Official Title of the Study: Alcohol use and mental health – Pilot test of video-assisted drinking topography

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2. Abstract

Alcohol use especially high-risk drinking remains a serious public health concern. Recent calls for "precision intervention" require more in-depth understanding of drinking behavioral patterns for more individualized treatment. Currently, alcohol research has relied on self-reported questionnaire or biomarkers to measure alcohol use. However, self-reports are often subjected to social desirability bias or recall errors; whereas biomarkers are prone to measurement errors, confounders for false positives, and individual variations in alcohol metabolism. There is need for an objective, reliable, and nonintrusive way to measure alcohol use with high ecological validity.

Topography can provide objective measures of consumption behavior patterns in fine grained detail. While it's been widely used in tobacco research, alcohol topography has not been well-studied. Smoking topography has been shown to provide indicative information for nicotine dependence. We hypothesize that alcohol topography can also be used as an objective measure indicative of alcohol use disorder. In this project, we propose to conduct a video-assisted drinking topographical study. The main objectives of this study include: (1) characterize drinking behavioral patterns by converting videotaped drinking episodes into various drinking related parameters (e.g., sipping frequency, sipping interval, sipping duration, rest duration, sipping amount, and etc.); (2) compare drinking behavioral patterns across groups defined by drinking status (social vs. heavy drinkers) and mental health status (depressed vs. non-depressed); and (3) use advanced nonlinear modeling to quantify the behavioral pattern and to derive potential indicators for alcohol use disorder.

This will be the first study to ever use videotaped topography to analyze alcohol drinking behavioral pattern using a quantum model and link it to alcohol use disorder. The study will be conducted in the simulated bar laboratory located in Yon Hall at the University of Florida (UF). Conducting alcohol topography in such a setting greatly enhances ecological validity, further increasing the capacity of this method to capture real life drinking patterns and to potentially detect alcohol use disorder.

3. Background

Alcohol use continues to be a major public health concern in the United States. The 2015 National Survey on Drug Use and Health (NSDUH) showed that 26.9% of American adults engaged in binge drinking and 7% reported heavy drinking in the past month (i.e., binge drinking on 5 or more days).[1] About 15 million adults in this country (about 6% of the population) meet criteria for a current alcohol use disorder (AUD). [1] However, only 8.3% of this population received treatment for their AUD,[1] and overall interventions tend to show small effects in ameliorating problem drinking.[2] Recent calls for "precision intervention" underscore the importance of understanding individual drinking behavioral patterns as the first step for more effective, personalized AUD treatment.[3]

Currently, measures of alcohol use have relied on self-report questionnaire or biomarkers. The limitations of subjective self-report for alcohol use have been long recognized. Recall bias (e.g., unable to remember, incorrect memory about drinking events) [4] and social desirability bias (e.g., underreporting due to concern of being judged by the care provider) [5] often lead to incorrect diagnosis of alcohol use problems. Objective measures including different types of biomarkers (e.g., GGT, PEth, and FAEE) have been developed to address these limitations. However, these biomarkers often fail to perform satisfactorily due to measurement errors, confounders for false positives, and individual variations in alcohol metabolism.[6-8]

Topography is the study of consumption behaviors in extensive details in either laboratory or natural settings.[9] Data can be obtained objectively and noninvasively through a topography device or videotaping. This approach been widely applied to tobacco research in investigating puffing behaviors (e.g., puff duration, puff volume, and puff speed). The characteristics of puffing behavior measured by topography such as puff speed and puff duration are shown to be reliable indicators for individual differences, [10-13] nicotine dependence, [11,14] and abstinence after quitting.[15]

Despite its utility, alcohol topography has not been as well-established as smoking topography. Alcohol topography measures have been used successfully as alternate measures of alcohol self-administration in human laboratory studies.[16,17,24] Despite calls for the use of alcohol topography to expand (e.g., as a longitudinal predictor of drinking outcomes)[25] these research efforts have not yet materialized. To explore the potential of using alcohol topography as a noninvasive objective measure of alcohol drinking behavior and the possibility of using the identified behavioral pattern as an indicator for alcohol use disorder.

4. Preliminary Study

The video-assisted topography method was developed as an indicator of nicotine dependence by our group in previous research.[18] The procedure involves videotaping one smoking episode of a whole cigarette and coding the video frame by frame to generate parameters of puffing behaviors (e.g., puff speed, puff duration, puff interval, and etc.). The temporal pattern of each parameter is plotted using time (in seconds) as the x-axis, and fitted to both linear and nonlinear (i.e., fold catastrophe) models. Results from the smoking topography study showed that the indicators derived from the fitted catastrophe model were significantly associated with self-reported nicotine dependence scores, especially DSM-IV criteria. This study provided an impetus for us to explore the potential of using the same method to develop topographic indicators for alcohol use disorder.

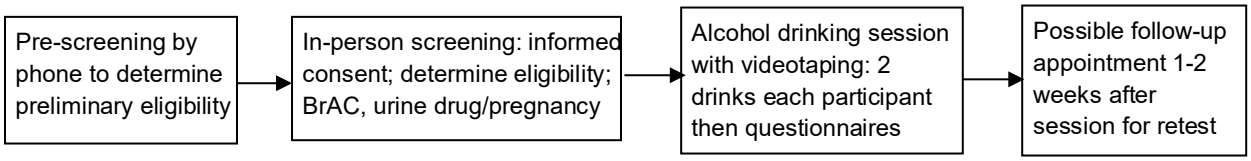
5. Specific Aims

The overall goal is to pilot test and establish a procedure for video-assisted alcohol topography and explore its utility as an indicator of alcohol use disorder. Our specific aims include the following: (1) characterize drinking behavioral patterns by converting videotaped drinking episodes into various drinking related parameters (e.g., sipping frequency, sipping intervals, sipping duration, rest duration, sipping amount); (2) compare drinking behavioral patterns across groups defined by drinking status (social vs. heavy drinkers) and mental health status (elevated vs. non-elevated depressed mood); and (3) use advanced nonlinear modeling to quantify the behavioral pattern and to derive potential indicators for alcohol use disorder.

6. Research plan

Overview

There are 4 phases to this study: 1) pre-screening by phone; 2) in-person screening appointment; 3) the first alcohol drinking session with videotaping; and 4) follow-up appointment for retest. The figure below gives a timeline of the steps involved in the study. Each alcohol drinking session including all testing will require 3-4 hours.



Participants

Recruitment: Participants will be recruited through recruiting flyers (Attached) posted on the UF campus and vicinity, along with ads posted on online classified sites such as Craigslist and newspapers. Prospective participants who see one of these

advertisements and are interested in the study will contact the study initially via telephone, text, or email message. Study staff will answer any questions and conduct a preliminary phone screen among those who would like to pursue study participation.

General inclusion & exclusion criteria: Participants must be 21-55 years of age, able to read English and complete study surveys, report liking beer and consuming it at least once in the past 30 days, and report having consumed at least two alcoholic drinks on at least one day during the past 30 days (i.e., current drinkers). Participants will be excluded if their urine drug test indicates recent use of illegal drugs (except cannabis) and pregnancy for women. In addition women who report engaging in sexual activity with opposite sex partners without use of reliable birth control will be excluded. Participants will also be excluded for any of the following conditions: a history of medically-assisted detoxification; present with signs of current alcohol withdrawal; currently meet the severe threshold for alcohol use disorder according to DSM-5 (i.e., 6 criteria or more); currently meet DSM-5 substance use disorder criteria at any level (i.e., 2 or more criteria) for any substance besides alcohol; are currently seeking treatment for problem substance use; have engaged in intensive outpatient or inpatient treatment for substance use in the past 12 months; meet criteria for severe depression or have any serious psychological or medical history that contraindicates alcohol consumption; currently taking any medication that contraindicates alcohol use at the levels included in this study; and have BMI under 18.5 or over 35. Given that video recording is a critical aspect of the study, participants will be required to agree to video recording in order to take part in the study. Undergraduates enrolled at the University of Florida will be excluded from participating. Graduate and non-matriculating students will be allowed to participate as long as they are not enrolled in the College of Health and Human Performance.

Subgroup division: Participants will be further divided by drinking status (social vs. heavy drinkers) and mental health status (elevated vs. non-elevated depressed mood). This creates four combinations of subgroup category (2×2). Efforts will be made to recruit equal numbers of men and women in each of the 4 categories.

Sample size: As a pilot study, we will target enrollment of up to 40 participants (~10 in each subcategory as defined in the previous section).

Procedure

Pre-screening by phone:

Study stuff will conduct a brief phone screen to determine whether the participant meet the general criteria to be included in the study. If the participant is eligible based on the phone screen, study stuff will schedule an appointment for in-person screening.

Screening phase:

An in-person screening will be conducted to give information about the study and determine eligibility. The initial screening appointment will take about 2 hours. During this appointment, we will interview the participants about their drinking habits, cigarette use, mood, menstrual cycle if female, medical and mental health histories. Participants will also be engaged in a timeline followback interview to update their alcohol, cigarette smoking and electronic cigarette use. The alcohol drinking that is part of this study may not be safe for those who are also using cocaine, opiates, phencyclidine, amphetamines, methamphetamine, barbiturates, methadone or benzodiazepines. For this reason, individuals whose urine drug test indicates use of one of these drugs will be excluded. Also, participants who arrive with a positive breath alcohol reading no higher than 0.02% may be able to remain at the research office until their breath alcohol level declines to 0.00% and then continue with the appointment or reschedule the appointment one time. However, individuals who arrive at an appointment with a positive breath alcohol reading a second time will be excluded from the study and offered local referral options for treatment. Finally, women who are pregnant, nursing or sexually active with opposite sex partners without use of birth control will not be able to participate in the study.

As part of the screening procedure, participants will be asked to complete a web-based questionnaire that covers topics including drinking motives; current drinking behaviors; reasons for drinking; and physical activity level.

Information will also be gathered to categorize the participants into subgroups based on their drinking behaviors and depressive symptoms:

a. *Drinking behaviors*: Past 30-day drinking behaviors and DSM-5 criteria for alcohol use disorder will be used as the basis for distinguishing social and heavy drinkers. The social drinker group will be those who (1) consume at least 1 but no more than 5 standard alcoholic drinks per week and (2) engage in infrequent binge drinking (i.e., 5 or fewer times per year, but allowing for 1 past interval of a maximum of 6 months' duration of up to twice weekly binge drinking). The heavy drinker group will be those who (1) consume at least 10 alcoholic drinks per week ; (2) engage in regular binge drinking (i.e., consume 5 or more drinks on one occasion or ≥ 4 for women 1 to 5 times on average per week); and (3) meet DSM-5 criteria for mild or moderate alcohol use disorder. These criteria are based on criteria outlined by King et al.[19] The timeline followback (TLFB) interview will be used to obtain self-reports of drinking behavior with a focus on past-30-day behavior, however the extent to which recent drinking behavior resembles past-12-month and lifetime drinking behavior will be queried in order to make sure participants meet criteria for

one of these two categories. Those who drink but who did not clearly fall into one of these two groups will be excluded from participation.

b. *Depression*: Patient Health Questionnaire (PHQ-2 and PHQ-9) will be used for depression screening. The non-elevated depressed mood group will be those who scored less than 3 on PHQ-2 (i.e., negative PHQ-2). Elevated depressed mood group will be those who scored 3 or more on the PHQ-2 (i.e., positive PHQ-2) and 5 or more on the follow-up PHQ-9. Those who scored 20 or more (i.e., severe depression) will be excluded from the study and offered local referral options for treatment.

Once the participants pass the breath alcohol and urine testing, and meet all the eligibility criteria, they will be scheduled for the first of two alcohol drinking sessions. Compensation for the in-person screening appointment will be $10 for those deemed ineligible during the first hour of the appointment and $20 for those who complete the two hour appointment, regardless of eligibility or interest in continuing with the study.

Videotaped drinking session:

Laboratory setting: The videotaped drinking session will take place in the simulated bar laboratory, located in Yon Hall North on the UF campus. This laboratory has been established to maximize ecological validity by simulating an actual bar. Two protocols have been approved by IRB01 to take place in this laboratory setting (IRB201500990, 201600614). It includes the drinking bar itself (seats 3 people), alcohol brand signage, television, glassware, music, and a beer tap (nonoperational). A high-definition camcorder (Sony FDR-AX53, DVD format, 100 frames/s or equivalent) will be set up in the wall cabinet after the participant is seated at the bar. The distance from the camcorder to participants is around 1.5 meters. The camcorder will be adjusted each time before videotaping to focus on the upper body of the participant to capture the detailed drinking behaviors. A digital scale (IDAODAN nutrition food scale, 5kg max, 1g/0.1oz accuracy) will be set up in front of the participant on the bar counter. The scale is equipped with wireless bluetooth technology that automatically uploads measurement to the research computer. A coaster will be placed on top of the scale. Participants will return their drink to the coaster on top of the scale after each sip. Readings from the scale will not be observable to participants.

Videotaped drinking session: An initial alcohol drinking session will take place following in-person screening. Participants will be asked not to drink any alcohol on the day of an alcohol drinking session prior to coming to the lab for the session. They will also be asked to abstain from food during the 4 hour period leading up to their session. Transportation will be provided by the study to and from the research facility using either a university-owned vehicle or a commercial transportation service. Participants can be

picked up from any convenient location in the Gainesville area though transportation after the session must be taken directly home only. Participants within an 0.5 mile radius of the research facility may be walked to and from the facility by a study staff member rather than driven.

When participants arrive, they will have a short rest period during which they will be asked to consume a 150-200 calorie snack. After they consume the snack, the alcohol drinking period will begin. This part of the session will take place in a laboratory space that has been built and decorated to look like an actual bar. There will be a camcorder set up in the lab to record the whole drinking session. Beer will be the only beverage that we provide. We will provide several common brands with similar calorie (125-150) and alcohol level (approximately 4.5% ABV) for the participants to choose from (e.g., Yuengling lager, Yuengling black and tan, Smithwicks Ale). We will pour the beer of their choice into a standard glass for them to drink. The participants will be asked to drink as they usually do. They will be requested to put the glass on a food scale that we provide throughout the drinking process whenever they are not holding it.

After completing the first beer, they will take a 30 minute break before they can drink the second beer. It must be the same brand as the first beer. During the break, they may take part in recreational activities (e.g., watching television, playing games). They will be allowed to read magazines but will not be permitted to complete work during the alcohol drinking period (either academic or for a job). When they are ready after the required break time, they can start drinking the second beer. The request will be the same for them as for the first beer, and only the same type of beer as their first drink will be provided to them.

To obtain an additional objective measure of alcohol consumption, we will also ask the participants to wear the BACtrack Skyn, a wristband-type alcohol monitor during their whole drinking session. The wrist-worn alcohol monitor looks like a fitness tracker or wristwatch (see figure 1). It can detect alcohol as it evaporates through the skin, providing objective data of alcohol consumption in a nearly real-time basis.[20,21] The research assistant will help participants put on the wristband monitor when they arrive at the bar lab, and set up the Skyn App for data streaming. This allows us to establish baseline readings and make sure that the monitor functions properly. The monitor will be worn during the whole session for continuous monitoring and will be taken off from participants upon their departure from the lab. There is no reading shown on the wristband monitor itself, which ensures no interference on participants' drinking behavior. Data will be stored in the microchip in the monitor and can be later streamed into a smartphone App after the monitor is retrieved from participants.

Figure 1. BACtrack Skyn Alcohol Monitor

Survey and post-administration:

When the drinking session is completed, participants will be asked to complete a web-based questionnaire using REDCap, which covers topics including subjective response to alcohol, craving, and mood.

Participants will be required to stay in research facility for at least 2 hours and until their breath alcohol drops to the safe level of 0.02%, at which point they will be provided with transportation directly home by the study. It is important that all participants be required to remain in the lab for a minimum amount of time following alcohol consumption in order to avoid participants drinking differently (i.e., faster) in an effort to depart from the laboratory sooner. This transportation can only be taken directly home.

Follow-up for retest:

Participants may be selected for a follow-up appointment for the retest after 1-2 weeks, which includes repeating the same procedure alcohol drinking session procedures as their first appointment. To make data comparable, only the same type of beer as their first drinking session will be provided to them. At the outset of this pilot study, all participants will be invited for a second session, however the study Co-PIs reserve the right to limit participation to one alcohol drinking session per individual subsequently based on limitations with preliminary study funding and/or time limitations in terms of obtaining preliminary data in support of subsequent grant applications.

Compensation for drinking session:

Participants will receive $40 for completing each drinking session, provided they complete all study procedures and remain in the laboratory until their breath alcohol level declines to .02%. Participants leaving before this point will be given a prorated payment based on a rate of $10 per hour. Those departing before their breath alcohol declines to a safe level during the first alcohol drinking session will be excluded from the second session.

List of instruments

Pre-Screening phase:

Demographic information: Basic demographics will be collected, including age, gender, race/ethnicity, height and weight.

Frequency and quantity of alcohol consumption: Four questions will be used to assess alcohol use: (1) number of days used alcohol in the past 30 days; (2) number of binge drinking (i.e., 5 or more drinks for men, 4 or more drinks for women) days in past 30 days; (3) highest number of alcoholic drinks consumed on any given day in the past 30 days; and (4) number of binge drinking days in the past year. Five response options will be given for each question

Frequency and quantity of cigarette smoking: Two questions will be used to assess (1) number of days smoked in the past 30 days and (2) the average number of cigarettes smoked per day on the days they smoke in the past month. Five response options will be given for each question

Preferences for different alcoholic beverages: One question will assess participants' preferences for beer, wine, and/or liquor, followed by questions asking on how many days respondents have consumed each type of alcohol in the past 30 days.

General questions regarding other inclusion/exclusion criteria: Two questions will list the other inclusion and exclusion criteria respectively, and ask participants whether or not any of the criteria pertain to them.

In-Person Screening

Withdrawal symptoms: The 10-item Clinical Institute Withdrawal Assessment for Alcohol (Revised) (CIWA-AR)[22] will be used to assess severity of current withdrawal syndromes.

Depression: Patient Health Questionnaire (PHQ-2 and PHQ-9)[23,24] will be used for depression screening.

Medical and psychiatric history: A medical and psychiatric history will be taken from all participants, which will cover the following conditions: hypertension, diabetes, high cholesterol, cardiac abnormalities, pancreatitis, renal insufficiency, cancer, pulmonary disease, thyroid conditions, history of head injury or other neurological problems, stomach or intestinal disorders and liver disease. Participants will also be asked whether they have ever been diagnosed with a psychiatric condition or received treatment for such a condition. Participants will be asked to report all medications, including over the counter medications and those that they are currently taking, including psychotropic medications. The Structured Clinical Interview for DSM-5 (First et al., 2015) will be used to classify patients according to the presence or absence of past or present alcohol and other substance use disorders.

Self-reported alcohol consumption: The Timeline Followback Interview (TLFB) (Sobel & Sobel) will be administered at the in-person screening and updated at outset of each alcohol drinking session. Participants will be given a blank calendar including memory prompts (e.g., holidays), which covers the designated time interval (the prior 30 days at initial screening) and asked to reconstruct their drinking behavior, cigarette and electronic cigarette usage over that interval. The TLFB has good test-retest reliability and good validity for verifiable events.

Family history of problem drinking: Family history is measured with a subscale taken from the *Addiction Severity Index*.[26]Participants are asked to indicate whether or not four classes of relatives on both their mother's and father's side ever "had a significant problem with alcohol or drugs, one that either lead to treatment or should have led to treatment."

Drinking history: Participants will be asked to report the age when they first started drinking, not counting small tastes or sips of alcohol and their age of first intoxication. They will also be asked to report the highest number of drinks they have ever consumed over a 24-hour period in their lifetimes.

Drinking motives: The Drinking Motive Questionnaire Revised Short Form (DMQ-R SF)[25] will be used to assess various motives for drinking (i.e., enhancement, social, coping).

Alcohol expectancies: The *Comprehensive Effects of Alcohol* (*CEOA*) (Fromme et al.) measure will be used to assess the extent to which participants report experiencing alcohol-related expectancies (e.g., "After a few drinks of alcohol, I would be more likely to feel dizzy").

Subjective response to alcohol: An adapted version of the *Self-rating of Effects of Alcohol* (*SRE*; Schuckit et al., 1997) will be used at intake to assess the number of alcoholic drinks it took for participants to experience a series of subjective effects (e.g., stimulation,

arousal) the first time they drank alcohol, in the past three months and during their period of heaviest drinking. Responses to the adapted SRE will be used to assess self-reported *tolerance* as well. A tolerance score is created by subtracting the score for the first five drinking occasions (α = .83) from the score for the recent drinking experiences (α = .86).

Alcohol Use Disorders Identification Test (AUDIT): The AUDIT[33] is an established, valid 10-item measure assessing both quantity/frequency of alcohol consumption and symptoms of alcohol use disorder

Impaired control: The *Impaired Control Scale (ICS;* Heather et al., 1993) consists of three parts including 5 items concerning actual attempts at limiting alcohol consumption (Part 1); 10 items assessing the frequency of past failures at controlling drinking (Part 2) and 10 items assessing beliefs regarding future ability to control drinking (Part 3). Parts 1 and 2 will be administered in this study. The ICS is reliable and has been validated in clinical and community samples. Items are rated on a 0 to 4 scale and summed with higher scores indicating greater difficulty in controlling consumption.

Facets of impulsivity: Impulsivity and risky decision making will be measured using the *UPPS Impulsive Behavior Scale*: a 59-item measure that assesses five subdimensions of impulsivity (premeditation, positive urgency, negative urgency, sensation seeking and perseverance). The *Kirby delay discounting measure*[27] and the *Probabilistic Choice Questionnaire (PCQ)*[39] will be administered at in-person screening and during alcohol self-administration sessions. The Kirby is a 27-item measure that assesses preferences as to whether participants would prefer smaller, immediate or larger, delayed hypothetical monetary amount. Length of delay and amount of hypothetical funds vary across items. The PCQ is made up of 30 items comparing certain with uncertain hypothetical monetary amounts of varying sizes.

Alcohol purchase task: This is a simulation measure to assess self-reported alcohol consumption and expenditure were alcohol to cost varying amounts of money. The measure generates a number of variables pertaining to reinforcement from alcohol, including intensity of demand.

Physical activity level: The General Practice Physical Activity Questionnaire (GPPAQ)[34] a validated physical activity screening tool for patients aged 16-74, will be used to assess physical activity level. This tool generates a simple, 4-level Physical Activity Index (PAI): Active, Moderately Active, Moderately Inactive, and Inactive.

Breath alcohol concentration: Breath alcohol concentration will be assessed using a hand-held Intoxilyzer breathalyzer unit at the in-person screening at outset of each alcohol drinking session and then at several points during the sessions, including determining the point at which participants can be dismissed safely from the session.

Urine drug and pregnancy tests: Urine drug dips will be used to detect opiates, cocaine, phencyclidine, amphetamines, methamphetamine, barbiturates, methadone and benzodiazepines. Urine pregnancy tests will also be administered to all female participants. A positive test for any of the above drugs or a positive pregnancy test will lead to immediate exclusion from the study.

Vital signs (i.e., blood pressure and pulse readings), *height and weight*.

Menstrual cycle data: Self-reports will be obtained from all women on their menstrual/gynecological status. We will include women who are cycling normally and/or on birth control pills. Three months of self-report data recording the start of their menses will be obtained prior to the laboratory sessions. This information will be obtained initially at the in-person screening and updated at the outset of each alcohol drinking session.

Symptoms: Adverse experiences are collected on standardized forms, using the *SAFTEE*[35] The SAFTEE includes 1) open-ended questions about any changes in physical or health problems, appearance, or activity level, and 2) yes/no responses to a specific list of symptoms for a specified time period. For each symptom reported on the SAFTEE a rater also records the severity (mild, moderate, or severe) and action taken.

Suicidality: The *Columbia Suicide Severity Rating Scale*[36] is a semi-structured interview that assesses past and current suicidal ideation, intent, and attempts. It will be used to monitor the safety of participants. Any participant reporting current suicidal ideation including intent to carry out a suicide attempt will be excluded from the study and the study physician, Dr. Hobbs, will be alerted immediately.

<u>Measures taken following the alcohol drinking period</u>:

These measures will be administered twice per session after the conclusion of the alcohol drinking period: once immediately following the end of the alcohol drinking period and again one hour later.

Mood: The *Positive Affect and Negative Affect Scale* (*PANAS*)[37] provides a measure of current mood. Participants indicate their agreement with 20 adjectives, including 10 each to assess positive (e.g., attentive, interested) and negative affect (e.g., hostile,

Subjective effects of alcohol: The *Biphasic Alcohol Effects Scale*[28] is an established 14-item self-report, unipolar adjective rating scale that focuses on positively-valenced stimulant and negatively-valenced sedative effects. The Subjective Effects of Alcohol Scale[40] is a new measure, also made up of 14 items, which covers both positively and negatively-valenced stimulant and sedative effects of alcohol.

Craving: Craving will be assessed using two measures. The *Alcohol Urge Questionnaire (AUQ)*[38] an 8-item questionnaire, derived from a larger 49-item "Questionnaire of

Alcohol Urges" and assesses *desire for a drink, expectation of positive effect from drinking,* and *inability of avoid drinking if alcohol was available.* The AUQ is a reliable and valid scale for the measurement of self-reported alcohol urges and scores have been shown to be strongly related to alcohol dependence severity and to cognitive preoccupation with alcohol. Its brevity and time frame for ratings (i.e. right now) makes it suitable for administration during the alcohol drinking period. Craving will also be assessed with a *single item assessed using a 100-point visual analog scale*. Participants will be asked to report the extent to which they "want alcohol."

Liking for alcohol: An item from *The Drug Effects Questionnaire* (DEQ)[29] will be used to assess the extent to which participants like the effects of alcohol they are experiencing at the time, rated on a 100-mm line (from "not at all" to "very much"). The DEQ has been utilized in previous alcohol studies. The aforementioned alcohol purchase task, delay discounting and probability discounting measures will be repeated post-alcohol-consumption as well.

7. Possible Discomforts and Risks

Potential risks in this study were identified in accordance with the recommended guidelines on ethyl alcohol administration in human experimentation put forth by the National Advisory Council on Alcohol Abuse and Alcoholism[30] and two reviews on this subject.[31,32] Steps taken to minimize these risks were also developed in accordance with these documents.

Alcohol consumption: A number of medical conditions could potentially be worsened by acute alcohol administration (e.g., liver disease, cardiac abnormality, pancreatitis, diabetes, neurological problems, and gastrointestinal disorders). As a result, participants with such medical problems or who currently take medications contraindicating alcohol consumption at the level in this study will be excluded.

Alcohol self-administration in a research study by individuals who are severely alcohol dependent as evidenced by current withdrawal, a history of withdrawal or diagnosis of current severe alcohol use disorder may pose a risk to their health and safety. Alcohol self-administration in a research study by individuals who are seeking treatment for alcohol dependence or who have recently engaged in intensive treatment for alcohol dependence may compromise their efforts to reach or to maintain abstinence or moderate levels of alcohol use.

Alcohol may cause nausea in high doses, however, nausea is not expected at the doses that will be consumed in this sample of frequent heavy drinkers. Only current drinkers who had consumed at least 2 drinks on at least one day in the past month are selected for the study, thus ensuring that any amount of alcohol consumed during an

alcohol administration session is less than or equal to an amount of alcohol they consume on their own on a regular basis.

Another area of potential risk to participants under the influence of alcohol involves their safety during the experimental procedures. Although impairment of gross motor coordination in drinkers is rare at the alcohol doses to be consumed in this study, all participants will be under the close supervision of the experimenters to prevent possible accidents such as falls. Alcohol is a reinforcing agent, which may cause changes in behavior including repetitive or excessive alcohol consumption.

Breath screening and urine collections: Breath screening and urine collections are performed primarily as safeguards and should add no risks other than those normally associated with these procedures.

Interviews, rating scales and questionnaires: The assessments used in this study deal with some sensitive issues including family history of high-risk alcohol use and participants' own experience of alcohol-related problems. The major disadvantages of these assessments are the time taken to complete them and possible breach of confidentiality. Our past experience with these measures indicates that they are acceptable to participants.

Videotaping: Participants will be videotaped through the alcohol drinking period which may generate some confidentiality risks and potentially cause some uncomfortable feelings for those who are not used to be videotaped. Our past experience with videotaping cigarette smoking indicates that the procedure is acceptable to participants and they usually get used to it after the first few minutes of recording.

Alcohol monitoring: Participants will be requested to wear the wristband-type alcohol monitor during the whole drinking session up to their departure. The wristband monitor itself is noninvasive and adjustable for different wrist sizes. It's very unlikely to cause any discomfort based on our experience.

8. Procedures to protect against or minimize potential discomforts and risks

Alcohol consumption: Participants will only be enrolled in the study if they self-report consuming the requisite level of alcohol use. Participants will also be excluded should they self-report any condition that contraindicates alcohol consumption (e.g., a history of clinically significant withdrawal detected at the in-person screening). Females will be screened for pregnancy at the in-person screening, as well as during the pre-session appointment on the day of the alcohol drinking session.

Alcohol drinking sessions will be conducted by the P.I. and by research staff who are experienced with these methods and have been carefully trained. As described above,

all participants will be under supervision to prevent possible accidents. Several steps will be taken to ensure that alcohol consumption in this study occurs in a safe manner, in accordance with the recommended guidelines on ethyl alcohol administration in human experimentation, set forth by the National Advisory Council on Alcohol Abuse and Alcoholism. All alcohol drinking sessions will be supervised by Dr. Leeman himself or by a senior research assistant (post-doctoral fellow/associate, graduate student or professional research assistant/coordinator) who has training and experience with alcohol self-administration. Dr. Leeman will either be present at the alcohol drinking session himself or readily available on call to make any determination regarding serious versus non-serious adverse events. In the event of an immediate medical emergency, 911 will be called right away and study physician Dr. Hobbs will be notified. In the event of a non-emergent adverse event, Dr. Hobbs will be available for consultation as needed.

Participants will be asked to remain at the research facility for at least two hours after the end of the alcohol drinking period and until their breath alcohol concentration (BrAC) drops to the safe level of 0.02% or lower (according to 2 breathalyzer readings). When it is time for dismissal, participants will be provided transportation directly home by the study.

Several protocol features diminish the chance that study participants will leave the bar lab before dismissal by study staff and we have plans in place in case this occurs. As part of the informed consent process, we advise all participants of study requirements, including the requirement to stay until their BrAC falls to a safe level. We reiterate these requirements verbally and in the form of a printed handout the day before the alcohol drinking session and on the day of the session, just before the beginning of the alcohol self-administration period. Thus, participants are made aware multiple times of the requirement to remain in the facility for at least two hours after the end of the alcohol drinking period and until they reach a safe BrAC, along with other study requirements.

The pay structure of the study also discourages early departure. We pay participants $40 per alcohol drinking session, however participants will receive only a prorated portion of the payment should they end the session early. While there is a possibility of some benefit to participants in the form of referrals for behavior change that we will provide at the conclusion of the second alcohol drinking session (participants in the heavy drinking group will also receive a brief motivational interview including personalized information about their drinking), participants in laboratory studies take part primarily for the monetary compensation, making it unlikely that they will intentionally engage in behaviors that are certain to reduce their payment.

Nonetheless, it is possible that a participant could elect to leave the research facility early. We have procedures in place should this occur. Study staff will ask individuals

who wish to end their participation early to remain in the facility until their breath alcohol reaches the safe level of 0.02% or lower. Study staff will offer these participants transportation to their home, provided for by the study regardless of their willingness to remain in the research facility until their BrAC reaches a safe level.

Administration of alcohol to individuals in treatment for addictive behaviors could potentially impede the progress of their recovery. As a result, we will not enroll individuals who have taken part in inpatient or intensive outpatient treatment for alcohol use or other addictive behaviors in the past 12 months. Further, we will not enroll individuals with a lifetime history of clinically significant withdrawal from alcohol; a lifetime history of medical intervention for withdrawal or who currently present in a manner suggestive of withdrawal, based on the Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar). These steps regarding withdrawal will also have the benefit of excluding individuals who are severely dependent on alcohol, for whom alcohol consumption in this study may not be safe. Study activities take place in a controlled, simulated bar lab environment.

Interviews, rating scales and questionnaires: The major risk of the assessments is potential loss of confidentiality, which we address above. To minimize any discomfort associated with reporting sensitive behaviors, participants will be informed that they may refuse to respond to questions that they are not comfortable answering. Questions related to eligibility determination and monitoring of safety and treatment response are not optional. If a person declines to answer these questions, we will advise them that they will not be able to participate.

Confidentiality: Whenever possible, research participants will be referred to by study-assigned ID numbers rather than by their name or other personal information. Accordingly, results of clinical interviews, vital signs, breath alcohol and urine drug/pregnancy screening are recorded by staff members on paper forms using study IDs only. Urine testing will take place only at our research offices. Urine samples will be used for the purposes of this testing only and will be discarded after tests are completed.

However, some private identifiable information about individuals will be collected to enroll and contact participants. This information will be collected primarily via paper forms, which will be stored in locked filing cabinets in a locked room in the research facility in Yon Hall North. This includes a master list connecting participant study identification numbers to participant names.

Electronic mail is an invaluable means of communicating with prospective and enrolled study participants. All email communication with participants in this study will be via secure email accounts administered by the University of Florida. In the proposed study,

electronic mail is an option for prospective participants to self-identify as being potentially interested in the study. Prospective participants also have the option of communicating with study staff by phone. Email communication will be used primarily to schedule appointments and to respond to questions about the study. Telephone and in-person are the preferred methods for conversations regarding protected health information (PHI). Conversations via email regarding PHI will occur only after participants consent to engaging in these conversations via email after being advised of potential risks of breach of confidentiality, which will be minimal given our use of secure email accounts administered by the University of Florida.

Some self-report data will be collected via the web, however no protected health information (PHI) will be collected via web-based forms on REDCap. Participants will be identified on web-based forms in REDCap by a study-issued identification number. Even though no PHI will be collected on these forms, steps will be taken to maintain the confidentiality of this information. Data transmitted from the server will be encrypted and secured within a password-protected file that will only be accessed by study staff. These steps will provide the highest level of security for web-based data in this study.

In order to be compensated, participants' identifiable information will be entered into a secure, online system maintained by the University of Florida. Participants' names, street addresses and social security numbers will be entered into this system, however no study data will be entered and study id will not be included either thus preventing study data from being linked to the identifiers stored in this system. Use of this system enables us to compensate participants via a debit or gift card to which funds can be added as participants complete different stages of the study. Social security numbers will be collected only for the purpose of providing payment.

Electronic data sets not containing any PHI will be stored on the P.I.'s desktop computer in his office at Florida Gym, on computer in the research facility in Yon Hall North and on space in a secure server maintained by the University of Florida. Any data from this study that is shared with collaborators or other qualified individuals from institutions outside the University of Florida with whom we may collaborate on secondary data analyses will first be de-identified. Thus, no investigators outside the University of Florida will have access to any protected health information collected in this study. Individually identifiable health information will be protected in accordance with the Health Insurance Portability and Accountability Act of 1996. All research personnel will be trained on human participants' protection and HIPAA procedures.

Video recorded data will be used for data analysis conducted by authorized research team members only. No unauthorized individuals can have access to the video recordings. If there is need to use the video for educational purpose, it will not be done until the participants give us written permission. The recordings will be stored in a

locked file cabinet and linked with a code to subject's identity. Participant's name will not be revealed in the videotape. After the data analysis is completed, the video recordings will be retained for one year in case there is a need for go back to the original recording for validation. The video recordings will be destroyed after that.

In Case of Injury: If a participant is injured as a direct result of participation in this study and is clearly in need of immediate emergency treatment, 911 will be called right away. Study physician Dr. Hobbs will be consulted in the case of any injury. In the case of injuries that are not clearly emergencies, the next steps will be taken in accordance with Dr. Hobbs' advice. Efforts will be made to assist participants in obtaining any necessary treatment. If injury is a direct result of study participation, healthcare will be provided at the University of Florida Health Science Center at no charge. The participant and/or his or her insurance carrier will be expected to pay the costs of any further treatment, including any treatment at Shands Hospital. No additional financial compensation for injury or lost wages is available. Participants will not waive their legal rights by participating in this study. Participants will be provided with this information as part of the informed consent process.

9. Possible Benefits

Participants may not benefit directly from study participation. They will receive referral information should they be interested in changing their drinking behavior at the conclusion of the second alcohol drinking session. Participants in the heavy drinker group will also be engaged in a motivational interview including personalized feedback regarding their drinking behavior. Should the participant decide after the first alcohol drinking session not to return for the second session or if the investigators decide in the interim to limit study participation to one session per individual, referral information will be offered by electronic mail or postal mail. For heavy drinking participants in this scenario, a motivational interview will be offered either in person or by telephone. The results of this study could benefit society at large by exploring the possibility of using videotaped topography data as an inexpensive and noninvasive objective measure to indicate AUD. The development of such measures could be widely applied for those who seek more individualized treatment based on their own drinking behavioral patterns.

10. Conflict of Interest

None.

11. Data Safety and Monitoring Plan

Designation of Serious Adverse Events:

Dr. Robert Leeman, the Co-PI in charge of overseeing the data collection, has primary responsibility for monitoring the data, assuring protocol compliance, and conducting regular safety reviews after each alcohol drinking session has been completed. Dr. Leeman will have primary responsibility for distinguishing serious from non-serious adverse events and has sufficient clinical research expertise to make this distinction. In addition to his own experience conducting clinical research for several years, Dr. Leeman will also base determination of serious adverse events on consultation with Co-PI Dr. Xinguang (Jim) Chen, who has over 20 years of clinical and behavioral research experience. In addition, Dr. Leeman will consult with Study Physician Dr. Hobbs regarding medical issues associated with a Serious Adverse Event.

Reporting of Serious Adverse Events

Dr. Leeman will report serious adverse events in writing within 48 hours to the UF IRB 01 following their policies. The investigator will apprise fellow investigators and study personnel of all adverse events that occur during the conduct of this research project through regular weekly study meetings. An annual report will be submitted to UF IRB 01 summarizing all adverse events.

Female participants:

Women who are pregnant or nursing, or who report engaging in sexual activity with an opposite sex partner and refuse to use a reliable method of birth control (e.g., condoms +spermicide; birth control pills, diaphragm) will not be allowed to participate in this study. Urine pregnancy tests will be completed at the in-person screening appointment and at an appointment at the research office just prior to alcohol self-administration.

Supervision of Alcohol Administration Sessions:

The National Advisory Council on Alcohol Abuse and Alcoholism - Recommended Council Guidelines on Ethyl Alcohol Administration in Human Experimentation - Revised May 2005 will be followed. All alcohol drinking sessions will be supervised by Dr. Leeman himself or by a graduate student or other senior research staff member who will be carefully trained in alcohol self-administration methods and this specific protocol. Dr. Leeman will either be present at the alcohol drinking session himself or readily available on call to make any determination regarding serious versus non-serious adverse events. In addition, the Study Physician Dr. Hobbs will be available for consultation as needed. In cases of illness or injury where medical treatment is needed, the necessary treatment will be provided.

Procedures for Data Quality Assurance and Confidentiality:

Data quality will be ensured through training of research staff, the development of data collection tools, and monitoring of data quality. Study staff will monitor the quality of data after completion of each participant. Right to privacy for participation in this research will be protected through coding of data using study-assigned identification numbers and proper storage of research records. Access will be limited to the co-P.I.s and their designates involved in the study. A master list linking participants' names to their study ID numbers will be maintained, but it will be stored in a locked cabinet separate from other study materials. Identifiers will be destroyed when all study activities are completed. Protected health information will not be collected or stored electronically. Web-based data collection using REDCap will be encrypted and stored on secure servers, but will not contain any identifiers. Individually identifiable health information will be protected in accordance with the Health Insurance Portability and Accountability Act of 1996. All research personnel will be trained on human participants' protection and HIPAA procedures.

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