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## Pain, hedonic regulation, and opioid misuse: Modulation of momentary experience by Mindfulness-Oriented Recovery Enhancement in opioid-treated chronic pain patients



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### ABSTRACT

**Background:** Given the risk of opioid misuse among chronic pain patients being treated with long-term opioid pharmacotherapy, non-pharmacological treatments are needed. Further, in light of hedonic deficits in this population, therapies that enhance positive affect may be useful. The purpose of this study was to examine effects of a Mindfulness-Oriented Recovery Enhancement (MORE) intervention on ecological momentary assessments (EMA) of pain and positive affective experience, and to determine if changes in pain, affect, and their interaction were associated with opioid misuse at post-treatment.

**Methods:** This study examined unpublished EMA data from a subset of participants (N = 55) in a previously published RCT (NCT01505101) of MORE versus a support group (SG) control. Across 8 weeks of treatment, patients completed up to 224 EMA measures of pain and affect. Multilevel models and generalized estimating equations examined effects of treatment on momentary pain and positive affect, and generalized linear models examined associations between pain and affect and changes in opioid misuse by post-treatment.

**Results:** Patients in MORE reported significantly greater improvements in momentary pain ( $p = 0.01$ ) and positive affect ( $p = 0.004$ ) than patients in the SG. Further, over the entire course of treatment, patients in MORE were significantly more likely to exhibit positive affect regulation (OR = 2.75) than patients in the SG. Finally, improvements in positive affect (but not pain) over the course of intervention were associated with reduced risk of misusing opioids by post-treatment ( $p = 0.02$ ).

**Conclusion:** MORE may be a useful non-pharmacological treatment for pain and hedonic deficits among chronic pain patients at risk for opioid misuse.

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### 1. Introduction

Chronic pain presents a significant burden to the approximately 100 million individual sufferers within the U.S. (Institute of Medicine (US) Committee on Advancing Pain Research, Care, and Education, 2013) and to American society at large, due in part to high rates of co-occurring psychological distress and functional impairment (Dersh et al., 2002; McWilliams et al., 2003). Over the past twenty years biomedical conceptualizations of chronic pain have dominated. However, outcome studies on most of the

conventional approaches to pain management (e.g., spinal injections, opioid therapy, spinal cord stimulators) suggest that positive treatment responses are transient and not clinically significant (Jamison, 2011; Shaheed et al., 2016). Moreover, exclusive reliance on biomedical interventions including surgery and opioid analgesia may have serious unwanted effects including worsened pain or hyperalgesia and opioid misuse that can escalate to opioid use disorder (Chan and Peng, 2011; Chou et al., 2015; Chu et al., 2008; Manchikanti and Singh, 2008). In that regard, recent estimates suggest that approximately 22–29% of chronic pain patients engage in aberrant medication-related behaviors associated with opioid misuse (Vowles et al., 2015). Misuse as used in this paper is defined as use contrary to the directed or prescribed pattern, regardless of

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harm or adverse effects; this could include dose escalation, use for non-pain purposes, and a variety of drug-seeking behaviors.

The potential adverse effects of chronic opioid therapy (e.g., misuse, development of opioid use disorders, overdose) have led to increased interest in alternative approaches to treatment of chronic pain (Deter, 2012). The panoply of alternatives include exercise regimens such as aerobic conditioning, muscle strengthening, and flexibility training (Ambrose and Golightly, 2015; Bertozzi et al., 2013; Peek and Stevens, 2016; Searle et al., 2015) as well as massage therapy and spinal manipulation (Tan et al., 2007), acupuncture (Lam et al., 2013), and electrical nerve stimulation (Johnson and Martinson, 2007). While some of these approaches may be promising, evidence has not yet definitively substantiated their effects on physical or emotional functioning (Turk et al., 2011).

There has also been growing interest in more complex, integrative and multidimensional models of pain that reflect an understanding of the profound role that psychological factors play in pain chronicity (Gatchel et al., 2007; Kerns et al., 2011). In this arena, cognitive-behavioral therapies (CBT) that integrate classical behavioral principles with techniques designed to target beliefs and appraisals about pain (Gatchel et al., 2007; Turner et al., 2000), have become the dominant psychological treatment for chronic pain and are a staple of multidisciplinary treatment programs (Scascighini et al., 2008). Systematic reviews have revealed positive effects on pain reduction and emotional well-being for traditional CBT in comparison to treatment as usual or wait list controls, with generally small effect sizes (Williams et al., 2012). More recently, “third wave” CBT approaches like Acceptance and Commitment Therapy and mindfulness-based interventions, which teach acceptance of pain and decoupling of emotional reactivity from pain experience, have also been applied to chronic pain treatment (McCracken and Vowles, 2014).

To date, mindfulness approaches for chronic pain have been shown to be efficacious but not superior to traditional CBT in well-controlled trials (Cherkin et al., 2016) and meta-analyses (Veehof et al., 2011). However, it should be noted that these trials and meta-analyses have not focused specifically on opioid-treated chronic pain patients. It is possible that different findings with regard to mindfulness-based treatment effects on pain and affect would be obtained in pain patients engaging in long-term opioid therapy. Effects of mindfulness therapies on aberrant medication-related behaviors including misuse of opioid medications would also be of great interest. The basis for effectiveness of mindfulness approaches overall is highlighted in recent theories positing functional interconnections between prolonged exposure to pain, increased pain sensitization, decreased affective sensitivity to natural rewards, and disruption of affective regulation marked by an impaired ability to maintain and recover positive affect in the face of painful and stressful experiences; this cluster of dysregulation is thought to result in a hedonic deficit that propels a downward spiral of opioid dose escalation and other aberrant medication-related behaviors (Elman and Borsook, 2016; Garland et al., 2013; Shurman et al., 2010). In light of such proposed hedonic (dys)regulatory mechanisms, interventions that promote positive emotions by enhancing natural reward processing may be especially efficacious for concurrent treatment of pain and opioid misuse (Garland, 2016; Finan and Garland, 2015; Navratilova et al., 2016).

Given growing concerns about the risk of opioid misuse and addiction among chronic pain patients (Chou et al., 2015), there is also a need for empirically-validated treatments to concurrently target pain and opioid misuse (Wachholtz et al., 2011). Integrated treatment approaches have been recommended (Portenoy, 1996), but controlled research on interventions to reduce comorbid chronic pain and opioid use/misuse is extremely limited. Jamison et al. (2010) conducted a randomized controlled trial (RCT) of CBT for comorbid opioid misuse and chronic pain. The intervention

was efficacious but was focused mainly on prescription compliance. More recently, Ilgen et al. (2016) conducted a RCT of a CBT and acceptance-based intervention for Veterans with chronic pain and substance use disorders. That study found significant intervention effects on pain severity, functioning, and alcohol consumption, but not on opioid use. A recent pilot RCT investigated a mindfulness intervention for opioid-treated chronic back pain patients, and found significant effects on pain severity and sensitivity, but no effects on opioid use (Zgierska et al., 2016).

In addition to the relative paucity of good research on integrated therapies, there is also a measurement issue in that the majority of relevant studies have retrospectively assessed global outcomes at a limited number of time points (e.g., pre and post-treatment). This measurement approach makes it difficult to elucidate the effects of interventions on the temporal dynamics of pain and affective experience. Ecological Momentary Assessment (EMA, also referred to as experience sampling method) is a method of data collection that overcomes many of the biases that arise with retrospective measures by gathering data via real-time reports of momentary experiences in the context of everyday life (Csikszentmihalyi and Larson, 1987; Hektner et al., 2007; Shiffman et al., 2008; Stone and Shiffman, 1994; Wenze and Miller, 2010). EMA may allow for more accurate observation of phenomena in real-world contexts and facilitate a more nuanced analysis of interrelationships between changes in pain and affect that underpin the treatment of chronic pain and opioid misuse.

The purpose of the present study was to employ EMA to examine the effects of a novel, integrated therapy for chronic pain and opioid misuse, Mindfulness-Oriented Recovery Enhancement (MORE). MORE integrates mindfulness training with techniques from CBT and positive psychology designed to restructure reward processing and boost positive affect. In a previously published RCT, relative to a support group (SG) active control, MORE was shown to significantly reduce pain severity and functional interference, as well as opioid craving and misuse (Garland et al., 2014c). Notably, there was a 63% reduction in the occurrence of opioid misuse from pre- to post-treatment in the MORE group compared to a 32% reduction in the SG group ( $p=0.05$ ). The present secondary analysis had three goals: 1) to replicate MORE versus SG effects on global pain ratings obtained pre and post-treatment using detailed data gathered from EMA during the treatment episode; 2) to examine effects of MORE versus SG on momentary affective state and affect regulation (ability to maintain and recover positive affect) using EMA data; 3) to determine whether changes in pain intensity and/or affective state were related to improvement in measures of opioid medication misuse. We hypothesized that: a) MORE would produce significantly greater improvements in momentary pain and positive affective experience relative to SG control; b) MORE would enhance positive affect regulation, evidenced by a greater ability to maintain and recover positive affect relative to the SG; and c) improvements in momentary pain and positive affect would predict decreases in medication misuse from pre- to post-treatment.

## 2. Method

### 2.1. Participants and procedure

The current secondary analysis examined unpublished data from a subset of participants (21 men and 34 women, mean age=48.9, SD=11.6) enrolled in a previously published RCT of MORE vs. a support group (SG) for chronic pain patients on long-term opioid analgesic pharmacotherapy (ClinicalTrials.gov identifier NCT01505101; please refer to Garland et al., 2014c for a CONSORT diagram). Individuals who had completed at least one EMA measurement over the 8 week study interventions (MORE

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