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Translating Preclinical Models of Alcohol Seeking and Consumption into the Human Laboratory using Intravenous Alcohol Self-Administration Paradigms

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Abstract

Preclinical models of Alcohol Use Disorder (AUD) have advanced theoretical, mechanistic, and pharmacological study of the human condition. "Liking" and "wanting" behaviors reflect core processes underlying several models of AUD. However, the development and application of translational models of these preclinical approaches are at an incipient stage. The goal of this study was to examine how intravenous free-access and progressive-ratio, operant-response human alcohol self-administration paradigms can be used as translational human model parallel of preclinical "liking" and "wanting". Participants were 40 adults (Mean age=23.7, SD=2.0; 45% Female) of European descent who reported 12.6 drinking days (SD=5.2) out of the previous 30 (average= 4.1 drinks/drinking day (SD=1.7)). Individuals diverged in their alcohol self-administration behavior, such that free-access and progressive-ratio paradigm outcomes were not significantly correlated (p=.44). Free-access alcohol seeking was related to enjoying alcohol (p<.001), but not craving (p=.48), whereas progressive-ratio seeking at similar levels of alcohol exposure was related to craving (p=.02), but not enjoying (p=.30). Family history of alcoholism, venturesomeness traits, and disinhibition traits were unrelated (p's>.70) to preferred level of breath alcohol concentration (BrAC) in the free-access session, a measure of liking alcohol. Family history of alcoholism, disinhibition traits, and recent drinking history were significantly related (p's<.05) to alcohol seeking in the progressive-ratio paradigm, a measure of wanting

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Author Contributions

Authors' contributions: SO, USZ, MHP, AK and DK conceptualized and conducted the research study. SO, MHP, and AK performed preliminary data analyses. MAC provided the main conceptualization and writing of the manuscript, MHP and MAC provided the reconceptualization, and MAC conducted analyses. MHP, SO, and ZW provided guidance and feedback in structuring the manuscript. All authors approved the final manuscript.

alcohol. We conclude that intravenous alcohol self-administration paradigms show promise in modeling behaviors that characterize and parallel alcohol “liking” and “wanting” in preclinical models. These paradigms provide a translational link between preclinical methods and clinical trials.

Keywords

addiction; alcohol use disorder; human laboratory; intravenous alcohol self-administration

Preclinical models of Alcohol Use Disorder (AUD) have advanced theoretical, mechanistic, and pharmacological study of the human condition. Appetitive behaviors, defined as the seeking or procurement of the substance or “wanting”, and consummatory behaviors, defined as consumption of the substance or “liking”, reflect core processes underlying many theoretical models of substance use disorders [1–3]. However, the development and application of translational models of these preclinical approaches are at an incipient stage. The goal of the current study was to examine intravenous alcohol self-administration paradigms as translational human model parallels of preclinical “liking” and “wanting” behaviors.

Appetitive and consummatory behaviors have been successfully modeled in multiple preclinical studies as separate and distinct responses [4–8]. Rodents that are genetically bred based on alcohol consumption show different wanting and liking behavioral patterns: “Alcohol-preferring” (“P”) rat lines [9] show greater appetitive and consummatory behaviors than other lines, working more and longer in pursuit of alcohol (“wanting”) and consuming more once given the opportunity (“liking”) while High Alcohol Drinking (“HAD”) rats show high “liking” but not high “wanting” of alcohol [10]. Liking and wanting behaviors are differentially influenced by medications in preclinical models [6, 11], suggesting the potential for human interventions to modify separable alcohol seeking behaviors.

“Liking”, commonly measured with alcohol challenge or free-access self-administration, and “wanting”, most directly assessed with progressive ratio and similar operant designs, underlie core features of several prominent models of the development and maintenance of AUD [12–15]. The Incentive Sensitization Theory posits that repeated pleasurable substance use, “liking”, results in eventual “wanting” or craving as induced by the substance and/or the cues associated with it [1, 3]. Koob’s three-stage model of addiction elaborates Incentive Sensitization and seeks to explain the development, maintenance, and course of AUD through three overlapping and recurring stages: (1) *binge/intoxication,* where alcohol seeking and consumption are driven by the rewarding effects of alcohol; (2) *negative affect/ withdrawal,* where alcohol seeking and consumption are driven by avoidance of negative affect or withdrawal symptoms; and (3) *preoccupation/anticipation,* which captures aspects of motivation, and then compulsivity as the individual becomes increasingly preoccupied with obtaining and consuming alcohol despite its negative consequences [2]. Thus, liking is considered indicative of the binge-intoxication stage while wanting reflects preoccupation/ anticipation[2]. “Liking” and “wanting” are then core constructs of AUD development across both preclinical and these clinical models.

Human laboratory alcohol self-administration paradigms could constitute a viable, and objective "bench-to-bedside" platform for testing the efficacy of interventions designed for *specific* seeking behaviors and that have shown promise in preclinical models. However, human laboratory models of distinct behaviors have generally trailed preclinical assessments. In the current study, we employed a within-subject's design to compare drinking behavior using two intravenous self-administration techniques based on the preclinical literature– free-access and progressive-ratio operant response paradigms. We hypothesized that individuals would diverge in their alcohol use behavior, such that the two behaviors would track in the same direction, but not be significantly related to each other.

We conceptualized alcohol "liking" as a free-access paradigm in which participants requested each alcohol reward (an incremental breath alcohol concentration, BrAC, trajectory) through a single button press, yielding an *ad-lib* exposure up to a preset safety limit. Sensation and thrill seeking (i.e., the impulsive tendency to seek out new and exciting experiences and sensations) are thought to be key in alcohol use, including associations with a higher likelihood of drinking more frequently; conceptually linked to repeated exposure ("liking") in the Incentive Sensitization Model [16, 17]. Thus, we hypothesized that the free-access paradigm would correspond with enjoying (but not craving) the alcohol infusion, as well as sensation and thrill seeking traits (e.g., venturesomeness, thrill and adventure seeking, and experience seeking) and total drinks and days drinking in the previous 30 days [2, 16].

We conceptualized alcohol "wanting" as a progressive-ratio, instrumental response paradigm, in which access to an alcohol reward required progressively greater effort over the course of the experiment. More disinhibited, compulsive, and emotion-driven forms of impulsivity relate to more problematic and compulsive alcohol use, including greater alcohol consumption and binge drinking [17–19], linking conceptually to wanting or craving in the Incentive Sensitization Model [1, 3]. Thus, we hypothesized that this progressive-ratio paradigm would correspond to craving (but not enjoying) the alcohol infusion, as well as disinhibited forms of impulsivity (impulsiveness, disinhibition, boredom susceptibility), drinks per drinking day, a history of reported alcohol-related externalizing behaviors, and the participant's biological family history of alcoholism (FHA) [2, 17].

Materials and Methods

Participants

Participants were healthy volunteers enrolled in a larger study (clinicaltrials.gov identifier NCT00681655) recruited through community advertisements. Inclusion criteria included regular moderate-to-heavy drinking (i.e., 3 or more drinks per week) and good health. Since the parent study focused on the expression of specific phenotypes within a shared gene pool, all participants in the current study were of European descent. Exclusion criteria included prior AUD treatment, current/prior history of serious medical conditions including DSM-IV alcohol or drug dependence (but not alcohol abuse), alcohol-induced flushing reactions, or serious psychiatric illness; positive urine drug screen (for substances including cocaine, amphetamine, methamphetamine, tetrahydrocannabinol, methadone, morphine, phencyclidine, barbiturate, benzodiazepine, and tricyclic antidepressants); pregnancy, the

intent to become pregnant, or breast-feeding; any alcohol intake on the day of or day prior to test day; and current use of medications that interact with alcohol.

Procedure

Infusions were achieved using the Computer-assisted Alcohol Infusion System (CAIS) [20] using an IMED GEMINI PC-2TX dual channel volumetric infusion pump. Prior to infusion, the participant's age, height, weight, and sex were entered into the CAIS software, which transforms those measurements into individualized parameters of a physiologically based pharmacokinetic (PBPK) model of alcohol distribution and elimination [21, 22]. CAIS then calculates and updates the infusion rate profile of 6.0% ethanol in half-normal saline required to achieve the same, prescribed *incremental* BrAC trajectory in response to a reward across every individual [20, 23, 24]. Participants performed the free-access paradigm first and the progressive-ratio paradigm within 2 weeks on the same day of the week. On the day of each infusion, participants arrived at the outpatient clinical research center ~7:30 am and provided a BrAC reading and a urine sample for urine pregnancy (women only) and drug testing. Participants were given a light breakfast and fitted with a 20-gauge indwelling intravenous catheter in a vein of the antecubital fossa of the non-dominant arm.

Each experiment began at ~10:00am and ended ~12:30 pm. During each session, participants completed a 2.5-hour voluntary alcohol self-administration of alcohol paradigm, where they were free to request more alcohol, or to refrain from doing so, according to preference. Participants received the video-monitor message that "the bar is temporarily closed" during the 2.5 minutes required for each incremental ascending limb or whenever a new request would have raised the BrAC above the 115 mg/dL preset safety limit. Between rewards, the infusion maintained a constant descending rate of minus 1.0 mg/dL/min as long as was pharmacokinetically possible. BrAC samples were obtained at approximately 15 min intervals by a Draeger Alcotest meter, model 7410 or 6510 (Draeger, Irving, Texas) and not shared with the participant. Once all procedures were complete, participants remained in the clinic until their BrAC was at or below 20mg/dL or 7pm, whichever occurred later; they were then were compensated and dismissed.

Free-access session.—The design of the free-access session allowed participants to achieve their preferred level of BrAC without any required work. This session began with a 30-minute priming interval during which participants were prompted to request an alcohol reward four times in a row, each request made by pressing the button as soon as the BrAC increment peaked. Each request increased the BrAC by 7.5 mg/dL in 2.5 minutes; a linear ascending limb slope of +3 mg/dL per minute for the increment. Thus, the four requests produced a priming alcohol exposure of 30 mg/dL after 10 minutes, followed by a 20-minute break during which the BrAC fell at the prescribed slope, resulting in a target BrAC of approximately 10 mg/dL at the end of the priming interval. The 2-hour, voluntary alcohol self-administration period then began, where a single button-press initiated delivery of the additional alcohol exposure, with the instruction to achieve each participant's typical experience when drinking at a party. In the consequent, self-administered exposure trajectories, each participant's preferred level of BrAC was defined as the average value of CAIS-based BrAC estimates that exhibited the least variance within any 40-minute window

that began when the voluntary self-administration segment of the experiment began and ended 40 min after the last request for additional alcohol was made. See Supplemental Figure 1 for a detailed description of the procedure.

Progressive-work session.—Our progressive-ratio session required participants to complete a progressively larger amount of work to earn successive rewards, up to the point that the work required for alcohol made it difficult or impossible to prevent a BrAC decline. Thus, the procedure optimally yields a "breakpoint" in work, such that participants may decide the amount of work required for the next reward is not worth the effort. An alternative reward was provided (credit for $0.49/work-set); rewards were kept on a single schedule, such that work for either reward would increase the requirement for either successive reward. We included an alternative reinforcer to ensure that effects reported were not due to boredom and so that we could more closely approximate real-life choices between alcohol and money. Our Continuous Attention Task (CAT) [25] was employed as work. To complete a work-set and earn the reward, participants needed to successfully complete a predetermined and escalating number of successful CAT trials. To initiate a work-set, the participant chose the reward to be earned upon completion by pressing a labeled button. To initiate each trial in a set, participants depress and hold the button. An image of the button on the screen changes color to reflect trial onset; after a random interval of 0.5–2.0 seconds, the button image changes color again, signaling the participant to release the button quickly. If the release occurs within the current response window, the trial is counted as a success. Successful trials are counted toward the work-set requirement; per-trial feedback is provided to the participant. The CAT response window adapts after each trial so that approximately 50% of all completed trials are successful, minimizing any effects of learning, distraction, or intoxication. The amplitude of the BrAC increment in this paradigm was scaled such that all participants would need to perform the same amount of work for alcohol to achieve their preferred BrAC, as determined from their free-access session.

Measures

Liking alcohol.—Liking was quantified as the preferred level of BrAC (mg/dL) achieved during the free-access self-administration session.

Wanting alcohol.—Wanting was quantified by the total number of CAT trials completed for the last earned alcohol reward ('breakpoint') in the progressive-ratio paradigm.

Subjective Effects of Alcohol Infusion.—When the participant achieved their apparent preferred level of BrAC, each was asked to rate how much they were *enjoying* the infusion and how much they were *craving* the infusion they were receiving, on a scale of 0–100, using a sliding bar consistent with our prior studies (e.g. [26, 27]).

Recent drinking history.—Recent drinking history during the past month was measured using a 30-day Timeline Followback (TLFB) [28], using standardized procedures: variables extracted comprised the total number of standard drinks, number of drinking days, the mean number of drinks per drinking day, and the maximum number of drinks in one drinking day during the past 30 days.

Family history of alcoholism.—Family history of alcoholism was obtained through the family history module of the Semi-Structured Assessment of the Genetics of Alcohol (SSAGA) [29]. A categorical definition of family history of alcoholism was employed for analysis. To be defined as positive (FHP), a participant had to report at least one first degree biological relative, plus at least one other first or second degree biological relative, with a lifetime history of significant alcohol problems. All others were defined as negative (FHN).

Impulsivity.—Impulsive personality was assessed using the I-7 Impulsiveness Questionnaire [30] and the Sensation Seeking Scale [31]. For the I-7, individual items are marked “yes” or “no” and item responses are summed onto one of three separate subscales: impulsiveness (19 items; alpha=0.73), venturesomeness (16 items; alpha=0.75), and empathy (19 items; alpha=0.68). The Sensation Seeking Scale comprised 40 forced-choice items; individual items are coded so that 1=higher sensation seeking behavior and 0=lower sensation seeking behavior. Items are summed onto one of four 10-item separate subscales: thrill and adventure seeking (alpha=0.72), experience seeking (alpha=0.60), disinhibition (alpha=0.61), and boredom susceptibility (alpha=0.60).

Externalizing behaviors.—Antisocial externalizing behaviors were assessed using a modification of the Section M items from the SSAGA [29] assessing self-reported antisocial behaviors after age 15[32, 33]. Scores were summed to reflect overall externalizing behavior.

Data Analysis Plan

All analyses were conducted in SPSS Version 26. To assess divergence of behavior between paradigms, we examined correlations between the participants’ preferred BrAC in the free-access session and breakpoint for alcohol in the progressive-ratio session. To examine whether free-access responding is associated with liking indicators, we conducted a series of multiple linear regressions with the preferred BrAC as the dependent variable, entering sex first as a covariate. In the first analysis, self-reported subjective effects (enjoyment, craving) at the participant’s preferred level of BrAC were entered as the independent variables. In the second analysis, sensation seeking traits (venturesomeness, thrill and adventure seeking, and experience seeking) were entered in the second step and disinhibition traits (impulsiveness, disinhibition, boredom susceptibility, and externalizing symptoms) in the third step. In the third analysis, total number of drinks and total drinking days were entered into the second step. In the fourth set of analyses, family history of alcoholism was entered in the second step.

To examine whether progressive-ratio responding is associated with wanting indicators, we conducted a series of multiple linear regression analyses with breakpoint as dependent variables and sex as a covariate in the first step. In the first analysis, self-reported subjective effects (enjoyment, craving) of the alcohol infusion, when at the participant’s preferred level of BrAC, were entered as the independent variables. In the second set of analyses, sensation seeking traits (venturesomeness, thrill and adventure seeking, and experience seeking) were entered in the second step and disinhibition traits (impulsiveness, disinhibition, boredom susceptibility, and externalizing symptoms) entered in the third step. In the third set of

analyses, total number of drinks and drinking days in the previous 30 days were entered in the second step. In the fourth set of analyses, family history of alcoholism was included in the second step.

Results

The sample comprised 40 adults (Mean Age=23.7, SD=2.0, 45% Female, 65% FHP). The total sample reported drinking on average 12.6 days (SD=5.2) out of the previous 30, with an average of 4.1 drinks (SD=1.7) reported per drinking day. There were no significant mean differences in recent drinking history, impulsivity, or externalizing behaviors across sex and family history of alcoholism (Table 1).

Divergence of alcohol use behavior

Preferred level of BrAC in the free-access session ranged from 11 to 115 mg/dL (median=92.0 mg/dL). Breakpoint for alcohol from the progressive-ratio session ranged from 0 to 339 CAT trials (median=128 trials). Preferred level of BrAC was not significantly correlated with breakpoint (r= 0.13, p=.44), indicating that although they track in the same direction, these are separable alcohol behaviors (Figure 1). There were no significant differences between men and women on self-administration variables (preferred level t= −1.68, p=.10; breakpoint t= 0.69, p=.69).

Subjective Effects and Alcohol Responding

As hypothesized, preferred level of BrAC was significantly associated with enjoying the alcohol infusion (β=0.55, p<.001), but not with craving (β=0.11, p=.48) when at the preferred level of BrAC in the free-access session (Table 2, top). Also as hypothesized, breakpoint for alcohol was significantly associated with craving (β=0.38, p=.02), but not enjoying the alcohol infusion (β=0.17, p=.30), when at the preferred level of BrAC in the progressive-ratio session (Table 2, bottom).

Free-Access Responding and Liking Indicators

Contrary to hypotheses, impulsivity-related traits were not significantly related to the preferred level of BrAC in the free-access session (venturesomeness set of variables $R^2\Delta$= 0.05, p=.62; disinhibition set of variables $R^2\Delta$= 0.03, p=.93) (Table 3, top). As hypothesized, total number of drinks and drinking days in the previous 30 days were significantly related to the preferred level of BrAC in the free-access session, both as a set ($R^2\Delta$= 0.16, p=.04) and individually, with the total drinks positively associated with preferred level of BrAC (β= 0.56 p=.01) and drinking days negatively associated with preferred level of BrAC (β= −0.47, p=.03; Table 4, top). As hypothesized, family history of alcoholism was not significantly related to preferred level of BrAC in the free-access session (β= 0.04, p=.82; Table 5, top).

Progressive-Ratio Responding and Wanting Indicators

As hypothesized, the set of disinhibition variables were significantly related to breakpoint for alcohol in the progressive-ratio session $R^2\Delta$= 0.32, p=.02), whereas the venturesomeness set was not ($R^2\Delta$= 0.04, p=.72) (Table 3, bottom). Total number of drinks and drinking days in the previous 30 days were significantly related to breakpoint ($R^2\Delta$= 0.22, p=.01)

for alcohol in the progressive-ratio session, but only when included as a set in the model (p's>.20 for beta weight when included together or individually in the model; Table 4, bottom).[a] As hypothesized, family history of alcoholism was significantly related to breakpoint (β= 0.44, p=.005), with FHP performing more work than FHN (Table 5, bottom).

Discussion

Overall, the current study found initial support for the use of intravenous alcohol self-administration free-access and operant-based paradigms to model separate liking and wanting alcohol behaviors in the human laboratory. We perceive that free-access alcohol paradigms have potential as measures of liking behaviors, whereas progressive-ratio paradigms have potential as measures of wanting behaviors.

In the current examination, individuals diverged in their alcohol behavior in the laboratory. These are key human laboratory data that parallel work in preclinical models where consummatory and appetitive behaviors are separable [6, 10]. This divergence in alcohol-related behaviors has been minimally explored in the human laboratory and facilitates translational exploration. For example: if, in an animal model, a drug or intervention influences liking, but not wanting, a similar and parallel behavioral model could be utilized in the human laboratory. Such a paradigm can measure objective behavioral outcomes in clinical trial approaches, without relying on subjective self-report methods[34], which are limited by openness, awareness, and willingness to report, or implicit measures of such constructs [35, 36].

Importantly, our data support that free-access alcohol seeking was related to enjoying the alcohol exposure, but not craving alcohol, whereas progressive-ratio alcohol seeking showed the opposite pattern, further supporting these as behavioral measures tapping into liking and wanting, respectively. None of our participants had an AUD; thus, we cannot speak as to whether or not these intravenous paradigms can be used to assess Koob's AUD stages and associated behaviors. Other studies report some utility in this regard [37]. Our results do provide additional evidence that these laboratory behaviors track with AUD risk factors, as hypothesized. Family history of alcoholism was not related to free-access self-administration of alcohol, but was related to working for alcohol. In a manner similar to the genetically selected Alcohol Preferring (P) rat line[6, 10], our observation suggests that wanting alcohol may correspond with a family history of AUD, whereas liking might not, although this distinction should be examined in larger, more diverse samples. However, High Alcohol Drinking (HAD) rats are also genetically selected, but display more liking, as opposed to wanting, of alcohol[6, 10]. Other studies in humans have documented relationships between free-access alcohol self-administration and family history of alcoholism [24, 38], although with different experimental designs, analyses, and participant characterization approaches.

Findings with impulsivity-related constructs showed mixed results. Contrary to hypotheses, venturesomeness-type constructs were unrelated to free-access alcohol behavior, despite

[a]Breakpoint for alcohol and for money were negatively correlated (r=−.47, p=.002) in the current dataset. Importantly, relationships between risk indicators and breakpoint for money were not significant (p's>.17), suggesting that effects we report are unique to alcohol.

evidence that these types of traits contribute to intoxication and binge like behaviors [16]. Consistent with hypotheses and previous work [17], disinhibition-type constructs were related to progressive amounts of work performed for alcohol. This association suggests stronger associations between AUD risk and progressive-work paradigms as compared to free-access behaviors. However, another study found significant relationships between venturesomeness-type traits and free-access of alcohol in an intravenous paradigm [39]. A newer free-access paradigm, in which participants choose the rate of BrAC change every three minutes [40], may be a better measure of liking behaviors and may show better promise than simple free-access designs [41]. Although drinking frequency and quantity were significantly associated with free-access alcohol administration, only the combination of these two behaviors were associated with progressive-ratio alcohol administration, suggesting that pattern of drinking (for example, binging versus frequent but light drinking) may be more indicative of motivation to work for alcohol.

The current study should be interpreted in light of its limitations. First, due to the genetic focus of the parent study, the sample comprised only those of European descent, making it unclear if findings would generalize to more diverse samples. Second, participants undertook the sessions in a fixed order, which could have influenced behavioral patterns. Third, although intravenous alcohol offers exemplary control over brain exposures to alcohol across participants and sessions, the design and interpretation of alcohol self-administration paradigms are complex and its ecological validity is limited to the ability to achieve BrAC exposures relevant to usual drinking practices [41]. Consequently, ceiling effects, such as those apparent in some participants in our sample, limit the generalizability of our study and the safety limit should be increased in future studies with higher drinking individuals. Nonetheless, use of such paradigms for the human laboratory may be key for assessing experimental control of behaviors and “reward” which is defined by *brain exposure* rather than ingested dose. Future work should include biomarkers of alcohol intake in order to have more confidence in self-reported alcohol patterns of participants and how those might correspond with alcohol responding in the laboratory. Finally, participants’ current AUD “stage” or severity were not clinically assessed, so it cannot be asserted that these paradigms can quantify such characterizations. Testing such a hypothesis would be an important extension for future study.

We conclude that intravenous alcohol self-administration paradigms show initial evidence supporting the Incentive Sensitization Theory and the value of measuring divergent liking and wanting alcohol behaviors in the human laboratory. We perceive utility of these measures for multiple types of research, including using them as a platform for testing the efficacy of preclinical interventions designed to alter *specific* behaviors characterizing the transition from liking to wanting.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

The authors declare that they have no competing interests.

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CAIS is available at cost to investigators interested in the application of intravenous alcohol paradigms to laboratory research; write to mplaweck@iupui.edu

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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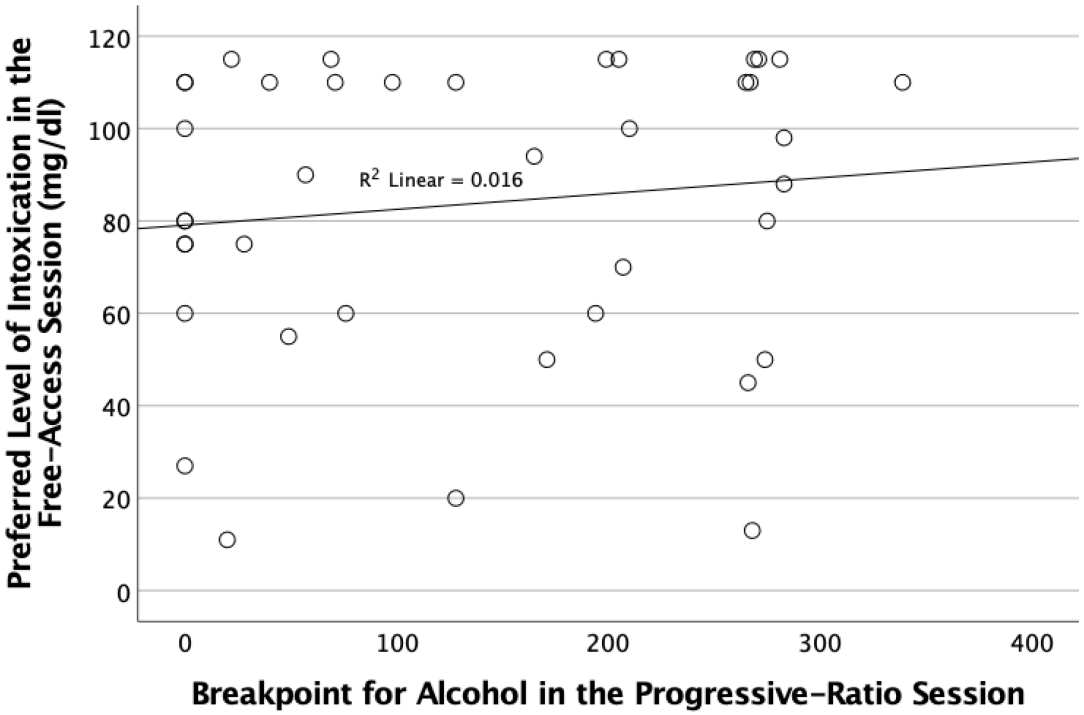

Figure 1.

Plot of 'Liking" Alcohol vs. 'Wanting' Alcohol in same participants. Preferred level of BrAC reached in the free-access session is plotted on the y axis ('liking'). Breakpoint (total CAT trials in the last completed work set for alcohol) in the progressive-ratio work session is plotted on the x axis ('wanting'), Line of best fit is included. Note: Three overlapping sets of individuals are represented in the figure at points (0,75), (0,80) and (0,110).

Table 1

Sample Characteristics, Stratified across Gender and Family History of Alcoholism

	Total Sample (n=40) M(SD)	Men(n=22) M(SD)	Women(n=18) M(SD)	Comparison t(df), p	FHN(n=14) M(SD)	FHP(n=26) M(SD)	Comparison t(df), p
Total drinks in previous 30 days	51.48 (32.31)	58.09 (38.51)	43.39 (20.91)	1.45(38), .16	50.64 (27.56)	51.92 (35.12)	−0.12(38), .91
# of drinking days in previous 30 days	12.60 (5.18)	12.50 (5.53)	12.72 (4.89)	0.13(38), .90	12.36 (5.80)	12.73(4.94)	−0.22(38), .83
Average drinks/ drinking day	4.53 (1.84)	3.59 (1.38)	2.22 (2.21)	1.79(38), .08	4.26 (1.64)	4.02 (1.76)	0.42(38), .68
Maximum # of drinks in one drinking day	9.00 (5.00)	9.68 (5.83)	8.17 (3.68)	0.96(38), .35	9.64 (5.21)	8.65 (4.92)	0.59(38), .56
Impulsiveness (Eysenck)	8.28 (3.65)	8.40 (3.24)	8.13 (4.23)	0.22(34), .83	8.00 (3.02)	8.42 (3.99)	−0.32(34), .75
Venturesomeness (Eysenck)	11.97(2.57)	12.55 (1.91)	11.25 (3.13)	1.54(34), .13	11.83 (3.16)	12.04 (2.29)	−0.23(34), .82
Empathy (Eysenck)	12.19 (3.76)	11.85 (3.86)	12.63 (3.70)	0.61(34), .55	11.67 (4.92)	12.46 (3.53)	−0.59(34), .56
Thrill/Adventure Seeking (Zuckerman)	8.33 (2.06)	8.70 (1.72)	7.88 (2.39)	1.20(34), .24	8.33 (2.19)	8.33 (2.04)	0.00(34), 1.00
Experience/ sensation seeking (Zuckerman	5.94 (2.03)	5.88 (1.96)	6.00 (2.13)	0.18(34), .86	6.00 (2.13)	5.92 (2.02)	0.12(34), .91
Disinhibition (Zuckerman)	7.06 (2.00)	7.15 (2.13)	6.94 (1.88)	0.31(34), .76	7.33 (2.23)	6.92 (1.91)	0.58(34), .56
Susceptibility to boredom (Zuckerman)	3.81 (2.14)	3.95 (2.19)	3.63 (2.13)	0.45(34), .66	4.58 (2.02)	3.42 (2.13)	1.58(34), .12
Externalizing behaviors	4.33 (3.83)	5.00 (4.46)	3.50 (2.76)	1.18(34), .24	4.08 (4.32)	4.32 (3.65)	−0.27(34), .79

Note: FHN=Family history of alcoholism negative; FHP=Family history of alcoholism positive

Table 2

Hierarchical Regressions with Subjective Effects of Alcohol at Preferred Level of BrAC

		B	SE	*β*	*p*	R^2	$R^2\Delta$	*p*
DV: Preferred Level of BrAC from the Free-Access Session								
Step 1						.07	.07	.10
	Sex	16.36	9,73	.26	.10			
Step 2						.42	.35	<.001*
	Sex	10.55	8.66	.17	.23			
	Enjoying the alcohol infusion	1.03	.26	.55	<.001			
	Craving the alcohol infusion	.21	.30	.11	.48			
		B	SE	*β*	*p*	R^2	$R^2\Delta$	*p*
DV: Breakpoint from the Progressive-Ratio Session								
Step 1						.01	.01	.60
	Sex	−19.69	36.83	−.09	.60			
Step 2								
	Sex	−33.50	33.82	−.15	.33	.22	.21	.01*
	Enjoying the alcohol infusion	1.03	.99	.17	.30			
	Craving the alcohol infusion	2.05	.85	.38	.02*			

Table 3

Hierarchical Regressions with Liking and Wanting Indicators

		B	SE	*β*	*p*	R^2	$R^2\Delta$	*p*
DV: Preferred Level of BrAC in the Free-Access Session								
Step 1						.03	.03	.30
	Sex	9.73	9.22	.18	.30			
Step 2						.09	.05	.62
	Sex	12.63	9.73	.23	.20			
	Venturesomeness	−1.12	3.09	−.10	.72			
	Thrill and Adventure Seeking	−1.97	3.83	−.15	.61			
	Experience Seeking	1.40	2.40	.10	.57			
Step 3						.03	.03	.30
	Sex	13.98	10.49	.26	.19			
	Venturesomeness	−.84	3.3	−.08	.80			
	Thrill and Adventure Seeking	−2.64	4.49	−.27	.43			
	Experience Seeking	2.45	2.87	.18	.40			
	Impulsiveness	−.63	1.46	−.08	.67			
	Disinhibition	.85	2.93	.06	.77			
	Boredom Susceptibility	−2.61	3.05	−20	.40			
	Externalizing	.25	1.49	.03	.87			
		B	SE	*β*	*p*	R^2	$R^2\Delta$	*p*
DV: Breakpoint for Alcohol in the Progressive-Ratio Session								
Step 1						.01	.01	.58
	Sex	−21.50	38.11	−.10	.58			
Step 2						.05	.04	.72
	Sex	−28.41	40.42	−.13	.49			
	Venturesomeness	13.10	12.87	.30	.32			
	Thrill and Adventure Seeking	−13.01	15.93	−.24	.42			
	Experience Seeking	4.94	10.00	.09	.63			
Step 3						.37	.32	.02*
	Sex	−37.21	36.21	−.17	.31			
	Venturesomeness	11.28	11.39	.26	.33			
	Thrill and Adventure Seeking	−22.77	15.49	−.42	.15			
	Experience Seeking	7.28	9.89	.13	.47			
	Impulsiveness	−2.11	5.04	−.07	.68			
	Disinhibition	8.58	10.10	.15	.40			
	Boredom Susceptibility	−21.99	10.52	−.42	.05			
	Externalizing	16.55	5.13	.56	.003*			

Note: Statistics presented are from the final step of the model

Table 4

Hierarchical Regressions with Recent Drinking History

		B	SE	*β*	*p*	R^2	$R^2\Delta$	*p*
DV: Preferred Level of BrAC from the Free-Access Session								
Step 1						.07	.07	.10
	Sex	16.36	9.73	.26	.10			
Step 2						.23	.16	.04*
	Sex	7.68	9.69	.12	.43			
	Total drinks in the last 30 days	.55	.21	.56	.01*			
	Drinking days in the last 30 days	−2.87	1.26	−.48	.03*			
		B	SE	*β*	*p*	R^2	$R^2\Delta$	*p*
DV: Breakpoint from the Progressive-Ratio Session								
Step 1						.01	.01	.60
	Sex	−19.69	36.83	−.08	.60			
Step 2						.23	.22	.01*
	Sex	−33.38	35.48	−.15	.35			
	Total drinks in the last 30 days	1.01	.76	.28	.19			
	Drinking days in the last 30 days	5.08	4.62	.23	.28			

Table 5

Hierarchical Regressions with Family History of Alcoholism

		B	SE	*β*	*p*	R^2	$R^2\Delta$	*p*
DV: Preferred Level of BrAC from the Free-Access Session								
Step 1						.07	.07	.10
	Sex	16.36	9,73	.26	.10			
Step 2						.07	.001	.82
	Sex	16.67	9.95	.27	.10			
	Family history of alcoholism	2.37	10.38	.04	.82			
		B	SE	*β*	*p*	R^2	$R^2\Delta$	*p*
DV: Breakpoint from the Progressive-Ratio Session								
Step 1						.01	.01	.60
	Sex	−19.69	36.83	−.09	.60			
Step 2						.20	.19	.01*
	Sex	−5.97	33.87	−.03	.86			
	Family history of alcoholism	104.46	35.35	.44	.01*			