Full length article

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

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ARTICLE INFO

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

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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
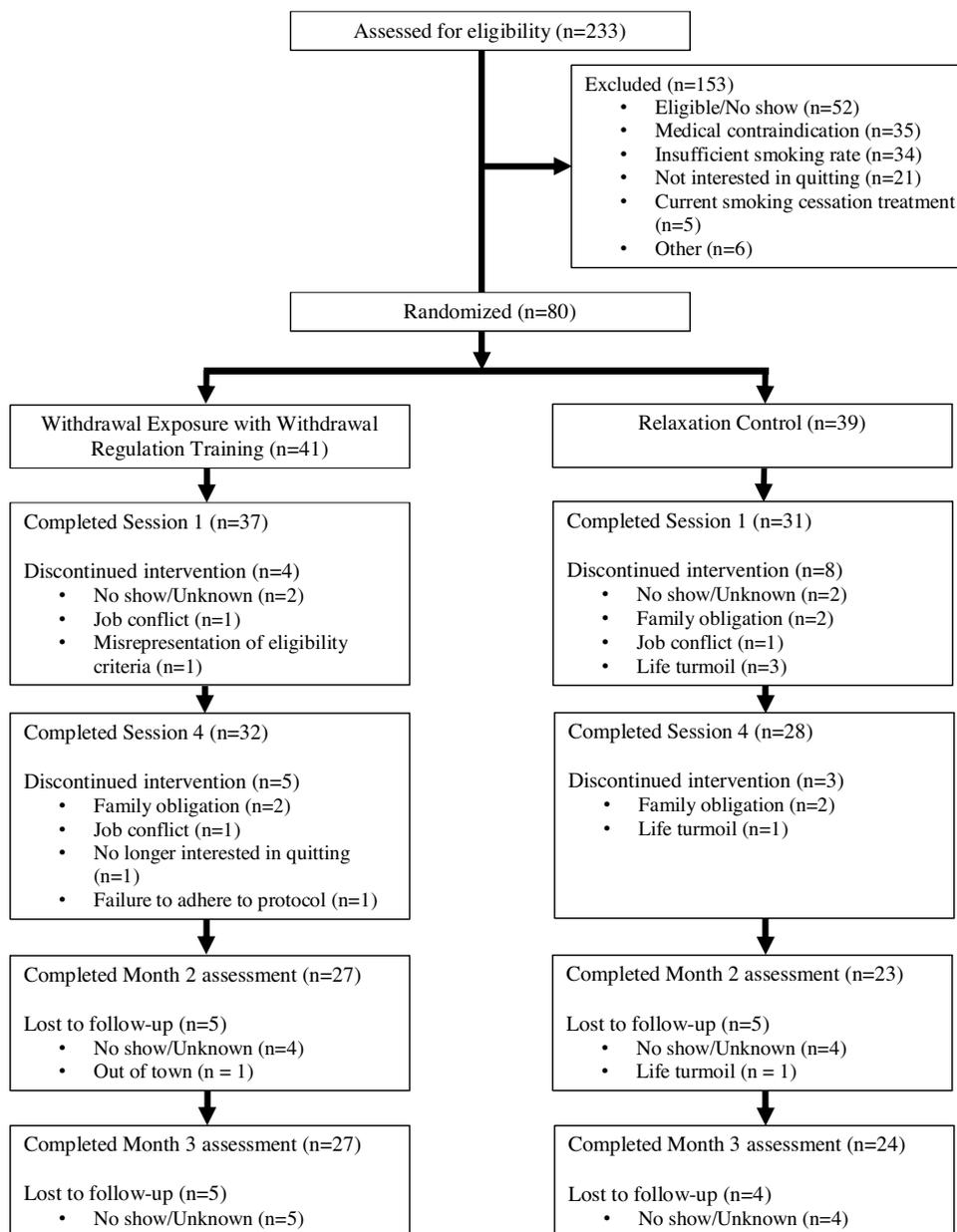
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                        │  Assessed for eligibility (n=233) │
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Fig. 1. Consort diagram.

with the principal investigator, and education in the treatment of tobacco dependence. In addition, the principal investigator directly observed the therapist during the first two sessions of each of the two conditions and intermittently thereafter, providing detailed feedback. Weekly and ad hoc meetings between the therapist and principal investigator served to ensure fidelity to treatment protocols and provide the opportunity to troubleshoot as needed. Treatment occurred over 28 months, with the therapist seeing a mean of 2.85 participants per month.

2.2.2. Informed consent, randomization, and compensation. Following telephone screening, participants met for an orientation session where informed consent was obtained and intake measures were administered. Upon completion of intake measures, participants were randomly assigned to either Withdrawal Exposure with Withdrawal Regulation Training or Relaxation Control, stratified by gender and cigarettes smoked per day (cut-point = 15). Participants received $10 for completing intake orientation, $40 for completing

Session 1, $15 for providing documentation of self-administered sessions (Sessions 2 and 3), $40 for completing Session 4, $20 for completing Month 2 assessment, $20 for completing Month 3 assessment, and a $40 bonus for completing both Month 2 and Month 3 assessments, for total possible compensation of $185.

2.2.3. Withdrawal exposure with withdrawal regulation training (WT). WT was informed in part by in-vivo exposure therapy paradigms for anxiety disorders (Deacon and Abramowitz, 2004; Nathan and Gorman, 2007) that involve gradual exposure to real-life anxiety provoking stimuli such as environmental cues or memories. Therapists prevent clients from engaging in avoidance behaviors to facilitate affective habituation to the stimuli (i.e., reduction of anxiety) and, in turn, extinction of avoidance responses and an instilled sense of mastery. Exposure therapy may not translate directly to a smoking cessation intervention designed to reduce withdrawal symptom severity, however, considering the stimuli (withdrawal symptoms) are themselves affective in

nature and increase in valence over time secondary to pharmacologic processes. Moreover, as smokers are routinely exposed to withdrawal symptoms as the result of environmental smoking restrictions, mere exposure may be insufficient to mitigate withdrawal, especially in light of the fact that extinction of the avoidance behavior (smoking) may be inhibited by the perceived availability of cigarettes at the conclusion of exposure sessions (Juliano and Brandon, 1998; Wertz and Sayette, 2001). The compound WT intervention was therefore conceived with the supposition that withdrawal exposure coupled with withdrawal regulation training may be the most appropriate translation of the exposure therapy paradigm for an intervention devised to alleviate the severity of smoking withdrawal.

Table 1 presents a summary of the WT protocol and the WT manual can be found in Supplementary material. During a precessation period, WT participants were scheduled to engage in an orientation session and four treatment sessions. The orientation session included psychoeducation regarding the withdrawal syndrome, its relationship to relapse, and the importance of effectively regulating withdrawal to achieving abstinence. Consistent with the treatment rationale, withdrawal was described as stemming from both pharmacologic and behavioral processes, with an emphasis on the latter. Participants were provided with a handout containing a list of potential withdrawal regulation strategies informed by contemporary smoking cessation and cognitive-behavioral therapy literature (e.g., Nathan and Gorman, 2007; Hall et al., 2004; O'Connell et al., 2007; see Supplementary material) and developed a preliminary, individualized set of such strategies for use during their first exposure session with assistance from the therapist.

Session 1 was held in the laboratory. As in earlier research (Hendricks et al., 2006, 2013), at the beginning of this session participants smoked one cigarette in a room equipped to ventilate cigarette smoke before being instructed to abstain from smoking in a room designed for therapeutic intervention. Exposure to withdrawal occurred during the first four hours after smoking this cigarette. During this time, the therapist instructed participants to use the withdrawal regulation strategies developed during the orientation session. Withdrawal severity and regulation strategy effectiveness were monitored by the therapist and regulation techniques were practiced and modified, or new techniques developed, to maximize withdrawal regulation effectiveness. The therapist vacated the intervention room for periods of time to allow participants to practice withdrawal regulation strategies independently. Withdrawal symptoms were formally assessed every 30 min via self-report (see Section 2.2.6 below). The therapist took note of those regulation strategies that appeared to be most effective for each participant and created a handout listing these techniques for each participant's future reference.

Upon conclusion of Session 1, participants were instructed to self-administer two withdrawal exposure sessions in their natural environment. The first, Session 2, occurred the day after Session 1 and comprised the first four hours immediately after waking in the morning. The second, Session 3, occurred the day after Session 2 and comprised four hours during which participants anticipated the greatest difficulty refraining from cigarette use. The purpose of these self-administered sessions was for participants to gain experience using withdrawal regulation strategies independently and in challenging real-world contexts. Participants were provided with diaries that included instructions regarding the self-administered sessions and self-report withdrawal forms to be completed every 30 min during the sessions.

The final session, Session 4, took place in the laboratory two days after Session 3. Participants' quit dates were scheduled on this day. Thus, the cigarette participants smoked at the beginning of this session was meant to represent their final use of tobacco. Session 4 focused on the resolution of any difficulties that may have arisen during Sessions 2 or 3 and the fine-tuning of withdrawal regulation techniques. As in Session 1, regulation strategy effectiveness was monitored by the therapist and withdrawal symptoms were formally assessed every 30 min. At the conclusion of Session 4, participants were given a summary handout containing an individualized list of effective withdrawal regulation techniques.

Participants also received a standard intervention from the therapist at the conclusion of Session 4 that included brief (approximately 20 min in length) cognitive-behavioral counseling, an eight-week supply of the nicotine patch, and empirically validated self-help smoking cessation material (Brandon et al., 2016, 2012; Maskrey et al., 2015; Unrod et al., 2015). The brief cognitive-behavioral counseling centered on: evaluating the cost-benefit of smoking and smoking cessation, stimulus control and behavior modification, managing abstinence-specific social support, urge coping skills, and relapse prevention strategies.

2.2.4. Relaxation control (RC). RC was designed to control for the therapeutic contact of WT. During a precessation period RC participants were scheduled to engage in an orientation session and four treatment sessions, similar to WT participants (see Table 1). Participants in this condition received relaxation training for the same duration and at the same frequency as participants who received WT, with analogous intervention materials, identical self-report assessment of withdrawal symptoms, and the same standard intervention delivered at the conclusion of Session 4. RC participants were instructed to smoke at their own pace for the duration of each session such that exposure to withdrawal did not take place. Participants initiated their quit attempt using the standard cessation intervention upon completing Session 4. Considering that relaxation training appears to have no effect on the efficacy of smoking cessation interventions ($OR = 1.0$, Fiore et al., 2008), RC was deemed an appropriate control.

2.2.5. Measures assessing participant characteristics at intake orientation.

2.2.5.1. Demographic and smoking history questionnaire. An author-constructed questionnaire was used to measure demographic and smoking characteristics (e.g., cigarettes smoked per day, years of regular smoking, etc.).

2.2.5.2. Fagerström test of cigarette dependence (FTCD; Fagerström, 2012). The FTCD is a widely used and well validated six-item measure of gradations in physical cigarette dependence. Scores range from zero to 10 with greater values reflecting greater dependence (Cronbach's α from this sample = 0.58).

2.2.5.3. Wisconsin Inventory of Smoking Dependence Motives-68 (WISDM-68; Piper et al., 2008a). The WISDM-68 is a 68-item measure designed to assess dependence as a motivational state on 13 scales: Affiliative Attachment (Cronbach's α from this sample = 0.93), Automaticity (Cronbach's α from this sample = 0.87), Loss of Control (Cronbach's α from this sample = 0.72), Behavioral Choice/Melioration (Cronbach's α from this sample = 0.88), Cognitive Enhancement (Cronbach's α from this sample = 0.92), Craving (Cronbach's α from this sample = 0.80), Cue Exposure/Associative Processes (Cronbach's α from this sample = 0.79), Negative Reinforcement (Cronbach's α from this sample = 0.87), Positive Reinforcement (Cronbach's α from this sample = 0.87), Social/Environmental Goads (Cronbach's α from this sample = 0.94), Taste/Sensory Processes (Cronbach's α from this sample = 0.88), Tolerance (Cronbach's α from this sample = 0.77), and Weight Control (Cronbach's α from this sample = 0.86). The Primary Dependence Motives (PDM) composite scale indexes the core features of tobacco dependence (Automaticity, Craving, Loss

Table 1
Summary of WT protocol.

Treatment Session	Procedures
Orientation Meeting	● Psychoeducation surrounding treatment rationale ● Initial development of individualized withdrawal regulation strategies
Session 1	● Application and modification of withdrawal regulation strategies across the first four hours of abstinence in the laboratory with assistance from the therapist
Session 2 *(1 day after Session 1)*	● Application and modification of withdrawal regulation strategies across the first four hours of abstinence immediately after waking in the morning
Session 3 *(1 day after Session 2)*	● Application and modification of withdrawal regulation strategies across the first four hours of abstinence during a time when participants anticipated the greatest difficulty refraining from cigarette use
Session 4 *(2 days after Session 3)*	● Initiation of the quit attempt at the beginning of the session ● Resolution of difficulties that may have arisen during Sessions 2 or 3 and fine-tuning of withdrawal regulation strategies across the first four hours of abstinence in the laboratory with assistance from the therapist ● Conclusion of treatment

Note: WT = withdrawal exposure with withdrawal regulation training.

of Control, and Tolerance) whereas the Secondary Dependence Motives (SDM) composite scale captures the remaining motives less central to cigarette use. Average scores per scale are reported (range 1–7) with greater values reflecting greater dependence motives.

2.2.5.4. Wisconsin smoking withdrawal scale (WSWS; Welsch et al., 1999). The WSWS is a 28-item measure that assesses smoking withdrawal symptoms on seven scales: Anger (Cronbach's α from this sample = 0.83), Anxiety (Cronbach's α from this sample = 0.70), Concentration Difficulty (Cronbach's α from this sample = 0.83), Craving (Cronbach's α from this sample = 0.72), Hunger (Cronbach's α from this sample = 0.52), Sadness (Cronbach's α from this sample = 0.76), and Sleep Disturbance (Cronbach's α from this sample = 0.87). Participants were instructed to respond based on how they felt "over the last week." Average scores per scale are reported (range 1–4) with greater scores representing more severe withdrawal effects.

2.2.5.5. Thoughts about abstinence questionnaire (TAA; Hall et al., 1990). The TAA assesses motivation to quit, abstinence self-efficacy, and perceived difficulty quitting with one item each. Participants indicated their desire to quit smoking (1 = "no desire to quit smoking" to 10 = "full desire to quit"), how successful they expected to be in quitting smoking (1 = "lowest expectation of success" to 10 = "highest expectation of success"), and how difficult they thought it would be to quit and remain abstinent (1 = "lowest amount of difficulty" to 10 = "highest amount of difficulty").

2.2.5.6. Smoking abstinence questionnaire (SASQ; Hendricks et al., 2011). The 55-item SAQ measures smokers' expectancies for the process of smoking cessation on 10 scales. Withdrawal, which measures expectancies for postcessation withdrawal effects, is reported here (Cronbach's α from this sample = 0.84). Average scores per scale are reported (range 0–6) with greater scores reflecting stronger expectancies.

2.2.6. Measure assessing early withdrawal symptoms during WT and RC sessions.

2.2.6.1. WSWS-revised. Consistent with previous research (Hendricks et al., 2006, 2013), participants completed a revised version of the WSWS indicating how they felt "right now … at this moment" at 30 min intervals over the four, four-hour WT and RC sessions following baseline assessment (i.e., at baseline and at 30 min, 60 min, 90 min, 120 min, 150 min, 180 min, 210 min, and 240 min post-baseline), for a total of nine assessments for each of the four sessions. The response scale was expanded from 0–4 to 0–8 to increase sensitivity and items on the Sleep Disturbance scale were removed as they do not apply to early withdrawal, leaving six

scales: Anger (mean Cronbach's α from this sample = 0.90), Anxiety (mean Cronbach's α from this sample = 0.79), Concentration Difficulty (mean Cronbach's α from this sample = 0.85), Craving (mean Cronbach's α from this sample = 0.92), Hunger (mean Cronbach's α from this sample = 0.82), and Sadness (mean Cronbach's α from this sample = 0.82). Average scores per scale are reported (range 0–8) with greater values representing more severe withdrawal symptoms.

2.2.7. Outcome measures.

2.2.7.1. Credibility/expectancy questionnaire (CEQ; Devilly and Borkovec, 2000). The CEQ was administered at the conclusion of the Session 1 and at end-of-treatment (EOT) to confirm that participants viewed the two treatments as equally plausible and effective for smoking cessation. This six-item measure yields two scales: Credibility, which assesses treatment credibility (Cronbach's α from this sample at Session 1 and EOT = 0.76 and 0.87, respectively); and Expectancy, which captures the expectation of treatment efficacy (Cronbach's α from this sample at Session 1 and EOT = 0.84 and 0.88, respectively). In this report, average scores on the two scales range from 0 to 10, with greater scores indicating greater perceptions of credibility and expectancy.

2.2.7.2. Abstinence. The primary outcome was seven-day point-prevalence abstinence ("no smoking, not even a puff" in the past seven days), assessed two months postcessation (Month 2; coinciding with the termination of the nicotine patch) and three months postcessation (Month 3), and biochemically verified by a CO value of three ppm or less. Although this CO cutoff is more conservative than the traditional cutoff of 8–10 ppm, it provides the best sensitivity and specificity for smoking cessation (Cropsey et al., 2015a; Emery and Levine, 2015).

2.2.8. Data analysis. The treatment conditions were compared on intake demographic and smoking-related characteristics using chi-square or *t*-tests as appropriate. Differences in treatment credibility and expectancy were evaluated using *t*-tests and differences in point-prevalence smoking abstinence were evaluated with Fisher's exact test. Consistent with contemporary recommendations (Blankers et al., 2016; Hedeker et al., 2007), missing abstinence data were coded as missing. However, to allow comparison with published research and enhance the robustness of findings, secondary analyses also were conducted with all missing abstinence data coded as smoking, as per intent-to-treat analysis.

To evaluate putative mechanisms of action, Generalized Estimating Equations (GEEs) were employed to determine mean and slope differences between the conditions in early withdrawal symptoms for each precessation period treatment session (Hendricks et al., 2006). Kendall's τ then evaluated the relationships

of early withdrawal symptom means and slopes from each of the four treatment sessions with smoking abstinence among WT participants only (Hendricks et al., 2013; these relationships were not evaluated among RC participants as RC participants were neither exposed to withdrawal nor provided withdrawal regulation training). To control for multiple comparisons and identify potentially meaningful relationships, only statistically significant τ's of at least 0.30 are reported (i.e., those corresponding to at least a moderate effect; Cohen, 1988).

3. Results

3.1. Sample characteristics

Sample characteristics are shown in Table 2. Participants were well distributed with regard to gender, and though most identified as White, 37.5% identified as African American, 1.3% identified as American Indian, and 2.5% identified as more than one race. Participants were middle-aged, and as typical of the smoking population (Hiscock et al., 2012), reported modest socioeconomic status. Participants were also moderately-to-heavily dependent on tobacco with extensive smoking histories, and reported past-week withdrawal symptoms in the mild-to-moderate range, high levels of motivation to quit, moderate-to-high levels of abstinence self-efficacy, moderate perceived difficulty quitting, and moderate expectancies for postcessation withdrawal. Seventy-eight percent of WT participants and 72% of RC participants completed treatment ($\chi^2 = 0.42$, $p = 0.52$), with 72% of WT participants (23/32) and 57% of RC participants (16/28) providing documentation of self-administered sessions ($\chi^2 = 1.4$, $p = 0.23$). The treatment conditions were similar with regard to loss to follow-up ($\chi^2 = 0.05$, $p = 0.99$).

3.2. Outcomes

3.2.1. CEQ. WT and RC participants reported similar Credibility scores at the end of the first session (WT $M = 7.64$, $SD = 1.31$; RC $M = 7.69$, $SD = 1.42$; $t = -0.13$, $p = 0.89$) and EOT (WT $M = 8.20$, $SD = 1.12$; RC $M = 8.11$, $SD = 1.03$; $t = 0.31$, $p = 0.76$), and similar Expectancy scores at the end of the first session (WT $M = 7.94$, $SD = 1.22$; RC $M = 7.86$, $SD = 1.78$; $t = 0.20$, $p = 0.84$) and EOT (WT $M = 8.56$, $SD = 1.19$; RC $M = 8.43$, $SD = 1.34$; $t = 0.38$, $p = 0.70$).

3.2.2. Abstinence. At Month 2, 22.2% (6/27) of WT participants reported seven-day point-prevalence abstinence confirmed by a CO value of three ppm or less as compared to 0% (0/23) of RC participants ($p = 0.02$). At Month 3, 22.2% (6/27) of WT participants reported seven-day point-prevalence abstinence confirmed by a CO of three ppm or less as compared to 4.2% (1/24) of RC participants ($p = 0.10$; $OR = 6.5$ [.73, 59.19]). In secondary analyses in which all missing abstinence data were coded as smoking, 14.6% (6/41) of WT participants reported seven-day point-prevalence abstinence confirmed by a CO value of three ppm or less at Month 2 as compared to 0% (0/39) of RC participants ($p = 0.02$) and 14.6% (6/41) of WT participants reported seven-day point-prevalence abstinence confirmed by a CO value of three ppm or less at Month 3 as compared to 2.5% (1/39) of RC participants ($p = 0.10$; $OR = 6.5$ [0.75, 56.84]). Mean CO values among abstinent WT participants were 1.33 ($SD = 1.36$) and 1.50 ($SD = 1.37$) at Months 2 and 3, whereas mean CO values among non-abstinent WT participants were 14.33 ($SD = 10.51$) and 15.61 ($SD = 12.35$) at these times. The CO value of the single abstinent RC participant at Month 3 was one, whereas mean CO values among non-abstinent RC participants were 14.10 ($SD = 7.65$) and 15.05 ($SD = 5.79$) at Months 2 and 3.

3.3. Mechanisms of action

Table 3 displays results of GEE models evaluating mean and slope differences between the conditions in early withdrawal symptoms for each precessation period treatment session. Fig. 2 depicts participant responses on the WSWS Craving scale for each treatment session as an exemplar of withdrawal symptom differences between treatment conditions (craving typically demonstrates the largest difference between abstaining and smoking participants across the first four hours of abstinence; Hendricks et al., 2006, 2013). As shown in Table 3 and depicted in Fig. 2, there were no significant differences in mean craving between WT participants and RC participants for any session. However, significant differences in craving slope were observed. Specifically, whereas craving tended to increase slightly over time for WT participants for Sessions 1, 3, and 4, it tended to remain stable for each of these sessions for RC participants. Results were similar for other WSWS scales but differences between conditions were generally less pronounced, with sadness evincing no mean or slope differences between conditions at any session.

Among WT participants, lower mean craving during Session 3 was associated with an increased likelihood of abstinence at Month 2 ($\tau = -0.42$, $p = 0.03$). Lower mean hunger during Session 3 was associated with an increased likelihood of abstinence at Month 3 ($\tau = -0.41$, $p = 0.04$) and an increased likelihood of abstinence at Month 2 that approached statistical significance ($\tau = -0.39$, $p = 0.055$). In addition, less steep anger slope during Session 3 was associated with an increased likelihood of abstinence at Month 2 ($\tau = -0.43$, $p = 0.03$) and an increased likelihood of abstinence at Month 3 that approached statistical significance ($\tau = -0.37$, $p = 0.07$). Finally, less steep anxiety slope ($\tau = -0.32$, $p = 0.06$) and sadness slope ($\tau = -0.33$, $p = 0.057$) across Session 4 were each associated with an increased likelihood of abstinence at Month 3 that approached statistical significance.

3.4. Exploratory moderator analyses

A series of logistic regression models evaluating a range of treatment condition by intake demographic/smoking-related variable interaction terms were conducted to identify moderators of treatment condition on smoking abstinence. Of particular interest were variables related to the withdrawal process (i.e., WISDM-68 Negative Reinforcement scale, WISDM-68 Craving scale, SAQ Withdrawal scale, WSWS scales) or prior withdrawal exposure (i.e., number of quit attempts of at least 24 h, number of quit attempts of at least 1 week). Results failed to reveal significant moderators among these or any other variables, though given the modest sample size, these analyses were likely underpowered.

4. Discussion

The objective of the present study was to pilot test a precessation compound intervention comprising withdrawal exposure with withdrawal regulation training for smoking cessation. Our first hypothesis was that this intervention would demonstrate feasibility and acceptability. In support of this hypothesis, nearly 80% of participants completed the treatment protocol, commensurate with adult psychotherapy completion rates in general (Swift and Greenberg, 2012) and smoking cessation treatment completion rates from recent trials conducted in the same geographic region in particular (Cropsey et al., 2015b, 2015c). Furthermore, participants rated the intervention as highly credible and efficacious, with scores of approximately eight on a 0–10 scale. These findings suggest that a larger trial making use of this treatment paradigm could be conducted with success.

Table 2
Sample characteristics.

Characteristic	WT (n = 41)	RC (n = 39)	*p*-value
Gender (%Men)	58.3	59.4	0.93
Race (%White)	52.8	56.3	0.77
Mean Age in Years (SD)	46.1 (14.0)	46.2 (13.5)	0.97
Educational Attainment (%)			0.16
High School Degree or Less	63.9	46.9	
Associate's Degree or More	36.1	53.1	
Employment Status (%Employed)	30.6	46.9	0.17
Annual Individual Income (%)			0.62
Less than $20,000	74.3	68.8	
$21,000 or more	25.7	31.2	
Mean Cigarettes Smoked per Day (SD)	17.3 (6.6)	20.6 (11.3)	0.15
Mean Years Smoked Regularly (SD)	25.9 (13.5)	26.0 (13.2)	0.96
Mean Quit Attempts of at least 24 hours (SD)	11.1 (19.5)	10.0 (19.3)	0.81
Mean Quit Attempts of at least 1 week (SD)	3.2 (3.9)	4.2 (5.6)	0.42
Mean FTCD (SD)	7.1 (2.2)	7.1 (2.3)	0.89
Mean WISDM-68 PDM (SD)	4.6 (1.3)	5.0 (1.0)	0.15
Mean WISDM-68 SDM (SD)	4.1 (1.1)	4.2 (1.2)	0.64
Mean WSWS Anger (SD)	2.0 (1.0)	2.1 (1.2)	0.57
Mean WSWS Anxiety (SD)	2.4 (.78)	2.5 (.88)	0.44
Mean WSWS Concentration Difficulty (SD)	1.8 (.99)	1.6 (.92)	0.43
Mean WSWS Craving (SD)	2.5 (.86)	2.5 (.80)	0.95
Mean WSWS Hunger (SD)	2.2 (.74)	2.1 (.69)	0.48
Mean WSWS Sadness (SD)	1.6 (.92)	1.6 (.90)	0.95
Mean WSWS Sleep Disturbance (SD)	2.1 (1.1)	1.8 (1.0)	0.27
Mean TAA Motivation to Quit (SD)	8.9 (1.3)	9.4 (.80)	0.09
Mean TAA Abstinence Self-efficacy (SD)	7.7 (2.1)	7.9 (2.2)	0.68
Mean TAA Perceived Difficulty Quitting (SD)	5.9 (2.5)	6.3 (2.3)	0.50
Mean SAQ Withdrawal (SD)	3.4 (1.3)	3.4 (1.1)	0.89

Note: WT = withdrawal exposure with withdrawal regulation training; RC = relaxation control; FTCD = Fagerström test of cigarette dependence (possible range 0–10); WISDM–68 = Wisconsin inventory of smoking dependence motives-68; PDM = primary dependence motives (possible range 1–7); SDM = secondary dependence motives (possible range 1–7); WSWS = Wisconsin smoking withdrawal scale (possible range on all scales 1–4); TAA = thoughts about abstinence questionnaire (possible range on all scales 1–10); SAQ = smoking abstinence questionnaire (possible range 0–6).

Table 3
Results of GEE models evaluating mean and slope differences between the conditions in early withdrawal symptoms for each precessation period treatment session.

	Session 1		Session 2		Session 3		Session 4	
	Mean difference	Slope difference	Mean difference	Slope difference	Mean difference	Slope difference	Mean difference	Slope difference
Anger	0.36	**1.45****	0.26	0.78	−0.0009	**1.45***	0.11	**.93***
Anxiety	0.43	**1.28***	−0.08	0.12	−0.08	1.01	0.01	**.97***
Concentration Difficulty	0.59	**1.77†**	0.56	−0.04	0.31	−0.32	0.74	0.57
Craving	0.15	**2.23†**	0.38	1.16	0.23	**2.48****	−0.12	**1.6****
Hunger	0.66	**1.39***	0.81	**2.18****	0.48	0.57	0.50	−0.51
Sadness	0.27	0.37	0.02	−0.05	−0.17	0.17	0.18	0.10

Note: Reported statistics are GEE parameter estimates. Positive estimates indicate greater mean withdrawal symptoms or steeper withdrawal symptom slopes in the WT condition whereas negative estimates indicate greater mean withdrawal symptoms or steeper withdrawal symptoms slopes in the RC condition. Significant findings presented in bold. $^* p < 0.05$ $^{**} p < 0.01$ $^† p < 0.001$.

Our second hypothesis was that this intervention would enhance short-term abstinence rates. Consistent with this hypothesis, 22% of participants in the experimental treatment condition were abstinent at Months 2 and 3, compared with 0% and 4.2% of participants in the control condition at Month 2 and 3, respectively. Though abstinence rates were especially low in the control condition, results should be interpreted in context of the small sample and possibility of randomization failure, conservative—though appropriate—CO cutoff of three ppm used to confirm smoking abstinence in the current study (the traditional CO cutoff of 8–10 ppm artificially inflates abstinence rates relative to a CO cutoff of three ppm; see Cropsey et al., 2015a), as well the woeful tobacco control in the state of Alabama, which earns failing "F" grades on all relevant American Lung Association metrics (American Lung Association, 2016). These outcomes yielded an *OR* of 6.5 at Month 3, which exceeds an *OR* of 4.25 corresponding to a large effect (Chinn, 2000). Although all participants received the nicotine patch and self-help materials (Brandon et al., 2016, 2012; Maskrey et al., 2015; Unrod et al., 2015), no postcessation behavioral support was provided.

This is unconventional in contemporary smoking cessation treatment, which typically provides the majority of treatment after the quit attempt (see Hall et al., 2004). The present results are therefore impressive and suggest that supplementing the prequit withdrawal exposure with withdrawal regulation training intervention with postcessation behavioral support might result in even higher abstinence rates. Future studies might also seek to improve efficiency (e.g., via group format or digital applications) should session length prove an obstacle to real-world dissemination.

Our final hypothesis was that the experimental intervention would prevent a significant increase in early withdrawal symptoms relative to the control intervention, and that less severe early withdrawal symptoms would be associated with a greater likelihood of abstinence among participants in the experimental condition. We did not include a condition in the current study that abstained from smoking without receiving withdrawal regulation training, which limits our ability to determine if the experimental intervention had an effect on the regulation of withdrawal. However, some evidence indirectly supports this inference. Participants in the
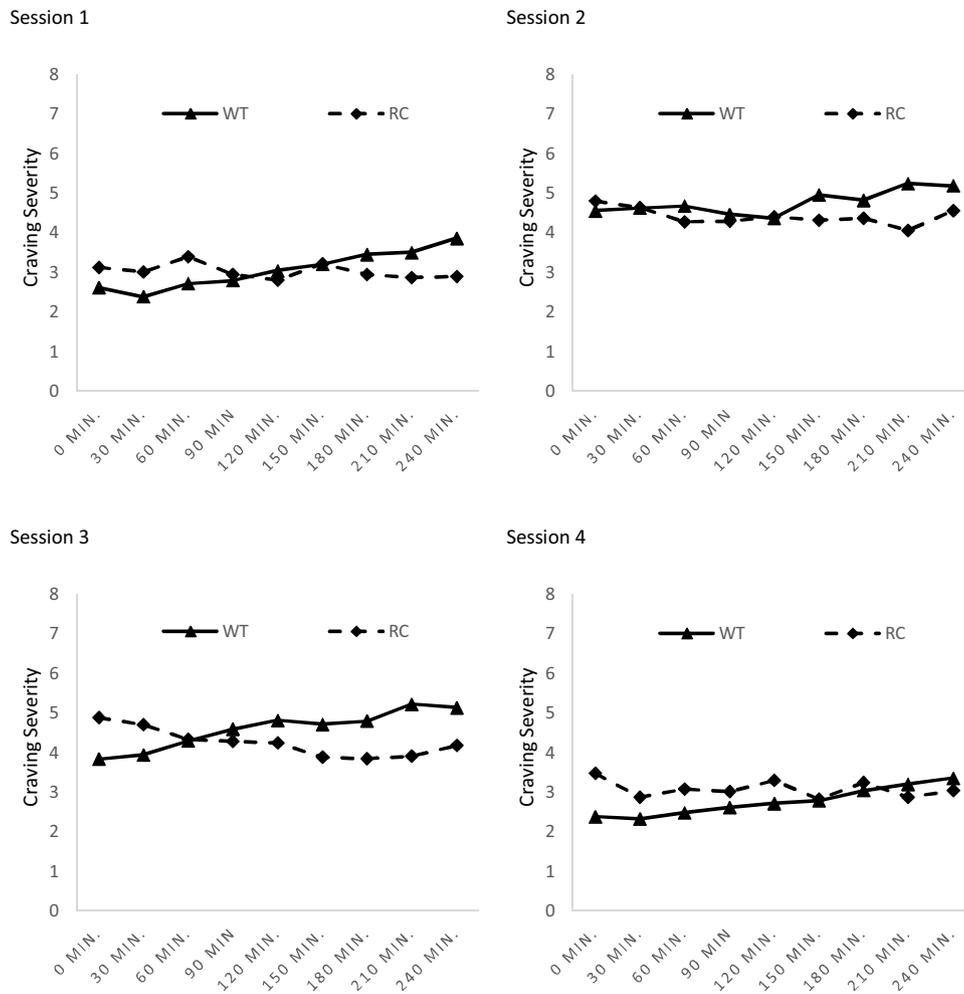
Fig. 2. Participants responses on WSWS Craving Scale for each precessation period treatment session.

experimental condition reported mean withdrawal symptoms across all four treatment sessions that were similar to those reported by participants in the control condition, who smoked ad libitum throughout those sessions. Some slope differences between conditions were found, but these differences were modest. This suggests enhanced withdrawal regulation given the strong, consistent impact of smoking abstinence on early withdrawal (Hendricks et al., 2006, 2013). There was also some evidence that lower levels of early withdrawal symptoms predicted an increased likelihood of abstinence among participants in the experimental condition. This is consistent with the putative mechanism of action thought to underlie the effects of the experimental intervention. Of course, lower withdrawal symptoms might be expected to predict superior clinical outcomes under almost any circumstance. Therefore, while the findings with regard to early withdrawal severity are consistent with the theoretical rationale for this research, they do not provide strong or unambiguous support. Nevertheless, the current findings suggest the WT intervention may have enhanced the ability to regulate negative affect withdrawal symptoms and craving without the use of cigarettes. If this is in fact the case, results align with contemporary theory underscoring the importance of these symptoms in the maintenance of cigarette use (e.g., Baker et al., 2004, 2006; Piper, 2015). Benefits of the experimental intervention relative to contemporary smoking cessation treatment (e.g., Hall et al., 2004) may include the opportunity to develop withdrawal regulation strategies in real-time during an exposure to withdrawal that resembles high-risk relapse contexts, and its advantages over other

smoking cessation treatments incorporating withdrawal exposure components may include the provision of withdrawal regulation training as opposed to withdrawal exposure only (McCarthy et al. 2016) and the provision of a range of individualized withdrawal regulation strategies versus one specific technique (Brown et al., 2013). The current findings also suggest that a renewed focus on the regulation of withdrawal in the treatment of tobacco dependence may indeed be warranted, and additional, complementary approaches to the current active treatment be pursued to achieve this objective. Furthermore, an emphasis on withdrawal regulation in the treatment of other drug dependencies may also lead to the development of novel and more efficacious interventions, and to that end translating the current active treatment may prove useful.

A number of limitations should be considered. First, of those who completed the experimental intervention, 72% provided documentation of self-administered treatment sessions and the completion of these sessions could not be verified. Future research should consider novel methods (e.g., telehealth) to ensure adherence to this component of the treatment protocol. Second, as this was a pilot study, the sample size was small. Pending a larger trial, the experimental intervention should be considered promising only. Third, the WT intervention was a compound intervention comprising both withdrawal exposure and withdrawal regulation training. Had RC participants been exposed to withdrawal, they would have been equated for a key ingredient of the active WT intervention. Still, since there was no condition that abstained from smoking without receiving withdrawal regulation training,

we cannot draw strong inferences regarding the effects of the experimental treatment on early withdrawal. Difficulties in proving the null hypothesis suggest that future research include such controls. Moreover, we are unable to identify which elements of the experimental treatment (i.e., withdrawal exposure, withdrawal regulation training, or the unique combination of the two) were responsible for the observed effects on abstinence. Future unpackaging studies may prove worthwhile. Fourth, the current trial did not seek to determine whether WT might promote the achievement of initial abstinence or prevent early lapse following abstinence, though successful accomplishment of these milestones may underlie the effectiveness of the WT intervention (see Brown et al., 2013 and McCarthy et al. 2016). Future research should seek to address these issues. Fifth, as in previous research on early smoking withdrawal (Hendricks et al., 2006, 2013), participants in the current trial smoked approximately one pack of cigarettes per day. Whether the current findings might generalize to the population of lighter smokers is therefore unknown. Finally, as with any behavioral intervention trial, the therapist was not blinded to condition and outcomes may reflect, at least in part, demand effects.

The present research indicates that an innovative smoking cessation treatment, withdrawal exposure with withdrawal regulation training, may promote smoking abstinence by enhancing withdrawal regulation. Given the public health impact of smoking and underperforming tobacco dependence interventions, this treatment paradigm warrants further study.

Role of funding

Contributors

PSH designed the study, planned and conducted the data analyses, and composed the first draft of the manuscript. SMH, KLC, and TBB helped design the study and contributed to results interpretation and manuscript preparation. LRT served as the study therapist, and assisted with data collection, results interpretation, and manuscript preparation. CBT assisted with data collection, results interpretation, and manuscript preparation. WCB served as the study physician, and assisted with results interpretation and manuscript preparation. SNL and MVM contributed to results interpretation and manuscript preparation. All authors contributed to and have approved the final manuscript.

Conflict of interest

No conflict declared.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.drugalcdep.2016.04.022.

References

American Lung Association, 2016. State of Tobacco Control, Retrieved from: http://www.lung.org/our-initiatives/tobacco/reports-resources/sotc/.

Baker, T.B., Piper, M.E., McCarthy, D.E., Majeskie, M.R., Fiore, M.C., 2004. Addiction motivation reformulated: an affective processing model of negative reinforcement. Psychol. Rev. 111, 33–51.

Baker, T.B., Japuntich, S.J., Hogle, J.M., McCarthy, D.E., Curtin, J.J., 2006. Pharmacologic and behavioral withdrawal from addictive drugs. Curr. Dir. Psychol. Sci. 15, 232–236.

Blankers, M., Smit, E.S., van der Pol, P., de Vries, H., Hoving, C., van Laar, M., 2016. The missing = smoking assumption: a fallacy in internet-based smoking cessation trials? Nicotine Tob. Res. 18, 25–33.

Bolt, D.M., Piper, M.E., Theobald, W.E., Baker, T.B., 2012. Why two smoking cessation agents work better than one: role of craving suppression. J. Consult. Clin. Psychol. 80, 54–65.

Brandon, T.H., Simmons, V.N., Meade, C.D., Quinn, G.P., Khoury, E.L., Sutton, S.K., Lee, J.-H., 2012. Self-help booklets for preventing postpartum smoking relapse: a randomized trial. Am. J. Public Health 102, 2109–2115.

Brandon, T.H., Simmons, V.N., Sutton, S.K., Unrod, M., Harrell, P.T., Meade, C.D., Craig, B.M., Meltzer, L.R., 2016. Extended self-help for smoking cessation: a randomized controlled trial. Am. J. Prev. Med. (in press) https://www.ncbi.nlm.nih.gov/pubmed/26868284.

Brown, R.A., Reed, K.M., Bloom, E.L., Minami, H., Strong, D.R., Lejuez, C.W., Kahler, C.W., Zvolensky, M.J., Gifford, E.V., Hayes, S.C., 2013. Development and preliminary randomized controlled trial of a distress tolerance treatment for smokers with a history of early lapse. Nicotine Tob. Res. 15, 2005–2015.

Centers for Disease Control Prevention, 2015. Current cigarette smoking among adults-United States, 2005–2014. MMWR, 64., pp. 1233–1240.

Chinn, S., 2000. A simple method for converting an odds ratio to effect size for use in meta-analysis. Stat. Med. 19, 3127–3131.

Cohen, J., 1988. Statistical Power Analysis For The Behavioral Sciences, second ed. Erlbaum and Associates, Mahwah, New Jersey.

Cox, L.S., Patten, C.A., Niaura, R.S., Decker, P.A., Rigotti, N., Sachs, D.P., Buist, A.S., Hurt, R.D., 2004. Efficacy of bupropion for relapse prevention in smokers with and without a past history of major depression. J. Gen. Intern. Med. 19, 828–834.

Cropsey, K.L., Clark, C.B., Hendricks, P.S., 2015a. Varenicline for smoking reduction prior to cessation. JAMA 313, 2284–2285.

Cropsey, K.L., Clark, C.B., Zhang, X., Hendricks, P.S., Jardin, B.F., Lahti, A.C., 2015b. Race and medication adherence moderate cessation outcomes in criminal justice smokers. Am. J. Prev. Med. 49, 335–344.

Cropsey, K.L., Jardin, B.F., Burkholder, G.A., Clark, C.B., Raper, J.L., Saag, M.S., 2015c. An algorithm approach to determining smoking cessation treatment for persons living with HIV/AIDS: results of a pilot trial. J. Acquir. Immune Defic. Syndr. 69, 291–298.

Deacon, B.J., Abramowitz, J.S., 2004. Cognitive and behavioral treatments for anxiety disorders: a review of meta-analytic findings. J. Clin. Psychol. 60, 429–441.

Devilly, G.J., Borkovec, T.D., 2000. Psychometric properties of the credibility/expectancy questionnaire. J. Behav. Ther. Exp. Psychiatry 31, 73–86.

Emery, R.L., Levine, M.D., 2015. Optimal carbon monoxide criteria to confirm smoking status among postpartum women. Nicotine Tob. Res. (in press) https://www.ncbi.nlm.nih.gov/pubmed/26386471.

Fagerström, K., 2012. Determinants of tobacco use and renaming the FTND to the Fagerström Test for cigarette dependence. Nicotine Tob. Res. 14, 75–78.

Fiore, M.C., Jaén, C.R., Baker, T.B., 2008. Treating tobacco use and dependence: 2008 update. In: Clinical Practice Guideline. U.S. Department of Health and Human Services, Public Health Service, Rockville, MD.

Hall, S.M., Havassy, B.E., Wasserman, D.A., 1990. Commitment to abstinence and acute stress in relapse to alcohol, opiates, and nicotine. J. Consult. Clin. Psychol. 58, 175–181.

Hall, S.M., Humfleet, G.L., Reus, V.I., Muñoz, R.F., Cullen, J., 2004. Extended nortriptyline and psychological treatment for cigarette smoking. Am. J. Psychiatry 161, 2100–2107.

Hall, S.M., Humfleet, G.L., Muñoz, R.F., Reus, V.I., Robbins, J.A., Prochaska, J.J., 2009. Extended treatment of older cigarette smokers. Addiction 104, 1043–1052.

Hall, S.M., Humfleet, G.L., Muñoz, R.F., Reus, V.I., Prochaska, J.J., Robbins, J.A., 2011. Using extended cognitive behavioral treatment and medication to treat dependent smokers. Am. J. Public Health 101, 2349–2356.

Hays, J.T., Hurt, R.D., Rigotti, N.A., Niaura, R., Gonzales, D., Durcan, M.J., Sachs, D.P.L., Wolter, T.D., Buist, A.S., Johnston, A., White, J.D., 2001. Sustained-release bupropion for pharmacologic relapse prevention after smoking cessation: a randomized, controlled trial. Ann. Intern. Med. 135, 423–433.

Hedeker, D., Mermelstein, R.J., Demirtas, H., 2007. Analysis of binary outcomes with missing data: missing = smoking, last observation carried forward, and a little multiple imputation. Addiction 102, 1564–1573.

Hendricks, P.S., Ditre, J.W., Drobes, D.J., Brandon, T.H., 2006. The early time course of smoking withdrawal. Psychopharmacology (Berl.) 187, 385–396.

Hendricks, P.S., Wood, S.B., Baker, M.R., Delucchi, K.L., Hall, S.M., 2011. The Smoking Abstinence Questionnaire: measurement of smokers' abstinence-related expectancies. Addiction 106, 716–728.

Hendricks, P.S., Delucchi, K.L., Humfleet, G.L., Hall, S.M., 2012. Alcohol and marijuana use in the context of tobacco dependence treatment: impact on outcome and mediation of effect. Nicotine Tob. Res. 14, 942–951.

Hendricks, P.S., Delucchi, K.L., Benowitz, N.L., Hall, S.M., 2013. Clinical significance of early smoking withdrawal effects and their relationships with nicotine metabolism: preliminary results from a pilot study. Nicotine Tob. Res. 16, 615–620.

Hiscock, R., Bauld, L., Amos, A., Fidler, J.A., Munafo, M., 2012. Socioeconomic status and smoking: a review. Ann. N. Y. Acad. Sci. 1248, 107–123.

Hurt, R.D., Krook, J.E., Croghan, I.T., Loprinzi, C.L., Sloan, J.A., Novotny, P.J., Kardinal, C.G., Knost, J.A., Tirona, M.T., Addo, F., Morton, R.F., Michalak, J.C., Schaefer, P.L., Porter, P.A., Stella, P.J., 2003. Nicotine patch therapy based on smoking rate followed by bupropion for prevention of relapse to smoking. J. Clin. Oncol. 21, 914–920.

Japuntich, S.J., Leventhal, A.M., Piper, M.E., Bolt, D.M., Roberts, L.J., Fiore, M.C., Baker, T.B., 2011. Smoker characteristics and smoking-cessation milestones. Am. J. Prev. Med. 40, 286–294.

Juliano, L.M., Brandon, T.H., 1998. Reactivity to instructed smoking availability and environmental cues: evidence with urge and reaction time. Exp. Clin. Psychopharmacol. 6, 45–53.

Killen, J.D., Fortmann, S.P., Murphy, G.M., Hayward, C., Arredondo, C., Cromp, D., Celio, M., Abe, L., Wang, Y., Schatzberg, A.F., 2006. Extended treatment with bupropion SR for cigarette smoking cessation. J. Consult. Clin. Psychol. 74, 286–294.

Killen, J.D., Fortmann, S.P., Schatzberg, A.F., Arredondo, C., Murphy, G., Hayward, C., Celio, M., Cromp, D., Fong, D., Pandurangi, M., 2008. Extended cognitive behavior therapy for cigarette smoking cessation. Addiction 103, 1381–1390.

Maskrey, V., Blyth, A., Brown, T., Barton, G.R., Notley, C., Aveyard, P., Holland, R., Bachmann, M.O., Sutton, S., Leonardi-Bee, J., Brandon, T.H., Song, F., 2015. Self-help educational booklets for the prevention of smoking relapse: a randomised controlled trial. Addiction (in press) https://www.ncbi.nlm.nih.gov/pubmed/26235659.

McCarthy, D.E., Piasecki, T.M., Lawrence, D.L., Jorenby, D.E., Shiffman, S., Baker, T.B., 2008. Psychological mediators of bupropion sustained-release treatment for smoking cessation. Addiction 103, 1521–1533.

McCarthy, D.E., Piasecki, T.M., Jorenby, D.E., Lawrence, D.L., Shiffman, S., Baker, T.B., 2010. A multi-level analysis of non-significant counseling effects in a randomized smoking cessation trial. Addiction 105, 2195–2208.

McCarthy, D.E., Bold, K.W., Minami, H., Yeh, V.M., 2016. A randomized clinical trial of a tailored behavioral smoking cessation preparation program. Behav. Res. Ther. (in press) https://www.ncbi.nlm.nih.gov/pubmed/26827293.

Nathan, P.E., Gorman, J.M., 2007. A Guide To Treatments That Work, third ed. Oxford University Press, Oxford.

O'Connell, K.A., Hosein, V.L., Schwartz, J.E., Leibowitz, R., 2007. How does coping help people resist lapses during smoking cessation? Health Psychol. 26, 77–84.

Piper, M.E., Bolt, D.M., Kim, S., Japuntich, S.J., Smith, S.S., Niederdeppe, J., Cannon, D.S., Baker, T.B., 2008a. Refining the tobacco dependence phenotype using the Wisconsin Inventory of Smoking Dependence Motives. J. Abnorm. Psychol. 117, 747–761.

Piper, M.E., Federman, E.B., McCarthy, D.E., Bolt, D.M., Smith, S.S., Fiore, M.C., Baker, M.B., 2008b. Using mediational models to explore the nature of tobacco motivation and tobacco treatment effects. J. Abnorm. Psychol. 117, 94–105.

Piper, M.E., 2015. Withdrawal: expanding a key addiction construct. Nicotine Tob. Res. 17, 405–415.

Swift, J.K., Greenberg, R.P., 2012. Premature discontinuation in adult psychotherapy: a meta-analysis. J. Consult. Clin. Psychol. 80, 547–559.

Tonstad, S., Tonnesen, P., Hajek, P., Williams, K.E., Billing, C.B., Reeves, K.R., 2006. Effect of maintenance therapy with varenicline on smoking cessation: a randomized controlled trial. JAMA 296, 64–71.

Unrod, M., Simmons, V.N., Sutton, S.K., Cummings, K.M., Celestino, P., Craig, B.M., Lee, J.-H., Meltzer, L.R., Brandon, T.H., 2015. Relapse-prevention booklets as an adjunct to a tobacco quitline: a randomized controlled effectiveness trial Nicotine. Tob. Res. (in press) https://www.ncbi.nlm.nih.gov/pubmed/25847293.

Vidrine, D.J., Arduino, R.C., Gritz, E.R., 2006. Impact of a cell phone intervention on mediating mechanisms of smoking cessation in individuals living with HIV/AIDS. Nicotine Tob. Res. 8, S103–S108.

Welsch, S.K., Simth, S.S., Wetter, D.W., Jorenby, D.E., Fiore, M.C., Baker, T.B., 1999. Development and validation of the wisconsin smoking withdrawal scale. Exp. Clin. Psychopharmacol. 7, 354–361.

Wertz, J.M., Sayette, M.A., 2001. A review of the effects of perceived drug use opportunity on self-reported urge. Exp. Clin. Psychopharmacol. 9, 3–13.

Williams, K.E., Reeves, K.R., Billing, C.B., Pennington, A.M., Gong, J., 2007. A double-blind study evaluating the long-term safety of varenicline for smoking cessation. Curr. Med. Res. Opin. 23, 793–801.

Wipfli, H., Samet, J.M., 2016. One hundred years in the making: the global tobacco epidemic. Annu. Rev. Public Health 37, 19.1–19.18.