Archival Report

Biological Psychiatry: CNNI

Decision-Making Signatures of Methamphetamine and Alcohol Use Disorders

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ABSTRACT

BACKGROUND: Aberrant decision making is a hallmark of substance use disorders (SUDs), often impeding recovery. While uncertainty, which comprises risk and ambiguity, is central to real-world choices, its distinct effects in SUDs remain underexplored. In this study, we disentangle risk and ambiguity to identify context-specific impairments in methamphetamine use disorder (MUD) and alcohol use disorder (AUD).

METHODS: We used a Choice under Risk and Ambiguity task to examine uncertainty decision making (UDM) in 101 individuals with MUD, 56 individuals with AUD, and their respective healthy control participant (HC) groups (n = 45 and n = 75). Group-level analyses applied a modified psychometric function to estimate decision parameters, while individual-level UDM indicators were derived using custom computational methods and subjective value models.

RESULTS: Individuals with MUD exhibited heightened reward sensitivity and a stronger preference for large rewards under high uncertainty, with flexible shifts across ambiguity levels. In addition, reward sensitivity under high ambiguity was linked to symptom severity. In contrast, individuals with AUD showed no evident decision-making impairments across conditions, and like HCs, they adopted conservative strategies under ambiguity. Direct comparisons confirmed more pronounced UDM impairments in MUD than in AUD.

CONCLUSIONS: These findings underscore the heterogeneity of decision-making patterns across SUDs, validating the need for precision in therapeutic strategies.

https://doi.org/10.1016/j.bpsc.2025.08.008

Individuals with addiction often continue substance use despite serious physical, psychological, and social consequences. This maladaptive decision making frequently persists after abstinence, contributing to high relapse rates. Understanding the mechanisms underlying detrimental choices in substance use disorders (SUDs) has been a major goal of psychiatry, psychology, and neuroscience (1–6).

In real-world settings, decisions are often made under uncertainty, where outcomes are unpredictable due to incomplete or variable information (7,8). To navigate such environments, humans rely on internal models to estimate outcome probabilities and adjust their behavior accordingly (7,9). Uncertainty could be categorized into 2 types: risk, where outcome probabilities are known (e.g., a coin toss), and ambiguity, where outcome probabilities are unknown (e.g., stock market fluctuations) (8). Importantly, risk and ambiguity are processed differently, both behaviorally and neurobiologically (10–12). Behaviorally, individuals tend to prefer risky options over ambiguous ones, even when the latter offer higher potential rewards, indicating an inherent aversion to ambiguity (11–14). Previous neuroimaging research suggests that risk engages the posterior parietal cortex and cerebellum, whereas ambiguity preferentially involves the lateral prefrontal and frontopolar cortices (8,15). These dissociable systems underscore the importance of differentiating risk and ambiguity when evaluating decision making in SUDs. As substance use affects widespread neural circuits (16–18), it is plausible that individuals with SUDs might show disrupted decision making under both uncertainty types, possibly with different impairment profiles. However, few studies have directly compared risk and ambiguity in SUDs, leaving these distinctions poorly understood.

Previous research on value-based decision making has highlighted cognitive deficits in SUDs using paradigms such as the Balloon Analogue Risk Task (BART) (19–21), delay discounting task (DDT) (22–25), and the Iowa Gambling Task (IGT) (26–28). For example, individuals with methamphetamine use disorder (MUD) show reduced earnings and disrupted right dorsolateral prefrontal connectivity in the BART (20), increased preference for immediate rewards in the DDT (25), and poor feedback-based learning in the IGT (27). While these paradigms provide important insights, they often conflate risk and ambiguity or fail to systematically manipulate them. Therefore, these tasks cannot be used to precisely isolate how different types and uncertainty levels influence decision making in SUDs.

Notably, relapse in SUDs is often triggered by single, high-stakes decisions made under uncertainty, underscoring the

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ISSN: 2451-9022

need for paradigms that isolate specific uncertainty contexts and quantify individual decision-making tendencies accordingly. Moreover, existing computational models (12,29) typically reduce preferences under uncertainty to a single summary value (e.g., risk or ambiguity aversion), without capturing how behavior varies across gradients of uncertainty (30,31). Thus, they may overlook critical aspects of uncertainty sensitivity.

To address these gaps, the current study introduces several methodological advances. First, we used a Choice under Risk and Ambiguity (CRA) task (12), which has previously been validated to reliably distinguish risk and ambiguity by applying overlays on options and parametrically varying uncertainty levels across low, medium, and high levels (12,32–34). Second, we adopted a psychophysical framework (35–37) to model decision making across uncertainty levels, enabling us to capture the continuous relationship between uncertainty and choice behavior. Among psychophysical approaches, psychometric functions (36) are particularly well suited to modeling probabilistic decisions in 2-alternative forced-choice tasks (37), as they yield interpretable parameters that map onto theoretical constructs of uncertainty valuation. Specifically, we used a modified psychometric function, tailored to the current task, to estimate key decision-making parameters: reward sensitivity (β), inflection point (α; reward magnitude where choice preference shifts), and the upper limit of lottery choice probability (L). This allowed us to examine how sensitivity and valuation vary across uncertainty levels. Existing evidence suggests that as uncertainty increases, higher rewards are required to motivate risk taking (38), while reward sensitivity (39) and lottery preference (40) decrease. Accordingly, we predicted that greater uncertainty would elevate the inflection point and reduce both reward sensitivity and choice probability ceilings, with potentially distinct effects under risk and ambiguity.

Additionally, we examined 2 prevalent forms of SUDs, MUD and alcohol use disorder (AUD), to assess whether different substances produce shared or divergent patterns of decision-making dysfunction. Methamphetamine, an illicit psychostimulant, and alcohol, a legal but widely abused substance, both pose major global public health challenges (41,42). Previous studies have linked MUD to impaired feedback learning (43) and AUD to increased risk taking for immediate rewards (44). Building on this, we hypothesized that both groups would exhibit uncertainty decision-making (UDM) impairments, potentially differing in severity and characteristics.

In summary, in the current study, we aimed to advance the understanding of decision-making impairments in SUDs by systematically dissociating risk from ambiguity and parametrically manipulating uncertainty levels. A psychophysical model was applied at the group level to capture context-specific patterns with greater granularity. To complement and validate the group-level results, we applied custom computational methods and subjective value models to estimate individual UDM indicators from different perspectives and examine their associations with symptom severity evaluated by DSM-5. Finally, by comparing UDM patterns in individuals with MUD and AUD, in this study, we seek to reveal substance-specific impairments and inform more targeted interventions. An overview of the task and analysis pipeline is illustrated in Figure 1.

METHODS AND MATERIALS

Participants

A total of 101 individuals with MUD (men, 35.98 ± 7.31 years), 45 healthy control participants (HCs) matched to the MUD group (men, 37.18 ± 6.98 years), 56 individuals with AUD (men, 42.70 ± 8.52 years), and 75 HCs matched to the AUD group (men, 42.12 ± 7.99 years) were recruited for the current study. Individuals with MUD and AUD were diagnosed according to ICD-11 criteria as inpatients in 5 different rehabilitation centers located in Hubei, Da Lian Shan, Tai Hu, Yunnan, and Shandong. Participants with other psychiatric, neurological, or major physical diseases were excluded from this study. All participants signed written informed consent forms, and this study was approved by the Ethics Committee of Shanghai Mental Health Center, in compliance with the Declaration of Helsinki.

CRA Task

In each trial, participants first viewed a 1-second fixation, followed by a stimulus screen presenting 2 options: a fixed option offering 35 points and a lottery option with a variable chance of winning higher rewards or nothing. The positions of the options (left-right) and reward amounts (vertical) were counterbalanced across trials. Options remained on screen for 3 seconds before disappearing, after which a green dot prompted participants to respond via keypress. Feedback was provided by highlighting the chosen option for 1 second without revealing outcomes (Figure 1A).

Two uncertainty conditions, risk and ambiguity, were distinguished by the absence or presence of an overlay on the lottery options, respectively, thereby rendering the probability of obtaining the reward either known or unknown. In the risk condition, winning probabilities were explicit, with failure probabilities of 25% (low risk), 50% (medium risk), and 75% (high risk) across 5 reward magnitudes (35, 56, 140, 350, 875 points). In the ambiguity condition, probabilities were concealed using a gray overlay, with ambiguity levels set at 24%, 50%, and 74%, using the same reward magnitudes. Overall, the design yielded 30 unique lottery conditions (context × uncertainty level × reward magnitude; 2 × 3 × 5) (Figure 1A). Participants were informed that task performance would influence their monetary compensation. Details on behavioral data exclusion criteria and task versions are provided in the Supplement.

Group-Level Behavioral Modeling for the CRA Task

To examine group-level decision-making patterns under varying risk and ambiguity (Figure 1B), we used MATLAB (version R2022b; The MathWorks, Inc.) for curve fitting. Lottery rewards were log transformed to accommodate the increasing reward intervals. For each uncertainty level, we calculated each individual's mean choice probability at each reward magnitude. These group-level data across the 5 reward magnitudes were then fitted using MATLAB's lsqcurvefit function, which applies nonlinear least squares to estimate model parameters. Candidate models were compared using the Bayesian information criterion (BIC) (45) to identify the best-fitting model (see Supplemental Methods). As

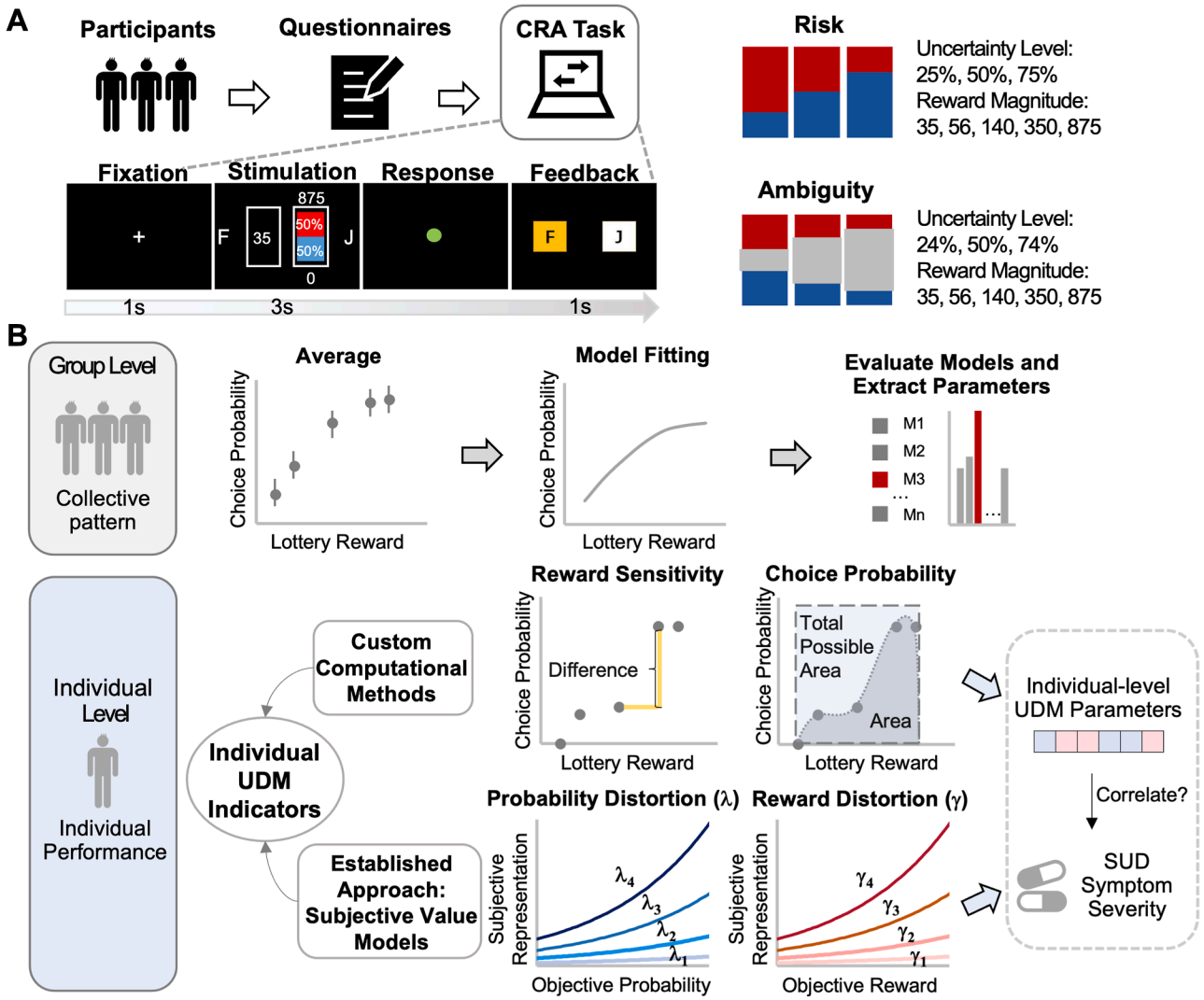


Figure 1. Task procedure and analysis workflow. **(A)** Schematic of the experimental procedure and the Choice under Risk and Ambiguity (CRA) task. Participants with methamphetamine use disorder and alcohol use disorder and healthy control participants completed clinical assessments and the CRA task. Each trial began with a 1-second fixation, followed by a 3-second display of choice options. Participants responded upon cue onset (green dot) and received feedback indicating the selected option. The lottery options were presented under 2 uncertainty contexts, risk and ambiguity, distinguished by the absence or presence of an overlay, with each context comprising 3 uncertainty levels and 5 reward magnitudes (see Methods and Materials for details). **(B)** Overview of group- and individual-level analyses. At the group level, mean choice probabilities averaged for each individual across reward magnitudes were modeled at each uncertainty level in 1 group, with optimal models selected using the Bayesian information criterion to derive group-level decision parameters. At the individual level, custom computational methods (i.e., 2 task-tailored mathematical formulas) and an established approach (i.e., subjective value models) were applied in this study to provide comprehensive evaluation of individual decision-making performance. For custom computational methods, reward sensitivity (defined as a greater increase in the probability of choosing the lottery option with increasing reward magnitude) and choice probability (defined as the area under the fitted choice probability curve as the proportion of the total possible area across the range of lottery reward magnitudes) were computed at each uncertainty level (including 25% risk, 50% risk, 75% risk, 24% ambiguity, 50% ambiguity, 74% ambiguity, overall risk, and overall ambiguity). For subjective value models, we constructed a series of models with hypotheses about whether or not distortions would be exhibited in probability and/or reward. The parameter estimation of these models could only be conducted under risk or ambiguity. Under risk or ambiguity, higher probability distortion parameter λ means higher subjective representation of probability to get rewards ($\lambda_4 > \lambda_3 > \lambda_2 > \lambda_1$); similarly, higher reward distortion parameter γ means higher subjective representation of reward magnitudes ($\gamma_4 > \gamma_3 > \gamma_2 > \gamma_1$). Choice randomness τ was also derived from subjective value models to indicate the randomness of participants' choices. Importantly, among the subjective value models, the model with λ fixed at 1 and γ as a free parameter provided the best fit. This indicates that distortion existed in reward magnitude but not in probability. Accordingly, only the reward distortion parameter γ is reported in Results. Finally, the associations between individual uncertainty decision-making (UDM) indicators and primary symptom severity (i.e., DSM-5 score) were examined using correlation analyses. SUD, substance use disorder.

expected, the modified psychometric function yielded the lowest BIC (Table S1). Its formula is shown below:

$$y = \phi(x;\ \alpha, \beta, L) = \frac{L}{1 + e^{-\beta(x-\alpha)}} \quad (1)$$

where x denotes the log-transformed lottery reward amount, and y signifies the probability of selecting the lottery. This model is a task-adapted 3-parameter psychometric with α (threshold), β (reward sensitivity), and L (curve's maximum).

Individual Decision-Making Performance

We applied the same curve-fitting procedure to individual data to estimate α, β, and L. However, due to choice variability and limited trials per condition, these estimates may not reliably reflect individual performance (Figure S1). To address this, we used alternative algorithms to compute individual-level reward sensitivity and choice probability at all uncertainty levels.

Reward sensitivity was defined as the summed differences in choice probabilities across reward magnitudes within each uncertainty level:

$$\textit{Reward Sensitivity} = \sum_{i=1}^{n-1} (P(A_{i+1}) - P(A_i)) \quad (2)$$

where $P(A_i)$ is the mean choice probability at reward amount A_i. This formula posits that a steeper increase in $P(A_i)$ with higher rewards indicates greater reward sensitivity.

To calculate overall choice probability at each risk or ambiguity level, we applied modified Akima interpolation (46) to fit a smooth curve [$f(x)$] to each individual's 5 mean choice probabilities across reward magnitudes (x). The area under this curve, normalized by the total possible area between the minimum (a) and maximum (b) lottery rewards, was used as the overall choice probability:

$$\textit{Choice Probability} = \frac{\int_a^b f(x)dx}{b - a} \quad (3)$$

This approach assumes that choice probability varies smoothly with reward magnitude, allowing the integrated area to reflect overall lottery preference within each uncertainty level.

A series of subjective value models based on established procedures (47–49) were applied to examine factors that influence decision making. These models assume that choices are driven by the subjective value (SV) of alternatives, with different models varying in how they estimate probabilities and reward magnitudes (see Supplemental Methods).

$$SV = P^{\lambda} V^{\gamma} \quad (4)$$

Here, λ and γ represent distortions in objective probabilities (P) and reward magnitudes (V), with higher values indicating greater subjective weighting. Subjective values were converted into choice probabilities using the softmax function:

$$p_{uncer} = \frac{\exp(\tau SV_{uncer})}{\exp(\tau SV_{uncer}) + \exp(\tau SV_{cer})} \quad (5)$$

where τ (inverse temperature) controls choice randomness, with lower τ indicating higher randomness. Parameters were fitted separately for risk and ambiguity contexts.

Model performance was evaluated using the BIC, Akaike information criterion (AIC) (45), and posterior exceedance probability (PXP) (50). Lower BIC and AIC values and higher PXP values indicate better model fit.

Statistical Analysis

Group differences in demographic and clinical variables were assessed using univariate general linear models. For group-level analyses, 1000-iteration permutation tests (51) evaluated differences in behavioral modeling parameters (*diff* in Results) between groups and uncertainty levels, with significance defined as values that fell below the fifth percentile (α) or above the 95th percentile (β, L) of the null distribution. Multiple comparisons were corrected using the Benjamini-Hochberg false discovery rate (BH-FDR) (52) at each uncertainty level. Wilcoxon rank-sum tests (53) compared choice probabilities between groups across reward magnitudes, with BH-FDR performed at each uncertainty level. Friedman's tests (53) were used to examine choice probability differences across uncertainty levels, and then Wilcoxon signed-rank tests (53) were used to examine pairwise differences, with BH-FDR performed at each group and uncertainty context.

In individual-level analyses, Wilcoxon rank-sum tests compared decision-making indicators in the SUD and HC groups, while generalized linear models adjusted for age and abstinence in comparisons between MUD and AUD, with BH-FDR correction applied within each uncertainty level and analysis approach.

Associations between decision-making indicators and clinical variables were examined using Pearson correlations, with BH-FDR correction applied within each SUD group. The primary focus was on correlations with DSM-5 symptom severity, as it reflects the core diagnostic criteria and severity of SUDs.

Analyses were performed using MATLAB version R2022b (behavioral modelings and comparisons), Python version 3.10 (subjective value modeling), RStudio (correlations, heatmaps), and SPSS version 24 (IBM Corp.) (demographic/clinical comparisons).

RESULTS

Individuals With MUD Exhibit Altered Sensitivity to Reward Magnitudes at the Group Level

Demographic and clinical characteristics of the 101 individuals with MUD and 45 matched HCs are shown in Table 1. Figure 2A–F shows the fitted curves illustrating group-level decision making across reward gradients and uncertainty levels, highlighting deviations in the MUD group relative to the HC group. Using 1000-iteration permutation tests, we compared estimated parameters of the modified psychometric function between the MUD and HC groups. The MUD group showed higher reward sensitivity (β) under 75%

Table 1. Demographics, Symptom Severity of SUD, and Secondary Clinical Symptoms in Individuals With SUDs and HCs

	MUD					AUD				
	MUD, n = 101	Matched HC, n = 45	F	p_{FDR}	η_p^2	AUD, n = 56	Matched HC, n = 75	F	p_{FDR}	η_p^2
Demographics										
Age, Years	35.98 (7.31)	37.18 (6.98)	0.859	.356	0.006	42.7 (8.52)	42.12 (7.99)	0.158	.692	0.001
Education, Years	9.13 (2.7)	9.67 (2.53)	1.283	.279	0.009	9.64 (3.58)	9.97 (2.9)	0.327	.62	0.003
Abstinence, Days	486.41 (341.3)	–	–	–	–	208.88 (544.48)	–	–	–	–
Symptom Severity										
DSM-5	7.29 (2.44)	–	–	–	–	6.54 (2.75)	–	–	–	–
Secondary Clinical Symptoms										
BDI	13.91 (7.99)	10.89 (10.88)	3.53	.072	0.024	13.3 (9.36)	10.28 (10.17)	3.033	.168	0.023
BAI	6.3 (6.94)	1.24 (2.89)	22.08	<.001	0.133	6.39 (7.82)	2.33 (4.24)	14.514	<.001	0.101
BIS Motor	24.1 (7.37)	17.71 (4.9)	28.18	<.001	0.164	20.61 (6.18)	18.59 (5.74)	3.721	.134	0.028
BIS Attention	29.07 (5.95)	23.22 (5.3)	32.11	<.001	0.182	27.36 (6.63)	23.47 (5.53)	13.383	.001	0.094
BIS Nonplan	29.83 (7.65)	20.42 (6.89)	49.97	<.001	0.258	27.48 (8.98)	20.83 (7.17)	22.236	<.001	0.147
BIS Total	27.67 (5.5)	20.45 (4.66)	58.67	<.001	0.289	25.15 (5.61)	20.96 (4.98)	20.339	<.001	0.136
PSQI	6.61 (2.62)	5.2 (2.34)	9.665	.003	0.063	6.04 (3.66)	5.12 (3.19)	2.325	.223	0.018
FTND	4.26 (2.99)	1.36 (1.98)	35.49	<.001	0.198	–	–	–	–	–
AUDIT	7.65 (8.02)	3.16 (4.27)	12.53	.001	0.08	–	–	–	–	–

Values are presented as mean (SD).

AUD, alcohol use disorder; AUDIT, Alcohol Use Disorders Identification Test; BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; BIS, Barrett Impulsivity Scale; FTND, Fagerström Test for Nicotine Dependence; HC, healthy control participant; MUD, methamphetamine use disorder; PSQI, Pittsburgh Sleep Quality Index; SUD, substance use disorder.

risk (*diff* = 1.581, p_{FDR} = .023), 74% ambiguity (*diff* = 1.237, p_{FDR} = .048), and 24% ambiguity (*diff* = 2.605, p_{FDR} = .012) (Figure 2M) but not under other conditions ($p_{FDR} > .10$). These results indicate increased reward sensitivity in MUD under high uncertainty. Choice probabilities for lotteries were higher in the MUD group than in the HC group at medium and large reward magnitudes across all risk and ambiguity levels ($ps < .05$) (Table S2), suggesting overestimation of these rewards under uncertainty. This preference was reflected in higher L parameters in the MUD group across all uncertainty levels ($p_{FDR} \leq .006$) (Figure 2M).

Individuals With MUD Mainly Focus on Reward Magnitude at the Group Level

To examine how uncertainty levels influence choice, we compared choice probabilities across the 3 risk and 3 ambiguity levels using 1000-iteration permutation tests.

In the risk context, parameters α, β, and L differed significantly across risk levels in both the MUD and HC groups (Figure 3A). As risk increased, higher rewards were needed to attract choices ($p_{FDR} \leq .023$), reward sensitivity decreased ($p_{FDR} \leq .002$), and the choice probability maximum declined ($p_{FDR} < .001$) in both groups. Choice probabilities also varied significantly across risk levels ($ps < .05$), indicating that participants adjusted their choices as known reward probabilities changed. Statistical details are shown in Table S6.

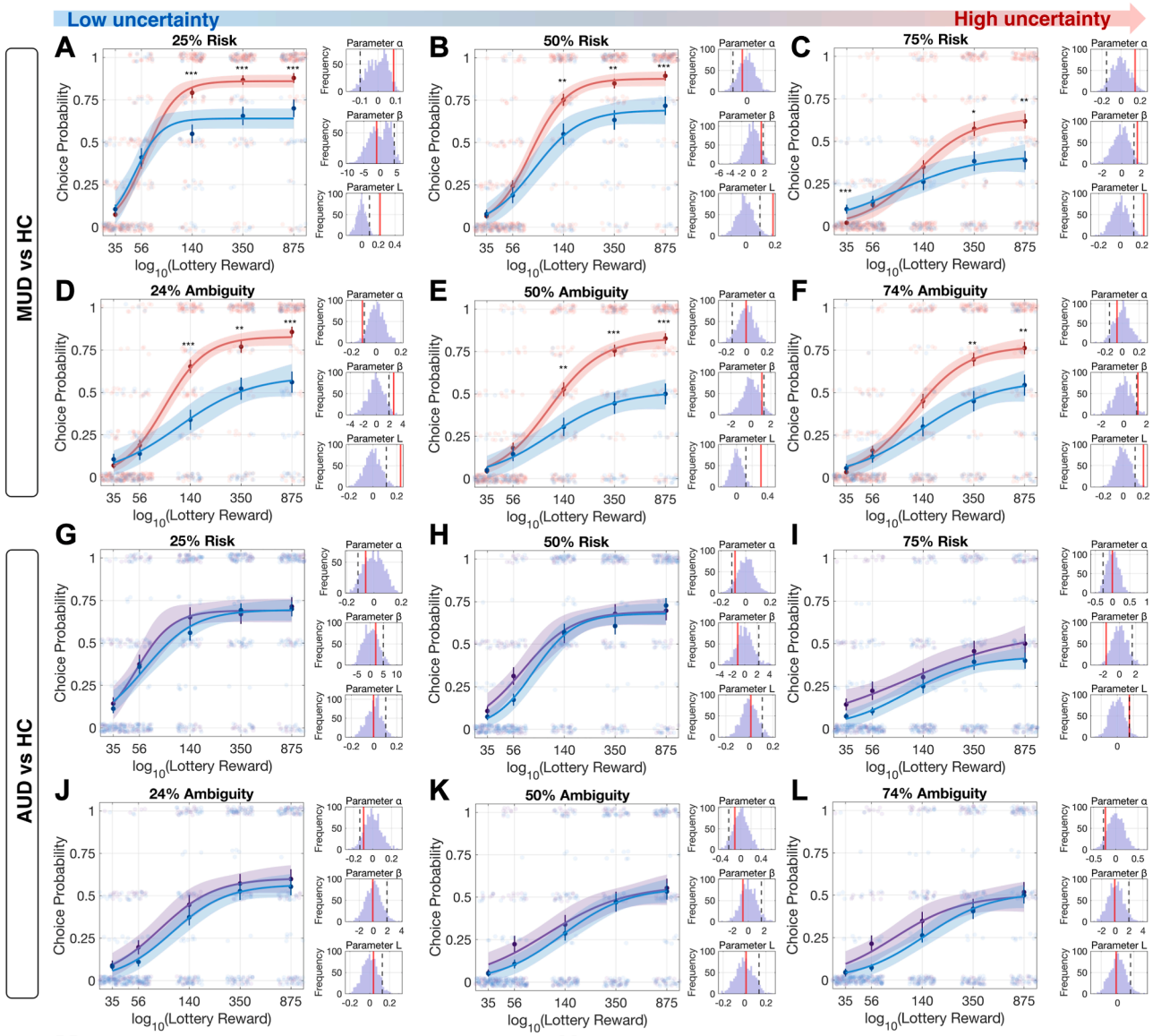
In the ambiguous context, the MUD group required higher reward to choose lotteries (α: $diff_{a74-a24}$ = 0.130, p_{FDR} = .015) and showed lower reward sensitivity (β: $diff_{a74-a24}$ = −1.418, p_{FDR} = .048) at high versus low ambiguity. Choice probabilities also differed across ambiguity levels at reward magnitudes of 140 (χ^2_2 = 28.352, $p_{FDR} < .001$) and 875 (χ^2_2 = 15.888, $p_{FDR} < .001$) (pairwise difference results are shown in Table S3), indicating strategy adjustments with ambiguity (Figure 3B). In contrast, the HC group showed no differences in behavioral parameters or choice probabilities across ambiguity levels ($ps > .05$), suggesting stable decision-making strategies.

The HC group showed consistent choice probabilities across ambiguity levels, with maxima around 0.5, while the MUD group exhibited greater variability, reaching approximately 0.8 (Figure 3B). This also suggests that ambiguity prompted HCs to adopt stable, conservative strategies, whereas individuals with MUD remained reward focused, adjusting choices to maximize outcomes.

UDM Deficits in MUD Are Associated With Clinical Severity at the Individual Level

To examine the relationship between UDM performance and clinical severity, individual-level indicators were needed. However, limited trials per condition increased data variability, hindering reliable parameter estimation using group-level curve-fitting methods (Figure S1). Therefore, custom computational methods were used to estimate reward sensitivity and choice probability, and subjective value models were used to assess distortions in probability and reward magnitude (Methods and Materials).

Consistent with group-level findings, individual-level analyses showed that the MUD group exhibited higher overall reward sensitivity (risk: z = 4.389, $p_{FDR} < .001$; ambiguity: z = 3.991, $p_{FDR} < .001$) and greater choice probability for lotteries (risk: z = 3.797, $p_{FDR} < .001$; ambiguity: z = 4.188, $p_{FDR} < .001$) than the HC group in both contexts (Figure 4A–D). At each uncertainty level, the MUD group also showed significantly higher reward sensitivity and choice probability ($p_{FDR} \leq .011$) (Figure S2A–L). Subjective value model results indicated that individuals with MUD showed no distortion in



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	Risk			Ambiguity		
	25%	50%	75%	24%	50%	74%
α	0.965	0.290	0.949	0.031	0.484	0.268
β	0.893	0.144	0.023	0.012	0.119	0.048
L	<0.001	<0.001	0.003	0.003	<0.001	<0.001

N

	Risk			Ambiguity		
	25%	50%	75%	24%	50%	74%
α	0.398	0.300	0.732	0.375	0.591	0.249
β	0.398	0.816	0.969	0.554	0.770	0.597
L	0.539	0.633	0.150	0.500	0.636	0.597

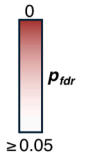

Figure 2. Collective patterns of decision-making behaviors at all uncertainty levels. **(A–F)** Curve-fitting plots of lottery choice probability across varied reward magnitude in the methamphetamine use disorder (MUD) and matched healthy control participant (HC) groups at all uncertainty levels. The MUD group showed deviant response curves compared with the matched HC group and a higher probability of choosing lotteries with moderate to large reward amounts ($ps < .05$). **(G–L)** Curve-fitting plots for the alcohol use disorder (AUD) and matched HC groups. The AUD group displayed similar response curves to the matched HC group. The right side of panels **(A–L)** displays frequency plots of the permuted null distribution of parameter differences between the 2 groups. Red solid lines indicate the observed parameter differences, and dashed lines mark the 1-tailed 5% significance thresholds (left tail for α, right tail for β and L). Colored dots represent mean choice probabilities of groups at each lottery reward magnitude, with vertical bars indicating the SEM. Semitransparent dots represent mean choice probability of individuals at each reward magnitude. Red represents MUD, purple represents AUD, and blue represents HC. Shaded areas represent 95% CIs of the fitted curves. **(M)** The heatmap summarizes the significance of group differences in parameters α, β, and L at all uncertainty levels between the MUD and HC groups. The MUD and HC groups differed significantly in parameter β, particularly at high levels of risk and ambiguity, in parameter L across all uncertainty levels, and in parameter α under 24% ambiguity ($ps < .05$). **(N)** The heatmap summarizes the significance of group differences in parameters α, β, and L between the AUD and HC groups. No significant differences in parameters α, β, or L were found between the AUD and HC

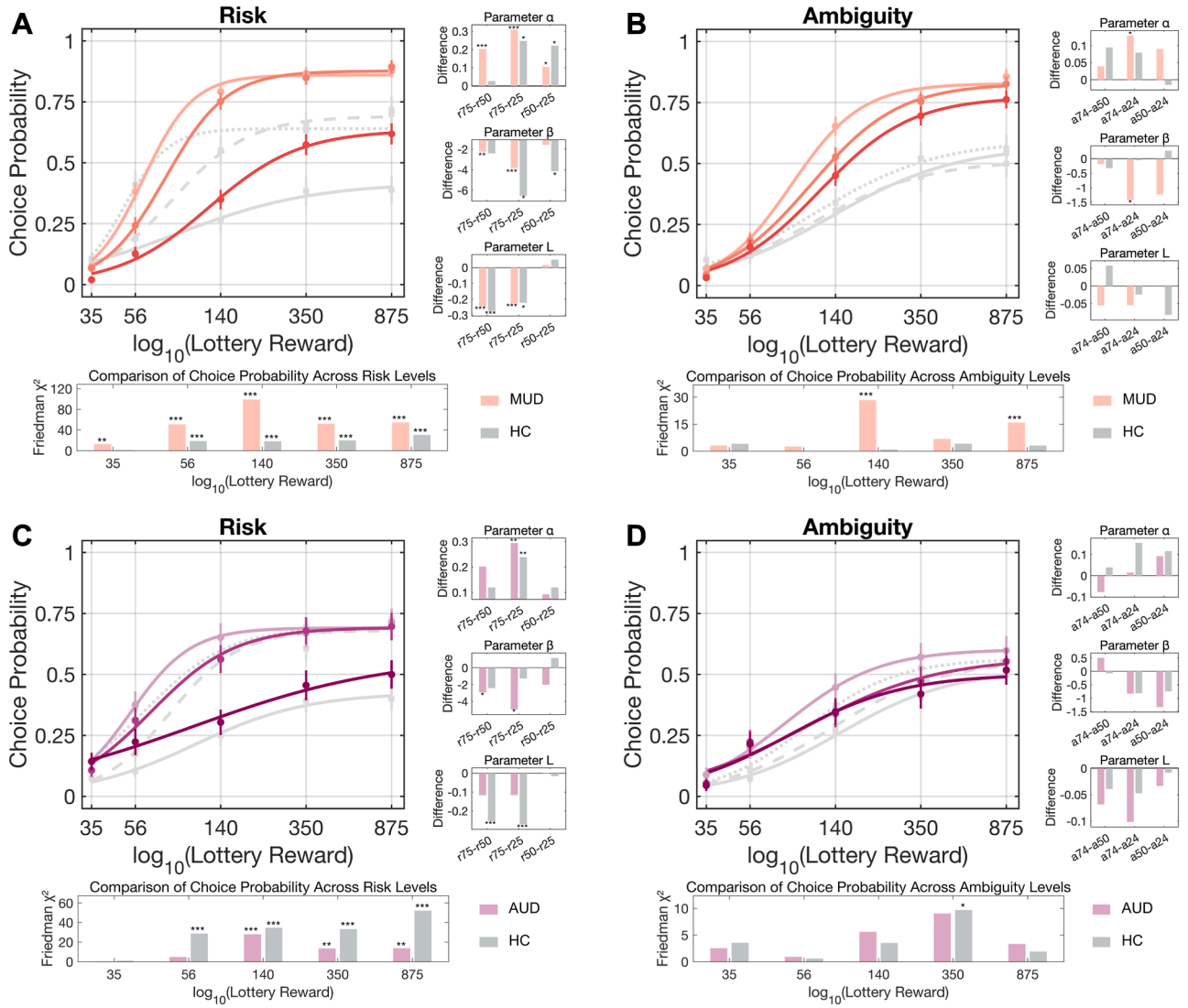

Figure 3. Collective patterns of decision-making behaviors across risk and ambiguity levels. **(A)** Curves of the methamphetamine use disorder (MUD) and matched healthy control participant (HC) groups across 25%, 50%, and 75% risk. Significant differences in parameter (α, β, and L) and choice probability were found across 3 risk levels in the MUD and HC groups ($ps < .05$). **(B)** Curves of the MUD and matched HC groups across 24%, 50%, and 74% ambiguity. Significant differences in parameter α and β between 74% and 24% ambiguity and in choice probability for lottery reward magnitudes of 140 and 875 points were found across 3 levels in the MUD group ($ps < .05$). **(C)** Curves of the alcohol use disorder (AUD) and matched HC group across 25%, 50%, and 75% risk. In the AUD group, significant differences were observed in parameter α between 75% and 25% risk, in parameter β between 75% and 50% risk, as well as between 75% and 25% risk, and in the choice probability for lottery reward magnitudes of 140, 350, and 875 points ($ps < .05$). In the HC group, significant differences were observed in parameter α between 75% and 25% risk, in parameter L between 75% and 50% risk, as well as between 75% and 25% risk, and in the choice probability for lottery reward magnitudes of 56, 140, 350, and 875 points ($ps < .05$). **(D)** Curves of the MUD and matched HC group across 24%, 50%, and 74% ambiguity. A significant difference was only found in choice probability for lottery reward magnitude of 350 in the HC group. In panels **(A–D)**, the right side shows the differences in parameters α, β, and L between different uncertainty levels; the bottom shows the comparison of choice probability across 3 uncertainty levels. All colored bars and lines represent patient groups, and gray ones represent HC groups. Darker fitted curves represent higher levels of uncertainty. $^*p < .05$, $^{**}p < .01$, $^{***}p < .001$; significant p values were corrected using the Benjamini-Hochberg false discovery rate.

groups ($ps > .05$). In panels **(M)** and **(N)**, colored cells indicate significant differences, with darker shades representing stronger significance; blank cells denote nonsignificant results. The p values are displayed within the cells. $^*p < .05$, $^{**}p < .01$, $^{***}p < .001$; p values were corrected using the Benjamini-Hochberg false discovery rate (FDR).

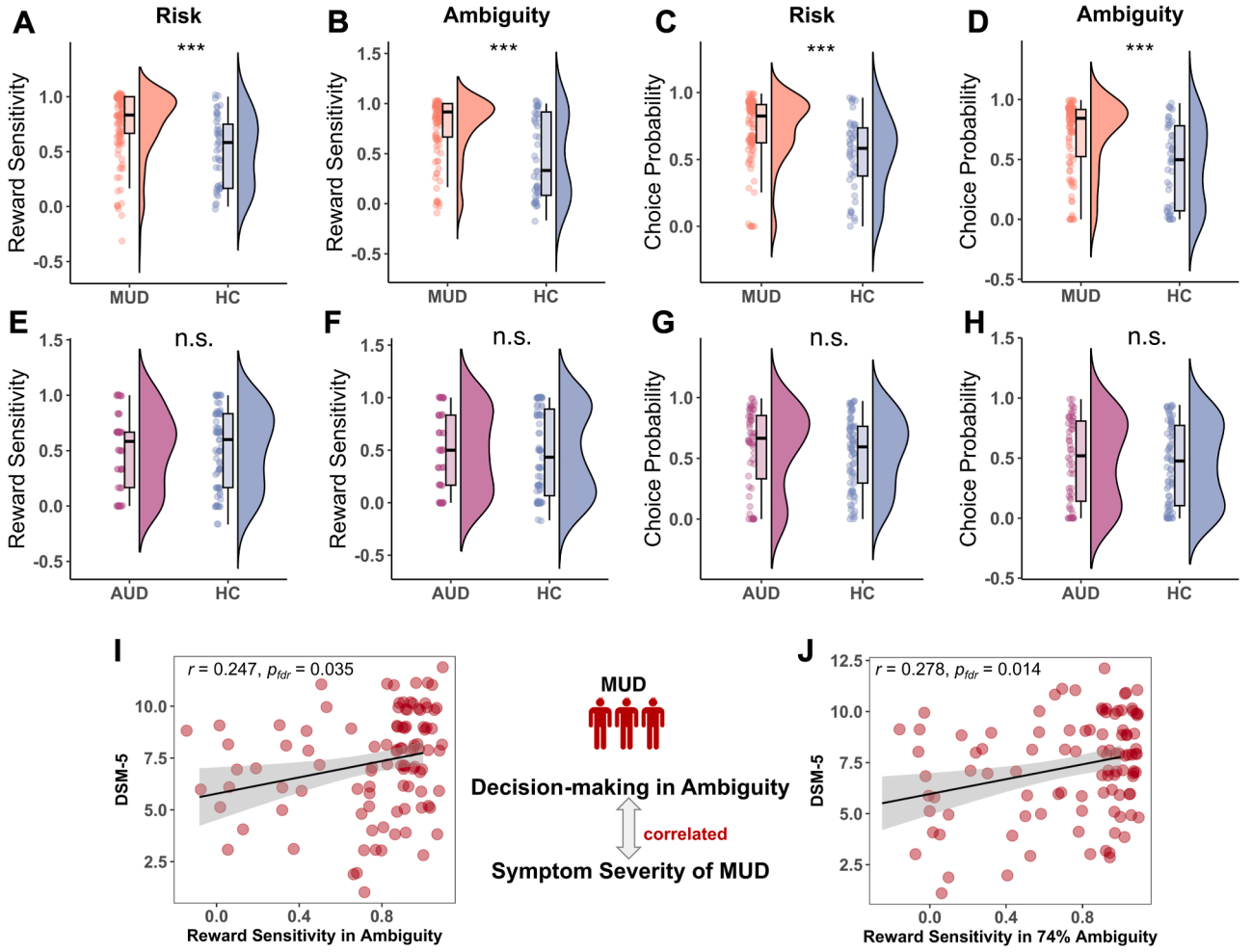

Figure 4. Individual decision-making behaviors in risky and ambiguous contexts. **(A–D)** Comparisons in reward sensitivity and choice probability under risk and ambiguity between the methamphetamine use disorder (MUD) and healthy control participant (HC) groups. **(E–H)** Comparisons of reward sensitivity and choice probability under risk and ambiguity between the alcohol use disorder (AUD) and HC groups. Panels **(I, J)** depict the correlations between DSM-5 scores and reward sensitivity under ambiguity, including overall ambiguity and specifically at 74% ambiguity. In the MUD group, there was a significant correlation between reward sensitivity and DSM-5 scores, especially 74% ambiguity. ***$p < .001$; significant p values were corrected using the Benjamini-Hochberg false discovery rate (FDR). n.s., nonsignificant.

uncertainty weighting but exhibited significant distortion in lottery reward valuation, as the model assuming objective probabilities and distorted reward values provided the best fit (Figure S3). Furthermore, the MUD group demonstrated higher subjective reward valuation than the HC group in both risky (γ: $z = 3.653$, $p_{FDR} < .001$) and ambiguous (γ: $z = 4.166$, $p_{FDR} < .001$) contexts, with no group differences in choice randomness ($ps > .05$) (Figure S2M–P).

We examined associations between UDM indicators and DSM-5 symptom severity using Pearson correlations. In the MUD group, reward sensitivity under ambiguity correlated with DSM-5 scores ($r = 0.247$, $p_{FDR} = .035$), particularly at 74% ambiguity ($r = 0.278$, $p_{FDR} = .014$) (Figure 4I–J). Other decision-making indicators showed no significant correlations ($ps > .05$) (Figure S4). These results suggest that reward sensitivity under high ambiguity may serve as a critical UDM indicator in MUD.

Individuals With AUD Exhibit Unaffected UDM Patterns

Demographic and clinical characteristics for 56 individuals with AUD and 75 matched HCs are presented in Table 1. Fitted curves illustrating responses across reward gradients at each uncertainty level are shown in Figure 2G–L. Modeling results indicated that the AUD group displayed decision-making patterns similar to those of the HC group, with no significant differences in parameters α, β, and L ($ps > .05$) (Figure 2N) or in choice probabilities across reward magnitudes ($ps > .05$) (Table S2).

In the risk context, parameter α differed significantly between 25% and 75% risk in both AUD (*diff* = 0.294, p_{FDR} = .009) and HC (*diff* = 0.239, p_{FDR} = .009) groups (Figure 3C), indicating that higher rewards were needed to attract choices as risk increased. In the AUD group, reward sensitivity (β)

decreased with increasing risk ($diff_{r75-r50} = -2.920$, $p_{FDR} = .042$; $diff_{r75-r25} = -4.945$, $p_{FDR} = .024$), while in the HC group, the maximum choice probability (L) decreased ($diff_{r75-r50} = -0.254$, $p_{FDR} < .001$; $diff_{r75-r25} = -0.270$, $p_{FDR} < .001$). Choice probabilities also differed across risk levels when lottery rewards exceeded 140 in the AUD group or 56 in the HC group ($ps < .05$) (pairwise results are shown in Table S4), suggesting that participants adjusted their choices as known probabilities changed. Statistical details are shown in Table S7.

In the ambiguous context, a significant difference in choice probability across ambiguity levels was observed only at a reward magnitude of 350 in the HC group ($\chi^2_2 = 9.700$, $p_{FDR} = .039$), with no other differences in choice probability or parameters α, β, and L between the AUD and HC groups (Figure 3D). This suggests that individuals with AUD and HCs showed similar decision making across ambiguity levels. Additionally, maximum choice probabilities remained around 0.5 in both groups, indicating a conservative strategy across all ambiguity levels.

At the individual level, decision making in the AUD group was similar to that of the HC group across all measures, including reward sensitivity, choice probability, reward distortion, and choice randomness under both risk and ambiguity ($p_{FDR} > .05$) (Figure 4E–H; Figure S5). These findings are consistent with the group-level results. Additionally, no correlations were found between decision-making indicators and DSM-5 scores in the AUD group ($ps > .05$) (Figure S6).

Different Substances May Have Distinct Impacts on Decision Making

To examine whether individuals with MUD differ from individuals with AUD in decision making, we compared UDM performance in the 2 groups at both group and individual levels, adjusting for age and abstinence differences (Table S5). At the group level, individuals with MUD showed higher reward sensitivity under high uncertainty ($p_{FDR} \leq .039$), higher maximum choice probabilities at all uncertainty levels except 75% risk (Figure S7), and a greater preference for lotteries with medium and large rewards across most conditions ($ps < .05$) (Table S2), suggesting more pronounced decision-making deficits than in individuals with AUD. At the individual level, the MUD group also exhibited higher reward sensitivity and choice probability under both risk and ambiguity ($p_{FDR} < .003$) (Figure S8A–P). In contrast, subjective value model results showed no differences in reward distortion under risk ($t_{153} = -1.388$, $p = .220$) (Figure S8Q). Collectively, these slight inconsistencies across analytic approaches suggest that AUD may involve only subtle decision-making impairments, with behavioral patterns intermediate between the MUD and HC groups.

DISCUSSION

Impaired decision making is a hallmark of SUDs and has been extensively studied for its clinical implications (20,54–56). Here, we utilized a CRA task, combined with group- and individual-level analyses, to identify context-specific impairments in different SUDs.

As expected and consistent with previous findings (57,58), individuals with MUD showed altered decision making, marked by heightened reward sensitivity and preference for large rewards, whereas individuals with AUD showed no significant deviations from HCs across uncertainty levels. Although neural activity was not directly assessed in this study, the distinct decision-making patterns in MUD and AUD may reflect substance-specific effects on reward and uncertainty-related neural circuits. Methamphetamine serves as a potent stimulant to enhance dopamine and norepinephrine signaling, producing intense euphoria and heightened arousal (59,60). Its use has been linked to hypofrontality, anterior cingulate cortex dysfunction, and parietal hyperactivity (61–63), potentially promoting reactive choices toward large rewards despite high uncertainty (64). In contrast, alcohol functions as a depressant to diminish prefrontal activation and induces milder hedonic effects (65,66). AUD is associated with broader disruptions across frontal, parietal, cerebellar, and limbic structures (67,68), which often emerge gradually with prolonged use (69–71). Given these differences, the stronger preference for large, uncertain rewards in MUD may reflect heightened neural reactivity not observed in AUD (72).

The observation that individuals with AUD showed UDM patterns comparable to those of HCs may be explained by several converging factors. First, previous research suggests that moderate or even chronic alcohol use does not consistently impair value-based decision making, especially in high-functioning individuals. For example, Bernhardt *et al.* (73) and Karlsson *et al.* (74) found no acute effects of alcohol on impulsivity or risk taking, indicating that core decision-making processes may remain intact. Second, value-based decision making consists of 5 basic processes, including representation, valuation, action selection, outcome evaluation, and learning (16), with most SUD studies focusing on the latter stages (75,76). Different from previous research, the current study primarily focuses on valuation and action selection, where participants with AUD showed minimal impairments. Third, alcohol-related neural deficits tend to be subtler and more gradual than those of methamphetamine (77,78), often emerging only in advanced stages marked by widespread brain atrophy (e.g., in the frontal, temporal, parietal, occipital, and subcortical regions) (79,80). Finally, abstinence might have supported recovery in our AUD sample. Several studies have found that abstinence facilitates brain recovery across a wide range of regions, including the frontal, parietal, and occipital cortices; cerebellum; and white matter (81–83).

We hypothesized that decision-making performance would vary between risk and ambiguity. Consistent with this, both the AUD and HC groups adjusted their behavior under risk, with increasing uncertainty leading to higher inflection points and reduced reward sensitivity and choice probability, but they maintained stable, conservative patterns under ambiguity. It indicates distinct processing of the 2 contexts. However, the MUD group exhibited similar patterns across both contexts, indicating a generalized, context-insensitive strategy. Specifically, in ambiguous contexts, individuals with MUD displayed atypical behavioral flexibility, shifting from optimism to conservatism as ambiguity increased and possibly reflecting maladaptive reward maximization. Unlike AUD and HC participants who consistently preferred safer options, participants in the MUD group prioritized large rewards despite uncertainty. This behavioral pattern is consistent with the well-established

understanding that repetitive and maladaptive reward seeking is a core feature of SUDs. Supporting this interpretation, animal studies have shown that addicted rats continue pressing a lever despite punishment by footshock (84–86), indicating stubborn actions directed toward narrow goals and blunted responses to negative consequences. Similarly, individuals with MUD appeared to disregard adverse contextual cues, maintaining a rigid preference for lottery options during UDM.

Overall, our findings underscore more severe decision-making deficits in MUD, with reward sensitivity under high ambiguity (74%) emerging as a key correlate of clinical symptom severity. This highlights that decision making with high-level ambiguity should be of great concern in MUD. Based on previous studies, it can be inferred that heightened striatal sensitivity may be elicited by large, uncertain rewards, increasing the incentive salience (87), while concurrent impairments in prefrontal cognitive control weaken the ability to regulate such impulses (61,88). Due to the dysfunction in salience processing and prefrontal regulation, persistent maladaptive reward seeking may occur despite high-level uncertainty, which could be also reflected in the symptom severity. Therefore, relevant brain regions could be potential targets for future neurobiological investigations of UDM in SUDs. Currently, neuropsychological interventions for SUDs often lack precision in targeting decision-making impairments (89). Incorporating disorder-specific decision-making profiles may enhance interventions such as cognitive behavioral therapy (90), goal management training (91), and working memory training (92). For MUD, strategies aimed at reducing reward sensitivity and improving risk processing may be particularly beneficial. For AUD, targeting outcome evaluation and learning, while considering disorder progression and individual alcohol use patterns, may offer more tailored therapeutic gains (75,76).

These findings raise the question of how individuals with SUDs balance reward and uncertainty during decision making. One possibility is that individuals with MUD prioritize reward, while individuals with AUD and HCs focus more on risk. Future studies could examine this from 2 angles. First, eye-tracking techniques may offer concrete evidence of an attentional bias during decision making (93), such as increased focus on rewards in MUD. Although previous work has applied eye tracking to gambling and healthy populations (94,95), its use in SUDs remains limited. Second, neuroimaging could help clarify the neural mechanisms behind these differences, thereby informing more precise interventions for decision-making impairments.

Limitations

This study has several limitations. First, the lack of longitudinal follow-up prevents evaluation of how UDM preferences relate to outcomes such as relapse. Second, individual-level modeling using the modified psychometric function was limited by the small number of trials per condition; increasing trial numbers in future studies would improve parameter reliability. Third, including individuals who use other substances (e.g., nicotine) would offer a more comprehensive view of how different addictions influence decision making.

Conclusions

This study reveals distinct UDM patterns in individuals with MUD and AUD, highlighting the heterogeneity of decision-making impairments across SUDs. These behavioral differences offer important insights for identifying core neural mechanisms and advancing disorder-specific therapeutic strategies.

ACKNOWLEDGMENTS AND DISCLOSURES

This work was funded by National Science and Technology Innovation 2030 Major Project of China (Grant No. 2021ZD0203900 [to DZ]), the Fundamental Research Funds for the Central Universities (Grant No. G2025ZD07 [to DZ]), National Natural Science Foundation of China grants (Grant Nos. 81822017 [to T-FY], 82422029 to [to DZ], 82325019 [to T-FY], 82271530 [to DZ], and 32441102 to [R-YZ], the Science and Technology Commission of Shanghai Municipality, China (Grant Nos. 24Y22800200 [to DZ], 23XD1423000 [to T-FY], 23ZR1480800 [to T-FY], and 2024AIZD014 [to R-YZ]), the Shanghai Municipal Commission of Health (Grant No. 2022JC016 [to T-FY]), the Scientific Research and Innovation Team of Liaoning Normal University (Grant No. 24TD004 [to DZ]), STI2030-Major Projects (Grant No. 2022ZD021170 [to YC]), and the Construction Fund of Key Medical Disciplines of Hangzhou (Grant No. 2025HZPY04 [to YC]).

We thank Tao Zhang, Tao Tang, Likan Liu, Meng Chen, Yujing Wang, Xi Li, Jiyu Xie, Yuanyuan Yin, Xuewei Qin, Yunhao Gu, Yirun Qi, Hangbin Zhang, Quanhao Yu, and Hong Wang for their help in collecting data.

XCh, T-FY, and DZ designed the experiment. XCh, YZ, JS, JL, XCa, YL, and JT performed the study in individuals with MUD. YZ, YC, WS, SH, WY, DW, and HW performed the study in individuals with AUD. XCh, YZ, YC, WS, SH, XCa, WY, DW, and HW performed the study in healthy participants. XCh, Y-FX, and R-YZ organized the data and analyzed the results. XCh, Y-FX, DZ, and T-FY wrote the article together. All authors read and approved the final version of the article.

The authors report no biomedical financial interests or potential conflicts of interest.

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Received Feb 10, 2025; revised Aug 16, 2025; accepted Aug 18, 2025.

Supplementary material cited in this article is available online at https://doi.org/10.1016/j.bpsc.2025.08.008.

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