



## Short communication

# Mindfulness-Oriented Recovery Enhancement reduces opioid craving among individuals with opioid use disorder and chronic pain in medication assisted treatment: Ecological momentary assessments from a stage 1 randomized controlled trial

Eric L. Garland<sup>a,\*</sup>, Adam W. Hanley<sup>a</sup>, Anna Kline<sup>b</sup>, Nina A. Cooperman<sup>b</sup>

<sup>a</sup> College of Social Work and Center on Mindfulness and Integrative Health Intervention Development, University of Utah, 395 South, 1500 East, Salt Lake City, UT 84112 USA

<sup>b</sup> Rutgers Robert Wood Johnson Medical School, 675 Hoes Ln W, Piscataway, NJ 08854 USA

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## ABSTRACT

**Background:** Methadone maintenance therapy (MMT) is an efficacious form of medication assisted treatment for opioid use disorder (OUD), yet many individuals on MMT relapse. Chronic pain and deficits in positive affective response to natural rewards may result in dysphoria that fuels opioid craving and promotes relapse. As such, behavioral therapies that ameliorate chronic pain and enhance positive affect may serve as useful adjuncts to MMT. This analysis of ecological momentary assessment (EMA) data from a Stage 1 randomized clinical trial examined effects of Mindfulness-Oriented Recovery Enhancement (MORE) on opioid craving, pain, and positive affective state.

**Methods:** Participants with OUD and chronic pain (N = 30) were randomized to 8 weeks of MORE or treatment as usual (TAU). Across 8 weeks of treatment, participants completed up to 112 random EMA measures of craving, pain, and affect, as well as event-contingent craving ratings. Multilevel models examined the effects of MORE on craving, pain, and affect, as well as the association between positive affect and craving.

**Results:** EMA showed significantly greater improvements in craving, pain unpleasantness, stress, and positive affect for participants in MORE than for participants in TAU. Participants in MORE reported having nearly 1.3 times greater self-control over craving than those in TAU. Further, positive affect was associated with reduced craving, an association that was significantly stronger among participants in MORE than TAU.

**Conclusion:** MORE may be a useful non-pharmacological adjunct among individuals with OUD and chronic pain in MMT.

## 1. Introduction

The United States is currently experiencing an opioid use disorder (OUD) epidemic. Medication assisted treatment (MAT) is the most effective intervention for OUD (Volkow et al., 2014), and methadone maintenance treatment (MMT) is a commonly used form MAT; however, nearly half of people in ongoing MMT continue to use opioids during treatment or relapse within six months (Naji et al., 2016). Chronic pain, which affects 55%–61% of people receiving MMT (Eyler, 2013), contributes to continued opioid use, relapse, and MMT dropout (Griffin et al., 2016; Mancino et al., 2010). Further, traditional MAT does not directly address the emotion regulation and reward processing deficits characteristic of OUD – critical mechanisms of addiction and

chronic pain (Elman and Borsook, 2016; Garland et al., 2013). Through opponent processes in the brain, emotion dysregulation and reward deficits may amplify stress sensitization (Koob, 2019) and opioid craving (Garland et al., 2017b, 2018), serving as critical risk factors for OUD that may be neglected by traditional MAT.

Novel behavioral interventions are needed to address the chronic pain, emotion dysregulation, and reward processing deficits associated with opioid use among people receiving MMT. Although several behavioral therapies have shown efficacy in separately treating pain and opioid use, a 2017 Cochrane review identified only five randomized controlled trials (RCTs) of interventions to address opioid use/misuse among people with chronic pain (Eccleston et al., 2017). Of the five interventions studied, only two evidenced significant effects (relative to

\* Corresponding author.

E-mail address: [eric.garland@socwk.utah.edu](mailto:eric.garland@socwk.utah.edu) (E.L. Garland).

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control conditions) on opioid-related outcomes and pain. One of those two was Mindfulness-Oriented Recovery Enhancement (MORE; Garland, 2013). MORE is an integrative behavioral therapy that unites training in mindfulness, reappraisal, and savoring skills to disrupt the downward spiral linking chronic pain to OUD and relapse. MORE is founded on the *restructuring reward hypothesis*, which states that increasing positive affective responses to naturally rewarding objects and events in the socioenvironment will decrease craving and addictive behaviors (Garland, 2016). Two Stage 2 RCTs (N = 115 and N = 95) have demonstrated MORE's efficacy in improving outcomes including pain and opioid misuse for people prescribed opioids for pain (Garland et al., 2014b, in press). However, no studies have evaluated MORE among people in MMT for OUD. Recently, we conducted the first Stage 1 RCT of MORE as a treatment for individuals with chronic pain in MMT for OUD (ClinicalTrials.gov identifier NCT03894501).

Here we present ecological momentary assessment (EMA) data from this trial to examine effects on opioid craving, pain, and affective state during the course of the MORE treatment. Ecological Momentary Assessment (EMA) is a method of data collection that overcomes retrospective biases by gathering data via real-time reports of momentary experiences in the context of everyday life (Csikszentmihalyi and Larson, 1987; Shimman et al., 2008). In particular, retrospective reports of craving are limited (Shiffman, 2000), whereas real-time reporting of craving via EMA may allow for more accurate observation and facilitate a more nuanced analysis of dynamic interrelationships between changes in craving and affective dysregulation that propel the downward spiral of chronic pain and OUD. In a prior Stage 2 RCT of MORE for chronic pain patients receiving long-term opioid analgesic therapy, MORE decreased momentary pain intensity and increased momentary positive affect regulation (Garland et al., 2017a); yet, this trial did not measure the impact of MORE on momentary craving experience.

The present study aimed to fill this gap and use EMA to obtain an initial indication of the therapeutic effect of MORE in MMT patients with pain and OUD. We hypothesized that: a) MORE would produce greater improvements in opioid craving, pain, positive affect, and stress relative to treatment as usual (TAU); b) MORE would result in greater self-control over craving than TAU; and c) improvements in momentary positive affect would predict decreases in craving over the course of treatment.

## 2. Method

### 2.1. Participants and procedure

Inclusion criteria were individuals with OUD who were 1) English-speaking; 2) age 18 or older; 3) admitted to MMT within the past year; and 4) had chronic non-cancer pain. (ClinicalTrials.gov identifier NCT03894501). Participants (see Table 1) were recruited from MMT clinics in New Jersey. Participants (N = 30) provided informed consent and were randomized to receive MORE in addition to TAU versus TAU alone. Study procedures complied with the Helsinki Declaration and the designated University IRB. Participants were compensated for completing study assessments.

### 2.2. Study interventions

#### 2.2.1. MORE

MORE is a manualized 8-session group therapy intervention (Garland, 2013) involving training in mindfulness, reappraisal, and savoring skills to address OUD and chronic pain. MORE sessions provide instruction in: mindfulness techniques to increase awareness of and self-control over craving and foster nonreactivity to emotional and physical pain; reappraisal skills to promote emotion regulation and restructure motivations for opioid use; and savoring pleasant events and emotions to remediate deficits in natural reward processing and boost positive affectivity. Sessions were 2 h long each week and led by a

**Table 1**  
Baseline Demographic and Clinical Characteristics, by Treatment Group (N = 30).

Measure	MORE (n = 15)	TAU (n = 15)
Female, n (%)	8 (53%)	7 (47%)
Age	47.9 ± 8.7	52.9 ± 8.4
Racial/ethnic background, n (%)†		
White	7 (47%)	4 (27%)
Black/African American	7 (47%)	9 (60%)
Hispanic	3 (20%)	3 (20%)
Other	1 (7%)	0 (0%)
Education, high school graduate or more, n (%)	10 (67%)	11 (73%)
Unemployed, n (%)	12 (80%)	13 (87%)
Primary pain condition, n (%)‡		
Low back pain	8 (53%)	8 (53%)
Arthritis	6 (40%)	6 (40%)
Migraine	2 (13%)	3 (20%)
Other	2 (13%)	2 (13%)
Used in the past 30 days, n (%)		
Heroin	9 (60%)	11 (73%)
Cocaine/crack	4 (27%)	3 (20%)
Pain medication (e.g., codeine, oxycodone)	2 (13%)	3 (20%)
Benzodiazepines	1 (7%)	1 (7%)
Stimulants (e.g., methylphenidate, amphetamine)	3 (20%)	1 (7%)
Marijuana	4 (27%)	3 (20%)
Baseline ecological momentary assessment ratings (week 1, 0-10 NRS)††		
Opioid wanting	4.3 ± 0.8	4.00 ± 0.8
Opioid urge	4.5 ± 0.8	3.92 ± 0.8
Pain intensity	4.7 ± 0.7	4.92 ± 0.7
Pain unpleasantness	5.1 ± 0.8	5.08 ± 0.8
Positive affect	5.3 ± 0.8	6.08 ± 0.8
Stress	5.3 ± 0.8	4.81 ± 0.8

Note. There were no significant between-groups differences on any of these variables. † = Participants could report more than one category. †† = Ecological momentary assessment ratings averaged over the first week of the study; mean ± 1 standard error. NRS = numeric rating scale; MORE = Mindfulness-Oriented Recovery Enhancement; TAU = Treatment as Usual.

Masters-level clinician. This clinician was trained and supervised weekly by the developer of MORE, who reviewed recordings of the sessions to monitor adherence to the MORE treatment manual and maintain treatment fidelity. Participants were asked to engage in daily 15-minute mindfulness, reappraisal, and savoring sessions at home guided by an audio recording.

#### 2.2.2. TAU

TAU consisted of MMT in addition to individual and group therapy provided by participating MMT treatment agencies. TAU therapeutic approaches included process-oriented, present-centered therapy and cognitive-behavioral coping skills training but did not include formal mindfulness-based intervention.

#### 2.2.3. Therapist contact time per week

MMT treatment agency policy required adjunctive psychotherapy sessions for patients. Participation in MORE counted towards this psychotherapy requirement. Over the 8-week study intervention period, the average number of hours per week of psychotherapy (individual and group, including MORE) received by participants in the MORE arm was 6.4 (SD = 3.9); the average hours of psychotherapy per week received by participants in the TAU arm was 6.4 (SD = 4.1); thus, the two arms were well matched on therapist contact time per week.

## 2.3. Measures

### 2.3.1. EMA

Following the first MORE treatment session, across 112 EMA measurement points (2 assessments/day X 56 days) participants in MORE

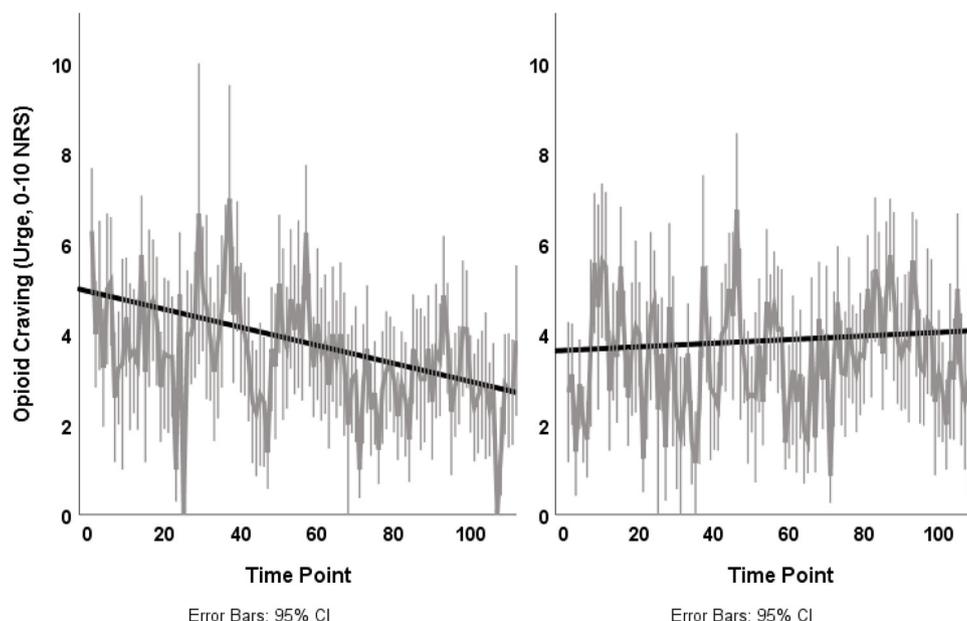


Fig. 1. Effects of MORE relative to TAU on opioid craving among patients with chronic pain in methadone maintenance therapy for OUD (N = 30).

and TAU completed EMAs via random smartphone probes delivered between 9 AM – 3 PM and again from 3 PM to 9 PM. Given the centrality of the construct of craving to this particular study, we opted to use two different items rated on a 0–10 numeric rating scale (NRS) to more broadly capture the construct: “How much do you want to use opioids right now?” (Garland and Howard, 2014) based on Robinson and Berridge (2001) concept of craving as mesolimbic dopamine-mediated wanting and an item previously validated for EMA assessment of opioid craving among individuals with chronic pain (Wasan et al., 2012), “How strong of an urge do you have to use opioids right now?”

Single NRS items assessed the following constructs: *pain intensity* - “How intense is your pain right now?” (Farrar et al., 2001); *pain unpleasantness* - “How unpleasant is your pain right now?” (Farrar et al., 2001); *positive affect* - “How positive are you feeling right now?” (Lindsay et al., 2018); and *stress* - “How stressed are you right now?” (Mason et al., 2015).

### 2.3.2. Event-contingent craving ratings

Following the first MORE treatment session, participants in MORE and TAU were instructed to complete event-contingent ratings of opioid craving (using the items above) via smartphone whenever they experienced a craving for opioids, as well as to rate their capacity to self-regulate the craving via a single item developed for the purpose of this study: “How much control do you have over your craving?” with a NRS.

### 2.4. Data analytic approach

Multilevel modeling with maximum likelihood estimation of missing data was used for linear analysis of random EMA data, which has a nested hierarchical structure with both between- and within-subjects’ predictors. The main effect of (MORE vs. TAU), Time, and the Group X Time interaction were the primary fixed effects of interest. Models included a random intercept, and the covariance structure for repeated effects (diagonal and AR1) was also evaluated by a chi-square test of the change in the -2LL fit statistics. Regarding analysis event-contingent EMA, because participants could register as many cravings as they experienced and at any frequency, time was highly variable in these models and so we chose to focus on the main effect of Group (rather than the Group X Time interaction) across all craving and control ratings.

## 3. Results

### 3.1. Sample characteristics

Half (50%) of the sample were women (n = 15), with a mean age of 50.4 years (SD = 8.5). The majority of the sample were African American (53%), followed by whites (36.67%), and non-white Hispanics (20%). Nearly one-third of participants had less than a high school education (30%). Low back pain (53%) and arthritis (40%) were the most commonly reported pain conditions, with a mean pain severity of 5.3 (SD = 2.7) out of 10. Two-thirds of participants (67%) reported using heroin in the past 30 days, with comparatively lower incidence of past 30 day cocaine (23%), marijuana (23%), painkiller (16%), stimulant (13%) and benzodiazepine use (7%). Participants had received a median of 7 months of MMT (range < 1 month to 35 years). There were no significant between-groups differences on any demographic or baseline clinical variable (Table 1).

Participants assigned to MORE completed an average of 6.1 (SD = 1.6) treatment sessions. One participant discontinued the MORE intervention after completing five sessions; two participants in the TAU arm discontinued MMT (see Supplementary Figure for CONSORT chart).

### 3.2. Craving, pain, and affective state

The daily response rate to random EMA probes over the two months of intervention was 62%.

#### 3.2.1. Craving

Compared to TAU, participants in MORE reported significantly greater decreases in opioid wanting (↓ 44%), Group X Time  $B = -0.019$  (SE = .005),  $p < .001$ , and opioid urge (↓ 50%),  $B = -0.019$  (SE = .005),  $p < .0001$  (Fig. 1).

#### 3.2.2. Pain

Compared to TAU, participants in MORE reported significantly greater decreases in pain unpleasantness (↓ 13%), Group X Time  $B = -.007$  (SE = .003),  $p = .025$ , but not pain intensity,  $p > .10$ .

#### 3.2.3. Positive affect and stress

Compared to TAU, participants in MORE reported significantly

greater decreases in stress ( $\downarrow$  26%),  $B = -.014$  ( $SE = .004$ ),  $p = .003$ , and significantly greater increases in positive affect ( $\uparrow$  22%), Group X Time  $B = .010$  ( $SE = .004$ ),  $p = .017$ .

### 3.2.4. Event-contingent craving

In event-contingent EMA, participants in MORE reported a greater number of cravings ( $n = 303$ ) than participants in TAU ( $n = 87$ ). Yet, participants in MORE reported those cravings as being significantly less intense than those experienced by participants in TAU: participants in MORE had 68% less severe opioid wanting,  $B = 1.35$  ( $SE = .40$ ),  $p = .001$ , and 56% weaker opioid urges,  $B = 1.69$  ( $SE = .39$ ),  $p < .0001$ , than participants in TAU. Participants in MORE also reported having 129% greater self-control over cravings,  $B = 1.81$  ( $SE = .34$ ),  $p < .0001$ , than participants in TAU.

### 3.2.5. Association between positive affect and craving

Increases in momentary positive affect were associated with decreases in opioid wanting  $B = -.49$  ( $SE = .04$ ),  $p < .0001$ . The inverse association between positive affect and opioid wanting was significantly stronger among MORE participants,  $p = .019$ .

## 4. Discussion

The present study examined the effects of MORE on EMAs of opioid craving, pain, and affective experience among a sample of individuals with OUD and chronic pain receiving MMT. Study hypotheses were largely supported by the data, which indicated that relative to TAU, participation in MORE was associated with statistically significant reductions in momentary opioid craving (wanting and urge), pain unpleasantness, and stress, as well as increases in positive affect from moment-to-moment. Further, although participants in MORE reported a greater number of cravings in event-contingent craving reports, these cravings (i.e., wanting and urges) were weaker in intensity, and participation in MORE was associated with significantly greater self-control over cravings. In that regard, participants treated with MORE reported being 1.3 times better able to control cravings than participants in TAU.

In the first week of the intervention, participants in MORE reported a moderate level of urge for opioids (approximately 5 on a 0–10 NRS); by the end of the 8 week intervention, the intensity of opioid urges had been nearly halved. Yet, paradoxically, participants receiving MORE reported nearly three times as many cravings as participants in TAU. This finding is sensible in light of the MORE treatment process. MORE teaches mindfulness skills to first enhance awareness of craving and then to increase the capacity to regulate craving. According to the cognitive processing model of addiction (Tiffany, 1999, 1990), the escalation from substance use to addiction is marked by the automatization of drug use; that is, drug use occurs in the absence of volition when automatic drug use action schemas are activated by conditioned stimuli, irrespective of any conscious awareness of craving. According to the model, when automatic drug use action schemas are blocked either by lack of access to the drug or by a conscious effort to resist drug use, craving arises, which then compels drug use as a means of alleviating the distress associated with the experience of craving. In MORE, participants use mindfulness to gain awareness of automaticity in the context of their addictive behavior, and to shift attention to the sensations of breathing as a means of interrupting activation of the drug use schema. During this process, when craving arises, participants are taught to deconstruct it into its cognitive, affective, and sensorial components, while metacognitively monitoring these experiential constituents from the psychological distance and perspective of a detached observer. Participants are then instructed to reappraise the meaning of the craving by contemplating the consequences of indulging the craving versus remaining abstinent, a technique that has been shown to decrease craving by increasing top-down prefrontal regulation of drug cue-reactivity in the ventral striatum (Kober et al., 2011, 2010).

Further, MORE teaches savoring natural rewards as a means of

reducing craving. In that regard, higher levels of momentary positive affect were correlated with lesser opioid wanting, and this inverse association was strengthened among individuals in MORE. These effects may have resulted from the savoring techniques taught in the MORE intervention, which leverage mindfulness to increase attention on the pleasurable features of salutary objects and events in the natural and social environment, as well as the positive emotions that flow from them (Garland et al., 2015a). Consistent with the *restructuring reward hypothesis* (Garland, 2016), participants in MORE may have utilized savoring to magnify the craving reducing effects of positive emotions, thereby reducing the intensity of their cravings.

In that regard, an earlier EMA study of MORE as an intervention for chronic pain patients receiving long-term opioid analgesic therapy demonstrated that increasing momentary positive affect via MORE was associated with significant reductions in opioid misuse (Garland et al., 2017a). In that study, participants in MORE were more than 2.75 times more likely than those in a support group control condition to exhibit positive affect regulation over the course of treatment, operationalized as the capacity to shift affect in a positive direction or maintain positive affect from moment to moment. The present study complements and extends these findings by replicating effects of MORE on momentary positive affective states and indicating that boosting positive affect with MORE may reduce addictive responses to opioids among individuals in MMT for OUD as well as among individuals taking prescription opioid analgesics for chronic pain. Both sets of findings support the *restructuring reward hypothesis* and contribute to the body of psychological (Garland et al., in press) and neurophysiological evidence (Froeliger et al., 2017; Garland et al., 2015b, 2014a) demonstrating effects of MORE on boosting positive affect and natural reward processing.

Although this Stage 1 RCT was not fully powered to test effects of MORE on opioid relapse, days of opioid use and time in MMT will be assessed as outcomes in an upcoming Stage 2 RCT of MORE. Future studies could use EMA to assess the effects of MORE and other behavioral MMT adjuncts on craving, positive affect, and stress in the moments preceding drug use to determine whether intervention can prevent relapse by modulating key antecedents and precipitants of relapse. The present analysis was also limited in its ability to assess durability of changes in craving, pain, and affect past the 8 weeks of treatment. Though the EMA response rate in this study was towards the lower end of the range observed across EMA studies of substance users (50%–90%; Shiffman, 2009), the treatment retention rate in the MORE intervention was excellent, with 93% of participants retained and completing an average of 6 out of 8 sessions. The closed cohort intervention format appeared to be a feasible way to deliver MORE in the MMT setting; nonetheless, a rolling group format might also increase the accessibility of the intervention. Although we were unable to determine whether the study arms differed in the amount of therapeutic homework practice (this was not assessed in the TAU arm), one notable strength of this study was the fact that the study arms were well-matched in terms of therapist contact time per week. Yet the therapeutic effects of MORE were evident above and beyond those provided by a structured program of TAU consisting of approximately six hours of group and individual therapy per week - attesting to the potency of the MORE intervention. Thus, in spite of the limitations and the preliminary nature of the research described herein, the present study provides suggestive evidence that MORE may be a useful adjunctive behavioral therapy for medication assisted treatment of OUD among individuals with chronic pain.

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The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

## Contributors

NC, AK, EG, and AH conceived of the study aims and hypotheses. NC and AK provided oversight in data collection. EG and AH performed the analysis. EG spearheaded manuscript preparation. All authors contributed to the final version of this manuscript.

Eric Garland, PhD, LCSW is the Director of the Center on Mindfulness and Integrative Health Intervention Development. The Center provides Mindfulness-Oriented Recovery Enhancement (MORE), mindfulness-based therapy, and cognitive behavioral therapy in the context of research trials for no cost to research participants; however, Dr. Garland has received honoraria and payment for delivering seminars, lectures, and teaching engagements (related to training clinicians in MORE and mindfulness) sponsored by institutions of higher education, government agencies, academic teaching hospitals, and medical centers. Dr. Garland also receives royalties from the sale of books related to MORE.

## Declaration of Competing Interest

Eric Garland, PhD, LCSW is the Director of the Center on Mindfulness and Integrative Health Intervention Development. The Center provides Mindfulness-Oriented Recovery Enhancement (MORE), mindfulness-based therapy, and cognitive behavioral therapy in the context of research trials for no cost to research participants; however, Dr. Garland has received honoraria and payment for delivering seminars, lectures, and teaching engagements (related to training clinicians in MORE and mindfulness) sponsored by institutions of higher education, government agencies, academic teaching hospitals, and medical centers. Dr. Garland also receives royalties from the sale of books related to MORE.

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## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.drugalcdep.2019.07.007>.

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