

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

20 Jun 2026

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

#### Protocol summary

##### Study aim

The current study aimed to investigate the efficacy of drug cue-exposure combined with episodic future thinking (CIREF) on craving and Delay Discounting in a sample of individuals with opioid use history receiving Methadone Maintenance Treatment (MMT).

##### Design

A randomized, double blinded clinical trial with a two arm parallel group designed of 28 Participants. Applying Python for the randomization.

##### Settings and conduct

This study will be performed in 4 one-hour sessions for four weeks with 28 subjects in one of the outpatient clinics for addiction treatment. After Initial and second screening, eligible individuals will be randomly allocated to trial and control groups. In the first session, momentary craving, craving in the past and delay discounting will be measured. Then, Individuals will be asked to generate opioid-related cues for 6 time intervals and rate each of them. (trial: 1 week, 1, 3, 6 months, and 1 year in future Control: 9,7,5 , Last 3, 1 and 11 days in the past). Cues which will receive normal score in arousal, valence, and vividness will be applied in the intervention. In second sessions, the cues will be presented again and 4 stages of EFT including simulation, prediction, Intention and Plan will be executed. At the end, the amount of craving and the value of procrastination will be measured again.

##### Participants/Inclusion and exclusion criteria

Inclusion Criteria: Individuals with a history of opioid use currently receiving Methadone maintenance treatment  $\leq$  150 mg 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

Episodic Future Thinking

##### Main outcome variables

Momentary Craving Craving in the past time frame Delay Discounting

#### General information

##### Reason for update

##### Acronym

CIREF

##### IRCT registration information

IRCT registration number: **IRCT20210804052079N1**

Registration date: **2022-06-02, 1401/03/12**

Registration timing: **prospective**

Last update: **2022-06-02, 1401/03/12**

Update count: **0**

##### Registration date

2022-06-02, 1401/03/12

##### Registrant information

##### Name

Matin Toulami

##### Name of organization / entity

Institute for Cognitive Science Studies

##### Country

Iran (Islamic Republic of)

##### Phone

+98 21 6642 6816

##### Email address

matin.toulami08@gmail.com

##### 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**

empty

**Actual recruitment end date**

empty

**Trial completion date**

empty

**Scientific title**

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

**Public title**

The Effect of Episodic Future Thinking (EFT) on Craving

**Purpose**

Education/Guidance

**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 **45 years** old

**Gender**

Both

**Phase**

N/A

**Groups that have been masked**

- Participant
- Data analyser

**Sample size**

Target sample size: **28**

**Randomization (investigator's opinion)**

Randomized

**Randomization description**

After screening, participants meeting the required inclusion criteria will be randomly allocated to the intervention and the active control group through block randomization. The randomization list will be created using Python. In block randomization, there would be only six conditions in which two cells get "C" control and two cells get "T" trial for a block of four cells. As a result, the 6 outcomes will be as follows: 1: CCTT, 2: TTCC, 3: CTCT, 4: TCTC, 5: TCCT, 6: CTTC. Also, a number will be randomly assigned to each participant.

**Blinding (investigator's opinion)**

Double blinded

**Blinding description**

In the present study, after screening and randomization, individuals will be officially included in the study. In the first session of the intervention, a brief description of the study process by the examiner will be provided to the participant. They will then be given an informed consent form. The information contained in the informed consent form and how to spend the study will be fully explained to the participants. In the process of conducting the study, participants will be blind to the intervention

received. It should be noted that the staff present at the outpatient clinic will be blind to the whole intervention process. These people are: nurse, psychologist, assistant and also the technical manager of the clinic. All data recorded during the intervention sessions will be stored in the computer of the outpatient clinic (the venue of the intervention sessions) in an encrypted folder that only the researcher has access to, and will be deleted after the intervention and follow-up sessions. At the end of the intervention sessions, only the data obtained from the questionnaires will be provided to the data analyzer.

**Placebo**

Not used

**Assignment**

Parallel

**Other design features**

In the present study, an intervention called " Intervention based on Episodic Future Thinking (EFT)" has been designed for the first time. It consists of 4 one-hour sessions. The protocol tries to be feasible and led participants to remain in the study. The set of opioid narrative cues, applied in the intervention have been completely personalized.

**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**

Tehran

**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, 14 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

Baseline and after 4-week interventions

#### Method of measurement

14-item Desire for Drug Questionnaire by Franken et al. will be used to assess the momentary craving.

### 2

#### Description

The 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

Trial group: Episodic Future thinking group: In the first session, the subjects of the intervention group will be asked to generate the opioid-related cues for the the following for the next 6 time intervals, including: 1 day, 1 week, 1 month, 3 months, 6 months and 1 year in future. Subjects will then scored them in terms of Valence, arousal, and vividness. Momentary craving, craving in the past period and the delay discounting will be measured. Next, the subject will be shown the cues of the relevant time intervals on the screen. In the first stage of the Episodic Future thinking, the subject will be asked to simulate a possible future event in his/her mind based on the related cue. In the second stage, he will be asked to predict all the details of the event in 2-3 minutes. The drug-related cues will trigger the drug-related memories which cause in negative retrieval. In the third stage, the subject's memory will be fragile and vulnerable due to stimulation. Now the person will be asked to think about the consequences of substance abuse and form a new interpretation and pursue this interpretation as a goal in his mind. This goal is actually a kind of new memory that is created in a person's mind called reappraisal. In the fourth step, the subject will be asked to plan small but strong steps to achieve the leading plan. These small steps will help him to have a predetermined plan to achieve his goal and also be able to manage his craving toward drug cues. After the intervention sessions, momentary craving, craving in the past period and delay discounting will be measured again.

#### Category

Behavior

### 2

#### Description

Control group: Control group: Episodic Recent thinking group: In the first session, the subjects of the intervention group will be asked to generate the opioid-related cues for the the following for the next 6 time intervals, including: 1,3,5,7,9 days in the past. Subjects will then scored them in terms of Valence, arousal, and vividness. Momentary craving, craving in the past period and the delay discounting will be measured. Next, the subject will be shown the cues of the relevant time intervals on the screen. In the first stage of the Episodic Recent thinking, the subject will be asked to simulate a possible event in the recent past based on the related cue. In the second stage, he will be asked to predict all the details of the event in 2-3 minutes. Now the person will be asked to set a new goal toward the drug-related cue. In the fourth step, the subject will be asked to plan small steps to achieve the leading goal. After the intervention sessions, momentary craving, craving in the past period and delay discounting will be measured again.

#### Category

Behavior

## Recruitment centers

1

### Recruitment center

**Name of recruitment center**

Marjan Outpatient Methadone Maintenance Treatment Clinic

**Full name of responsible person**

Keyvan Ghasemi

**Street address**

Shahid Motahari St. Ghomi Alley

**City**

Pakdasht

**Province**

Tehran

**Postal code**

3391657963

**Phone**

+98 21 3603 9800

**Email**

Keyvan.ghasemi.901@gmail.com

## Sponsors / Funding sources

1

### Sponsor

**Name of organization / entity**

Cognitive Sciences and Technologies Council

**Full name of responsible person**

Kamal Kharazi

**Street address**

No 35, CSTC Building, Alvand St, Argentina Sq, Tehran, Iran

**City**

Tehran

**Province**

Tehran

**Postal code**

1967875319

**Phone**

+98 21 2266 0770

**Fax****Email**

research.project@cogc.ir

**Web page address**

<https://cogc.ir/>

**Grant name****Grant code / Reference number****Is the source of funding the same sponsor organization/entity?**

Yes

**Title of funding source**

Cognitive Sciences and Technologies Council

**Proportion provided by this source**

100

**Public or private sector**

Public

**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

**Name of organization / entity**

Institute for Cognitive Science Studies

**Full name of responsible person**

Matin Toulami

**Position**

Master Degree Student

**Latest degree**

Bachelor

**Other areas of specialty/work**

Cognitive Neuroscience

**Street address**

No.7, Sheibani Alley, North Jamalzadeh St., West Keshavarz Blvd.

**City**

Tehran

**Province**

Tehran

**Postal code**

1418643514

**Phone**

+98 21 6642 6816

**Email**

matin.toulami08@gmail.com

## Person responsible for scientific inquiries

### Contact

**Name of organization / entity**

Institute for Cognitive Science Studies

**Full name of responsible person**

Tara Rezapour

**Position**

Full Professor

**Latest degree**

Ph.D.

**Other areas of specialty/work**

Neuroscience

**Street address**

Institute for Cognitive Science Studies, Cognitive Science Blvd.

**City**

Pardis

**Province**

Tehran

**Postal code**

1658344575

**Phone**

+98 21 7629 1130

**Fax**

+98 21 7629 1140

**Email**

tara\_rezapour@yahoo.com

## Person responsible for updating data

matin.toulami08@gmail.com

### Contact

**Name of organization / entity**

Institute for Cognitive Science Studies (ICSS)

**Full name of responsible person**

Matin Toulami

**Position**

Master Degree Student

**Latest degree**

Bachelor

**Other areas of specialty/work**

Cognitive Neuroscience

**Street address**

No7, Sheibani Alley, No. Jamalzadeh St., West  
Keshavarz Blvd

**City**

Tehran

**Province**

Tehran

**Postal code**

1418643514

**Phone**

+98 21 6642 6816

**Email**

## Sharing plan

**Deidentified Individual Participant Data Set (IPD)**

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

**Study Protocol**

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

**Statistical Analysis Plan**

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

**Informed Consent Form**

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

**Clinical Study Report**

Undecided - It is not yet known if there will be 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