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Reward, Relief, and Habit Drinking Profiles in Treatment Seeking Individuals with an AUD

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Abstract:

Aims: This study aimed to compare reward, relief, and habit treatment-seeking individuals on recent drinking, AUD phenomenology, and mood. The second aim of the study was to evaluate the predictive validity of reward, relief, and habit profiles.

Method: Treatment-seeking individuals with an AUD (n=169) were recruited to participate in a medication trial for AUD (NCT03594435). Reward, relief, and habit drinking groups were assessed using the UCLA Reward Relief Habit Drinking Scale. Group differences at baseline were evaluated using univariate analyses of variance. A subset of participants were enrolled in a 12-week, double-blind, placebo-controlled medication trial (n=102), and provided longitudinal drinking and phenomenology data. The predictive validity of group membership was assessed using linear regression analyses.

Results: At baseline, individuals who drink primarily for relief had higher craving and negative mood than those who drink for reward and habit. Prospectively, membership in the relief drinking group predicted greater alcohol use, greater heavy drinking, and fewer days abstinent compared to those in the reward drinking group. Membership in the relief drinking group also predicted greater alcohol craving, more alcohol-related consequences, and more anxiety symptoms over 12 weeks compared to those in the reward drinking group.

Conclusion: This study provides support for reward and relief drinking motive profiles in treatment-seeking individuals with an AUD. Membership in the relief drinking motive group was predictive of poorer drinking outcomes and more negative symptomology over 12 weeks, indicating that individuals who drink for relief may be a particularly vulnerable sub-population of individuals with AUD.

Running Title: Reward, Relief, and Habit in Treatment-Seekers

Short Summary: Reward and relief drinking motivation profiles were found in treatment-seeking individuals with an AUD. Membership in the relief drinking motive group was predictive of poorer drinking outcomes and more negative symptomology over 12 weeks, indicating that individuals who drink for relief may be a vulnerable sub-population of individuals with AUD.

Introduction

Alcohol use disorder (AUD) is a chronic, relapsing disease, often characterized by continued use despite adverse consequences. AUD is highly heterogenous, leading to varying clinical presentations (Litten et al., 2015). A diagnosis of AUD in the Diagnostic and Statistical Manual of Mental Disorders – 5 (DSM-5) can be met by endorsing as few as two and as many as 11 AUD criteria, with criteria ranging from physiological symptoms (i.e., tolerance and withdrawal) and social, interpersonal, and employment problems associated with use, to psychological phenomena (e.g., craving) (MacKillop et al., 2022). Therefore, individuals with the same diagnosis and same mental health condition can vary widely in their experience of AUD. As such, probing the heterogeneity of AUD is crucial to identify subgroups of individuals with the end goal of personalizing treatment for AUD.

One recent approach to understanding AUD heterogeneity is by separating motivations for drinking into reward, relief, and potentially habit categories. Reward drinkers are individuals who drink primarily for the pleasurable, rewarding effects of alcohol, or in other words, individuals who drink to feel good (Grodin et al., 2019). In contrast, relief drinkers are individuals who drink primarily to relieve negative affect, stress, and/or withdrawal symptoms, or in other words, individuals who drink to stop feeling bad (Grodin et al., 2019). Habit drinkers are individuals who primarily drink out of automaticity, in other words, out of routine or habit (Grodin et al., 2019). There are corresponding neurobiology and theoretical addiction models which are thought to underly reward, relief, and habit drinking profiles. One such model is the allostatic model of addiction, which is a framework of three stages of the addiction cycle: binge/intoxication, negative affect/withdrawal, and preoccupation/anticipation (Koob and Volkow, 2016a). The binge/intoxication stage, which corresponds most closely with the reward drinking profile, characterizes initial use, reflecting the rewarding effects of drugs and the development of incentive salience. This stage is mediated by changes in dopaminergic and opioidergic pathways in the basal ganglia. The negative affect/withdrawal stage, which corresponds most closely to the relief drinking profile, is characterized by increases in negative emotional states, dysphoria, stress, and withdrawal symptoms. The negative affect/withdrawal stage is mediated by the recruitment of stress-related neurocircuitry, including the extended amygdala, and stress-related neurotransmitters. Additionally, in this stage, the rewarding effects of alcohol diminish, and are thought to be replaced by increased dopaminergic and glutamatergic signaling in the dorsal striatum, contributing to habit and automaticity (Kalivas and Volkow, 2005; Robinson and Berridge, 1993). The preoccupation/anticipation stage reflects craving and increases in executive dysfunction, involving the dysregulation of prefrontal circuitry (Koob and Volkow, 2016a). While there is not a direct one-to-one correspondence between the allostatic model and the reward, relief, and habit profiles, the model provides a template to promote the understanding of these drinking profiles.

Several studies have found that the characterization of individuals by drinking motivation holds promise for precision medicine. These studies have largely used a more complex drinking motivation phenotyping method which derives four

phenotypes: high reward/high relief, high reward/low relief, low reward/high relief, and low reward/low relief. Naltrexone, an opioid antagonist, blunts alcohol-induced dopamine release (O'Malley et al., 1992), and therefore, may be an effective treatment for those motivated by alcohol's rewarding effects. Indeed, studies have shown that individuals who primarily drink for reward (e.g., high reward/low relief) show a more favorable response to treatment with naltrexone compared to those treated with placebo (Mann et al., 2018; Votaw et al., 2022; Witkiewitz et al., 2019a). However, one study did not find differences in naltrexone response among motivation to drink profiles (Roos et al., 2017). Conversely, acamprosate, which is thought to modulate glutamate transmission (Mann et al., 2009), may be more effective for those who drink for relief. One study found a benefit of acamprosate for those who drink for relief motives (e.g. high relief/moderate reward; (Roos et al., 2017)), while another study found a benefit of acamprosate for those who drink for reward motives (e.g. high relief/low reward; (Votaw et al., 2022)). While these studies have identified potentially useful drinking motivation profiles, they have largely used advanced methodological techniques, such as latent variable mixture models, to profile individuals, which limits implementation into clinics.

As such, our group developed and validated a brief, four-item measure to create reward, relief, and habit drinking motivation profiles (Grodin et al., 2019). This scale was designed with clinical translation in mind, such that complicated scoring metrics were not required to profile individuals by drinking motivation. The measure was initially tested in a laboratory-based sample of non-treatment-seeking heavy drinkers and was validated in a larger crowdsourced sample of heavy drinkers. We found that in non-treatment-seekers, the majority (71%) of the sample was classified as individuals who drank for reward, with a minority of the sample classified as individuals who drank for relief (13%) or habit (15%). Individuals who drank for reward were dissociable from those who drink for relief and habit motives; however, individuals who drink for habit and relief motives were not dissociable from one another. Specifically, those who drank for reward motives endorsed drinking for enhancement, while those who endorsed drinking for relief motives endorsed drinking for coping. Furthermore, those who drank for relief and habit motives had higher depressive symptomology and trait anxiety, and greater craving than those who drank for reward motives (Grodin et al., 2019). Those who drank for relief or habit motives also reported a greater decrease in negative mood during an experimental alcohol administration session compared to those who drank for reward motives (Grodin et al., 2019).

Importantly, non-treatment-seeking individuals differ from treatment-seeking individuals on a host of demographic and clinical factors, including age, severity of AUD, duration of AUD, alcohol consumption, subjective craving, and alcohol related-consequences (Ray et al., 2017; Venegas and Ray, 2020). Not only do treatment-seekers and non-treatment-seekers differ on clinical factors, but these same clinical factors are predictors of clinical outcomes during treatment (Ray et al., 2017), highlighting the significance of these factors. Given these notable sample differences, it is critical to evaluate reward, relief, and habit drinking profiles in a treatment-seeking sample, to complement previous work tested in a non-treatment-

seeking sample. Beyond evaluating drinking motivation profiles in treatment-seekers, it is also critical to investigate the predictive validity of these drinking motivation profiles to understand the clinical significance of these subtypes.

This study sought to evaluate reward, relief, and habit drinking motivation profiles in a treatment-seeking sample. The first aim of the study was to compare individuals who drink for reward, relief, and habit motives on quantity and frequency of recent drinking, AUD phenomenology, and mood at baseline. We hypothesized that those who drink for relief and habit motives would have more severe AUD, while those who drink for reward would consume more alcohol. We also hypothesized that those who drink for relief motives would report more negative mood, anxiety, and depression symptoms relative to those who drink for reward and habit motives. The second aim of the study was to evaluate the predictive validity of reward, relief, and habit motivation profiles. To do so, we tested if drinking group membership predicted alcohol use, craving, alcohol-related consequences, and anxiety and depression symptomology 3 months later. We hypothesized that membership in the relief and habit drinking motivation groups would predict more drinking, craving, and alcohol-related consequences compared to those who drink for reward motives.

Methods

Participants and design

Treatment-seeking individuals with an AUD (n=169) were recruited between 2018-2022 to participate in a medication trial for AUD (NCT03594435). Initial eligibility screening was conducted through telephone interviews and was followed by an in-person screening. After providing written informed consent, participants were breathalyzed, provided urine for toxicology screening, and completed a battery of self-report questionnaires and interviews. All participants were required to have a breath alcohol content (BrAC) of 0 mg% and to test negative on a urine drug screen for all drugs (except cannabis). Female participants were required to test negative on a urine pregnancy test. Data from the initial eligibility screening and from the medication trial were used for this study.

A subset of participants were enrolled in the 12-week, double-blind, placebo-controlled medication trial of ibudilast (n=102). Participants in the trial were followed for 12 weeks to assess drinking, mood, and craving over the course of the trial. Results from this trial are reported elsewhere (Ray et al., under review) and medication condition was controlled for in all prospective analyses. For participants who were enrolled in the medication trial, inclusion criteria included: (1) between the ages of 18-65; (2) moderate-to-severe AUD; (3) drinking ≥14 drinks/week for males, or ≥7 drinks/week for females; and (4) treatment-seeking for AUD. Exclusion criteria included: (1) recent suicide attempts or active suicidal ideation; (2) current substance use disorder diagnosis (other than alcohol or nicotine); (3) lifetime diagnosis of schizophrenia, bipolar disorder, or any psychotic disorder; (4) significant alcohol withdrawal symptoms as determined by a score >10 on the

Clinical Institute Withdrawal Assessment – Alcohol Revised (CIWA-Ar (Sullivan et al., 1989)); (5) current use of medication for AUD or psychotropic medication usage (excluding stable antidepressants). This study was approved by the Institutional Review Board at University of California, Los Angeles (UCLA).

Measures

Reward Relief Habit

Reward, relief, and habit drinking groups were assessed using the UCLA Reward Relief Habit Drinking Scale (UCLA RRHDS (Grodin et al., 2019)). The UCLA RRHDS is a brief, four-item self-report questionnaire which asks participants to identify their primary motivation for drinking (i.e., reward, relief, or habit). As with our prior work (Grodin et al., 2019), participants were classified into groups based on their ratings of drinking for reward, relief, and habit. In brief, participants were classified based on their answers to questions 2-4, in which they rated how often they drank for reward, relief, or habit motivations, where the highest scoring item was used to determine drinking motivation. Question 1 was used as a tie-breaker in cases where a participant rated more than 1 dimension as the highest, which was required for 37.3% of the participants.

Drinking Measures

At baseline, the 30-day Timeline Followback (TLFB) interview was used to assess recent drinking (Sobell et al., 1988). Over the course of the trial, participants completed TLFB interviews every two weeks (in person at weeks 4, 8, and 12; over the phone at weeks 2, 6, and 10). For this study, drinking both at baseline (past 30 days) and over the trial (12 weeks) were assessed. Several metrics of drinking were calculated including total number of drinks consumed, number of drinks per drinking day (DPDD), percent heavy drinking days (PHDD; defined as a drinking day with ≥5 drinks for males and ≥4 for females), and percent days abstinent (PDA).

AUD Diagnosis and Severity

The Structured Clinical Interview for DSM-5 (SCID) assessed for current (past 12-month) AUD (First, 2014). Symptom count was used as a measure of AUD severity. Participants also completed the Alcohol Use Disorders Identification Test (AUDIT (Allen et al., 1997)) as a secondary measure of AUD severity. Alcohol-related consequences were assessed through the ImBIBe (Werner et al., 2008), an abbreviated form of the Drinker Inventory of Consequences (Miller, 1996). Past week craving for alcohol was assessed through the Penn Alcohol Craving Scale (Flannery et al., 1999). The ImBIBe and PACS measures were collected at baseline and at week 12.

Mood

The Beck Anxiety Inventory (BAI) was used to assess past week anxiety symptoms (Beck et al., 1988). The Beck Depression Inventory-II (BDI-II) was used to assess past two-week depressive symptomatology (Beck et al., 1996). The Profile of Mood States (POMS) was used to assess transient mood state across four

dimensions: negative mood, positive mood, tension, and vigor (McNair, 1992). All mood measures were assessed at baseline and at week 12.

Individual Difference

The Fagerstrom Test for Nicotine Dependence (FTND) assessed for nicotine dependence (Heatherton et al., 1991) and was used to classify smoking status based on question 1, which assessed frequency of smoking (daily, occasionally, never). Demographic characteristics were assessed via the NIH Demographic Questionnaire.

Data Analysis

All analyses were conducted in SPSS v. 28. Baseline analyses were conducted on all participants who completed the baseline screening visit (n=174). Predictive validation analyses were conducted on participants who were randomized in the medication trial (n=102).

For the baseline analyses, univariate analyses of variance (ANOVAs) were conducted to evaluate group differences. Post-hoc t-tests were conducted to evaluate the direction of differences between the reward, relief and habit groups. As there were three areas of interest (recent drinking, AUD severity/phenomenology, and mood), a Bonferroni correction was applied, such that a corrected p-value of 0.017 was considered significant (0.05/3). Age and sex were included as covariates.

To examine the predictive validity of reward, relief, and habit group membership, linear regression analyses were conducted. Separate linear regressions were run examining alcohol use outcomes (total drinks consumed, DPDD. PHDD, and PDA), alcohol phenomenology outcomes (PACS for alcohol craving, and ImBIBe for alcohol-related consequences), and mood outcomes (BDI-II and BAI). All models examined the main effect of reward, relief, and habit group membership, controlling for age, sex, and medication condition. For these analyses, the reward group was selected as the reference group. Additional analyses were conducted with relief and habit groups as the reference groups (see Supplement Tables S2-S5). Multiple imputation was used to account for missing data due to drop-out in the trial (n=23; 22.5%) in the linear regression (predictive validity) analyses. Specifically, 5 imputations were performed using fully conditional specification, which is a Markov Chain Monte Carlo method. Participants with and without missing data were compared on baseline demographic and clinical characteristics (see Supplement **Table S1**). Participants without missing data were significantly older and had a higher proportion of non-smokers than participants with missing data.

Results

Participant Characteristics

Participants did not differ on baseline demographic characteristics (age, sex, or race and ethnicity) across reward, relief, and habit drinking subgroups. There were also no group differences on cigarette smoking status or on urine THC.

Participants did differ on their continuous ratings of drinking for reward, relief, and habit, as anticipated by their self-identification. Individuals who drank for reward scored higher than those who drank for relief and on reward drinking (ps < 0.001). Individuals who drank for relief scored higher on relief drinking than those who drank for reward and habit (ps < 0.001). Individuals who drank for habit had higher habit drinking than those who drank for reward and relief (ps < 0.001).

Table 1 Here.

Baseline Validation

For the full sample (n=169), there were significant differences between reward, relief, and habit drinking motive groups in recent alcohol craving, measured by the PACS, such that individuals who drank for reward had significantly lower craving than those who drank for relief (mean difference=-5.66, 95% CI[-8.33, -2.99], p<0.001) and habit (mean difference=-2.52, 95% CI[-4.66, -0.38], p=0.02), and those who drank for habit had significantly lower craving than those who drank for relief (mean difference=-3.14, 95% CI[-5.91, -0.47], p=0.03). There were also significant group differences in the POMS tension and happy subscales. Specifically, individuals who drank for relief reported significantly more tension than those who drank for reward (mean difference=-0.51, 95% CI[-0.79, -0.24], p<0.001) and habit (mean difference=-0.47, 95% CI[-0.76, -0.18], p=0.002). Conversely, individuals who drank for relief reported less happiness than those who drank for reward (mean difference=-0.53, 95% CI[-0.89, -0.17], p=0.004) and habit ((mean difference=-0.39, 95% CI[-0.77, -0.02], p=0.04). Individuals who drank for reward, relief, and habit motives did not differ on any recent drinking variables, as measured by the 30-day TLFB interview, after controlling for multiple comparisons. Without correction, individuals who drank for relief had higher percent days abstinent relative to those who drank for habit. Groups also did not differ on AUD severity as measured by AUD DSM-5 symptom count and AUDIT scores. While not significant after correcting for multiple comparisons, individuals who drank for relief reported more alcohol-related consequences than those who drank for reward. Groups did not differ in anxiety or depression symptomology (see **Table 2**).

Table 2 Here.

Prospective Validation

Linear regression models examining the predictive validity of reward, relief, and habit drinking groups at 12 weeks for randomized participants (n=102) are presented in **Table 3** (drinking) and **Table 4** (phenomenology) and in the Supplementary Materials (**Tables S2-S5)**. Group membership significantly predicted drinking over the course of the 12-week trial, controlling for age, sex, and medication. Specifically, membership in the relief drinking group predicted greater number total drinks consumed (*b*(SE)=90.36(31.97), p=0.03), higher percent heavy drinking days ((*b*(SE)=0.12(0.06), p=0.04), and lower percent days abstinent ((*b*(SE)=-0.20(0.07), p=0.005), compared to membership in the reward group. Membership in the habit drinking group predicted greater total drinks consumed

((*b*(SE)=73.91(36.24), p=0.04), compared to membership in the reward drinking group. Medication was not a significant predictor in any drinking model (see **Table 3**). When habit was the reference group, membership in the reward drinking group was predictive of total drinks consumed (p=0.04), but no other drinking outcomes were significant (**Table S4**).

Table 3 Here.

Group membership also significantly predicted alcohol craving, anxiety symptoms, and alcohol-related consequences over the course of 12-weeks. Specifically, membership in the relief drinking group predicted higher alcohol craving (*b*(SE)=3.09(1.34), p=0.02), greater anxiety symptoms (*b*(SE)=3.29(1.60), p=0.04), and greater alcohol-related consequences (*b*(SE)=6.25(2.64), p=0.02), compared to those in the reward drinking group. Group membership did not predict depressive symptomology. Medication was not significant for any models (see **Table 4**). When habit was the reference group, membership in the relief drinking group significantly predicted greater craving and anxiety symptomatology (p's <0.02) and predicted alcohol-related consequences at trend-level (p=0.09; **Table S5**).

Table 4 Here.

Discussion:

This study sought to characterize reward, relief, and habit drinking profiles in treatment-seeking individuals with an AUD. At baseline, individuals who drank for relief had higher craving and negative mood than those who drank for reward and habit. Prospectively, membership in the relief drinking motivation group predicted greater alcohol use, greater heavy drinking, and fewer days abstinent compared to membership in the reward drinking group over 12 weeks. Membership in the relief drinking group also predicted greater alcohol craving, more alcohol-related consequences, and more anxiety symptoms compared to membership in the reward and habit drinking groups over 12 weeks.

In partial support of our hypotheses, treatment seeking individuals with an AUD who drank for relief motives, and to some extent, habit motives, were distinguishable from those who drank for reward motives on craving and mood at baseline. Specifically, there was a medium effect of drinking motivation group on craving at baseline, such that individuals who drank for relief had the highest ratings of craving relative to those who drank for habit and reward; while individuals who drank for habit motives had higher craving than those who drank for reward. This extends our previous work in non-treatment-seekers, where significant differences were only found between those who drank for reward and relief motives (Grodin et al., 2019). Differences in baseline craving between drinking motive groups is in line with the allostatic model of addiction, where the *a-process*, consists of alcohol use motivated by reward, and the *b-process* consists of alcohol use motivated by relief from negative hedonic responses. Importantly, in the allostatic model, individuals transition from the *a-process* to the *b-process* and as such craving during the *b-process* is expected to be greater (Koob, 2013). In support of

the validity of the reward, relief, and habit drinking motive profiles, individuals who drank for relief motives had significantly greater baseline POMS tension (medium effect) and lower positive mood subscale scores (small effect) relative to those who drank for reward and habit motives. Similar patterns, although trend-level, were found for POMS negative mood and vigor sub-scales. In line with our findings in non-treatment-seekers (Grodin et al., 2019), reward, relief, and habit drinking motive profiles did not differ on recent drinking frequency or quantity or on AUD severity. This suggests that these drinking motivation profiles represent a construct, or potentially a phenotype, that is distinguishable from AUD severity and recent drinking patterns. Other studies have used an alternate phenotyping approach for reward and relief drinking, which highlights levels of reward and relief, and does not include habit. Using this approach, Votaw et al. (2022) found that individuals in the high reward/high relief subgroup were younger and drank more at baseline than those who endorsed low reward (low reward/high relief; low reward/low relief). Moreover, they found that individuals who endorsed high relief motives (high relief/low reward; high relief/high reward) had greater alcohol use severity, as indicated by AUDIT and ADS scores, higher craving, and more depressive and anxiety symptomology compared to low relief individuals. While the grouping methods differ between the present study and the study by Votaw et al. (2022), there are consistent indications that individuals who drink primarily for relief have higher craving and more mood-related symptoms than individuals who drink primarily for reward. However, results surrounding alcohol consumption and AUD severity measures seem to differ depending on if individuals are grouped by primary drinking motivation or by the four-class level approach.

Prospectively, membership in the relief drinking group predicted more drinking, greater craving, more alcohol-related consequences, and more anxiety at the 12-week follow-up and across medication conditions. Specifically, those in the relief drinking group had a greater number of total drinks, more heavy drinking, and less abstinence 12-weeks following the initial assessment relative to those in the reward and habit drinking groups. In the context of this treatment study, these findings suggest that individuals who drank for relief responded more poorly to treatment, with ibudilast or placebo, across the 12-week trial (Ray et al, under review). This set of findings align with previous work indicating that drinking for the positive or enhancing effects of alcohol is indicative of an earlier stage, or less severe presentation, of AUD (Koob, 2013). Other work has found that enhancement motives (i.e., drinking for reward) are associated with binge drinking, whereas coping motives (i.e., drinking for relief) are associated with alcohol-related consequences (Cooper et al., 2016a). It should be noted that in this study, all participants, including those who endorsed drinking primarily for reward, had at least a moderate AUD, and as such, were endorsing several diagnostic criteria of AUD.

One additional goal of this study was to test reward, relief, and habit drinking groups in a treatment-seeking sample to determine if habit drinking was distinguishable from relief drinking. In our previous work with non-treatment-seeking individuals with and without AUD, habit and relief drinking were not

distinguishable (Grodin et al., 2019). In the present study, we found some group differences between drinking motivation groups at baseline, such that individuals who drank for relief reported more tension and lower positive mood relative to those who drank for reward and habit, and all groups differed on craving, such that individuals who drank for reward motives had the lowest craving, followed by those who drank for habit, and individuals who drank for relief reporting the highest craving. The prospective validation found that membership in the relief drinking group was predictive of worse outcomes for craving, anxiety, and alcohol-related consequence outcomes, relative to the reward and habit drinking groups . Membership in the relief drinking group was predictive of worse drinking outcomes, but only relative to the reward group, as it was not predictive when the habit group was used as the reference group. This set of findings indicates that individuals with a relief drinking motivation do differ from individuals with a habit drinking motivation to predict alcohol-related phenomenology, but not as a predictor of actual alcohol consumption. Moreover, groups did not differ on AUD-severity, which does not align with predictions from the addiction cycle (Koob and Volkow, 2016b), where individuals who drink for reward would be hypothesized to be less severe than those who drink for relief who would be less severe than those who drink for habit.

Relatedly, the study findings call into question the conflation of habit with compulsivity. Compulsivity has been defined as an action which is repeated and persistent despite negative consequences, and is thus thought of as the end-stage of addiction (Burchi et al., 2019; Everitt and Robbins, 2005). In contrast to compulsion, habits (i.e., automation of behavior based on reinforcement learning), are more automatic, modifiable, and may be unrelated to the expected reward value of the substance (Everitt and Robbins, 2016; Hogarth, 2020) . The transition from reward-motivated drinking to consequence-resistant drinking, has been characterized as a transition from goal-directed behavior to habitual behavior (Gillan et al., 2016). However, recent work has questioned the conflation of habit and compulsivity as well as the role of habits in the development of AUD and addiction (Hogarth, 2020; Vandaele and Ahmed, 2021). It may be the case that while the two constructs are related, they occur in a sequential order in addiction, such that habit may serve as the building blocks for compulsive alcohol drinking (Everitt and Robbins, 2016). In line with this view, there were not significant group differences in alcohol-related consequences between individuals who drank for reward, relief, and habit motives. Qualitatively, individuals who drank for relief reported the highest number of alcohol-related consequences, followed by those who drank for habit, suggesting that those reporting habitual drinking do not have more “compulsive” or aversion-resistant alcohol seeking than those who drank for relief. Moreover, membership in the relief group was predictive of greater number of alcohol-related consequences over 12-weeks, relative to the habit group; further suggesting that habit is not the same as compulsivity. Our previous work has also failed to find associations between behaviorally-driven measures of habit and alcohol problem severity and recent alcohol consumption (Ray et al., 2020).

Finally, it is important to consider the clinical implications of these findings in regards to treatment planning. Overall, this study found that individuals with relief drinking motivations endorsed the most craving symptoms at baseline, and membership in this group was predictive of more craving during the 12-week longitudinal study, relative to both individuals with reward and habit drinking motivations. These findings suggest that craving may be a key treatment target for individuals who drink for relief. There are a number of promising pharmacotherapies which may be particularly beneficial for relief craving including pregabalin (Martinotti et al., 2013b), esketamine (Martinotti et al., 2021), and gabapentin (Mason et al., 2018), in addition to acamprosate which is already FDA-approved for AUD (Roos et al., 2017). Ibudilast, the pharmacotherapy used for the parent trial, may also be beneficial for individuals who experience greater withdrawal symptoms (Cooper et al., 2016b), thereby driving drinking to relieve withdrawal symptoms. However, the present study is underpowered to test this hypothesis and future work will be needed with larger samples to examine this question. These precision medicine questions are particularly important for individuals who drink for relief, as they consistently show worse outcomes when examined prospectively (Hebden et al., 2024).

The findings of this work should be interpreted in line with its strengths and limitations. Study strengths include the inclusion of a diverse, treatment-seeking sample, which increases the generalizability of the study findings, the use of a brief measure with easy clinical implementation, and the inclusion of a 12-week follow-up period. Study limitations include the single-time point collection of the UCLA RRHDS, thus limiting our ability to test the stability of reward, relief, and habit drinking motivation profiles throughout the study. Recent work has examined the stability of other assessments of drinking motivation and have found that drinking profiles are relatively stable in non-treatment seeking community samples; whereas drinking motivation profiles change during treatment (Hebden et al., 2024). Given the ease of assessment, future studies should similarly collect the UCLA RRHDS measure over the course of the study to assess the stability and trajectory of drinking motivation profiles in non-treatment and treatment-seeking individuals. Furthermore, this study was not designed to test the validity of these drinking motivation profiles, and results were limited to measures collected from the parent study protocol. Specifically, we were limited in our assessments of craving to a single assessment, the PACS, which was selected to be sensitive to changes over time for the parent study. Other measures of craving, including the Craving Typology Questionnaire (Martinotti et al., 2013a) would be ideally suited to answering questions related to drinking motivation subgroups and reward, relief, and obsessive craving for alcohol. Relatedly, the follow-up period for this study occurred in the context of a medication trial. While there were no significant effects of the medication in the trial (Ray et al., under review), and medication was controlled for in all predictive validity analyses and individuals in the drinking motivation subgroups were equally represented in the ibudilast and placebo conditions (ibudilast: reward n=23, relief n=10, habit n=18; placebo reward n=21, relief n=10, habit n=15), future studies should test the validity of these profiles without the confound of a medication trial. Additionally, participants in this study

were permitted to test positive for cannabis on a urine toxicology screen. Therefore, it is possible that cannabis use interacted with alcohol use to impact alcohol-related outcomes in this study. Of note, participants could not meet DSM-5 criteria for a substance use disorder, including cannabis use disorder, and as such, participants were likely not heavy cannabis users. Nevertheless, future studies should either exclude cannabis use, or collect large samples of alcohol only and alcohol and cannabis co-users to disentangle their role in drinking motivations and alcohol-related outcomes.

In sum, this study provides support for reward and relief drinking categories in treatment-seeking individuals with an AUD. This study highlights the high clinical severity of individuals who drink for relief motives, such that they have the highest craving and lowest mood at baseline. Moreover, membership in the relief drinking group was predictive of poorer drinking outcomes, greater craving and anxiety symptoms, and more alcohol-related consequences at the 12-week follow-up, indicating that individuals who drink for relief may be a particularly vulnerable sub-population. This study also found some support for a habit drinking profile; however, individuals who drank for habit were not distinguishable from those who drank for reward motives on prospective outcomes, except for total drinking over the 12-week period. As prior work has found support for precision medicine approaches using reward and relief drinking profiles defined *post hoc (Mann et al., 2009; Mann et al., 2018; Witkiewitz et al., 2019b)*, future studies should investigate the use of profiling by drinking motivation as an *a priori* predictor of medication and psychosocial treatment effects using the UCLA RRHDS measure.

Data Availability: The data underlying this article will be shared on reasonable request to the corresponding author.

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Declaration of Interest

The authors declare no competing interests.

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Table 1. Demographics for Full Sample

	Reward (n=77)	Relief (n=31)	Habit (n=61)	Statistic	P
Age	44.51 ± 11.67	41.29 ± 10.41	44.85 ± 10.49	F = 1.20	0.31
Sex (M/F)	52/25	21/10	41/20	χ^2 = 0.003	0.97
Smoking Status (Non-smoker / occasional / daily)	45/17/15	17/8/6	35/9/17	χ^2 = 2.80	0.60
Urine THC (-/+)	58/19	21/10	42/19	χ^2 = 0.98	0.61
Race				χ^2 = 6.80	0.86
White	34	14	22		
Black	20	8	19		
American Indian / Alaska Native	2	2	1		
Asian	0	1	2		
Pacific Islander	2	0	1		
Mixed Race	11	4	11		
Other	8	2	5		
Hispanic/Latino (N/Y)	48/29	22/9	47/14	χ^2 = 3.51	0.17
Reward Question	5.73 ± 1.47	3.97 ± 1.54	4.11 ± 1.53	25.77	<0.001
Relief Question	3.13 ± 1.72	5.48 ± 1.29	3.39 ± 1.68	24.19	<0.001
Habit Question	3.94 ± 1.83	3.68 ± 1.66	6.00 ± 1.92	34.12	<0.001

Table 2. Baseline Validation of Reward, Relief, and Habit Drinking Motivation Profiles

	Reward (n=77)	Relief (n=31)	Habit (n=61)	F	p	η_p^2
Recent Drinking (30-Day TLFB)						
Total Drinks	150.08 ± 100.62	140.02 ± 127.36	156.71 ± 104.16	0.23	0.80	.003
DPDD	7.31 ± 5.73	7.76 ± 6.38	6.67 ± 3.90	0.39	0.68	.005
PHDD	42.55 ± 32.32	42.15 ± 34.59	49.89 ± 33.21	0.88	0.42	.011
PDA	25.93 ± 24.94	36.77 ± 31.64	20.38 ± 22.97	3.43	0.04	.040
AUD Severity						
AUD Symptoms (DSM-5)	5.86 ± 2.31	6.58 ± 2.64	6.80 ± 2.27	2.82	0.06	.034
AUDIT Total Score	18.34 ± 7.58	21.84 ± 7.30	20.26 ± 7.24	2.35	0.10	.028
ImBIBe	14.94 ± 9.31	19.97 ± 10.04	18.25 ± 11.19	3.05	0.05	.036
PACS[a,b,c]	**11.17 ± 6.09**	**16.81 ± 7.40**	**13.64 ± 6.43**	**9.15**	**<0.001**	**.100**
Mood						
BAI	7.95 ± 7.62	12.00 ± 9.38	8.57 ± 9.19	2.23	0.11	.026
BDI-II	10.58 ± 8.71	14.71 ± 8.30	12.92 ± 10.03	2.19	0.12	.026
POMS – Tension[a,c]	**1.02 ± 0.64**	**1.54 ± 0.62**	**1.07 ± 0.70**	**7.10**	**0.001**	**.080**
POMS – Negative Mood	0.85 ± 0.64	1.20 ± 0.69	0.88 ± 0.67	2.88	0.06	.034
POMS – Vigor	1.60 ± 0.90	1.18 ± 0.74	1.52 ± 0.86	2.61	0.08	.031
POMS – Positive Mood[a,c]	**1.82 ± 0.91**	**1.29 ± 0.70**	**1.69 ± 0.85**	**4.19**	**0.02**	**.049**

[a] = reward vs. relief
[b] = reward vs. habit
[c] = relief vs. habit
DPDD = Drinks per drinking day; PHDD = percent heavy drinking days; PDA = percent days abstinent. All calculated based on 30-day Timeline Followback.
AUDIT = Alcohol Use Disorders Identification Test; ImBIBe = negative drinking-related consequences; PACS = Penn Alcohol Craving Scale; BAI = Beck Anxiety Inventory; BDI = Beck Depression Inventory – II; POMS = Positive and Negative Mood States
Note: $\eta_p^2 = 0.01$ indicates a small effect; $\eta_p^2 = 0.06$ indicates a medium effect; $\eta_p^2 = 0.14$ indicates a large effect.

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Table 3. Predictive Validity of Drinking Motivation Groups – Drinking over 12 weeks (n=102)

Variable	Unstandardized B	Std. Error	p-value	f^2
Total Drinks Model				
Intercept	110.22	80.69	0.18	
Age	-1.34	1.55	0.39	0.007
Sex	20.74	35.27	0.56	0.003
Medication	18.56	32.56	0.57	0.003
Relief	**95.04**	**42.7**	**0.03**	**0.05**
Habit	**76.83**	**36.87**	**0.04**	**0.04**
Baseline Total Drinks	**0.62**	**0.16**	**<0.001**	**0.15**
DPDD Model				
Intercept	0.93	1.48	0.53	
Age	0.02	0.03	0.36	0.007
Sex	0.06	0.60	0.92	0.001
Medication	0.76	0.56	0.18	0.02
Relief	0.62	0.74	0.41	0.006
Habit	0.88	0.64	0.18	0.02
Baseline DPDD	**0.29**	**0.05**	**<0.001**	**0.29**
PHDD Model				
Intercept	0.11	0.11	0.30	
Age	-0.002	0.002	0.26	0.01
Sex	0.06	0.05	0.18	0.02
Medication	-0.001	0.05	0.98	0.001
Relief	**0.13**	**0.06**	**0.03**	**0.04**
Habit	0.08	0.05	0.11	0.02
Baseline PHDD	**0.32**	**0.07**	**<0.001**	**0.20**
PDA Model				
Intercept	0.18	0.13	0.19	
Age	**0.005**	**0.002**	**0.04**	**0.03**
Sex	-0.08	0.05	0.12	0.02
Medication	0.02	0.05	0.71	0.001
Relief	**-0.20**	**0.07**	**0.004**	**0.06**
Habit	-0.11	0.06	0.06	0.03
Baseline PDA	**0.76**	**0.11**	**<0.001**	**0.45**

Note: The reference group for sex was male and the reference group for medication was placebo. f^2 = 0.02

indicates a small effect; $f^2 = 0.15$ indicates a medium effect; $f^2 = 0.35$ indicates a large effect.
DPDD = Drinks per drinking day; PHDD = percent heavy drinking days; PDA = percent days abstinent.

Table 4. Predictive Validity of Drinking Motivation Groups – Alcohol Phenomenology over 12 weeks (n=102)

Variable	Unstandardized B	Std. Error	p-value	f^2
PACS Model				
Intercept	1.70	1.35	0.21	
Age	-0.003	0.02	0.89	0.001
Sex	0.87	0.53	0.10	0.007
Medication	-0.75	0.51	0.15	0.005
Relief	**2.46**	**0.67**	**<0.001**	**0.03**
Habit	0.69	1.20	0.24	0.003
Baseline PACS	**0.72**	**0.04**	**<0.001**	**0.60**
BDI Model				
Intercept	3.35	2.96	0.26	
Age	-0.03	0.06	0.60	0.002
Sex	-0.07	1.21	0.95	0.001
Medication	1.07	1.18	0.37	0.006
Relief	0.84	1.56	0.59	0.002
Habit	-1.10	1.33	0.41	0.005
Baseline BDI	**0.46**	**0.08**	**<0.001**	**0.36**
BAI Model				
Intercept	0.94	1.73	0.59	
Age	-0.01	0.03	0.69	0.001
Sex	0.19	0.71	0.79	0.001
Medication	0.94	0.70	0.18	0.006
Relief	**2.81**	**0.92**	**0.003**	**0.03**
Habit	0.34	0.05	.67	0.001
Baseline BAI	**0.70**	**0.05**	**<0.001**	**0.55**
ImBIBe Model				
Intercept	11.00	4.17	0.01	
Age	-0.11	0.08	0.17	0.01

Sex	-1.53	1.68	0.37	0.006
Medication	2.87	1.71	0.10	0.02
Relief	**6.12**	**2.17**	**0.006**	**0.06**
Habit	2.14	1.88	0.26	0.009
Baseline ImBIBe	**0.31**	**0.06**	**<0.001**	**0.26**

Note: The reference group for sex was male and the reference group for medication was placebo. $f^2 = 0.02$ indicates a small effect; $f^2 = 0.15$ indicates a medium effect; $f^2 = 0.35$ indicates a large effect.

PACS = Penn Alcohol Craving Scale; BDI = Beck Depression Inventory – II; BAI = Beck Anxiety Inventory; ImBIBe = negative drinking-related consequences