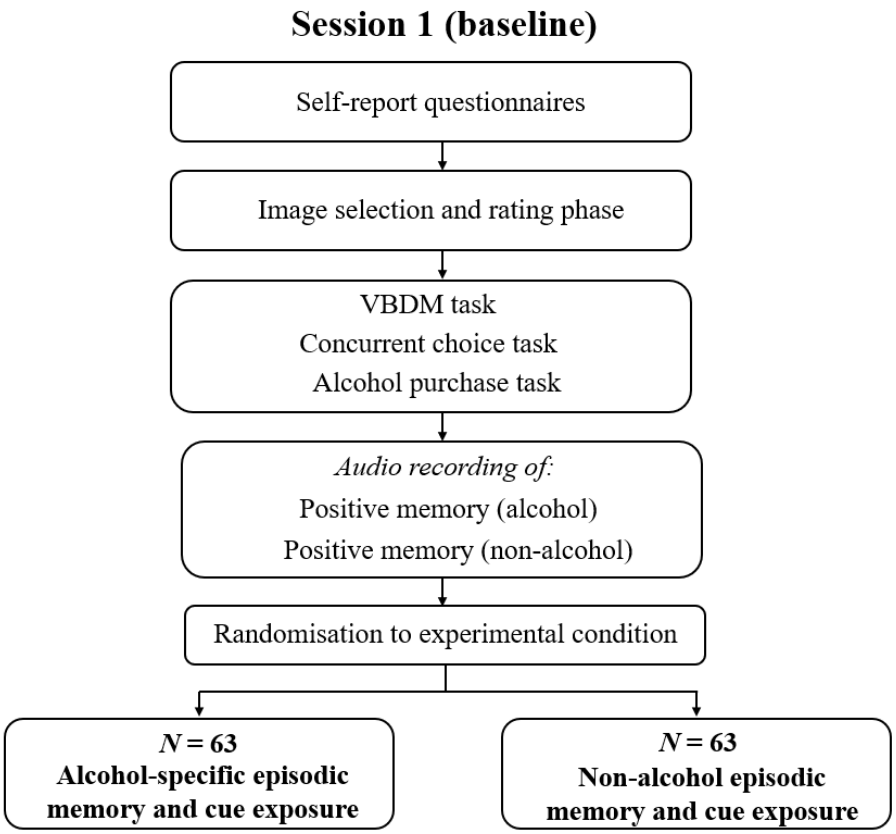
The rationale for having two categories of comparator images (soft drinks, and alcohol-free reinforcement) is to expand upon our existing VBDM work where only images of alcohol and soft drinks were contrasted. Retention of the soft-drink comparator yields an alcohol-free '*appetitive*' contrast that might be particularly important for some VBDM parameters (e.g., in some of our previous VBDM research tobacco and animal contrasts were confounded by animal EA rates always being higher). But the addition of a different comparator that is

better mapped to the complexity of alcohol-free reinforcement should increase the ecological validity of our findings.

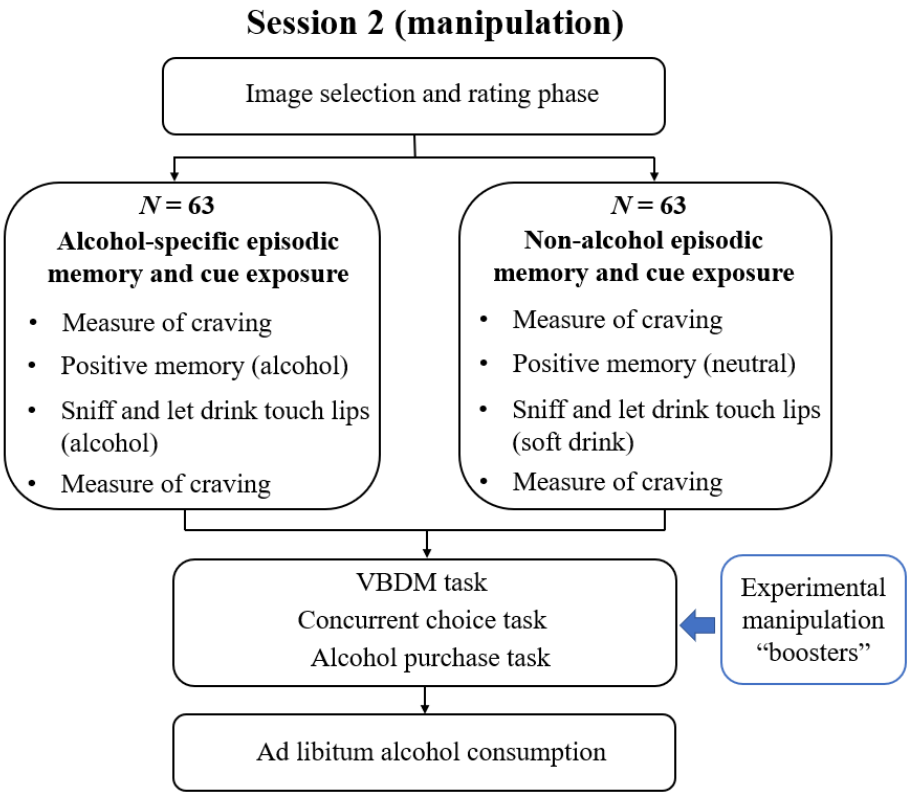
Procedure

Participants will be recruited from the local community in Sheffield to attend the lab where they will complete two in-person sessions (a baseline session followed by an experimental manipulation session; see schematics below for a visual depiction of the study procedure):

Schematic overview of session 1



Schematic overview of session 2



Session 1 (baseline): Upon arrival, we will firstly check participants ID (age-verification) and confirm that they have not consumed alcohol with a breathalyser. The remainder of this session will involve completion of self-report questionnaires, experimental tasks (behavioural measures of value), and the audio recording of positive memories, all of which are detailed below:

<u>Self-report questionnaires</u>

- *Alcohol use disorders identification test* (10-item AUDIT; Saunders et al., 1993): To measure patterns of alcohol that are hazardous or harmful to health. We will include additional response options from Dutey-Magni et al. (2022) that will allow us to calculate an extended AUDIT-C score.

- *The drinking motive questionnaire revised short form* (DMQ-R SF; 12-item questionnaire; Kuntsche & Kuntsche 2009): To measure people's motives for drinking alcohol (social, enhancement, coping, conformity).

- *Alcohol symptom checklist* (Hallgren et al., 2022): To measure how many (if any) of the DSM-5 AUD criteria a person meets within the past year. This has been found to be a highly consistent measure that was able to capture and discriminate across different AUD diagnoses.

- *Hypothetical alcohol purchase task* (APT; Murphy & MacKillop, 2006): A 14-item version (0, 50p, £1, £1.50, £2, £2.50, £3, £4, £6, £9, £11, £15, £18, £22) will be used to have a (relatively) brief version of the APT, but with enough price points to precisely estimate indices of demand. The high price point of £22 is intended to encourage a breakpoint across participants, reflecting both inflation and typical drink pricing in the UK (it is common for a cocktail to be £12-15).

- *Hypothetical soft drink (soda) purchase task* (SPT; Strickland et al., 2019): the price points and procedure will be identical to that of the APT listed above. This measure is included for exploratory analyses.

- *Drinking refusal self-efficacy* (9-item version of the drinking refusal self-efficacy questionnaire; Young et al., 1991): This will be measured for exploratory analyses.

- *Alcohol-free reinforcement* (17-item activity level questionnaire; Copeland et al., 2022): This will be to capture a self-report measure of alcohol-free reinforcement and to provide prompts for the memory recollection (via enjoyment ratings for different activities when alcohol was and was not consumed).

- *The Prospective and Retrospective Memory Questionnaire* (Smith et al., 2000): we will administer the 8-item subscale that assesses retrospective memory ability.

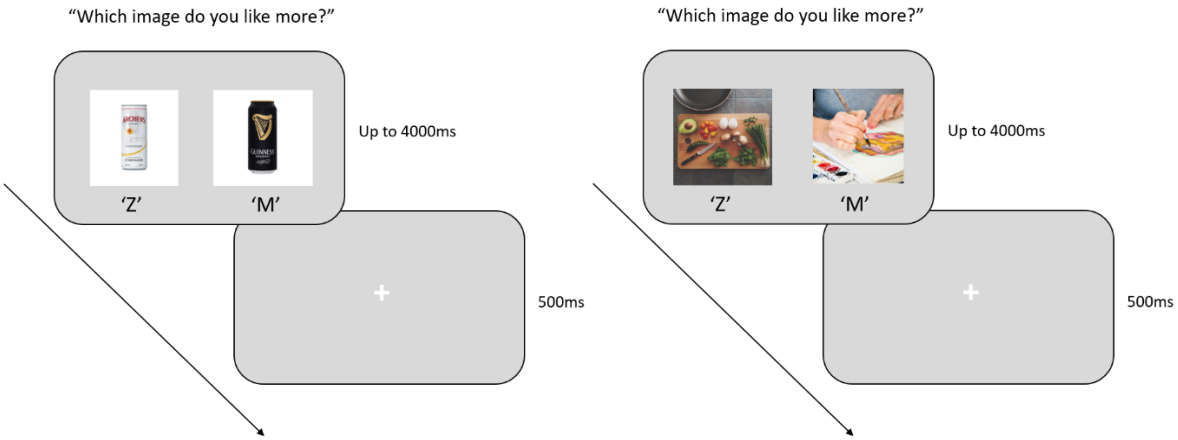
- *Participant demographics, tobacco use, and drink preferences* (multiple choice questions about age, gender, socioeconomic status, relationship status, employment status). We will also ask questions about smoking-related behaviour (smoking status, cigarettes smoked per day, potential e-cigarette (vape) use). Participants will be asked to state their alcohol and soft drink preferences; this will be used to select the drinks for each participant that will be used during the cue exposure and ad libitum taste test.

<u>Image rating phase</u>

Participants will make value judgements about 35 images that depict alcohol, alcohol-free reinforcement, and soft drinks (separately) by placing the images into one of four boxes using a computer mouse to indicate how much they like the image (or more broadly what the image represents), ranging from: ‘A lot’, ‘A little bit’, ‘Not really’, and ‘Not at all’. Participants will be instructed to rate all 35 images (from each category) while being instructed to assign at least five to each value category. Subsequently, for all three image categories (alcohol, alcohol-free reinforcement, and soft drink), five images will be randomly selected from each value category for use in the VBDM and concurrent choice task (therefore 3 x 4 x 5 = 60 images in total).

VBDM task (Copeland et al., 2022)

On each trial, two images from the same category will appear (one on the left and one on the right) over repeated trials, and participants will be instructed to press one of two computer keys ('Z' for left and 'M' for right) to select the image they like more, as quickly as possible. Block order will be randomised, with 150 trials in each, making 450 trials in total with a short break after every 50 trials. Difficulty levels will vary, in that the difference in rating between the two images can be 1, 2 or 3 (hard, medium, and easy choices respectively). On each trial, there will be a correct answer (based on previous value rankings), and whether this appears on the left or the right of the screen will be random.

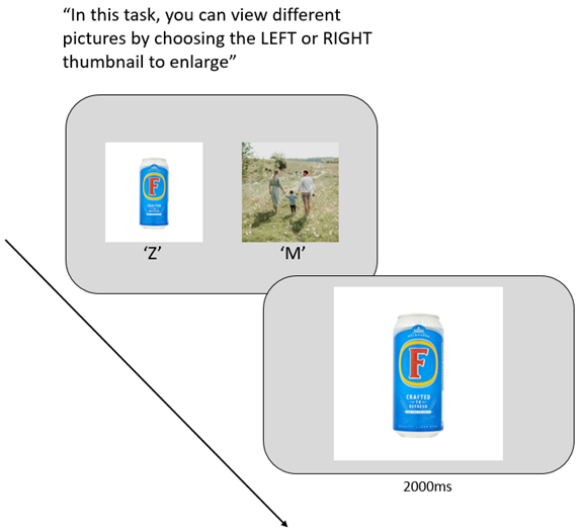


Schematic depiction of the VBDM task (alcohol (left) and alcohol-free reinforcement (right) blocks)

Concurrent choice task (Dyer et al., 2020)

Two images will appear side-by-side (one substance-related and the other substance-free) On each trial, participants choose which image to enlarge (for 2000ms) before progressing to the next trial. There will be two blocks of trials (this is to aid comparability to VBDM parameters derived from each block using behavioural data from the VBDM task):

- Alcohol vs alcohol-free reinforcement
- Alcohol vs soft drink



Schematic depiction of a concurrent choice task in the alcohol vs alcohol-free reinforcement block

Each block in the task will have 50 trials in total, where each trial randomly selects from the 5 most highly rated alcohol and 5 most highly rated non-alcohol images, with each possible combination being presented twice (5 x 5 = 25; 25 x 2 = 50). Whether the alcohol image appears on the left or the right of the screen will be random. On this task, the % choice of alcohol (relative to the alternative) will be the dependent variable.

<u>Retrieving, identifying, and talking about two positive memories (audio recorded)</u>

Participants will then be instructed to retrieve, identify, and talk about two different types of positive memories (one memory related to alcohol and the other not related to alcohol), both of which will be audio recorded. Participants will recall both types of positive memory to minimise participant expectancies prior to the second testing session. The order of memory recollection will be counterbalanced across participants with a short distraction task in between (participants will be presented with, and then asked to recall, random facts). We will measure and contrast participants' moods after recalling each of the memories (Positive and Negative Affect Schedule–Expanded; Watson & Clark, 1999). The Activity Level Questionnaire (ALQ; as used in Copeland et al., 2022) will be used to prompt participants to generate alcohol-related and non-alcohol positive memories with the following wording:

- Alcohol memory:

  *"We would like you to tell us about a positive memory that you have that **involved** drinking alcohol or being drunk. For example, some things you rated as high in enjoyment are (X, X, X). Tell us about a **particular time** that really stands out in your mind. Picture this memory in your mind and try to remember as vividly as possible*

*what the event entailed and focus specifically on the **positive role that alcohol played**. Please describe this memory in as much detail as possible"*

– Non-alcohol memory:

*"We would like you to tell us about a positive memory that you have that **did not** involve drinking alcohol or being drunk. For example, some things you rated as high in enjoyment are (X, X, X). Tell us about a **particular time** that really stands out in your mind. Picture this memory in your mind and try to remember as vividly as possible what the event entailed. Remember that we want you to think of a positive memory when **alcohol was not consumed.** Please describe this memory in as much detail as possible"*

Crucially, the following instructions will follow for both types of memory: *"When recalling your memory to us, please do not disclose anything relating to sexual activity, or any illegal activity such as illicit drug use"*. The reason we add this sentence is to minimise any possibility of us having to breach confidentiality to report any illegal activity that poses serious and immediate harm to others, such as admission of regular drink-driving.

The researcher will probe for key aspects of the event(s), crucially the time and place of the event so that how long ago it occurred can be calculated (after discussion we have decided not to limit this (e.g., to the past year) as we want people to have flexibility in recalling a "good high" which may have occurred before COVID or at a younger age for some people), as well as probing about emotions, thoughts, and bodily sensations. Following this, participants will be randomly assigned to one of two conditions (they will not be aware of which experimental condition they have been assigned to).

<u>Creation of episodic memory scripts</u>

After participants leave the lab, the researcher will listen to the audio recordings and create a condensed script that lasts approximately 1 minute for use in the subsequent manipulation. The scripts will be created from the information provided by participants in the audio taped responses (relevant to the experimental condition that the participant was randomly assigned to). Scripts will be created by summarising and condensing participant responses, and will be put together in the first person, present tense. The recording of the episodic memory scripts (by researchers) will match the gender of the participant (by Cameron and Amber).

Session 2 (experimental manipulation; completed within 10 days of session 1): Upon arrival, participants will again be breathalysed to confirm that they have not consumed any alcohol prior to the session. Participants will then complete the image selection and rating phase, undergo the experimental manipulation (depending on the condition they have been

randomly assigned to), complete measures of craving, and complete a taste test, all of which are detailed below:

Experimental manipulation (episodic memory and cue exposure)

- *Re-exposure to episodic memories*

As in Jobes et al. (2016), before each script, participants will be instructed to close their eyes while listening back to the script, to imagine themselves in the scene, and then to continue imagining until told to stop (30 s after the script ended). Participants will be given headphones and will only listen back to the positive memory relevant to the experimental condition that they have been assigned to.

- *Cue exposure (Field & Jones, 2017)*

Before and after listening to their positive memory, participants will be presented with a glass of their preferred alcoholic or soft drink (depending on experimental condition; drinks will be cold). For this cue exposure, participants will initially be instructed to sniff the drink (before listening to the memory), and will subsequently be asked to sniff the drink and allow it to touch their lips (3 times each), but to refrain from drinking it (after listening to the memory). They will also be asked to think about what it would be like to drink the beverage, and how this would make them feel. The alcohol exposure is intended to augment the craving effect elicited by memory of vivid positive drinking experiences. To avoid the possibility of conditioning between soft drinks and alcohol among those that use mixed drinks, the instructions will explicitly state whether the drink contains alcohol or not (a soft drink example is "this drink contains diet coke only").

Participants will complete self-report measures of craving before and after the experimental manipulation to explore whether alcohol-specific episodic memory and cue exposure augment alcohol craving as intended. This will be done using the *approach and avoidance of alcohol questionnaire – 'right now' version* (AAAQ; McEvoy et al. 2004) and *a single item of craving* (West & Ussher, 2010): This 14-item questionnaire will measure subjective alcohol craving (as in Field & Jones, 2017) by assessing momentary motivational tendencies to approach or avoid drinking. Participants will also answer the single question "How strong is your urge to consume alcohol now?". Participants will respond on a visual analogue scale ranging from 0 (no urge to consume alcohol) to 100 (extreme urge to consume alcohol).

Experimental tasks (behavioural measures of value; all detailed above)

Next, participants will complete the VBDM task, concurrent choice task, and APT. We will "boost" the experimental manipulation (exposure to cues only) in-between these measures to minimise any habituation of induced craving (this will be done at least 6 times, such as between task trial blocks).

Taste test to measure ad libitum alcohol consumption (Field & Jones, 2017)

First participants will report their current level of thirst (100-mm visual analogue scale with anchors at 0 (not thirsty at all) to 100 (extremely thirsty) prior to the ad libitum alcohol taste test): This will be measured for exploratory analyses, such as whether current level of thirst impacts the volume of alcohol consumed in the taste test (regardless of craving).

Participants will then be provided with two of their preferred alcoholic drinks (1 UK unit, or 8g alcohol, of each) and will be instructed to complete a taste test. Prior to starting this test, participants will be informed that afterwards they will complete another cognitive task in which they could win a financial reward of up to £5 and that alcohol is known to have a detrimental effect on the performance of that task. Like previous research (Jones et al., 2016; Field & Jones, 2017) participants will be asked to rate each alcoholic drink on ten different dimensions (e.g., gassy, pleasant, light, fizzy, etc) using 10-point Likert scales and we will supplement this with additional questions (e.g., "which of the two drinks do you prefer and why?"). The instructions of the taste test will be:

- *"Please taste and rate the alcoholic drinks in front of you using the scales provided. You can consume as little or as much of the drink as you would like in order to make accurate judgements, and you will have a maximum of 30 minutes to make your judgements".*

Once participants have completed this, the glasses (and remaining alcohol) will be removed, and the total volume of each drink consumed will be measured. The information regarding completion of an additional cognitive task is false – this is presented to motivate participants to restrict their alcohol (participants will not actually complete an additional task). This procedure or slight variations thereof have been used to measure the motivation to consume alcohol in the laboratory and have good construct validity and sensitivity to experimental manipulations (Jones et al. 2016). This simple procedure aligns with that used in Field et al. (2017) who found there to be sufficient variation in alcohol consumption that could be predicted by the effects of alcohol cues on inhibitory control, using mediation analysis. We will pilot the procedure to determine the optimal amount of time that participants will be given to taste the drinks - so consider 30 minutes stated here as a rough guide. Finally, participants will complete a "cool down" phase where they will complete a word search and watch a relaxing video (aquatic life) used in previous alcohol cue-exposure research (Hochster et al., 2018) to help participants 'recover' to baseline following the experimental manipulation. They will finally be breathalysed and will provide a craving rating (if their craving is above 75/100 or BAC above the drink driving limit, we will advise them to remain in the lab until these reduce).

Data preparation and analysis plan:

For primary pre-registered analyses, we will fit the EZ-DDM (Wagenmakers et al., 2007) to RT and accuracy data from the VBDM task. The EZ-DDM takes the mean correct RT, variance

of correct RT, and response accuracy as input and produces three key parameters, which are drift rate (v), boundary separation (a), and non-decision time (T_{er}).

Trials will be excluded if responses < .03 seconds or > 4 seconds. If any participants always give the same answer (such as always responding with the left key, or always responding with the right key) they will be excluded from the analyses.

We will explore the behavioural data to explore whether they meet assumptions for the EZ-DDM (Wagenmakers et al., 2007) by:

1. Exploring the shape of the RT distributions
2. Exploring the relative speed of error responses
3. Exploring whether the starting point is unbiased

Analysis of Covariance (ANCOVA) will be conducted on the post-manipulation VBDM parameters, with a between-subject factor of group, and pre-manipulation values as covariate(s). Between subject *t*-tests will explore differences in measures between groups. Mediation analyses will be used to explore the effect of the experimental manipulation on ad lib alcohol consumption, in particular mediation of this effect by VBDM parameters and % alcohol choice post-manipulation, using multilevel mediation models. We predict that the effect of the experimental group on the volume of alcohol consumed will be mediated by higher EA rates, and lower response thresholds, when making alcohol decisions, and lower EA rates, and higher response thresholds, when making non-alcohol decisions.

Exploratory analyses (will be included in the pre-registration):

- Contrasts across stimulus types in the VBDM task, e.g., in the alcohol craving condition, when making alcohol-related decisions, drift rates will be higher, and response thresholds lower, compared to drift rates and response thresholds when making alcohol-free decisions. This would be interesting because it would allow us to explore the importance of the type of alternative reinforcers (alcohol vs soft drink; alcohol vs. alcohol-free reinforcement).
- Whether there is a 'difficulty effect' in the VBDM task (determine whether the task can discriminate between different types of trials (e.g., easy, medium, or difficult determined by pairings on across trials, i.e., the difference in comparison determined by participant's own value ratings), and whether people are responding in accordance with their initial value ratings).
- Correlational analyses to explore relationships between VBDM parameters, % alcohol choice, self-report indices of demand, volume of alcohol consumed, and other self-report questionnaire measures (e.g., self-report thirst, drinking refusal self-efficacy, craving).
- Whether non-decision time differs for decisions relating to alcohol compared to non-alcohol stimuli.
- Whether the core conclusions differ depending on the type of computational model fitted to the data (e.g., EZ-DDM, *fast-dm-30*, hierarchical drift diffusion models).

- Whether VBDM metrics predict change in craving produced by the episodic memory and cue exposure manipulation.
- Whether there are any significant differences in self-report demand for soft drinks between the experimental conditions.
- Repeating analyses on units consumed as the dependent variable as opposed to % of total drink consumed.

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