Journal of Evidence-Based Psychotherapies,
Vol. 26, No. 1, March 2026, 93-116.

10.24193/jebp.2026.1.5

EFFECT OF AEROBIC EXERCISE ON RELAPSE TENDENCY IN INDIVIDUALS WITH METHAMPHETAMINE USE DISORDER IN A VIRTUAL SOCIAL ENVIRONMENT: MEDIATED BY CUE-INDUCED CRAVING AND INTEROCEPTIVE SENSIBILITY

Xiaoxia Liu and Zefan Fan[1]*

[1] Department of Physical Education, Tongling University, Tongling 244061, China.

Abstract

Interoceptive sensibility (IS) is a novel therapeutic target in drug relapse prevention. The beneficial mechanisms of exercise on methamphetamine relapse remain unclear. This study assessed the effects of aerobic exercise on cue-induced craving reactivity (including heart rate variability [HRV], methamphetamine-craving, and methamphetamine-using), IS, and relapse tendency in a methamphetamine-related virtual reality environment among individuals with methamphetamine use disorders (MUD). We further examined the role of craving reactivity and IS in aerobic exercise and relapse tendency. Exercise (n = 36) and control (n = 35) groups received eight weeks of aerobic exercise or health education, respectively (5 times/week, 60 minutes/session). HRV_{cue}, methamphetamine-craving, methamphetamine-using, IS, and relapse tendency were measured at pre-test and post-test on the same day. The exercise group exhibited a larger decrease in craving reactivity, IS, and relapse tendency from the pre-test to the post-test compared to the control group. Craving reactivity and IS changes mediated the relationship between exercise intervention and decreased relapse tendency (β = 1.505–2.009, 95% CI: 0.378–3.736). Aerobic exercise improves relapse tendency in individuals with MUD. The underlying mechanisms may include reduced cue-induced craving reactivity and IS.

Keywords: aerobic exercise; cue-induced craving; interoceptive sensibility; METH-related virtual reality environment; relapse tendency

* Correspondence concerning this article should be addressed to Zefan Fan, Department of Physical Education, Tongling University, 1335 Cuihu 4th Road Economic and Technological Development Zone, Tongling 244061, Anhui Province, People's Republic of China.
Telephone: +8613696527047.
E-mail: fl700615@163.com

1. Introduction

Methamphetamine (METH), a highly addictive psychostimulant, is the second most widely used class of illicit drugs worldwide (Chen et al., 2024; United Nations Office on Drugs and Crime, 2024). One main challenge in treating METH addiction is the high rate of relapse during abstinence (Tan et al., 2019; United Nations Office on Drugs and Crime, 2024). When drug users are exposed to drug-related cues, such as drugs, drug-use environments, and paraphernalia, an intense desire for the drug could be induced (Tan et al., 2019; Wang, Liu, & Shen, 2019). This reactivity to drug-related cues, including mental (e.g., craving and attention bias), psychophysiological (e.g., heart rate variability [HRV], skin conductance, and brain activity), and behavioral (e.g., the possibility of subsequent drug-using and drug-seeking) responses, is usually described as craving and results in drug-seeking and drug-taking behaviors, which can cause relapse (Chen et al., 2024; Sayette, 2016; Tan et al., 2019). For methamphetamine use disorder (MUD), craving is one of the most important symptoms and serves to maintain this addictive behavior and relapse (Wang et al., 2019). During abstinence from METH, craving is always elicited by the METH-related cues (Hormes, 2017; Wang et al., 2019). Therefore, reducing METH-related cue-induced craving reactivity may help prevent relapse in individuals with MUD.

Despite amphetamine being the second most common illicit drug abused worldwide (Chen et al., 2024; United Nations Office on Drugs and Crime, 2024), no approved pharmacotherapies are available for amphetamine dependence (AshaRani et al., 2020). Multiple systematic reviews of pharmacotherapies reveal that no medication provides sufficient evidence to support its use in the routine clinical management of amphetamine use disorder (AshaRani et al., 2020; Chan et al., 2019; Lee, Jenner, Harney, & Cameron, 2018). In the absence of effective pharmacotherapy, psychotherapy is considered the first line of treatment, although this approach lacks scientific evidence as a standalone treatment (Donovan & Wells, 2007) due to high relapse rates (AshaRani et al., 2020; McKetin et al., 2012). Nevertheless, a previous study investigated the effectiveness of an 8-week brief intervention compared with an 8-week psychoeducation program and showed that both the brief intervention and psychoeducation are effective in reducing methamphetamine use among individuals with MUD (Srisurapanont, Sombatmai, & Boripuntakul, 2007). Besides psychotherapy, other non-pharmacological interventions such as physical exercise and other programs targeting MUD have been studied in recent years (AshaRani et al., 2020; Liu & Wang, 2021, 2023; Rawson et al., 2015). Given the lack of evidence supporting the use of pharmacotherapies to treat MUD, the efficacy of alternative treatments must be evaluated.

Physical exercise is a promising, medication-free, and cost-effective adjunct treatment for MUD (AshaRani et al., 2020; Lynch, Peterson, Sanchez, Abel, & Smith, 2013). Studies have reported that exercise-based interventions may prevent relapse of MUD not only through a direct pathway but also through indirect pathways, such as the mediating roles of intrinsic restraint and yearning for drugs, as well as by remodeling the reward pathway (Lynch et al., 2013; Morais, Pita, Fontes-Ribeiro, & Pereira, 2018; Ouyang et al., 2020; Song et al., 2023). Traditionally, drug-cue craving reactivity relies mostly on pictures or videos presenting drugs and drug-associated paraphernalia. However, these methods typically elicit modest subjective craving (Avants, Margolin, Kosten, & Cooney, 1995), less effectively inducing a reliable physiological reactivity (Dudish-Poulsen & Hatsukami, 1997; Ooteman, Koeter, Verheul, Schippers, & van den Brink, 2006). Therefore, researchers have developed METH-related virtual reality (VR) social environments, which offer unique advantages due to their full immersion experience and realism (Culbertson et al., 2010; Tan et al., 2019) and are sufficient to elicit more reliable cravings and corresponding physiological reactivity than traditional methods (Wang, Shen, & Wu, 2018; Wang et al., 2019). Exploring the effects of physical exercise on METH-cue craving reactivity in VR cue-exposure environments may have significant practical and clinical implications for evaluating the effectiveness of exercise strategies.

Recently, interoception (i.e., receiving, processing, and integrating body-relevant signals with external stimuli to affect ongoing motivated behavior) has been recognized as another important process that contributes to the degree to which an individual approaches or avoids drug abuse and relapse (Paulus & Stewart, 2014; Reiner & Shaham, 2022). Long-term substance abuse has been found to negatively impact the brain's ability to process interoceptive information and impact the reward system (Paulus, Tapert, & Schulteis, 2009), leading to decreased sensitivity to natural rewards and increased sensitivity to drug stimuli (Herman, 2023; Volkow, Michaelides, & Baler, 2019). A recent analysis provided evidence that individuals with substance use disorder (SUD) show lower interoceptive accuracy and higher interoceptive sensibility (IS) compared to healthy controls (Jakubczyk et al., 2019a). In the context of SUD, higher IS has been associated with clinical correlates of relapse, such as craving, withdrawal, tolerance, and reward processing (Bonaz et al., 2021; Jakubczyk et al., 2019b; Reiner & Shaham, 2022). Therefore, reducing cue-induced or context-induced high IS may represent novel therapeutic targets for the treatment of drug relapse (Herman, 2023; Reiner & Shaham, 2022). Recent evidence suggests that physical exercise may help people with SUD to better decode and interpret bodily-related signals associated with transient states of homeostatic imbalances that usually trigger consumption (Brevers et al., 2024). Nevertheless, evidence regarding the effectiveness of physical exercise on IS and the role of IS in the relationship between physical exercise and relapse is currently very limited; therefore, further research is needed to examine this (Brevers et al., 2024; Reiner & Shaham, 2022).

This study aimed to compare the effects of physical exercise versus psychoeducation on METH-cue craving reactivity (including HRV, METH-craving, and METH-using), IS, and relapse tendency in a METH-related VR environment among individuals with MUD. We further examined the role of craving reactivity and IS in physical exercise and relapse tendency.

2. Methods

2.1 Participants

In total, 120 men with MUD from local residential illicit drug isolation and treatment centers were recruited for this study. The participants met the Diagnostic and Statistical Manual of Mental Disorders IV-revised diagnostic criteria, as determined via the Mini-International Neuropsychiatric Interview (Liu & Wang, 2021). The inclusion criteria were (1) physician-administered physical examination and collection of medical history with resting 12-lead electrocardiography (ECG; Mortara, Milwaukee, WI, USA) to determine study eligibility; (2) no history of neurological disease or physical disability; (3) no use of medication affecting cardiovascular and cognitive function over the preceding 3 months; (4) no cognitive disorder or medical contraindications to exercise; (5) sufficient capacity to provide informed consent and complete all assessment instruments; and (6) normal color vision, normal or corrected-to-normal visual acuity, and right-handedness. The exclusion criteria included the presence of musculoskeletal conditions and unstable cardiovascular, pulmonary, or other disorders. Finally, 82 participants who met the inclusion and exclusion criteria were randomly divided into two groups (Figure 1). All participants were informed that participation was voluntary, that they were free to withdraw at any time, and that their personal information would be kept confidential. This study was approved by the ethics committee of X Institutional Review Board, and written informed consent was obtained from all participants.

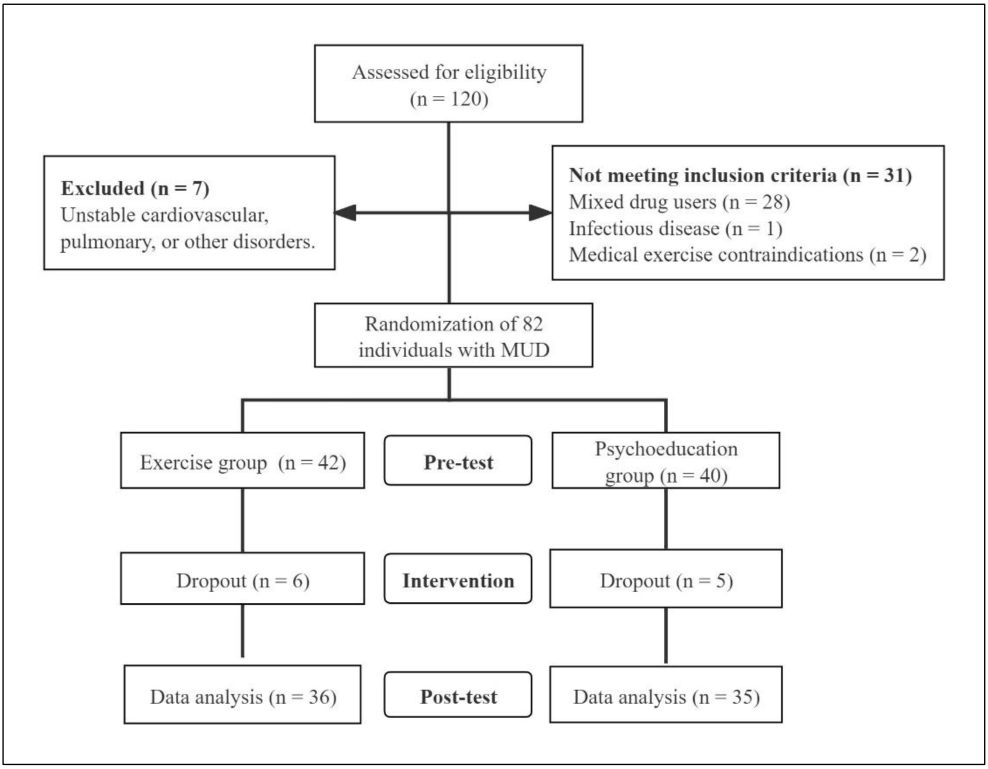

Figure 1. CONSORT diagram presenting the participant flow in the study

2.2 METH-related VR environment

We used the METH-related virtual social environment developed and tested in previous research and promoted in drug rehabilitation centers to elicit subjective psychological and physiological reactivity (Wang et al., 2018, 2019). The video depicts a real-life story of individuals who are using METH together and who invite the observers to take METH. Specifically, the video is divided into six scenes (Figure 2) (Wang et al., 2018; Wang et al., 2019). During the first scene (~60 s), the participants saw a black screen and heard voices luring them to take drugs (sounds likely to invite the participants to take METH, i.e., auditory cues with social interaction). In the second scene (~60 s), the participants viewed a person playing with "ice" and drug paraphernalia (i.e., drugs and drug-associated paraphernalia). During the third scene (~180 s), the participants experienced themselves in a room (with a first-person perspective), in which they could see six people using METH together (i.e., METH-use environment). During the fourth scene (~60 s), the participants viewed close-up scenes highlighting the facial expressions of all six people using METH (i.e., facial expression information). During the fifth scene (~60 s), the participants viewed close-up scenes highlighting the specific way that METH was being used (i.e., action cues). During the sixth scene (~60 s), the prepared drug and related paraphernalia were presented in a man's hand and moved toward the participants. This scene gave the participants the impression that they were being invited to use METH (i.e., "psychological interaction" with the observers). All the audio tracks were processed using Nuendo to create 5.1 analog sound channels. The VR video was rendered onto a spheroid to create a subject-centric immersive experience, and the viewing angle was pre-determined for specific scenes requiring close-ups (Wang et al., 2018, 2019).

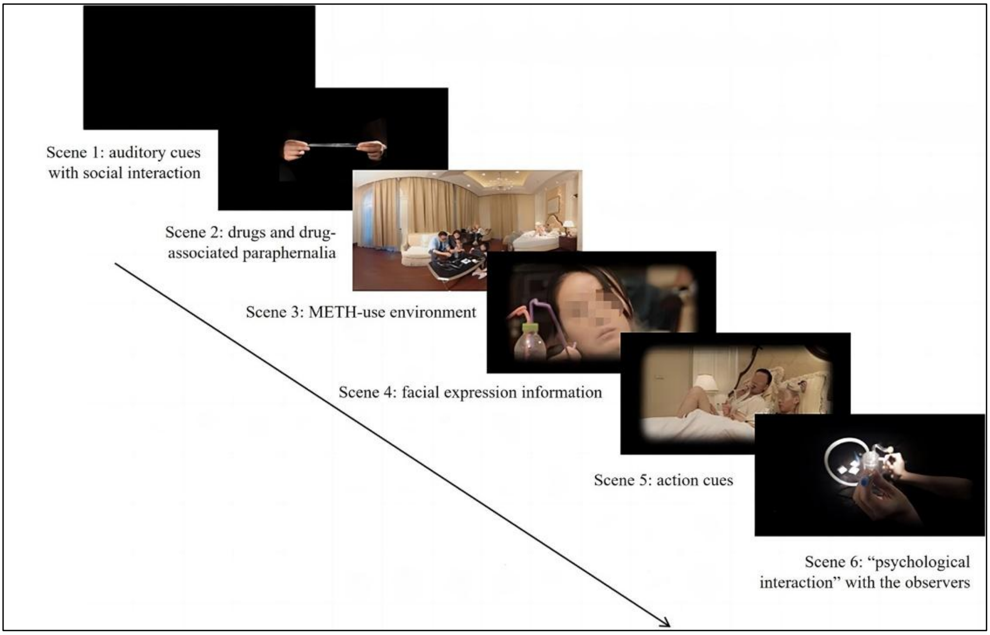

Figure 2. Diagram of the METH-related VR environment

2.3 Procedure and outcome measures

All outcome measures were assessed in a quiet room at a stable temperature (23–25 °C). The participants were asked to avoid strenuous exercise for 48 hours before the test. The participants' demographic characteristics, drug-use history, and $HRV_{baseline}$ were assessed at baseline. A researcher-developed questionnaire was used to assess age, education, and drug-use history (including duration of drug use, frequency, and total amount of METH used). Height, weight, and body mass index were measured using an electronic weight tester in the National Physical Fitness

Monitor (Beijing, China). Before testing the $HRV_{baseline}$, all participants rested comfortably in a chair for at least 5 minutes. They were then introduced to the equipment (i.e., HRV recording device and headphones) and assisted with putting on the equipment. After the participants felt comfortable with all the settings, they were asked to remain seated without speaking or moving. When the test began, the participants were instructed to breathe rhythmically at the same frequency to record an 8-minute $HRV_{baseline}$ (Liu & Wang, 2021). Meanwhile, a heart rate monitor (Polar FS2C, Polar Electro, Oy, Kempele, Finland) was used to measure the resting HR.

HRV_{cue}, METH-craving, METH-using, IS, and relapse tendency, in turn, were measured at pre-test and post-test on the same day. During the formal experiment, all participants were assisted with putting on the equipment (i.e., HRV recording device, VR helmet, and headphones). After the participants felt comfortable with all the settings, they were asked to remain seated without speaking or moving and breathe rhythmically at the same frequency. An 8-minute period of the resting condition continuous HRV signals (i.e., $HRV_{before\ video}$) was recorded. Then, the participants were required to view an 8-minute METH-cue VR video with concurrent recording of HRV signals (i.e., $HRV_{during\ video}$) (Wang et al., 2018; Wang et al., 2019). Immediately after the VR video finished, the participants self-reported METH-craving, METH-using, IS, and relapse tendency in turn. Unlike subjective reports, HRV is an objectively recorded natural physiological response that does not involve learning or practice effects but is highly influenced by the testing environment. Therefore, we calculated HRV_{cue} parameters (i.e., $HRV_{during\ video}$ minus $HRV_{before\ video}$) for statistical analysis.

2.3.1 METH-cue VR-induced HRV reactivity

As per the previously established method, HRV was measured using a wearable HR monitor and a chest belt (RS800CX Polar Electro Oy, Kempele, Finland) with a sampling rate of 1,000 Hz for subsequent analyses of HRV (Eggenberger et al., 2020; Williams et al., 2017). We calculated HRV parameters, including time-domain (i.e., standard deviation of normal-to-normal intervals [SDNN], root mean square differences of the standard deviation [RMSSD], percentage of beats that changed more than 50 ms from the previous beat [pNN50]), and frequency-domain (i.e., low-frequency [LF], high-frequency [HF], and low-frequency to high-frequency ratio [LF/HF]; using autoregressive estimates) (Dolezal et al., 2014; Gamelin, Berthoin, Sayah, Libersa, & Bosquet, 2007; Liu & Wang, 2021).

2.3.2 METH-cue VR-induced subjective METH-craving

A visual analogue scale (VAS) (Mottola, 1993) regarding subjective craving assessed the participants' METH-craving. The participants were asked: "How much do you crave METH/ice right now?" (possible scores ranged from 0–10, "0" indicating "no craving at all" and "10" indicating "extremely strong craving"). The VAS consisted of an 11-point scale, which has good reliability and validity. A higher score indicates greater METH-craving.

2.3.3 The possibility of METH-using immediately after exposure to VR cues

A VAS regarding the possibility of METH-using was used to assess the participants' METH-using: "If you had access to METH/ice right now, how likely would you be to use it right away?" (possible scores ranged from 0–10; "0" indicating "certainly not" and "10" indicating "certainly") (Wang et al., 2019).

2.3.4 IS immediately after exposure to VR cues

The Private Body Consciousness Subscale (PBCS) (Miller, Murphy, & Buss, 1981) from the Body Consciousness Questionnaire consists of 5 items reflecting the tendency to focus on internal body sensations. Specifically, it assesses awareness of internal bodily tensions, dry mouth/throat, heart beating, hunger, and body temperature (e.g., "I am sensitive to internal body tensions," "I'm very aware of changes in my body temperature") (Jakubczyk et al., 2019a). Items were rated for the extent to which they are characteristic of the respondent on a 5-point scale, ranging from 0 (extremely uncharacteristic) to 4 (extremely characteristic). Overall scores were computed as the mean of all items so that higher scores indicated greater IS. The PBCS has good reliability and validity in clinical samples (Mehling et al., 2009; Todd et al., 2022). Cronbach's alpha of the PBCS in this study was 0.79.

2.3.5 Relapse tendency immediately after exposure to VR cues

The Inclination of Relapse Scale of Drug Rehabilitated Addicts (Song et al., 2023; Wang, 2001) was used to assess the participants' subjective relapse tendency. The scale consists of 18 items, each rated on a 6-point Likert scale. Higher scores indicate a greater tendency to relapse. Cronbach's alpha of the scale in this study was 0.82.

2.4 Intervention

2.4.1 Physical exercise

The exercise group engaged in a treadmill aerobics program 5 times per week, 60 minutes per session, for 8 weeks. The exercise phase consisted of walking or jogging on a treadmill for 5 minutes (warm-up phase). After the warm-up phase, the participants gradually increased the treadmill speed and slope to reach 60–80% maximum HR (defined as 206.9 - 0.67×age) within 5 minutes under the guidance of a trainer (Liu & Wang, 2023). The participants then maintained this intensity for 40 minutes. If a participant was unable to complete 40 continuous minutes, rest periods were introduced until the participant accumulated a total of 40 minutes at this intensity (Dolezal et al., 2014; Liu & Wang, 2021). Finally, the participants performed 10 minutes of cool-down activities. The participants wore an HR monitor (Polar FS2C, Polar Electro, Oy, Kempele, Finland) connected to a system monitoring HR in real-time. At least three well-trained, experienced coaches guided each exercise process.

2.4.2 Psychoeducation

The psychoeducation group received an 8-week structured psychoeducation program (5 times per week, 60 minutes per session for 8 weeks) with three trained and experienced psychological health educators. The courses included education on health screening, healthy diet, stress reduction, healthy relationships, and healthy lifestyles.

2.5 Data processing

In line with previous studies, the Polar Pro-Trainer 5 software (RS800CX Polar Electro Oy, Kempele, Finland) was used to transmit the recorded data to the computer (Eggenberger et al., 2020; Liu & Wang, 2021; Williams et al., 2017). The first 30 recorded seconds were deleted to reduce initial motion artifacts, and the subsequent data were used for analysis. Artifacts were processed in two different ways: (1) interpolation of artifacts using Kubios HRV analysis software (version 2.2, Kubios Oy, Kuopio, Finland; settings: custom=0.2, interpolation rate=4 Hz); and (2) deletion of artifacts using MATLAB software (version R2016b, MathWorks Inc., Natick, MA, USA). R–R intervals <200 ms, >2,000 ms, or >20% interval-to-interval deviation were removed. Finally, using the aforementioned method, artifact examination with MATLAB software yielded a mean of 6.93% (±3.14%) artifacts per R–R interval recording. R–R interval time series with ≥80% non-artifact R–R intervals were used for further analyses (Peltola, 2012), while time series below this value (and the associated HRV indices) were replaced with the group mean value (Liu & Wang, 2021).

2.6 Statistical analyses

An a priori power analysis was conducted using G*Power (version 3.1) for a 2 (group: exercise vs. psychoeducation) × 2 (time: pre-test vs. post-test) repeated-measures ANOVA (within–between interaction). Based on prior studies of exercise interventions suggesting small-to-moderate effects on cue-induced craving reactivity (Liu & Wang, 2023; Peng, Chen, Su, Tao, & Wang, 2021; Shen, Du, Fan, Dai, & Wei, 2023; Wang, Zhu, Zhou, & Chang, 2017), we assumed a conservative effect size (Cohen's f = 0.25), with α = .05 and power (1 – β) = .90. The analysis indicated that a minimum of 23 participants per group was required to detect the Group × Time interaction. The current study exceeded this requirement (exercise group: *n* = 36; psychoeducation group: *n* = 35).

All data were analyzed using SPSS 20.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were first computed for participant demographic characteristics, drug-use history, and $HRV_{baseline}$. Data were expressed as means and standard deviations (SDs). The independent samples *t*-tests or chi-square tests were conducted to compare differences between the two groups in demographic characteristics, drug use history, and $HRV_{baseline}$ at baseline. A repeated-measures ANOVA was used to examine variable changes between the pre- and post-tests. Group was the between-subjects factor, and time point was the within-subjects factor. Further post-hoc multiple comparisons were conducted using the Bonferroni correction.

Pearson correlation was performed to analyze the relationship between changes (post-test – pre-test) for IS, METH-craving, METH-using, HRV_{cue}, and relapse tendency. Furthermore, mediation analysis was conducted using the PROCESS 3.5 macro developed by Hayes (2013). The significant indirect effect was examined using bias-corrected confidence intervals derived from 5,000 bootstrap samples (Shen et al., 2023). An effect was considered significant if its 95% bootstrap confidence interval (CI) did not include zero (Shen et al., 2023). All statistical tests were two-tailed. Statistical significance was indicated as $p < .05$. Effect sizes (η_p^2) were also reported.

3. Results

3.1 Baseline characteristics

No significant differences between groups were found at baseline in demographic characteristics, drug-use history, and $HRV_{baseline}$ (Table 1).

Table 1. Baseline characteristics

Variable	Exercise group (*n*=36)	Psychoeducation group (*n*=35)
Age (years)	35.31 ± 3.12	34.89 ± 4.60
Education (years)		
Elementary school	1 (2.78%)	1 (2.86%)
Junior high school	4 (11.11%)	9 (25.71%)

Variable	Exercise group (n=36)	Psychoeducation group (n=35)
Senior high school	27 (75.00%)	23 (65.71%)
College	4 (11.11%)	2 (5.71%)
Height (cm)	171.39 ± 4.99	170.03 ± 5.28
Weight (kg)	72.14 ± 7.57	70.86 ± 6.32
BMI (kg/m^2)	24.55 ± 2.22	24.50 ± 1.80
HR_{rest} (bpm)	73.81 ± 8.42	74.40 ± 7.41
Drug-use history		
Duration of drug use (years)	13.64 ± 3.31	13.81 ± 2.67
Frequency (times/week)	6.03 ± 1.86	5.66 ± 1.75
Total amount of METH used (g)	2394.93 ± 612.78	2381.39 ± 464.99
Withdrawal duration (months)	8.56 ± 3.12	9.03 ± 2.88
$HRV_{baseline}$		
SDNN	41.98 ± 0.36	42.85 ± 0.27
RMSSD	31.68 ± 0.61	31.57 ± 0.59
pNN50	13.59 ± 0.39	13.85 ± 0.44
nLF	0.62 ± 0.03	0.61 ± 0.02
nHF	0.26 ± 0.03	0.27 ± 0.03
LF/HF ratio	4.00 ± 0.65	3.90 ± 0.57

Note. Values are mean ± standard deviation. BMI, body mass index; bpm, beats per minute; HR_{rest}, resting heart rate.

3.2 Changes in indices before and after intervention

No significant differences between groups were found at the pre-test for all outcome measure scores. Repeated-measures ANOVA indicated significant interactions between time and group in METH-craving [$F_{(1,69)}$ = 17.204, p < .001, η_p^2 = 0.200], IS [$F_{(1,69)}$ = 12.935, p = .001, η_p^2 = 0.158], and relapse tendency [$F_{(1,69)}$ = 8.027, p = .006, η_p^2 = 0.104] and significant main effects of group in METH-craving [$F_{(1,69)}$ = 12.167, p = .001, η_p^2 = 0.150] and IS [$F_{(1,69)}$ = 4.866, p = .031, η_p^2 = 0.066], but no significant main effect of group in relapse tendency. The exercise group exhibited significantly lower scores on IS, METH-craving, and relapse tendency than the psychoeducation group in the post-test (Figure 3). For the VAS score on METH-using, there was a marginally significant interaction between time and group [$F_{(1,69)}$ = 3.893, p = .052, η_p^2 = 0.053], and a significant main effect of time [$F_{(1,69)}$ = 18.051, p < .001, η_p^2 = 0.289], reflected by a significant decrease from pre- to post-test in both groups. No significant main effect of group was found in METH-using.

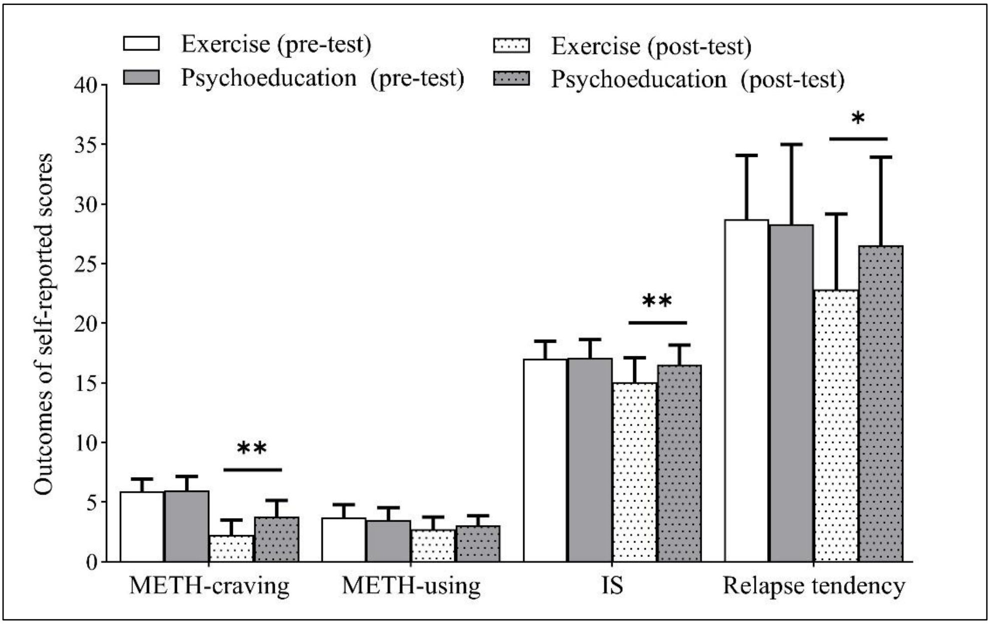

Figure 3. Outcomes of self-reported scores (*indicates $p < .05$, **indicates $p < .01$)

For HRV_{cue} parameters, there were significant interactions between time and group in SDNN [$F_{(1,69)} = 6.470$, $p = .013$, $\eta_p^2 = 0.086$], RMSSD [$F_{(1,69)} = 11.603$, $p = .001$, $\eta_p^2 = 0.144$], and pNN50 [$F_{(1,69)} = 6.969$, $p = .01$, $\eta_p^2 = 0.092$] and significant main effects of group in SDNN [$F_{(1,69)} = 6.991$, $p = .010$, $\eta_p^2 = 0.092$], RMSSD [$F_{(1,69)} = 17.154$, $p < .001$, $\eta_p^2 = 0.199$], and pNN50 [$F_{(1,69)} = 16.618$, $p < .001$, $\eta_p^2 = 0.194$]. The exercise group exhibited a significantly larger decrease in time-domain HRV_{cue} indices from pre- to post-test compared to the psychoeducation group (Table 2). There were significant main effects of time in nLF [$F_{(1,69)} = 5.507$, $p = .022$, $\eta_p^2 = 0.074$], nHF [$F_{(1,69)} = 19.192$, $p < .001$, $\eta_p^2 = 0.218$], and LF/HF ratios [$F_{(1,69)} = 6.152$, $p = .016$, $\eta_p^2 = 0.082$], reflecting a significant change from pre- to post-test in both groups. No significant main effect of group and no significant interaction between group and time were found in the frequency-domain HRV_{cue} indices.

Table 2. Parameters of HRV in different states at pre-test and post-test for the two groups

Group		Pre-test			HRV_{cue} $P_{between}$	Post-test			HRV_{cue} $P_{between}$
		Before video	During video	Cue-induced		Before video	During video	Cue-induced	
SDNN	Exercise	41.98 ± 0.84	44.96 ± 0.90	2.98 ± 0.19	NS	55.86 ± 0.73	49.86 ± 0.61	-6.00 ± 0.31	< .001
	Psychoeducation	42.86 ± 0.83	45.84 ± 0.76	2.98 ± 0.25		43.38 ± 0.84	39.87 ± 0.73	-3.52 ± 0.24	

	Group	Pre-test			HRV_{cue} $P_{between}$	Post-test			HRV_{cue} $P_{between}$
		Before video	During video	Cue-induced		Before video	During video	Cue-induced	
RMSSD	Exercise	31.68 ± 0.62	38.32 ± 0.65	6.64 ± 0.10	NS	49.68 ± 0.79	46.34 ± 0.80	-3.34 ± 0.23	< .001
	Psychoeducation	31.57 ± 0.52	38.43 ± 0.50	6.85 ± 0.18		34.48 ± 0.60	34.61 ± 0.69	0.13 ± 0.26	
pNN50	Exercise	13.59 ± 0.39	17.56 ± 0.43	3.97 ± 0.16	NS	34.25 ± 0.61	32.38 ± 0.58	-1.87 ± 0.24	< .001
	Psychoeducation	13.86 ± 0.45	18.33 ± 0.42	4.47 ± 0.15		18.24 ± 0.91	18.54 ± 0.80	0.29 ± 0.22	
nLF	Exercise	0.60 ± 0.08	0.56 ± 0.10	-0.04 ± 0.03	NS	0.52 ± 0.10	0.49 ± 0.10	-0.03 ± 0.05	NS
	Psychoeducation	0.61 ± 0.09	0.56 ± 0.09	-0.05 ± 0.01		0.58 ± 0.09	0.55 ± 0.09	-0.03 ± 0.02	
nHF	Exercise	0.28 ± 0.10	0.30 ± 0.10	0.02 ± 0.03	NS	0.38 ± 0.10	0.38 ± 0.10	0.00 ± 0.05	NS
	Psychoeducation	0.27 ± 0.09	0.30 ± 0.09	0.03 ± 0.02		0.32 ± 0.09	0.32 ± 0.09	0.00 ± 0.02	
LF/HF ratio	Exercise	4.01 ± 0.16	3.83 ± 0.14	-0.17 ± 0.04	NS	3.40 ± 0.17	3.36 ± 0.15	-0.05 ± 0.35	NS
	Psychoeducation	3.97 ± 0.15	3.75 ± 0.12	-0.22 ± 0.05		3.97 ± 0.10	3.93 ± 0.11	-0.04 ± 0.28	

Note. Values are mean ± standard deviation. LF, low-frequency component; LF/HF, low-frequency to high-frequency ratio; nHF, high-frequency component; pNN50, percentage of beats that changed more than 50 ms from the previous beat; RMSSD, root mean square differences of the standard deviation; SDNN, standard deviation of normal-to-normal intervals; NS, not significant.

3.3 Correlation analyses

METH-craving change correlated with changes in SDNN ($r = 0.576$, $p < .001$) and RMSSD ($r = 0.526$, $p = .001$), indicating that greater decreases in subjective drug craving in the METH-related virtual social environment were associated with greater decreases in physiological responses after 8 weeks of aerobic exercise intervention in the exercise group. In addition, changes in IS were positively correlated with changes in METH-craving ($r = 0.453$, $p = .005$), SDNN ($r = 0.439$, $p = .007$), and RMSSD ($r = 0.343$, $p = .041$). The results indicated that greater decreases in IS were associated with larger declines in METH-related cue-induced reactivity. Moreover, greater decreases in relapse tendency correlated with greater declines in IS ($r = 0.539$, $p = .001$), METH-craving ($r = 0.580$, $p < .001$), and time-domain HRV_{cue} reactivity ($0.332 < r < 0.594$, $p < .005$).

3.4 Mediation analyses

Mediation effect analyses showed that changes in METH-craving ($\beta = 2.009$, 95% CI: 0.862–3.736), SDNN ($\beta = 1.505$, 95% CI: 0.378–3.256), and IS ($\beta =$

1.580, 95% CI: 0.380–3.551) mediated the relationship between the physical exercise intervention and changes in relapse tendency.

4. Discussion

This study compared the effects of physical exercise versus psychoeducation on METH-cue reactivity, IS, and relapse tendency in the VR cue-exposure environment among individuals with MUD. We further examined the role of METH-cue craving reactivity and IS in physical exercise and relapse tendency. As predicted, compared with the psychoeducation intervention, the 8-week aerobic exercise intervention produced greater reductions in craving reactivity (i.e., METH-craving and time-domain HRV_{cue}), IS, and relapse tendency from the pre-test to the post-test. METH-cue craving reactivity and IS mediated the relationship between physical exercise and relapse tendency. This suggests that the decreased METH-cue craving reactivity and IS in the VR cue-exposure environment might contribute to the effects of physical exercise on relapse tendency. To our knowledge, this is the first study to provide evidence that IS may be one of the mechanisms underlying the effect of physical exercise on the risk of relapse.

It is well-known that one main challenge in treating MUD is the high rate of relapse during abstinence (Reiner & Shaham, 2022). Cue-induced craving is widely regarded as a primary target in relapse prevention (Wang et al., 2019). The METH-VR model serves as a powerful clinical and research tool for manipulating acute craving in METH abusers (Culbertson et al., 2010). Studies have shown that craving has different forms, including mental, psychophysiological, and behavioral (Chen et al., 2024; Sayette, 2016; Tan et al., 2019). To comprehensively assess the effects of physical exercise on the improvement of acute craving induced by a METH-related VR social environment, we measured different forms of METH-cue craving reactivity. Our results showed that compared with the psychoeducation group, the VAS score for METH-craving in the exercise group significantly decreased after 8 weeks of aerobic exercise intervention. This suggests that physical exercise may effectively attenuate subjective craving in individuals with MUD. The METH-craving results obtained from METH-related VR cue exposure in this study agree with those reported using traditional exposure methods in previous studies (Huang, Zheng, Gao, Hu, & Yuan, 2019; Liu & Wang, 2023; Wang et al., 2017). However, we did not find a significant beneficial effect of physical exercise on the VAS score of METH-using. This may be attributed to the strict restrictions on drug use in the detoxification environment, which make it impossible to obtain drugs during the confinement period, resulting in low self-reported pre- and post-test scores for both groups. Additionally, a floor effect for VAS scores of METH-using may, in part, be responsible for the relatively small differences between groups, as speculated by previous studies (Wang et al., 2019).

The HRV_{cue} results showed that, compared with participants receiving the psychoeducation intervention, those receiving the aerobic exercise intervention exhibited a larger decrease in time-domain HRV_{cue} indices when exposed to VR cues. This suggests that the exercise group had a lower level of physiological arousal when exposed to METH-related VR cues. These results are consistent with the observations of previous studies in the resting state (Cabral et al., 2018; Dolezal et al., 2014; Liu & Wang, 2021), namely, that aerobic exercise contributes to the homeostasis of the autonomic nervous system in individuals with MUD. Moreover, changes in time-domain HRV_{cue} and METH-craving were positively correlated. As different manifestations of METH-cue reactivity, the reduction in METH-craving and HRV_{cue} components may be the mental and psychophysiological representation of decreased cue-related craving. This further supports that an 8-week aerobic exercise intervention may be a useful strategy in suppressing METH-cue reactivity in a VR cue-exposure environment in individuals with MUD.

In addition, reduced subjective craving and autonomic arousal upon exposure to substance-related cues help individuals with SUD experience fewer subjectively abnormal bodily sensations, which may ultimately reduce urges and the risk of relapse (Sharpe, Tarrier, Schotte, & Spence, 1995). In the present study, our findings revealed significant reductions in relapse tendency after physical exercise, which is consistent with the findings of previous studies (Lynch et al., 2013; Morais et al., 2018; Song et al., 2023). We also found that the change in METH-cue reactivity (i.e., METH-craving and $SDNN_{cue}$) mediated the relationship between physical exercise and decreased relapse tendency. This suggests that reducing METH-cue craving reactivity might contribute to the effects of physical exercise in preventing relapse in individuals with MUD, which is also consistent with previous research (Song et al., 2023). However, no significant improvement was found in the frequency-domain HRV_{cue} parameters in association with physical exercise. Several physiological studies have shown that many physiological parameters (e.g., respiratory rhythm) can influence frequency-domain HRV indices, and these confounders might lead to large individual differences (Billman, 2013; Billman, Huikuri, Sacha, & Trimmel, 2015; Shaffer & Ginsberg, 2017; Wang et al., 2019). We speculate that this may have masked the beneficial effects of exercise interventions on frequency-domain HRV_{cue}.

A novel finding of this study was the beneficial effect of physical exercise on IS and the significant positive correlation between the altered IS scores and the change in METH-related cue-induced reactivity resulting from the exercise intervention. This is consistent with prior work demonstrating that body-oriented therapy may help decrease craving and improve interoception (Price et al., 2019a, 2019b). More intriguingly, we found that IS mediated the relationship between aerobic exercise intervention and relapse tendency, suggesting that the improved IS in METH-related cue exposure may be one of the potential pathways underlying the effect of physical exercise on the risk of relapse. Several studies have shown that physical exercise may help people with SUD better decode and interpret bodily-related signals associated with transient homeostatic imbalances that usually trigger consumption (Brevers et al., 2024). For example, the inflow of active inference mechanisms triggered by exercise should allow one to strategically regulate the pace and intensity of effort throughout the exercise session, which may lead to better awareness of stimuli arising within the body and help maintain bodily homeostasis (Brevers et al., 2024; Osypiuk et al., 2020).

Moreover, by training individuals to formulate prospective, momentary, and retrospective judgments toward physical states, exercise would allow individuals with SUD to explore and resolve homeostatic imbalances while adopting healthy behaviors (Brevers et al., 2024). Exercise may also help individuals discriminate between sensations triggered by physical exercise and those triggered by reward-seeking and consumption (Brevers et al., 2024). Vicarious reward processing might be linked to people's sensitivity to internal body states and could facilitate a tendency to act pro-socially (Herman, 2023). This preliminary study supports the notion that individuals with MUD may benefit from interventions focused on redirecting interoceptive input toward competitive natural reinforcers like physical exercise (Jakubczyk et al., 2019a).

The present study is the first to find that physical exercise may decrease relapse tendency in individuals with MUD through improved IS, indicating that IS may be one of the potential mechanisms underlying the reduction in relapse tendency induced by physical exercise. Previous research has revealed that physical activity can affect the relapse tendency of individuals with MUD undergoing compulsory detoxification not only through a direct pathway but also through indirect pathways, such as the mediating roles of intrinsic restraint and yearning for drugs (Lynch et al., 2013; Morais et al., 2018; Ouyang et al., 2020; Song et al., 2023); the current study expanded on these findings.

In addition, regarding the efficacy of physical exercise in improving IS and cue-induced reactivity, previous studies provide some evidence at the neural mechanism level. Research suggests that the insular cortex is the central hub for processing interoception, and insular dysfunction has been reported in several addictive disorders (Bonson et al., 2002; Engelmann et al., 2012; Goudriaan, de Ruiter, van den Brink, Oosterlaan, & Veltman, 2010; Paulus & Stewart, 2014; Prisciandaro, Myrick, Henderson, McRae-Clark, & Brady, 2013). An animal study demonstrating the causal role of the insula in nicotine-induced cue approach behavior (Scott & Hiroi, 2011) supports the central role of this structure in IS and cue reactivity processing. Intense physical exercise has been shown to cause changes in insular activity and potentially decrease the heightened internal response to stimuli related to drug use (Herman, 2023; Paulus, Stewart, & Haase, 2013). Therefore, in this preliminary study, we hypothesize that insular modulation may be the underlying neural mechanism by which physical exercise improves IS and cue-induced reactivity, leading to a greater reduction in relapse tendency in individuals with MUD. However, we did not provide any evidence regarding the neural mechanisms by which physical exercise improves IS and cue-induced reactivity; instead, we offered directions for future research. More interventional trials are needed to test this hypothesis.

The current study has several strengths. It has provided evidence supporting the notion that physical exercise may be a useful strategy for suppressing VR cue-induced craving reactivity, IS, and relapse tendency in individuals with MUD, with physical exercise showing superior results compared to psychoeducation. In addition to craving reactivity, this study provided new evidence that IS may also be one of the underlying mechanisms by which physical exercise reduces relapse tendency. Second, this preliminary study aimed to understand the interoceptive mechanisms driving drug relapse and may lead to an enhanced understanding of relapse mechanisms, as well as to new treatment strategies for METH addiction. The relationship between interoception and addiction may apply not only to substance dependence but also to behavioral addictions (Herman, 2023). This study also has important implications for the clinical treatment of drug addiction, behavioral addictions, psychiatric disorders, and non-pharmacological therapy. Furthermore, we used one of the most ecologically valid drug-related cue-induced methods, which can more reliably detect subjective cravings and physiological reactivity and may have a greater impact on the participants' perceptions of their own bodily signals.

It should be noted that, although positive results have been found, these findings should be interpreted and applied with caution. As IS assessment is based on subjective self-reported acute responses, further studies are needed to develop new methods for studying how individuals with addiction who receive exercise interventions perceive the process and perceive internal bodily sensations, such as utilizing structural and functional neuroimaging to explore relevant neural mechanisms. Second, interoception consists of interoceptive accuracy, IS, and interoceptive awareness (Garfinkel & Critchley, 2013). Whether interoceptive accuracy and awareness alterations are associated with physical exercise-induced changes in METH-cue reactivity and relapse tendency remains unknown. Third, due to the repetitive nature of measuring acute craving and IS, scales with more items might be optimal and could provide more useful information (Culbertson et al., 2010; Wang et al., 2019). Fourth, the relatively small sample size used in this study may have been insufficient to detect small effects, particularly for frequency-domain HRV indices that are sensitive to physiological influences; therefore, the results should be interpreted with caution. Future studies with larger samples, improved psychoeducation, expanded measurement of key physiological confounders (e.g., respiration), and designs that minimize floor effects in behavioral outcomes are needed to test the robustness of these findings. Finally, there may be gender differences between interoception (Prentice & Murphy, 2022); however, our sample was composed exclusively of males, which may limit our ability to generalize the results of the current study to females with MUD. Future studies should include both male and female participants to enhance comparability and generalizability. Overall, evidence regarding the relationship between interoception and drug relapse and the effects of exercise interventions on IS remains limited. Therefore, more research aimed at understanding interoceptive mechanisms driving drug relapse is needed, which may lead to a better understanding of the mechanisms of relapse and new treatment strategies for drug addiction.

5. Conclusion

Physical exercise may improve METH-cue craving reactivity, IS, and relapse tendency in association with VR cue exposure in individuals with MUD, yielding greater improvements than psychoeducation. In the current study, reduced relapse tendency attributable to physical exercise was positively correlated with changes in METH-cue craving reactivity and IS. In addition to drug craving, IS may have a mediating effect on the relationship between physical exercise and relapse tendency, indicating that IS may be one of the potential mechanisms underlying the decrease in relapse tendency induced by physical exercise.

Authors' Notes

Acknowledgments: The author would like to thank all participants, exercise specialists, cognitive psychologists, and health educators involved in this study.

Funding: This work was supported by the Tongling University Research Project Program [Grant No. 2025tlxykj05] and the Talent Research Start-up Fund Project of Tongling University [Grant No. 2025tlxyrc147].

Data availability: Deidentified data are available upon reasonable request to the corresponding author.

Ethics approval: The ethics committee of the Tongling University Institutional Review Board approved this study.

Informed consent to participate: Informed consent was obtained from all patients for inclusion in the study.

Conflict of interest: I hereby declare that there are no potential conflicts of interest associated with this publication, and that any financial support has been noted in the Acknowledgment section.

References

AshaRani, P. V., Hombali, A., Seow, E., Ong, W. J., Tan, J. H., & Subramaniam, M. (2020). Non-pharmacological interventions for methamphetamine use disorder: A systematic review. *Drug and Alcohol Dependence*, *212*, Article 108060. https://doi.org/10.1016/j.drugalcdep.2020.108060

Avants, S. K., Margolin, A., Kosten, T. R., & Cooney, N. L. (1995). Differences between responders and nonresponders to cocaine cues in the laboratory. *Addictive Behaviors, 20*(2), 215–224. https://doi.org/10.1016/0306-4603(94)00066-2

Billman, G. E. (2013). The LF/HF ratio does not accurately measure cardiac sympatho-vagal balance. *Frontiers in Physiology, 4*, Article 26. https://doi.org/10.3389/fphys.2013.00026

Billman, G. E., Huikuri, H. V., Sacha, J., & Trimmel, K. (2015). An introduction to heart rate variability: Methodological considerations and clinical applications. *Frontiers in Physiology, 6*, 55. https://doi.org/10.3389/fphys.2015.00055

Bonaz, B., Lane, R. D., Oshinsky, M. L., Kenny, P. J., Sinha, R., Mayer, E. A., & Critchley, H. D. (2021). Diseases, disorders, and comorbidities of interoception. *Trends in Neurosciences, 44*(1), 39–51. https://doi.org/10.1016/j.tins.2020.09.009

Bonson, K. R., Grant, S. J., Contoreggi, C. S., Links, J. M., Metcalfe, J., Weyl, H. L., Kurian, V., Ernst, M., & London, E. D. (2002). Neural systems and cue-induced cocaine craving. *Neuropsychopharmacology, 26*(3), 376–386. https://doi.org/10.1016/S0893-133X(01)00371-2

Brevers, D., Billieux, J., de Timary, P., Desmedt, O., Maurage, P., Perales, J. C., Suárez-Suárez, S., & Bechara, A. (2024). Physical exercise to redynamize interoception in substance use disorders. *Current Neuropharmacology, 22*(6), 1047–1063. https://doi.org/10.2174/1570159X21666230314143803

Cabral, D. A. R., Tavares, V. D. O., da Costa, K. G., Nascimento, P. H. D., Faro, H. K. C., Elsangedy, H. M., & Fontes, E. B. (2018). The benefits of high intensity exercise on the brain of a drug abuser. *Global Journal of Health Science, 10*(6), 123–135. https://doi.org/10.5539/gjhs.v10n6p123

Chan, B., Freeman, M., Kondo, K., Ayers, C., Montgomery, J., Paynter, R., & Kansagara, D. (2019). Pharmacotherapy for methamphetamine/amphetamine use disorder-a systematic review and meta-analysis. *Addiction*, *114*(12), 2122–2136. https://doi.org/10.1111/add.14755

Chen, C.-C., Chung, C.-R., Tsai, M.-C., Wu, E. H.-K., Chiu, P.-R., Tsai, P.-Y., & Yeh, S.-C. (2024). Impaired brain-heart relation in patients with methamphetamine use disorder during VR induction of drug cue reactivity. *IEEE Journal of Translational Engineering in Health and Medicine, 12*, 1–9. https://doi.org/10.1109/JTEHM.2022.3206333

Culbertson, C., Nicolas, S., Zaharovits, I., London, E. D., De La Garza, R. II, Brody, A. L., & Newton, T. F. (2010). Methamphetamine craving induced in an online virtual reality environment. *Pharmacology Biochemistry and Behavior, 96*(4), 454–460. https://doi.org/10.1016/j.pbb.2010.07.005

Dolezal, B. A., Chudzynski, J., Dickerson, D., Mooney, L., Rawson, R. A., Garfinkel, A., & Cooper, C. B. (2014). Exercise training improves heart rate variability after methamphetamine dependency. *Medicine & Science in Sports & Exercise, 46*(6), 1057–1066. https://doi.org/10.1249/MSS.0000000000000201

Donovan, D. M., & Wells, E. A. (2007). 'Tweaking 12-Step': The potential role of 12-Step self-help group involvement in methamphetamine recovery. *Addiction*, *102*(Suppl 1), 121–129. https://doi.org/10.1111/j.1360-0443.2007.01773.x

Dudish-Poulsen, S. A., & Hatsukami, D. K. (1997). Dissociation between subjective and behavioral responses after cocaine stimuli presentations. *Drug and Alcohol Dependence, 47*(1), 1–9. https://doi.org/10.1016/S0376-8716(97)00054-9

Eggenberger, P., Annaheim, S., Kündig, K. A., Rossi, R. M., Münzer, T., & de Bruin, E. D. (2020). Heart rate variability mainly relates to cognitive executive functions and improves through exergame training in older adults: A secondary analysis of a 6-month randomized controlled trial. *Frontiers in Aging Neuroscience, 12*, Article 197. https://doi.org/10.3389/fnagi.2020.00197

Engelmann, J. M., Versace, F., Robinson, J. D., Minnix, J. A., Lam, C. Y., Cui, Y., Brown, V. L., & Cinciripini, P. M. (2012). Neural substrates of smoking cue reactivity: A meta-analysis of fMRI studies. *NeuroImage, 60*(1), 252–262. https://doi.org/10.1016/j.neuroimage.2011.12.024

Gamelin, F. X., Berthoin, S., Sayah, H., Libersa, C., & Bosquet, L. (2007). Effect of training and detraining on heart rate variability in healthy young men. *International Journal of Sports Medicine, 28*(7), 564–570. https://doi.org/10.1055/s-2007-964861

Garfinkel, S. N., & Critchley, H. D. (2013). Interoception, emotion and brain: New insights link internal physiology to social behaviour. Commentary on: "Anterior insular cortex mediates bodily sensibility and social anxiety" by Terasawa et al. (2012). *Social Cognitive and Affective Neuroscience, 8*(3), 231–234. https://doi.org/10.1093/scan/nss140

Goudriaan, A. E., de Ruiter, M. B., van den Brink, W., Oosterlaan, J., & Veltman, D. J. (2010). Brain activation patterns associated with cue reactivity and craving in abstinent problem gamblers, heavy smokers and healthy controls: An fMRI study. *Addiction Biology, 15*(4), 491–503. https://doi.org/10.1111/j.1369-1600.2010.00242.x

Hayes, A. F. (2013). *Introduction to mediation, moderation, and conditional process analysis: A regression-based approach.* Guilford Press.

Herman, A. M. (2023). Interoception within the context of impulsivity and addiction. *Current Addiction Reports, 10*(2), 97–106. https://doi.org/10.1007/s40429-023-00482-7

Hormes, J. M. (2017). The clinical significance of craving across the addictive behaviors: A review. *Current Addiction Reports, 4*(2), 132–141. https://doi.org/10.1007/s40429-017-0138-y

Huang, J., Zheng, Y., Gao, D., Hu, M., & Yuan, T. (2019). Effects of exercise on depression, anxiety, cognitive control, craving, physical fitness and quality of life in methamphetamine-dependent patients. *Frontiers in Psychiatry, 10*, Article 999. https://doi.org/10.3389/fpsyt.2019.00999

Jakubczyk, A., Skrzeszewski, J., Trucco, E. M., Suszek, H., Zaorska, J., Nowakowska, M., Michalska, A., Wojnar, M., & Kopera, M. (2019). Interoceptive accuracy and interoceptive sensibility in individuals with alcohol use disorder: Different phenomena with different clinical correlations? *Drug and Alcohol Dependence, 198*, 34–38. https://doi.org/10.1016/j.drugalcdep.2019.01.036

Jakubczyk, A., Trucco, E. M., Klimkiewicz, A., Skrzeszewski, J., Suszek, H., Zaorska, J., Nowakowska, M., Michalska, A., Wojnar, M., & Kopera, M. (2019). Association between interoception and emotion regulation in individuals with alcohol use disorder. *Frontiers in Psychiatry, 10*, Article 1028. https://doi.org/10.3389/fpsyt.2019.01028

Lee, N. K., Jenner, L., Harney, A., & Cameron, J. (2018). Pharmacotherapy for amphetamine dependence: A systematic review. *Drug and Alcohol Dependence*, *191*, 309–337. https://doi.org/10.1016/j.drugalcdep.2018.06.038

Liu, X.-X., & Wang, S. (2021). Effect of aerobic exercise on executive function in individuals with methamphetamine use disorder: Modulation by the autonomic nervous system. *Psychiatry Research, 306*, Article 114241. https://doi.org/10.1016/j.psychres.2021.114241

Liu, X.-X., & Wang, S. (2023). Effects of aerobic exercise combined with attentional bias training on cognitive function and psychiatric symptoms of individuals with methamphetamine dependency: A randomized controlled trial. *International Journal of Mental Health and Addiction, 21*, 1727–1745. https://doi.org/10.1007/s11469-021-00686-w

Lynch, W. J., Peterson, A. B., Sanchez, V., Abel, J., & Smith, M. A. (2013). Exercise as a novel treatment for drug addiction: A neurobiological and stage-dependent hypothesis. *Neuroscience & Biobehavioral Reviews, 37*(8), 1622–1644. https://doi.org/10.1016/j.neubiorev.2013.06.011

McKetin, R., Najman, J. M., Baker, A. L., Lubman, D. I., Dawe, S., Ali, R., Lee, N. K., Mattick, R. P., & Mamun, A. (2012). Evaluating the impact of community-based treatment options on methamphetamine use: Findings from the Methamphetamine Treatment Evaluation Study (MATES). *Addiction*, *107*(11), 1998–2008. HTTPS://DOI.ORG/10.1111/J.1360-0443.2012.03933.X

Mehling, W. E., Gopisetty, V., Daubenmier, J., Price, C. J., Hecht, F. M., & Stewart, A. (2009). Body awareness: Construct and self-report measures. *PLOS ONE, 4*(5), Article e5614. https://doi.org/10.1371/journal.pone.0005614

Miller, L. C., Murphy, R., & Buss, A. H. (1981). Consciousness of body: Private and public. *Journal of Personality and Social Psychology, 41*(2), 397–406. https://doi.org/10.1037/0022-3514.41.2.397

Morais, A. P. D., Pita, I. R., Fontes-Ribeiro, C. A., & Pereira, F. C. (2018). The neurobiological mechanisms of physical exercise in methamphetamine addiction. *CNS Neuroscience & Therapeutics, 24*(2), 85–97. https://doi.org/10.1111/cns.12788

Mottola, C. A. (1993). Measurement strategies: The visual analogue scale. *Decubitus, 6*(5), 56–58.

Ooteman, W., Koeter, M. W. J., Verheul, R., Schippers, G. M., & van den Brink, W. (2006). Measuring craving: An attempt to connect subjective craving with cue reactivity. *Alcoholism: Clinical and Experimental Research, 30*(1), 57–69. https://doi.org/10.1111/j.1530-0277.2006.00019.x

Osypiuk, K., Ligibel, J., Giobbie-Hurder, A., Vergara-Diaz, G., Bonato, P., Quinn, R., Ng, W., & Wayne, P. M. (2020). Qigong mind-body exercise as a biopsychosocial therapy for persistent post-surgical pain in breast cancer: A pilot study. *Integrative Cancer Therapies, 19*, Article 1534735419893766. https://doi.org/10.1177/1534735419893766

Ouyang, Y., Luo, J., Wang, K., Zhang, T., Zhou, C., & Lu, Y. (2020). Impact of physical activity on relapse tendency of AIDS patients undergoing compulsory detoxification: A chain mediation analysis of intrinsic restraint and yearning for drugs. *Journal of Shanghai University of Sport, 44*(10), 48–57. https://doi.org/10.16099/j.sus.2020.10.006

Paulus, M. P., & Stewart, J. L. (2014). Interoception and drug addiction. *Neuropharmacology, 76* (Part B), 342–350. https://doi.org/10.1016/j.neuropharm.2013.07.002

Paulus, M. P., Stewart, J. L., & Haase, L. (2013). Treatment approaches for interoceptive dysfunctions in drug addiction. *Frontiers in Psychiatry, 4*, Article 137. https://doi.org/10.3389/fpsyt.2013.00137

Paulus, M. P., Tapert, S. F., & Schulteis, G. (2009). The role of interoception and alliesthesia in addiction. *Pharmacology Biochemistry and Behavior, 94*(1), 1–7. https://doi.org/10.1016/j.pbb.2009.08.005

Peltola, M. A. (2012). Role of editing of R-R intervals in the analysis of heart rate variability. *Frontiers in Physiology, 3*, Article 148. https://doi.org/10.3389/fphys.2012.00148

Peng, B., Chen, J., Su, R., Tao, W., & Wang, D. (2021). Effects of resistance exercise on subjective craving and inducing factors of methamphetamine-dependent individuals. *Chinese Journal of Sports Medicine, 40*(1), 46–54. https://doi.org/10.16038/j.1000-6710.2021.01.009

Prentice, F., & Murphy, J. (2022). Sex differences in interoceptive accuracy: A meta-analysis. *Neuroscience & Biobehavioral Reviews, 132*, 497–518. https://doi.org/10.1016/j.neubiorev.2021.11.030

Price, C. J., Thompson, E. A., Crowell, S., & Pike, K. (2019a). Longitudinal effects of interoceptive awareness training through mindful awareness in body-oriented therapy (MABT) as an adjunct to women's substance use disorder treatment: A randomized controlled trial. *Drug and Alcohol Dependence, 198*, 140–149. https://doi.org/10.1016/j.drugalcdep.2019.02.012

Price, C. J., Thompson, E. A., Crowell, S. E., Pike, K., Cheng, S. C., Parent, S., & Hooven, C. (2019b). Immediate effects of interoceptive awareness training through mindful awareness in body-oriented therapy (MABT) for women in substance use disorder treatment. *Substance Abuse, 40*(1), 102–115. https://doi.org/10.1080/08897077.2018.1488335

Prisciandaro, J. J., Myrick, H., Henderson, S., McRae-Clark, A. L., & Brady, K. T. (2013). Prospective associations between brain activation to cocaine and no-go cues and cocaine relapse. *Drug and Alcohol Dependence, 131*(1–2), 44–49. https://doi.org/10.1016/j.drugalcdep.2013.04.008

Rawson, R. A., Chudzynski, J., Mooney, L., Gonzales, R., Ang, A., Dickerson, D., Penate, J., Salem, B. A., Dolezal, B., & Cooper, C. B. (2015). Impact of an exercise intervention on methamphetamine use outcomes post-residential treatment care. *Drug and Alcohol Dependence*, *156*, 21–28. https://doi.org/10.1016/j.drugalcdep.2015.08.029

Reiner, D. J., & Shaham, Y. (2022). Recent findings on the role of sensory and interoceptive-related circuits in relapse to drug seeking. *Neuropsychopharmacology, 47*(2), 373–374. https://doi.org/10.1038/s41386-021-01081-8

Sayette, M. A. (2016). The role of craving in substance use disorders: Theoretical and methodological issues. *Annual Review of Clinical Psychology, 12*, 407–433. https://doi.org/10.1146/annurev-clinpsy-021815-093351

Scott, D., & Hiroi, N. (2011). Deconstructing craving: Dissociable cortical control of cue reactivity in nicotine addiction. *Biological Psychiatry, 69*(11), 1052–1059. https://doi.org/10.1016/j.biopsych.2011.01.023

Shaffer, F., & Ginsberg, J. P. (2017). An overview of heart rate variability metrics and norms. *Frontiers in Public Health, 5*, Article 258. https://doi.org/10.3389/fpubh.2017.00258

Sharpe, L., Tarrier, N., Schotte, D., & Spence, S. H. (1995). The role of autonomic arousal in problem gambling. *Addiction, 90*(11), 1529–1540. https://doi.org/10.1046/j.1360-0443.1995.9011152911.x

Shen, H., Du, X., Fan, Y., Dai, J., & Wei, G.-X. (2023). Interoceptive sensibility mediates anxiety changes induced by mindfulness-based tai chi chuan movement intervention. *Mindfulness, 14*(7), 1662–1673. https://doi.org/10.1007/s12671-023-02162-z

Song, L., Huang, Z., Zhou, J., Rao, X., Chen, Y., Li, H., & Du, X. (2023). Effects of aerobic exercise combined with mindfulness-based relapse prevention programs on the relapse tendency in drug abusers. *China Sport Science, 43*(1), 69–77. https://doi.org/10.16469/j.css.202303007

Srisurapanont, M., Sombatmai, S., & Boripuntakul, T. (2007). Brief intervention for students with methamphetamine use disorders: A randomized controlled trial. *The American Journal on Addictions*, *16*(2), 111–116. https://doi.org/10.1080/10550490601184431

Tan, H., Chen, T., Du, J., Li, R., Jiang, H., Deng, C.-L., Song, W., Xu, D., & Zhao, M. (2019). Drug-related virtual reality cue reactivity is associated with gamma activity in reward and executive control circuit in methamphetamine use disorders. *Archives of Medical Research, 50*(8), 509–517. https://doi.org/10.1016/j.arcmed.2019.09.003

Todd, J., Swami, V., Aspell, J. E., Furnham, A., Horne, G., & Stieger, S. (2022). Are some interoceptive sensibility components more central than others? Using item pool visualisation to understand the psychometric representation of interoception. *PLOS ONE, 17*(12), Article e0277894. https://doi.org/10.1371/journal.pone.0277894

United Nations Office on Drugs and Crime. (2024). *World drug report 2024*. United Nations Publications. https://www.unodc.org/unodc/en/data-and-analysis/world-drug-report-2024.html

Volkow, N. D., Michaelides, M., & Baler, R. (2019). The neuroscience of drug reward and addiction. *Physiological Reviews, 99*(4), 2115–2140. https://doi.org/10.1152/physrev.00014.2018

Wang, D., Zhu, T., Zhou, C., & Chang, Y.-K. (2017). Aerobic exercise training ameliorates craving and inhibitory control in methamphetamine dependencies: A randomized controlled trial and event-related potential study. *Psychology of Sport and Exercise, 30*, 82–90. https://doi.org/10.1016/j.psychsport.2017.02.001

Wang, R. (2001). *Psychological health and relapse tendency of male compulsive drug abusers* [Master's thesis, East China Normal University]. https://kns.cnki.net/kcms2/article/abstract?v=WNLjQhMUSxJ-_gmRRojD5gxFQ_qJWYbotEVw7_vzUB4wZEDALS8nib1JCUXqQ_QadinQkjMdhs5Tm7ig8beu1-p_h0tGNmSG1GBSO6refd-J-c-14sKeXGoqvJVW6izBy4nPXwSZogGYVHSsc5M5TFoxsQZuuf--toiDy_6OlZD27NvZxyH5A0qEv3_L6XXQ&uniplatform=NZKPT&language=CHS

Wang, Y.-G., Liu, M.-H., & Shen, Z.-H. (2019). A virtual reality counterconditioning procedure to reduce methamphetamine cue-induced craving. *Journal of Psychiatric Research, 116*, 88–94. https://doi.org/10.1016/j.jpsychires.2019.06.007

Wang, Y.-G., Shen, Z.-H., & Wu, X.-C. (2018). Detection of patients with methamphetamine dependence with cue-elicited heart rate variability in a virtual social environment. *Psychiatry Research, 270*, 382–388. https://doi.org/10.1016/j.psychres.2018.10.009

Williams, D. P., Jarczok, M. N., Ellis, R. J., Hillecke, T. K., Thayer, J. F., & Koenig, J. (2017). Two-week test-retest reliability of the Polar® RS800CX™ to record heart rate variability. *Clinical Physiology and Functional Imaging, 37*(6), 776–781. https://doi.org/10.1111/cpf.12321