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A preliminary randomized controlled trial of a distress tolerance treatment for opioid dependent persons initiating buprenorphine

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ABSTRACT

Background: Buprenorphine opioid agonist treatment (OAT) has established efficacy for treating opioid dependency but early relapse rates are high and are often associated with withdrawal-related or emotional distress.
Methods: To determine whether a novel distress tolerance (DT) intervention during buprenorphine initiation decreases opioid relapse, we conducted a preliminary randomized controlled trial with opioid-dependent outpatients. Participants received buprenorphine-naloxone induction and 3-months of maintenance buprenorphine plus seven, 50-min manualized, individual sessions (DT vs. health education (HE) control) over a 28-day period, linked to clinician medication dosing visits, and beginning 2 days prior to buprenorphine induction. Primary outcomes included use of illicit opioids (positive defined as any self-reported use in the prior 28 days or detected by urine toxicology) and treatment drop out.
Results: Among 49 participants, the mean age was 41 years, 65.3% were male. Persons randomized to DT had lower rates of opioid use at all three monthly assessments, and at 3-months, 72% of HE participants were opioid positive compared with 62.5% of DT participants. Rates of dropout were 24% and 25% in the HE and DT arms, respectively.
Conclusions: This distress tolerance treatment produced a small, but not statistically significant reduction in opioid use during the first three months of treatment although no differences were found in drop-out rates between conditions. If replicated in a larger study, DT could offer clinicians a useful behavioral treatment to complement the effects of buprenorphine.

1. Introduction

The nonmedical use of opioids, including prescription pain relievers and heroin, is a growing public health concern. In 2011, an estimated 2.2 million Americans met DSM-IV (APA, 1994) criteria for opioid abuse or dependence (Substance Abuse and Mental Health Services Administration, 2012). Buprenorphine, an opioid agonist treatment (OAT) that has been prescribed to more than a million individuals in the U.S. since it became available in 2003 (Boothby and Doering, 2007). Offered as an office-based maintenance treatment alternative to methadone, buprenorphine has demonstrated efficacy in reducing cravings, ameliorating withdrawal discomfort, and increasing periods of abstinence. In regard to treatment effectiveness (variously defined as reducing street crime, illicit drug use, HIV risk, or improving vocational development and psychological functioning), buprenorphine has long-term positive outcomes (Mattick et al., 2008). However, buprenorphine treatment drop-out rates are high, with observational studies reporting 50–65% retention rates at 6 months, and the great majority of attrition occurring during the *first three months* of treatment (Cunningham et al., 2008; Finch et al., 2007; Fudala et al., 2003; Lee et al., 2009; Magura et al., 2007; Mintzer et al., 2007; Soeffing et al., 2009; Stein et al., 2005).

Lapse to opioid use soon after initiation of buprenorphine is common and a strong predictor of poor treatment retention and return to chronic opioid use. Evidence from our group suggests that a significant proportion of persons initiating buprenorphine will lapse within the first week of treatment and those with a positive opioid toxicology by week four are at five times higher risk for continuing opioid use during treatment, treatment drop-out,

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and relapse (Stein et al., 2010). In subsequent work, we demonstrated that opioid craving, particularly during the first two weeks of buprenorphine treatment, similarly portends worse treatment outcome (Tsui et al., 2014). Thus, convergent evidence indicates that early craving and lapses to opioid use are both frequent and highly predictive of continued opioid use during buprenorphine treatment and of subsequent relapse (Stein et al., 2005, 2010).

Reasons for early attrition from buprenorphine treatment include inadequate dosing of buprenorphine, a desire to continue illicit drug use, social pressures due to a partner's or friend's drug use, and barriers to ongoing medication receipt such as cost and difficulty keeping medical appointments (Gryczynski et al., 2014; Mattick et al., 2008; Stein et al., 2005). However, these factors do not account for all instances of relapse. Early illicit opioid lapse despite motivation for abstinence and pharmacologic treatment of acute withdrawal with buprenorphine implicates the substantial role that early events or situations play in increasing craving and motivating drug-seeking behavior (Goldstein and Volkow, 2002; Lubman et al., 2004; Robinson and Berridge, 2001). Indeed, early recovery situations and events that are associated with emotional distress, including the sensation of inadequate opioid substitution and prolonged withdrawal symptoms, continued exposure to environmental drug cues, stresses of everyday life (e.g., financial, familial), or concurrent mood disorder symptoms, reliably induce craving among treated opioid users (Hyman et al., 2007). Indeed, negative affect is well-established as a primary precipitant of early lapse and features prominently in current models of addiction maintenance and relapse (e.g., Baker et al., 2004; Hendershot et al., 2011; Witkiewitz and Marlatt, 2004), which have informed the development of behavioral treatments unrelated to opioid agonist treatment. Skills for the management and reduction of negative affect (e.g., stress management techniques, avoidance of triggers) are primary elements of these treatments. Meta-analyses indicate that cognitive-behavioral intervention for the treatment for substance use disorder is efficacious (Magill and Ray, 2009). However, recent trials evaluating cognitive-behavioral treatment (Fiellin et al., 2013; Ling et al., 2013) and additional drug counseling (Weiss et al., 2014) have not shown significant benefit over physician management for patients taking buprenorphine (Amato et al., 2011). But earlier studies have not initiated behavioral treatment prior to buprenorphine initiation in preparation for the increased challenge of opioid withdrawal and the risk of early lapse.

Research in the area of nicotine dependence has revealed that it is not solely the severity or intensity of distress, but also one's ability to tolerate both physical and psychological distress (i.e., distress tolerance) occurring in the context of withdrawal and early abstinence that predicts whether one succumbs to a lapse (Brandon et al., 2003; Brown et al., 2002, 2009; Quinn et al., 1996). In these studies, distress tolerance was measured as duration of persistence on psychological and physical challenge tasks that served as analogs for the types of stresses experienced during nicotine withdrawal.

Like nicotine withdrawal and craving, acute opioid withdrawal, which is required as part of standard clinical care in the hours prior to initiating buprenorphine, and craving in the days and weeks after the initiation of buprenorphine, produce uncomfortable interoceptive symptoms such as bone and muscle aches, restlessness, and nausea. Such experiential discomfort, to a greater or lesser degree, demands the use of distress tolerance skills in order to be successful in maintaining abstinence. Evidence suggests that opioid users are overly sensitive to the discomfort associated with anxiety symptoms (Lejuez et al., 2006; Tull et al., 2007). It seems likely then, that for those opioid users initiating buprenorphine treatment who have a low threshold for tolerating distress, and/or difficulty controlling, avoiding, or suppressing the experience of distress, ongoing illicit drug use may serve as a way to manage discomfort. These illicit substance-based efforts to avoid or escape distress are maintained by negatively reinforcing effects such as the reduction of urges or negative affect, even as euphoria is blocked by the agonist properties of buprenorphine.

Supporting this hypothesis, we have recently extended findings from research on nicotine dependence to opioid dependence. The pattern of lower persistence times on the PASAT (Paced Auditory Serial Addiction Task; Diehr et al., 1998; Holdwick and Wingenfeld, 1999) showed that the probability of opioid lapse was greatest soon after initiating buprenorphine, stabilized over subsequent weeks, and was highest among those with low persistence scores (Strong et al., 2012). Given that inability or reduced ability to tolerate distress interferes with efforts to establish longer-term opioid-free behavior change (Strong et al., 2012), individuals who are initiating buprenorphine treatment may benefit from learning new skills or strategies to tolerate these withdrawal symptoms, cravings, and negative affect during early abstinence.

In the current study, we present an adaptation of a distress tolerance treatment (DT), originally developed for smokers (Brown et al., 2008, 2013), that was tailored for opioid dependent individuals initiating buprenorphine treatment. This treatment combines behavioral exposure to opioid craving with training in skills based in Acceptance and Commitment Therapy (Hayes, 2006) to promote maintenance of abstinence. By teaching buprenorphine initiators to minimize avoidance or efforts to escape this discomfort, treatment is meant to strengthen their ability to remain opioid abstinent. We have reported on the development piloting of a novel DT treatment for buprenorphine initiators previously (Brown et al., 2014). Based on feedback from this open trial work, we have created a treatment that we now test in a preliminary randomized trial comparing the distress tolerance treatment (DT) to a health education (HE) comparison condition.

2. Methods

2.1. Participants

Participants were recruited via advertisements (newspaper, bus). Inclusion criteria were age 18–65, seeking buprenorphine treatment, and planning to remain on buprenorphine for at least 3 months. Individuals were excluded for: current participation in methadone maintenance treatment; 15 or more days of benzodiazepine or cocaine use in the last month; daily alcohol use or binges weekly or more; medically necessary opioid treatment for chronic pain; surgery in the next 3 months; current suicidality; neuropsychological dysfunction; justice system involvement that might interfere with participation; bipolar or psychotic disorder; or pregnancy.

Between April, 2013 and October, 2013, 278 individuals were screened after calling the study line. Of these, 194 did not meet eligibility criteria for the following reasons: 65 reported bipolar symptoms or disorder, 52 had a history of psychotic symptoms, 28 had high levels of benzodiazepine, cocaine, or binge alcohol use, 21 had suicidal ideation, 17 were leaving the area in the next 3 months, and 11 were receiving methadone. Of the 84 eligible persons invited for an interview, 31 did not show up and 53 completed a baseline interview. Four were ruled ineligible (3 due to buprenorphine use and negative opioid toxicology and one due to heavy alcohol). Of the remaining 49 persons, 25 were assigned to health education (HE) and 24 to DT condition using permuted block (block sizes of 4 or 6) randomization generated by an off-site statistician (Fig. 1).