Drug and Alcohol Dependence xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Full length article

# Withdrawal exposure with withdrawal regulation training for smoking cessation: a randomized controlled pilot trial

Peter S. Hendricks[a,*], Sharon M. Hall[b], Leslie R. Tyus[a], Christopher B. Thorne[a], Sara N. Lappan[a], Megan V. McMurray[c], William C. Bailey[d], Karen L. Cropsey[c], Timothy B. Baker[e]

[a] University of Alabama at Birmingham, School of Public Health, Department of Health Behavior, 227L Ryals Public Health Building, 1665 University Blvd., Birmingham, AL 35294 USA
[b] University of California, San Francisco, Department of Psychiatry, 401 Parnassus Ave., San Francisco, California 94143 USA
[c] University of Alabama at Birmingham, Department of Psychiatry and Behavioral Neurobiology, Sparks Center 1016, 1720 2nd Ave. South, Birmingham, AL 35294 USA
[d] University of AL at Birmingham, School of Medicine, Department of Medicine, Division of Pulmonary, Allergy and Critical Care Medicine, 1720 2nd Ave. S., Birmingham, AL 35294 USA
[e] University of Wisconsin, School of Medicine and Public Health, Center for Tobacco Research and Intervention, 1930 Monroe St. Suite 200, Madison, Wisconsin 53711 USA

ARTICLE INFO

*Article history:*
Received 26 January 2016
Received in revised form 30 March 2016
Accepted 10 April 2016
Available online xxx

*Keywords:*
Smoking
Tobacco
Withdrawal
Exposure
Treatment
Cessation

ABSTRACT

*Introduction:* Although withdrawal processes form a key motivational basis for cigarette use, smoking cessation treatments appear to exert only modest effects on withdrawal. One treatment option for further reducing withdrawal severity would be to provide smokers with withdrawal regulation training. The objective of this study was to pilot a smoking cessation intervention comprising withdrawal exposure with withdrawal regulation training.

*Methods:* Adult smokers (N = 80) were randomized to one of two conditions: 1) Withdrawal Exposure with Withdrawal Regulation Training (WT), which included the development and application of individualized withdrawal regulation strategies over four separate sessions that spanned the first four hours of abstinence; 2) or Relaxation Control (RC) training, which controlled for the therapeutic contact of WT. All sessions occurred before the quit date, after which differential treatment was discontinued and all participants received brief counseling, nicotine replacement therapy, and self-help literature. Biochemically-confirmed (CO ≤ 3) seven-day point-prevalence abstinence was assessed at Months 2 and 3 after end-of-treatment.

*Results:* Treatment completion and ratings of credibility and efficacy were high and equivalent across conditions. 22.2% of participants in the WT condition were abstinent at both time points, whereas 0% and 4.2% of participants in the RC condition were abstinent at Months 2 and 3 (Month 3 *OR* = 6.5 [0.73, 59.19]). In-session withdrawal ratings suggested WT improved regulation of withdrawal symptoms, which were in turn associated with abstinence.

*Conclusions:* This small pilot study suggests that WT promotes abstinence by enhancing withdrawal regulation. Results warrant further investigation of this innovative treatment approach.



## 1. Introduction

Although the prevalence of tobacco use has declined in many countries, smoking remains the single most preventable cause of morbidity and mortality worldwide (Centers for Disease Control and Prevention, 2015; Wipfli and Samet, 2016). Unfortunately, long-term abstinence rates for even the most intensive of typical smoking cessation treatments are usually 25% or less, with the most successful of atypical extended interventions yielding abstinence

* Corresponding author at: 227L Ryals Public Health Building, 1665 University Blvd, Birmingham, AL 35294, USA.
*E-mail addresses:* phendricks@uab.edu (P.S. Hendricks), sharon.hall@ucsf.edu (S.M. Hall), lware200@uab.edu (L.R. Tyus), cbthorne@uab.edu (C.B. Thorne), lappansa@uab.edu (S.N. Lappan), mvmcmurr@uab.edu (M.V. McMurray), wcbailey@uab.edu (W.C. Bailey), kcropsey@uab.edu (K.L. Cropsey), tbb@ctri.wisc.edu (T.B. Baker).

http://dx.doi.org/10.1016/j.drugalcdep.2016.04.022
0376-8716/

rates no greater than about 55% (Cox et al., 2004; Hall et al., 2004, 2009, 2011; Hays et al., 2001; Hurt et al., 2003; Killen et al., 2006, 2008; Tonstad et al., 2006; Williams et al., 2007). It is therefore critical that novel and more efficacious smoking cessation treatments be developed.

In current leading models of drug dependence, the escape or avoidance of negative affect withdrawal symptoms constitutes a strong motivational basis for continued cigarette use (e.g., Baker et al., 2004, 2006; Piper, 2015). Whereas pharmacologic withdrawal is believed to result from the homeostatic adaptation of the nervous system to chronic nicotine administration, behavioral withdrawal is thought to stem from repeated pairings of cigarette use with withdrawal relief. Through these pairings smokers learn the act of smoking is a powerful tool for regulating negative affect and craving. From this perspective, smokers are likely to relapse in the face of negative affect and craving if they lack adequate non-smoking regulation strategies.

In contemporary smoking cessation treatment, withdrawal regulation strategies are typically administered *after* a smoker's quit date (e.g., Hall et al., 2004). However, the timing of such treatment means that smokers could lapse or relapse prior to their acquiring effective withdrawal regulation techniques (see Japuntich et al., 2011), or develop maladaptive regulation strategies in the initial stages of abstinence that increase later relapse risk (e.g., alcohol use; Hendricks et al., 2012). The concurrent use of pharmacotherapy may also limit the efficacy of withdrawal regulation strategies. Because pharmacotherapies alleviate withdrawal (albeit somewhat modestly), smokers may learn withdrawal regulation techniques when symptoms are muted, leaving them poorly equipped to regulate more severe symptoms associated with relapse. Whether owing to the timing of treatment, or the lack of highly effective interventions, smoking cessation treatments tend to reduce withdrawal severity only modestly and this no doubt limits their effects on abstinence (Bolt et al., 2012; McCarthy et al., 2008, 2010; Piper et al., 2008b; Vidrine et al., 2006). Thus, current smoking cessation treatments may be augmented by a renewed focus on the regulation of withdrawal.

Not only might it be most effective to practice withdrawal regulation prior to the quit date, but it also might be especially effective for practice to occur early in the course of abstinence and without the use of pharmacotherapy. This approach would provide the opportunity to generate, modify, and refine withdrawal regulation strategies in real-time during an exposure to withdrawal that more closely approximates post-treatment high-risk relapse contexts. Indeed, among those who smoke approximately 20 cigarettes (one pack) per day withdrawal symptoms increase within the first four hours of abstinence—craving as early as 30 min after the last cigarette—and withdrawal symptom severity across the first four hours of abstinence approximates longer-term withdrawal severity among smokers attempting to quit in real-world settings (Hendricks et al., 2006; Welsch et al., 1999). In addition, withdrawal symptoms across the first four hours of abstinence predict smoking cessation treatment outcome, suggesting interventions that focus on this time period might demonstrate efficacy (Hendricks et al., 2013). Thus, withdrawal regulation training early in the course of abstinence may provide an important foundation for adaptive coping with withdrawal later in the quit attempt.

To our knowledge, only two randomized controlled trials have evaluated withdrawal exposure components in smoking cessation treatment. Brown et al. (2013) incorporated four sessions of withdrawal exposure ranging from one to four hours as part of a larger distress tolerance intervention that emphasized Acceptance and Commitment Therapy approaches (i.e., acceptance of withdrawal distress). Results favored the distress tolerance intervention at end of behavioral and pharmacologic treatment, but not at subsequent follow-up periods. (McCarthy et al. 2016) tested the efficacy of prescribing seven sessions of escalating abstinence prior to the quit date. No specific withdrawal regulation strategies were provided. This intervention increased latency to lapse and prevented progression from lapse to relapse, but only modestly increased smoking abstinence four weeks post-quit. These findings suggest that withdrawal exposure components may hold promise in the treatment of tobacco dependence, but that withdrawal exposure in the absence of withdrawal regulation training may not be sufficient to maintain abstinence.

The objective of the current investigation was to pilot test a precessation compound intervention comprising withdrawal exposure with withdrawal regulation training for smoking cessation. In this study, participants were randomly assigned to abstain from smoking for four hours over four separate sessions while engaging in individually tailored withdrawal regulation strategies, or to smoke at their own pace for four hours over four sessions while enacting individualized relaxation techniques. All participants received a standard intervention consisting of brief cognitive-behavioral counseling, nicotine replacement therapy, and self-help smoking cessation material after withdrawal regulation or relaxation interventions. We hypothesized that the experimental withdrawal regulation intervention would be feasible, acceptable to participants, effective in increasing short-term abstinence rates, and activate change mechanisms consistent with its theoretical rationale—specifically, that the experimental intervention would prevent a significant increase in early withdrawal symptoms relative to the control intervention (suggesting enhanced regulation of withdrawal among participants in the experimental condition), and that less severe early withdrawal symptoms would be associated with a greater likelihood of abstinence among participants in the experimental condition.

## 2. Material and methods

### 2.1. Participants

Participants were 80 treatment-seeking cigarette smokers from the Birmingham, Alabama area who responded to community advertisements. Eligibility criteria were: (1) fluent in English; (2) ≥19 years old; (3) smoking ≥10 cigarettes/day; (4) reported the intention to quit smoking; (5) residing in the area with no plan to relocate in the next six months; and (6) having telephone access. Exclusion criteria were: (1) expired breath carbon monoxide (CO) <8 parts per million (ppm) at intake; (2) current participation in a smoking cessation treatment program; (3) current use of pharmacotherapy for smoking cessation; (4) presence of any condition contraindicating the use of the nicotine patch; and (5) presence of conditions that might interfere with adherence to the protocol or greatly complicate treatment (i.e., dementia, psychotic disorders, bipolar disorders, suicidal or homicidal ideation, and any disease acutely life-threatening or so severe that the participant could not comply with the protocol). Fig. 1 shows the CONSORT flow diagram. This study was registered with ClinicalTrials.gov (NCT02192762) and was approved by the University of Alabama at Birmingham Institutional Review Board.

### 2.2. Procedures

*2.2.1. Therapist training and fidelity.* Manuals were developed for standardized delivery of treatment components for both conditions. The therapist was a student obtaining a Master of Arts degree in Counseling from the University of Alabama at Birmingham selected for having previously completed training in health behavior intervention. Prior to study implementation, the therapist underwent training that included mentoring and practice sessions

Please cite this article in press as: Hendricks, P.S., et al., Withdrawal exposure with withdrawal regulation training for smoking cessation: a randomized controlled pilot trial. Drug Alcohol Depend. (2016), http://dx.doi.org/10.1016/j.drugalcdep.2016.04.022