Clinical Trial Protocol
Iranian Registry of Clinical Trials

17 Sep 2026

A Pilot Study of Cue-Exposure Combined with Episodic Future Thinking (CIREF) Intervention on Craving and Delay Discounting in Opioid Users Receiving Methadone Maintenance Treatment.

Protocol summary

Study aim

The current study aimed to evaluate the efficacy of Cue-Induced Reconsolidation and Episodic Future Thinking (CIREF) in reducing craving and delay discounting in individuals with opioid use disorder (OUD) receiving methadone maintenance treatment (MMT).

Design

The current study aimed to evaluate the efficacy of Cue-Induced Reconsolidation and Episodic Future Thinking (CIREF) in reducing craving and delay discounting in individuals with opioid use disorder (OUD) receiving methadone maintenance treatment (MMT).

Settings and conduct

This multicentre study was conducted at two outpatient addiction treatment centres in Tehran. After screening, participants were randomized to CIREF or ERT. Ten personalized opioid-related cues were generated and rated, and six were selected. Participants then completed three 75-minute intervention sessions. CIREF used future intervals, whereas ERT used recent-past intervals. DDQ was assessed before and after each session; OCDUS and MCQ were assessed before and after the intervention.

Participants/Inclusion and exclusion criteria

Inclusion Criteria: Individuals with a history of opioid use currently receiving Methadone maintenance treatment Acquire normal score on the Beck Depression Inventory, Snaith-Hamilton Pleasure Scale and Montreal Cognitive Assessment in the initial Screening Ability to generate the opioid-related cues in the second screening Exclusion Criteria: Not having the mentioned criteria above

Intervention groups

CIREF

Main outcome variables

Phasic Craving Toic Craving Delay Discounting

General information

Reason for update

Post-recruitment update to accurately reflect the study as conducted and to correct administrative inaccuracies in the original registration. Updates include final recruitment/completion information, multicentre recruitment, session structure, masking, outcome-measure descriptions and assessment timepoints, intervention procedures, funding information, and the data-sharing plan. These changes are reported transparently after study completion and do not alter the original prospective registration date.” The existing registration date (2 June 2022) must remain unchanged.

Acronym

CIREF

IRCT registration information

IRCT registration number: **IRCT20210804052079N1**
Registration date: **2022-06-02, 1401/03/12**
Registration timing: **prospective**

Last update: **2026-08-10, 1405/05/19**
Update count: **1**

Registration date

2022-06-02, 1401/03/12

Registrant information

Name

Matin Toulami

Name of organization / entity

Institute for Cognitive Science Studies

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date
2022-06-06, 1401/03/16

Expected recruitment end date
2022-11-21, 1401/08/30

Actual recruitment start date
2022-09-11, 1401/06/20

Actual recruitment end date
2022-12-23, 1401/10/02

Trial completion date
2023-03-18, 1401/12/27

Scientific title
A Pilot Study of Cue-Exposure Combined with Episodic Future Thinking (CIREF) Intervention on Craving and Delay Discounting in Opioid Users Receiving Methadone Maintenance Treatment.

Public title
Effect of CIREF on craving and delay discounting in people with opioid use disorder receiving methadone treatment.

Purpose
Treatment

Inclusion/Exclusion criteria

Inclusion criteria:
History of Opioid Use Methadone Maintenance Treatment Receivers Ability to Read and Write

Exclusion criteria:
Chronic Mental Disorder History

Age
From **18 years** old to **50 years** old

Gender
Both

Phase
N/A

Groups that have been masked

- Care provider
- Data analyser

Sample size
Target sample size: **28**
Actual sample size reached: **28**

Randomization (investigator's opinion)
Randomized

Randomization description
After screening and informed consent, eligible participants were randomly allocated in a 1:1 ratio to the CIREF or ERT group using computer-generated block randomization with a fixed block size of four, applied independently at each recruitment site. Each block contained two CIREF and two ERT assignments, with one of the six possible balanced permutations selected randomly. The allocation sequence was generated in Python by a statistician who was not involved in recruitment, enrollment, or intervention delivery. Allocation concealment was maintained using sequentially numbered assignment codes.

Blinding (investigator's opinion)
Single blinded

Blinding description
Due to the experiential nature of the interventions—future-oriented episodic simulation in CIREF and recent-past episodic retrieval in ERT—participants could not be blinded to their assigned condition. However, participants were not informed which condition was considered the experimental intervention or active control, and they were not informed of the study hypotheses. The intervention providers were aware of group allocation because this was necessary to deliver the condition-specific procedures. Clinic staff involved in participants' routine clinical care, including nurses, psychologists, assistants, and the clinic technical manager, remained blinded to group allocation.

Placebo
Not used

Assignment
Parallel

Other design features
This pilot study provides the first empirical evaluation of Cue-Induced Reconsolidation and Episodic Future Thinking (CIREF), a manualized intervention integrating personalized drug-cue exposure, memory reactivation, and episodic future thinking. Participants completed one screening and personalized cue-development session followed by three 75-minute intervention sessions. Six individualized opioid-related cues were selected for each participant based on ratings of arousal, salience, valence, and vividness and were used throughout the intervention. The active control condition, Episodic Recent Thinking (ERT), followed a comparable structure while using recent-past rather than future-oriented episodic processing.

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee
Research Ethics Committees of Institute for cognitive science studies

Street address
Institute for Cognitive Science Studies, Cognitive Science Blvd, Pardis

City
Pardis

Province
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Postal code
۱۶۵۸۳۴۴۵۷۵

Approval date
2021-10-04, 1400/07/12

Ethics committee reference number
IR.UT.IRICSS.REC.1400.011

Health conditions studied

1

Description of health condition studied
Opioid Substance Use
ICD-10 code
F11
ICD-10 code description
Opioid related disorders

Primary outcomes

1

Description
The primary outcome measure of the present study will be momentary craving assessed by the score of 3 sub-scales of the Desire for Drug Questionnaire. The sub-scales including: questions 1, 2, 4, 6, 7, 10, 13 investigate the patient's "desire and intention to drug use", questions 5, 9, 11, 12 investigate the "negative reinforcement for drug use" and questions 3 and 8 which are related to "drug abuse control". There is no normal score for this questionnaire and the significance level of change is the evaluation criterion. Score received in each sub-scales will be assessed at baseline and after intervention.
Timepoint
Before and after each intervention session
Method of measurement
13-item Desire for Drug Questionnaire by Franken et al. will be used to assess the momentary craving.

2

Description
14The primary outcome measure of the present study will be craving in the past period assessed by the score of 4 sub-scales of Obsessive Compulsive Drug Use Scale. The sub-scales including: questions 1, 2, 7, 8 investigate "desire and mental preoccupation with drugs", questions 3 and 9 could be called as "the effect of desire for drug, and drug-related thoughts on the patient's work and life", questions 4, 6, 11 and 12 are related to "motivation, emotion, and lack of control" and questions 5 and 10 evaluate "resistance to drug use". score for this questionnaire and the significance level of change is the evaluation criterion. Score received in each sub-scales will be assessed at baseline and after intervention.
Timepoint
Baseline and after 4-week interventions
Method of measurement
10-item Obsessive Compulsive Drug Use Scale by Franken et al. will be used to assess the craving in the past period.

Secondary outcomes

1

Description
The secondary outcome of the present study is the score obtained in the dual monetary selection questionnaire.
Timepoint
At baseline and after 4-weeks of intervention
Method of measurement
Delay Discounting will be assessed by Monetary Choice Questionnaire.Monetary Choice Questionnaires is a 27-item, brief dichotomous choice tasks that assess preference between small immediate and larger delayed monetary outcomes.

Intervention groups

1

Description
Participants in the CIREF group completed three 75-minute intervention sessions following baseline assessment and personalized cue development. Six individualized opioid-related cues were selected for future time intervals (1 day, 1 week, 1 month, 3 months, 6 months, and 1 year). In each session, cue exposure was followed by four stages of episodic future thinking: (1) simulation of a future cue-related event, (2) prediction and appraisal of possible responses and outcomes, (3) formation of a specific adaptive intention or goal, and (4) development of concrete action plans. Phasic craving (DDQ) was assessed before and after each session, while tonic craving (OCDUS) and delay discounting (MCQ) were assessed before and after the intervention period.
Category
Behavior

2

Description
Participants in the ERT active control group completed the same intervention dose, session structure, cue-exposure procedures, and therapist-guided exercises as the CIREF group. Six individualized opioid-related cues were linked to recent-past intervals (1, 2, 3, 5, 7, and 9 days earlier). Each cue was followed by episodic retrieval of a recent-past event, prediction and appraisal of responses and outcomes, intention formation, and planning. The main difference from CIREF was temporal orientation: past-oriented retrieval in ERT versus future-oriented simulation in CIREF. DDQ was assessed before and after each session, while OCDUS and MCQ were assessed before and after the intervention period.
Category
Behavior

Recruitment centers

1

Recruitment center
Name of recruitment center
Marjan Outpatient Methadone Maintenance Treatment Clinic
Full name of responsible person

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Sponsors / Funding sources

1

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Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes
Title of funding source
Institute for Cognitive Science Studies
Proportion provided by this source
10
Public or private sector
Private
Domestic or foreign origin
Domestic
Category of foreign source of funding
empty
Country of origin
Type of organization providing the funding
Academic

Person responsible for general inquiries

Contact
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Person responsible for updating data

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Sharing plan

Deidentified Individual Participant Data Set (IPD)

Yes - There is a plan to make this available

Study Protocol

Yes - There is a plan to make this available

Statistical Analysis Plan

Yes - There is a plan to make this available

Informed Consent Form

Yes - There is a plan to make this available

Clinical Study Report

Yes - There is a plan to make this available

Analytic Code

Undecided - It is not yet known if there will be a plan to make this available

Data Dictionary

Undecided - It is not yet known if there will be a plan to make this available

Title and more details about the data/document

De-identified participant-level dataset and supporting analysis materials for the CIREF pilot randomized controlled trial. Details: De-identified participant-level data used in the reported analyses may be shared upon reasonable request, including demographic and clinical variables, cue ratings, treatment-group assignment, DDQ, OCDUS, and MCQ outcomes, together with relevant derived variables, a data dictionary, and statistical analysis code. Direct identifiers and potentially identifying free-text information, including personalized cue content, will not be shared.

When the data will become available and for how long

The de-identified participant-level data and supporting materials will be available upon reasonable request after publication of the primary study results. There is no predetermined end date for data availability; requests may be submitted for as long as the study team is able to maintain and securely share the data.

To whom data/document is available

De-identified participant-level data and supporting documents may be shared, upon reasonable request, with qualified researchers from academic, clinical, governmental, or other legitimate research institutions. Requests from researchers outside academia may also be considered if the proposed use is scientifically appropriate and consistent with ethical and confidentiality requirements.

Under which criteria data/document could be used

De-identified participant-level data and supporting materials may be used for scientifically appropriate secondary analyses, replication and reproducibility studies, meta-analyses, methodological research, or related academic purposes. Requests should describe the research question, planned analyses, investigators, and data-security procedures. Requests will be reviewed by the corresponding author and study team for scientific appropriateness, ethical acceptability, participant confidentiality, and feasibility. Approved users may be required to sign a data-use agreement and must not attempt to re-identify participants.

From where data/document is obtainable

The de-identified participant-level data and supporting documents may be requested from the corresponding author, Dr. Tara Rezapour, Department of Cognitive Psychology, Institute for Cognitive Science Studies (ICSS), Tehran, Iran, by email at tara.rezapour@gmail.com. The OSF project overview is available at https://osf.io/q6w9d/. Participant-level data are not publicly downloadable and will be provided only after review and approval of a reasonable request.

What processes are involved for a request to access data/document

Requests should be submitted by email to the corresponding author and should briefly describe the research purpose, planned analyses, investigators, and data-security procedures. The corresponding author and study team will review the request for scientific appropriateness, ethical acceptability, participant confidentiality, and feasibility. If approved, the requester may be asked to sign a data-use agreement before receiving the de-identified data and supporting materials. Applicants should generally allow approximately 2–4 weeks for review and response.

Comments