FATIGUE and SMOKING RELAPSE

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ABSTRACT

The majority of smokers in the US report a desire to quit and most, who smoke, make a serious quit attempt each year, primarily on their own (i.e., self-guided quit). Smoking prevalence has stabilized as the remaining population becomes increasingly representative of "at-risk smokers" who are unable to quit. The experience of prolonged fatigue may be one underrecognized but highly common problem that may help in understanding smoking maintenance and relapse. Prolonged fatigue is defined as self-reported, persistent fatigue lasting 1 month or longer. Emerging work suggests that prolonged fatigue is common among smokers and that nicotine may be used to combat fatigue. However, there has been no research on prolonged fatigue in relation to actual smoking behavior. Therefore, the purpose of the present study was to better understand whether and how individual differences in severity of fatigue predict smoking behavior during an experimental relapse analogue task. Participants attended two counterbalanced experimental sessions- (1) smoking deprivation (16 hours smoking deprived) and (2) smoking as usual. It was hypothesized that greater fatigue severity would predict greater number of cigarettes smoked, puff velocity, smoking urges, smoking withdrawal, and shorter latency to first cigarette and inter-puff intervals. In addition, it was hypothesized that smoking deprivation would significantly moderate such relations. Participants in the current study included 36 (M_{age}= 49.25; *SD*=8.83; 54.1% male) daily cigarette smokers that reported past month fatigue. Results were partially consistent with prediction. Specifically, results suggest that fatigue severity statistically significantly predicted smoking withdrawal (b=0.16, p<.05). Smoking deprivation condition statistically

significantly predicted number of cigarettes smoked (b=1.35, p<.05) and puff velocity (b=28.24, p<.05). Lastly, the interaction between fatigue severity and smoking deprivation condition statistically significantly predicted number of cigarettes smoked (b=-0.29, p<.05), such that individuals that were smoking deprived reported lower levels of fatigue and smoked more cigarettes. However, due to sample size limitations, more work is needed to better understand the role of severe fatigue in the context of smoking behavior. Future work would benefit from more directly manipulating fatigue among smokers, such as through behavioral tasks or sleep deprivation, to determine the impact of severe fatigue on smoking behavior.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION

Public Health Significance

Cigarette smoking is the leading cause of preventable death in the United States (US), contributing to over 480,000 deaths each year (CDCP, 2018; Cornelius, 2023). In 2017, 14 of every 100 US adults currently smoked cigarettes, reflecting approximately 34.3 million people (CDCP, 2018). Further, approximately 16 million smokers in the US live with smoking-related disease (CDCP, 2018; Health & Services, 2014). Other research has documented high rates (~35%) of current psychological distress among smokers compared to nonsmokers (CDCP, 2018). The majority of smokers (68%) in the US report a desire to quit (Babb, 2017) and most (55.4%) of the 34 million Americans who smoke make a serious quit attempt each year, primarily on their own (i.e., self-guided quit), and to a lesser extent, with assistance from formal treatment (Jamal et al., 2018). Unfortunately, fewer than 7.5% of adult smokers are successful in quitting each year (CDCP, 2022), with most ending in early relapse (approximately 8 days; Pierce et al., 2019). Smoking prevalence has stabilized as the remaining population becomes increasingly representative of “at-risk smokers” who are unable to quit (Hughes & Brandon, 2003; Kulik & Glantz, 2017). Yet, there remains little understanding of the subgroups of "at-risk smokers" and the processes governing relapse among them (Hughes, 1999; Kulik & Glantz, 2017). The experience of prolonged fatigue may be one underrecognized but highly common problem that may help in understanding smoking maintenance and relapse.

Prolonged Fatigue

There is a theoretical and empirical distinction between peripheral and central fatigue (Ream & Richardson, 1996). Peripheral fatigue is defined as a reduction in the maximal muscle force or motor output and is commonly due to overexertion, prolonged or strenuous physical activity (Ream & Richardson, 1996). Central fatigue conversely refers to the general feeling often described as 'tiredness', 'weakness', or 'languor' (Ream & Richardson, 1996). Central fatigue or prolonged fatigue may exist independently or may be due to an underlying psychological or medical condition(s) (Fukuda et al., 1995). Although 'normal' fatigue is a state of general tiredness that is the result of overexertion and can be ameliorated by rest, 'clinical' fatigue is a state characterized by weariness unrelated to previous exertion levels and is usually not ameliorated by rest (Shen et al., 2006). Both peripheral and central fatigue may exist in normal and abnormal states (Fukuda et al., 1995). Central fatigue is defined as self-reported, persistent fatigue lasting 1 month or longer. In the US, almost 25% of the general adult population has had fatigue lasting 2 weeks or longer (Price et al., 1992; Shen et al., 2006); the majority of these persons (59% to 64%) report that their fatigue has no defined medical cause (Price et al., 1992; Shen et al., 2006; Walker et al., 1993). Further, it is important to note that fatigue is theoretically and empirically distinct from related states such as sleepiness (i.e., the inability to stay awake even in situations in which wakefulness is required (Lichstein et al., 1997; Shen et al., 2006)).

Fatigue and Smoking

Research on fatigue states is emerging but presently modest in scope. One study found that smokers compared to non-smokers self-reported higher severity of fatigue symptoms (Corwin et al., 2002). Other research has found that while muscle mass and contractile properties are similar in smokers and non-smokers, smokers experience greater peripheral muscle fatigue (Wüst et al., 2008). These findings are in line with those observed among cancer survivors (Novy et al., 2012). For example, among a large sample of cancer survivors (n = 947), smokers had a significantly higher self-reported fatigue than nonsmokers and continued to report higher fatigue than non-smokers at 6-month follow-up (Peppone et al., 2011). Moreover, participants who quit smoking before cancer treatment reported similar levels of fatigue compared to nonsmokers (Peppone et al., 2011). Other research has found that smoking compared to non-smoking can improve cognitive functioning in sleep-deprived states (Parkin et al., 1998); these data are line with the perspective that nicotine can be used to cope or regulate fatigue states (Hamidovic & de Wit, 2009). More recent work has found that greater fatigue severity is associated with greater perceptions of more barriers for quitting, higher levels of dependence, and more severe symptoms when trying to quit among adults who use combustible and electronic cigarettes (Manning et al., 2019; Zvolensky et al., 2019). Additionally, research focused on adult e-cigarette users has found that greater fatigue severity is associated with more positive and negative expectancies of e-cigarette use (Manning, Garey, Viana, et al., 2020). Although none of the past research has expressly focused on prolonged fatigue and smoking, available research indicates that (1) smokers experience more fatigue than non-smokers; (2) smoking may be used to offset fatigue symptoms; (3) fatigue is related to several problematic features of use (e.g., dependence, perceived barriers for quitting); and (4) quitting may reduce fatigue.

Integrative Model

No formal model to explain the relation between severe fatigue and prolonged smoking exists. Although several different mechanisms may be involved, one working perspective is that smokers with prolonged fatigue are more behaviorally, cognitively, and affectively intolerant to distressing internal cues. Research suggests that smokers experience greater rates of fatigue compared to non-smokers, and report using cigarettes as a method to combat feeling fatigued (Hamidovic & de Wit, 2009). Thus, during periods of smoking deprivation, smokers with prolonged fatigue may interpret the onset of fatigue as intolerable or catastrophic, exacerbating the experience of acute withdrawal symptoms and craving. This perspective is in line with fatigue research that has found prolonged fatigue is related to catastrophizing fatigue and bodily symptoms (Romano et al., 2016). Consequently, smokers with severe fatigue may rely on smoking to cope with aversive stimuli, and thus, increase smoking behavior to cope with withdrawal symptoms. The acute effects of nicotine can reduce the severity of fatigue symptoms (Warburton, 1985), thereby reinforcing smoking to escape or avoid fatigue symptoms. This negative reinforcement model of addiction has been supported in the smoking literature (Baker et al., 2004), however, it has yet to be applied to the smokers with severe fatigue.

Clinical Significance of (Early) Lapse for Relapse

The majority of smokers will lapse within the first week or two after initial cessation and subsequently relapse (Herd & Borland, 2009; Hughes et al., 2004; Hughes et al., 2003). These results highlight the importance of the early stages of cessation as a particularly critical period (Shiffman et al., 1997), even when psychological and nicotine replacement therapies are used (Cook et al., 1995). Further, smokers with emotional or physical vulnerabilities are significantly more apt to lapse within the first 24-48 hours of a quit attempt (Farris et al., 2016). Thus, although there is convergent evidence indicating that early lapse to smoking is a common problem that is often predictive of subsequent (full-blown) relapse, current models of relapse and corresponding research have devoted insufficient attention to the phenomenon of early lapse.

Withdrawal/Craving

One possible reason that smokers with prolonged fatigue may be at higher risk for relapse is that their heightened sensitivity to internal perturbation may make them particularly sensitive to the bodily sensations associated with withdrawal or craving. Indeed, tobacco withdrawal leads to a variety of undesirable affective, cognitive, and somatic symptoms (Hughes, 2007) and these may provoke compulsive motivation to return to smoking in order to modulate their symptoms (Baker et al., 2004). Withdrawal symptoms might be particularly salient to smokers with prolonged fatigue, as they may be more apt to perceive these internal sensations as uncontrollable because they have diminished self-regulation resources (due to fatigue) to regulate withdrawal states. In fact, research has found that fatigue states are related to a greater tendency to catastrophize internal sensations (Kauffman et al., 2020; Manning, Kauffman, et al., 2020; Petrie et al., 1995; Rimes & Wingrove, 2013; Sohl & Friedberg, 2008). This work is consistent with a large corpus of work that has found moderate to large sized effects for catastrophizing and fatigue severity across a range of clinical groups (Andrykowski et al., 2010; Jacobsen et al., 1999; Jacobsen et al., 2004; Kangas & Montgomery, 2011; Skerrett & Moss-Morris, 2006). Yet, it is presently unclear if smokers with prolonged fatigue demonstrate more withdrawal and craving during abstinence.

Deprivation as a Moderator of the Fatigue-Smoking Association

One way to examine the role of fatigue severity in early lapse is to examine the predictive power of fatigue symptom severity under two states – during a period of nicotine deprivation vs. smoking as usual. Although individual differences in fatigue are stable (Joyce et al., 1997), fatigue symptom severity is sensitive to state (and pharmacological) manipulations (Brower et al., 1988; Grillon et al., 2015; Lukkahatai & Saligan, 2013; Tran et al., 2009). McKee and associates have established a protocol for assessing lapse behavior that uses empirically-derived monetary reward levels so that smokers, on average, can delay smoking for the median of the delay window (i.e., ~25 min of the 50 min window), and provides measures of two critical features of lapse behavior: (a) the ability to resist the first cigarette and (b) subsequent smoking if a participant decides to “give in” and starts to smoke (Roche et al., 2014). The McKee procedure has been shown to reflect non-laboratory predictors of smoking behavior

(Roche et al., 2014), and to be sensitive to the effects of stress (McKee et al., 2011) and alcohol (Kahler et al., 2014; McKee et al., 2006) on attenuating the latency and increasing the amount of smoking during the protocol. As such, the protocol provides an ideal format for efficiently assessing the relationship between putative risk factors and lapse behaviors. Importantly, fatigue severity has been shown to be particularly heightened in experimentally induced aversive/stressful contexts (Grillon et al., 2011; Robinson et al., 2012), leading to the prediction (i.e., Aim 2) that the magnitude of the fatigue severity and smoking behavior association will be greater in the deprivation condition.

The Importance of Smoking Topography

The current proposal seeks to innovate work on the McKee paradigm by integrating it with an assessment of smoking topography (how a person smokes); smoking topography measures puffing volume CO (plus a complex combination of particles and vapors). This advancement is clinically important, as smokers can control the timing, and to a large extent, the amount/dose of nicotine they consume (Perkins et al., 2011) by altering the depth, speed, and/or frequency of each cigarette puff. For example, increased levels of nicotine can be absorbed from taking more frequent and deeper/longer puffs (i.e., shorter inter-puff intervals and greater puff volume/duration). Empirical data convincingly indicate that smokers will change (compensate) how they smoke to maintain stable levels of nicotine (Epstein et al., 1981). Therefore, we can gain empirical insight into the affective-regulatory aspects of smoking (e.g., delay to smoking) and the actual nature of smoking itself (e.g., puff, inhalation) by measuring smoking topography in the context of a lapse paradigm.

Present Study

The purpose of the present study was to better understand whether and how individual differences in fatigue severity predict smoking behavior during an experimental relapse analogue task. The association between fatigue severity and smoking behavior during the task, however, may depend on whether individuals are in a period of abstinence as the experience of withdrawal during abstinence may be particularly aversive for those with higher fatigue symptoms, leading to greater urges and lapse behavior for these individuals. That is, even though fatigue severity has been shown to have trait-like qualities (Hoofs et al., 2017), it also has been shown to be sensitive to state effects (Lukkahatai & Saligan, 2013). Consequently, the predictive power of fatigue severity may be particularly (or perhaps only) evident while the individual is experiencing the stress induced by substance deprivation. Therefore, participants attended two counterbalanced experimental sessions– (1) smoking deprivation (16 hours of smoking abstinence) and (2) smoking as usual – during which fatigue severity was assessed.

First, it was hypothesized that greater fatigue severity would significantly relate to multi-modal facets of smoking behavior (i.e., shorter latency to first cigarette, greater number of cigarettes smoked, greater puff velocity, and shorter inter-puff intervals) and greater subjective withdrawal and urge/craving, among adult smokers.

In addition, it was hypothesized that smoking deprivation condition would significantly moderate the relation between current fatigue severity and smoking behavior (i.e., latency to first cigarette, number of cigarettes, greater puff velocity, and shorter inter-puff intervals) and subjective urge and withdrawal, such that the hypothesized relations would evince greater significance during smoking deprivation. Such results were expected over and above the effects of CO level and sleepiness.

METHOD

Participants[1]

The current study included 36 adults (M_{age}= 49.25; SD=8.83; 54.1% male) who reported daily combustible cigarette use. All participants were recruited through newspaper and community flyer advertisements targeting individuals interested in participating in research examining their current cigarette use and symptoms of fatigue in Houston, Texas.

Participants were included in the current study if they reported (a) prolonged fatigue (defined as self-reported, persistent fatigue lasting 1 month or longer (Bültmann et al., 2000; Fukuda et al., 1995)); (b) $\geq$ 20 years old; (c) regular (daily) cigarette smoking for $\geq$ 1years; (d) currently smoking $\geq$ 6 cig/day; and (e) English fluency. Participants were excluded if (a) they met criteria for lifetime psychotic symptoms or untreated bipolar disorder, (b) breath carbon monoxide (CO) levels <

[1] Please note that some of the original eligibility criteria changed, in order to improve recruitment efforts. It was originally proposed that participants must smoke 10 or more cigarettes per day, endorse regular daily smoking for 2 or more years, and must not have met criteria for a substance use disorder, based on the MINI-7. No changes were made to the intake ppm levels, or other criteria outlined above. However, despite these changes, participants, on average, met the original eligibility criteria. One participant was included in the sample that endorsed past year substance use disorder, but they denied use in the past 5 months. It is therefore not likely that changes to the eligibility criteria impacted study results.

10ppm at intake; (c) use of other tobacco products (including e-cigarettes) to prevent the confounding of alternative tobacco use on the outcomes; and (d) pregnant.

For the current project, 63 individuals completed baseline appointments (See Figure 1.1). Thirty-nine participants met inclusion criteria during the baseline appointment and were scheduled for an experimental session. Of the 39 participants that were scheduled for the first experimental session, 35 completed the abstinent appointment and 36 completed the non-abstinent appointment.

Measures

Descriptive Measures and Eligibility

Demographics Questionnaire. Demographic-Treatment History Questionnaire was used to assess participant sex, age, race/ethnicity, education level, income, and marital status.

Medical History Form (MHF; Scheftner & Endicott, 1984). The MHF contains a checklist of 96 health conditions or symptoms. The MHF was used to collect information on physical health and the presence of any chronic medical conditions to determine safety of participation according to the eligibility criteria.

Mini International Neuropsychiatric Interview-7 (MINI-7; Lecrubier et al., 1997). The MINI-7 is a structured clinical interview used to assess symptoms of mental health disorders such as anxiety, depression, and substance use, defined in the DSM-5. The MINI-7 was used to assess for exclusionary diagnostic criteria including lifetime psychotic disorder and untreated bipolar disorder.

Centers for Disease Control and Preventions Chronic Fatigue Symptom Inventory (CDC CFS; Wagner et al., 2005). The CDC CFS is a validated interview that asses the frequency and severity of 19 fatigue symptoms over the past month. Of the 19 fatigue symptoms, 8 of them are considered typical CFS symptoms and the remaining 11 symptoms are considered non-CFS symptoms. All 19 symptoms are included in the total score. Participants rate the frequency of these symptoms on a 4-point Likert type scale ranging from 1 (*a little of the time*) to 4 (*all of the time*), as well as the severity of the symptoms on a 3-point Likert type scale ranging from 1 (mild) to 3 (severe). Severity scores were transformed into equidistant scores (0 = symptom not reported 1 =mild, 2.5 = moderate, 4 = severe), and then multiplied with severity scores, resulting in a range of 0-16 for each symptom. All 19 symptom scores were summed for a total score (range=0-304). The symptom inventory total score demonstrated excellent internal consistency (α = 0.91).

Fagerström Test for Cigarette Dependence (FTCD; Fagerström, 2012; Heatherton et al., 1991). The FTCD is a well-established 6-item scale designed to assess gradations in tobacco dependence. Total scores range from 0-16, with higher scores indicating greater cigarette dependence. The measure exhibits a high degree of test-retest reliability (Pomerleau et al., 1994), and positive relations with key smoking variables (Heatherton et al., 1991; Payne et al., 1994). The FTCD was used to describe smoking characteristics in the current sample. The FTCD demonstrated fair internal consistency (α = 0.60), consistent with past work (Berlin et al., 2015; Korte et al., 2013).

Smoking History Questionnaire (SHQ; Brown et al., 2002). The SHQ is a 30 item self-report questionnaire used to assess smoking history and patterns of smoking (e.g. smoking rate, age of onset, number of years smoking). It has been successfully used in previous studies as a measure of smoking history (Zvolensky et al., 2004). This measure was used to describe smoking characteristics in the current sample.

Timeline Follow-Back (TLFB; Sobell & Sobell, 1992). The TLFB is a calendar-based assessment of substance use, in which data are collected using clinician guided retrospective recall. Participants are encouraged to use notable events (e.g., birthdays, holidays, special events) and patterns of use (e.g., weekends versus week days, locations, time of day) to complete the calendar. These data were used, in combination with other assessment, to determine presence of regular smoking patterns in the past month. The assessment has demonstrated good reliability and validity with biochemical indices of smoking (Sobell and Sobell, 1992).

Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989). The PSQI is a 19-item self-report measure assessing sleep quality and sleep disturbances over the past month. The PSQI generates 7 component scores measuring subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. The PSQI demonstrated good psychometric properties ($\alpha = 0.88$), consistent with past work (Buysse et al., 1989).

Covariates

Carbon Monoxide (CO) Analysis. See Table 1.1 for a list of measures included in the analyses. A Smokerlyzer Breath Co carbon monoxide monitor was used to measure the amount of carbon monoxide (in parts per million [ppm]) in an expired breath sample, which is an indirect, noninvasive measure of blood carboxyhaemoglobin. Levels of CO typically range from 0-10ppm (non-smoker), 11-

20 (light smoker), 21-100 (heavy smoker). To provide a breath sample, the hand-held device prompts the participant to complete a 15 second breath-hold before exhaling completely into a single-use disposable cardboard mouthpiece. For the present study, a CO sample of ≥ 10 ppm was required for study inclusion. In addition, CO level at each experimental session was included as a covariate.

Epworth Sleepiness Scale (ESS; Johns, 1991). The ESS is an 8-item self-report measure assessing an individual's likelihood of falling asleep in certain situations, such as watching TV. Items are rated on a 4-point Likert-type scale ranging from 0 (*would never doze*) to 3 (*high chance of dozing*). The ESS has demonstrated good psychometric properties in past work. The ESS score from each experimental session was included as a covariate in the current study and demonstrated good to excellent internal consistency across the three appointments (α = .83-.90).

Dependent and Independent Variables

Fatigue Severity Scale (FSS; Krupp et al., 1989). The FSS is a 9-item self-report measure of fatigue severity. Individuals are asked to indicate on a 7-point Likert-type scale ranging from 1 (*strongly disagree*) to 7 (*strongly agree*) which best fits each statement regarding fatigue within the *last week*. The FSS has demonstrated good psychometric properties in previous work (see Whitehead, 2009). In the current study, the FSS demonstrated excellent internal consistency (α = .93-.95). For the current study, the FSS from both experimental sessions was included as a predictor.

Minnesota Nicotine Withdrawal Scale (MNWS; Hughes & Hatsukami, 1986). The MNWS is an 8-item measure that assesses symptoms of nicotine withdrawal during the last period of smoking deprivation. Items are rated on a 5-point Likert type scale ranging from 0 (*not present at all*) to 4 (*severe*). The MNWS has demonstrated good internal consistency in past work (Hughes & Hatsukami, 1986). The MNWS score from each experimental session was included as an outcome across all analyses. In the current sample, it demonstrated excellent internal consistency across all three appointments (α = .87-.93).

Questionnaire of Smoking Urges-Brief (QSU; Cox et al., 2001; Tiffany & Drobes, 1991). The QSU-brief is a 10-item self-report measure that assesses symptoms of nicotine craving over the past 24 hours. Items are rated on a 1 (*strongly disagree*) to 7 (*strongly agree*) Likert-type scale. The QSU-brief score from each experimental session was included as a criterion variable across all analyses. The QSU-brief demonstrated excellent internal consistency (α = .96-.98), consistent with past work (Cox et al., 2001).

Clinical Research Support System (CReSS; Plowshare Technologies, Borgwaldt KC, Inc., Virginia). The portable CReSS pocket has a sterilized flow meter mouthpiece that is connected to a pressure transducer, which converts pressure into a digital signal that is sampled at 1,000Hz. CReSS computer software transforms the signal to a flow rate (mL/s), from which puff topography data are computed. The reliability and acceptability of use of the portable CReSS device is well documented (Blank et al., 2009; Perkins et al., 2011) and is recommended over direct observation (Blank et al., 2009). Puff topography data included: latency to first cigarette puff (seconds), puff volume (volume of CO in mL of smoke taken in during each puff), and inter-puff interval (amount of time between puffs in seconds). Puff level data were averaged to compute mean topography variables for each participant, by smoking deprivation condition.

Procedure

All study procedures will follow guidelines form the institutional review board of the University of Houston. Participants were recruited from the University of Houston campus and the greater Houston area through advertisements and physician referrals. Recruitment techniques included electronic media (university listservs, Facebook, Craigslist, etc.) and flyers in community-based organizations (UH campus, community health centers). The current study involved four stages: (1) pre-screener over the phone (eligibility); (2) baseline appointment consisting of additional eligibility screening; (3) two counterbalanced experimental sessions.

During the initial pre-screening over the phone, participants were asked about current health conditions, smoking history, use of other tobacco products, and fatigue symptoms. If determined to be eligible, participants were given a description of the study procedures and compensation schedule, and if they agreed to participate, were scheduled for a baseline appointment that was conducted in person.

During the baseline appointment, participants met with a trained researcher who obtained informed consent. The participants were then assessed for current smoking status using a CO measurement and the TLFB, as well as current mental health symptoms, using the MINI-7. Lastly, participants completed an online survey.

Participants that were deemed to be eligible following the baseline appointment were then scheduled for two nearly identical experimental visits (one abstinent and one non-abstinent; order counterbalanced). For abstinent visits, participants were instructed not to smoke after 6pm the day before the session. For non-abstinent visits, they were be instructed to smoke normally. A CO level of 10 ppm for non-abstinent and below 10 ppm for the abstinent condition were used (as per prior studies; Pang & Leventhal, 2013) to document procedural compliance. Participants' with CO > 9ppm at their abstinent session were rescheduled. After the CO assessment, participants completed assessment measures.

After the survey administration on the non-abstinent visit, participants smoked a cigarette of their preferred brand in the laboratory to standardize recency of smoking. Next, participants completed the McKee Experimental Relapse Analogue Task (RAT; Kahler et al., 2014; McKee et al., 2006)**.** During this task, participants received a tray containing eight cigarettes (their usual brand) and a lighter. At the outset of the delay period, participants were instructed they could begin smoking at any point during the next 50 minutes, but they would earn $0.20 for each 5 minutes they delayed smoking, for a total of $2 maximum for delaying smoking. Thus, the delay period could span 0-50 minutes. Once participants indicated that they wished to initiate smoking or following 50 minutes (whichever occurred first), the participants were informed that they could smoke as much or little as they wanted during the next 60 minutes. Participants were told they had a $1.60 credit, and for each cigarette lit, it would cost $0.20. Participants were compensated $50 for completing the baseline appointment, $50 for completing the first experimental session and $100 for completing the second experimental session.

Data Analytic Plan

Analyses were conducted using SPSS version 28. First, data were screened for entry errors or inconsistencies. Frequency distributions, indices of skewness and kurtosis, and tests of normality (Kolmogorov-Smirnov test statistic and Shapiro-Wilk test statistic) were examined to determine the underlying distribution of variables by condition.

Next, bi-variate correlations and descriptive statistics among the variables were examined by condition. Paired samples t-tests were conducted to examine mean difference scores between the abstinent and non-abstinent condition for each predictor and outcome variable. Cohens d was used as an indicator of effect size, with values of .2, .5, and .8 indicating small, medium, and large effects, respectively (Cohen, 1988), with 95% confidence intervals.

Then, two-level random intercept multi-level models (visit type within-person), using linear modeling, were used to examine the main effects of fatigue severity and smoking deprivation manipulation, and the interaction effects of fatigue severity and smoking deprivation on latency to first cigarette, number of cigarettes smoked, average puff velocity (rate of flow during puff; mL/s), average inter-puff interval (amount of time between puffs; seconds), smoking urges, and smoking withdrawal. Data were nested within individual. The estimation of unknown parameters in the models was based on restricted maximum-likelihood estimation. To examine the main effects of fatigue severity and smoking deprivation manipulation for each of the smoking outcomes, models were built hierarchically. First, empty models were constructed to determine the intra-class correlation (ICC; Muthen & Satorra, 1995). Second, fatigue severity was included as a fixed predictor of smoking outcomes. Then, fatigue severity and smoking deprivation manipulation were included as fixed predictors. Fourth, the interaction between fatigue and smoking deprivation condition was entered. Lastly, the interaction model that included covariates was examined. Covariates included experimental session CO level and sleepiness score. For all models, effect sizes for the fixed effects were calculated via a partial correlation from the *t*-statistic for each parameter (Altman, 1990). The following equation was used: $r_k = \frac{t_k}{\sqrt{t_k^2 + \mathrm{df}}}$ where *k* represents the parameter. Effect sizes were interpreted as .10=small, .30=medium, and .50=large (Cohen, 1988). Given smoking topography variables have a meaningful zero point, variables were included in their raw, un-centered form. The unstructured covariance matrix was used for covariance parameter estimates of the random effects to allow for the estimation of the variance and covariance to be greater than zero (Raudenbush & Bryk, 2002).

RESULTS

Correlations and Descriptive Statistics

Bivariate correlations and descriptive statistics for the non-abstinent and abstinent condition are presented in Table 2.1 and 2.2, respectively. Of note, in both the non-abstinent and abstinent session, smoking urges and withdrawal were statistically significantly, positively correlated (r=.71, p<.01 and r=.52, p<.001 respectively). In addition, fatigue severity was statistically significantly positively correlated with CO ppm during the non-abstinent session (r=.39, p<.05), and smoking withdrawal during the abstinent session (r=.37, p<.05).

Demographic Characteristics. The present sample consisted predominately of Black/African American (56.8%) individuals, followed by 35.1% White/Caucasian, and 5.4% other. In addition, 5.4% identified as Hispanic or Latinx. About 46% of the sample indicated they completed some college, 18.9% of the participants received a high school diploma or equivalent, 16.2% were college graduates, 11% of the sample indicated they did not graduate high school, and 5.4% earned a graduate degree. Most participants indicated they were single (62.2%), followed by 16.2% of participants indicating they were divorced, 8.1% currently living with a partner, 5.4% separated, and 5.4% married. About 59% of the sample reported making less than $50,000 per year.

Mental Health Characteristics. Based upon the Mini International Neuropsychiatric Interview version 7 (MINI-7), 22.9% of the sample met diagnostic criteria for Major Depressive Disorder, 14.3% endorsed low risk suicidal ideation, 11.4% met criteria for Post-Traumatic Stress Disorder, 5.7% met criteria for Panic Disorder, 5.7% met criteria for Agoraphobia, 5.7% met criteria for Generalized Anxiety Disorder, 5.7% met criteria for Social Anxiety Disorder, 2.9% of the met criteria for a lifetime Substance Use Disorder, but denied past month use, 2.9% met criteria for Bipolar I Disorder (past manic symptoms), and 2.9% met criteria for Obsessive Compulsive Disorder. Approximately 25% of the sample met criteria for one mental health disorder, 8.3% met criteria for two mental health disorders, and 2.8% met criteria for three mental health disorders.

Smoking Characteristics. In terms of smoking characteristics, participants were, on average, 15.61 (SD = 3.54) years old when they first started smoking and were 19.94 (*SD* = 6.63) years old when they began daily cigarette smoking. Respondents endorsed regular daily smoking for an average of 27.44 years (*SD* = 8.56) years and reported smoking 16.25 (*SD* = 9.01) cigarettes per day, on average. Participants endorsed, on average, 3.36 (*SD*=4.91) serious attempts to quit smoking in their lifetime. The average level of cigarette dependence in the current sample was 5.83 (*SD*=1.99), indicating moderate dependence (Fagerstrom et al., 1990). The average CO level at the baseline appointment in the current sample was 17.69 (*SD*=8.83).

Fatigue, Sleep, and Health Characteristics. At the baseline appointment, the average level of fatigue severity observed in the current sample was 4.68 (*SD*=1.70). Past work indicates that a score of 5 or above indicates clinically significant fatigue (Bakshi et al., 1999). The average global sleep score observed in the current sample was 8.90 (*SD*=4.61). On average, participants reported sleeping 6.31 (*SD*=2.24) hours prior to the non-abstinent experimental appointment, and 7.15 (*SD*=1.99) hours prior to the abstinent experimental appointment. The most common symptoms endorsed on the Centers for Disease Control Chronic Fatigue Syndrome symptom inventory were fatigue (*M*=5.78, *SD*=4.76), sleep problems (*M*=5.14, *SD*=5.18), unrefreshing sleep (*M*=4.40, *SD*=4.48), muscle aches (*M*=4.36, *SD*=4.05), and joint pain (*M*=4.18, *SD*=4.69). The average body mass index (BMI) observed in the current sample was 29.76 (*SD*=9.12), which is classified as 'overweight'.

Paired Samples T-Test

Fatigue Severity. A paired samples t-test was conducted to determine the effect of smoking deprivation condition on fatigue severity (See Table 3.1). The results indicate a non-statistically significant difference between fatigue severity during smoking deprivation (M=3.79; SD=1.48) and smoking as usual conditions (M=3.81; SD=1.56); [$t(26) = -0.06$, $p = .952$, d=-.01].

Latency to Cigarette. A paired samples t-test was conducted to determine the effect of smoking deprivation condition on latency to first cigarette. The results indicate a non-statistically significant difference between latency to smoke during smoking deprivation (M=599.29; SD=1196.22) and smoking as usual conditions (M=970.81; SD=1323.45); [$t(30) = -1.16$, $p = .255$]. However, effect size estimates indicate a small effect (d=-.21), such that latency to the first cigarette was shorter in the abstinent condition compared to the non-abstinent condition.

Number of Cigarettes. The results indicate a non-statistically significant difference between number of cigarettes smoked during smoking deprivation (M=2.40; SD=1.06) and smoking as usual conditions (M=2.26; SD=1.48); [$t(34) = 0.76$, $p = .454$, d=.13].

Puff Velocity. The results for puff velocity indicate a non-statistically significant difference between smoking deprivation (M=82.38; SD=63.40) and smoking as usual conditions (M=60.08; SD=39.35); [$t(31) = 1.98$, $p = .057$]. However, effect size estimates indicate a medium effect, such that puff velocity is greater in the abstinent condition, compared with the non-abstinent condition.

Inter-Puff Interval. The results for inter-puff interval indicate a non-statistically significant difference between smoking deprivation (*M*=28.75; *SD*=35.45) and smoking as usual conditions (*M*=24.10; *SD*=18.78); [t(34) = 0.76, p = .473, d=.12].

Smoking Urges. The results for smoking urges indicate a statistically significant difference between smoking deprivation (*M*=38.74; *SD*=20.96) and smoking as usual conditions (*M*=28.77; *SD*=18.11); [t(30) = 2.52, p <.05]. Examination of effect size estimates indicates a medium sized effect (Cohens d=.45, 95% CI [0.08, 0.82]).

Smoking Withdrawal. The results for smoking withdrawal indicate a non-statistically significant difference between smoking deprivation (*M*=1.36; *SD*=0.83) and smoking as usual conditions (*M*=1.25; *SD*=1.06); [t(27) = 0.68, p = .503, d=.13].

Multilevel Models

Latency to Cigarette. Inspection of data distribution, skewness (.83), kurtosis (-1.30), and the Kolmogorov-Smirnov (.33, $p < .001$) and Shapiro-Wilk (.66, $p < .001$) test statistics indicated a non-normal distribution for latency to first cigarette in the smoking as usual condition, as well as for the smoking deprivation condition (skewness (1.63), kurtosis (.70), the Kolmogorov-Smirnov (.44, $p < .001$) and Shapiro-Wilk (.51, $p < .001$)). The data distribution indicated clustering at the minimum value (0s) and maximum value (3000s). The empty model failed to converge, indicating a redundant covariance parameter. As such, the ICC could not be calculated due to an intercept estimate of 0. Multi-level modeling is typically robust to violations of normality (Heck et al., 2013); however, the clustering of the data indicates that a linear model may not be the best fit. Based on past work dealing with a non-normally distributed latency to smoke variable (Zvolensky et al., 2014), a change score was computed (abstinent time to smoke-non-abstinent time to smoke; range -3000 to 3000). In addition, similar to past work, a change score for fatigue severity was computed (abstinent fatigue-non-abstinent fatigue; range -7 to 7), and the correlation between the change scores was examined as an indicator of abstinence induced changes in the interaction between fatigue severity and time to smoke (Wong et al., 2014). The mean change score for latency to smoke was -334.66 (SD=1676.41), indicating, on average, an increase in time to smoke in the non-abstinent condition. The mean change score for fatigue severity was -0.06 (SD=2.71), indicating, on average, an increase in fatigue severity in the non-abstinent condition. The correlation between the change scores was not statistically significant (r=-.19, p=.298; 95% CI [-0.52, 0.16]). These results indicate that there is not a statistically significant abstinence induced effect in the relation between fatigue severity and time to smoke.

Number of Cigarettes. Inspection of data distribution, skewness (1.02), kurtosis (1.85), and the Kolmogorov-Smirnov (.26, $p < .001$) and Shapiro-Wilk (.90, $p < .01$) test statistics indicated a non-normal distribution for number of cigarettes in the smoking as usual condition, as well as in the smoking deprivation condition (skewness (.20), kurtosis (.18), the Kolmogorov-Smirnov (.22, $p < .001$) and Shapiro-Wilk (.93, $p < .05$)).

Results from the empty model suggest that 63% of the variance in number of cigarettes is at the between-subjects level. For a full breakdown of parameter estimates for each step of the model, see Table 4.1. In model 2, fatigue severity was not a statistically significant predictor of number of cigarettes (b=0.04, se=0.10, p= .663, r=.06). In model 3, the addition of smoking deprivation condition was not statistically significant (b=0.22, se=0.19, p= .256, r=.22). While the fully conditional model, including the fixed effect of fatigue severity, deprivation condition, and the interaction term, suggest that within each individual, fatigue severity was not a statistically significant predictor of number of cigarettes (b=0.18, se=0.11, p= .108, r=.23). However, smoking deprivation condition (b=1.35, se=0.52, p<.050, r=.42) was a significant predictor of number of cigarettes, indicating that those in the abstinent condition smoke about 1.35 cigarettes more than those in the non-abstinent condition. Further, the interaction term was a statistically significant predictor of number of cigarettes (b=-0.29, se=0.13, p<.050, r=-.38), indicating that those in the abstinent condition with greater fatigue severity smoked about 0.29 cigarettes fewer than those in the non-abstinent condition with greater fatigue severity. Lastly, the model with covariates exhibited statistically significant results for smoking deprivation condition and the interaction term.

Puff Velocity. Inspection of data distribution, skewness (1.80), kurtosis (6.36), the Kolmogorov-Smirnov (.18, $p < .01$) and Shapiro-Wilk (.85, $p < .001$) test statistics indicated a non-normal distribution for average puff velocity, in the smoking as usual condition, as well as in the abstinent condition (skewness (2.18), kurtosis (5.90), Kolmogorov-Smirnov (.23, $p < .001$) and Shapiro-Wilk (.77, $p < .001$)). Although the empty model converged, the conditional model with the fixed effects of fatigue severity did not converge, indicating a redundant covariance parameter. As such, the output generated an intercept estimate of 0. However, past work indicates that examination of average puff velocity of the first cigarette smoked is a robust indicator of smoking lapse behavior smoked (Kassel et al., 2007; Perkins et al., 2010). Inspection of this data distribution, skewness (2.48), kurtosis (10.89), Kolmogorov-Smirnov (.18, $p < .01$) and Shapiro-Wilk (.78, $p < .001$) test statistics also indicated a non-normal distribution for average puff velocity of first cigarette in the smoking as usual condition, as well as in the smoking deprivation condition (skewness (2.33), kurtosis (5.31), Kolmogorov-Smirnov (.24, $p < .001$) and Shapiro-Wilk (.70, $p < .001$)).

Results from the empty model suggest that 23% of the variance in puff velocity is at the between-subjects level. For a full breakdown of parameter estimates for each step of the model, see Table 4.2. In model 2, fatigue severity was not a statistically significant predictor of puff velocity (*b*=-5.64, *se*=4.76, *p*= .242), however, examination of effect size estimates indicates a small effect (*r*=-.17) such that a 1 unit increase in fatigue severity results in a 5.79 mL/s decrease in puff velocity. The addition of the smoking deprivation condition in model 3 was statistically significant (*b*=28.24, *se*=12.43, *p*<.05, *r*=.38), indicating that those in the abstinent condition evinced a greater puff velocity. The fully conditional model, including the fixed effect of fatigue severity, deprivation condition, and the interaction term, suggests that within each individual, fatigue severity was not a statistically significant predictor of average puff velocity (*b*=-5.89, *se*=6.14, *p*=.342, *r*=-.13). In addition, smoking deprivation condition (*b*=27.27, *se*=34.16, *p*=.430, *r*=.13) nor the interaction term (*b*=0.25, *se*=8.28, *p*=.976, *r*=.001) were statistically significant predictors of puff velocity. Lastly, the model with covariates did not exhibit statistically significant results.

Inter-Puff Interval. Inspection of data distribution, skewness (1.30), kurtosis (2.79), Kolmogorov-Smirnov (.15, $p < .05$) and Shapiro-Wilk (.91, $p < .01$) test statistics indicated a non-normal distribution for inter-puff interval in the smoking as usual condition, as well as in the smoking deprivation condition (skewness (4.65), kurtosis (25.06), Kolmogorov-Smirnov (.31, $p < .001$) and Shapiro-Wilk (.50, $p < .001$)).

Results from the empty model suggest that 11% of the variance in inter-puff interval is at the between-subjects level. For a full breakdown of parameter estimates for each step of the model, see Table 4.3. In model 2, fatigue severity was not a statistically significant predictor of inter-puff interval (b=1.98, se=2.60, p= .449, r=.11). The addition of the smoking deprivation condition in model 3 was not statistically significant (b=6.32, se=7.04, p=.377, r=.17). The fully conditional model, including the fixed effect of fatigue severity, deprivation condition, and the interaction term, suggest that within each individual, fatigue severity was not a statistically significant predictor of inter-puff interval (b=0.79, se=14.87, p= .826, r=.03). In addition, smoking deprivation condition (b=-1.35, se=4.83, p=.947, r=-.001) nor the interaction term (b=1.97, se=4.83, p=.686, r=.07) were statistically significant predictors of inter-puff interval. Lastly, the model with covariates did not exhibit statistically significant results.

Smoking Urges. Inspection of data distribution, skewness (1.17), kurtosis (0.45), Kolmogorov-Smirnov (.16, $p < .05$) and Shapiro-Wilk (.85, $p < .001$) test statistics indicated a non-normal distribution for smoking urges in the smoking as usual condition, as well as in the smoking deprivation condition (skewness (0.10), kurtosis (-1.59), Kolmogorov-Smirnov (.15, p =.08) and Shapiro-Wilk (.89, p < .01)).

Results from the empty model suggest that 33% of the variance in smoking urges is at the between-subjects level. For a full breakdown of parameter estimates for each step of the model, see Table 4.4. In model 2, fatigue severity was not a statistically significant predictor of smoking urges (b=1.97, se=1.79, p= .277), however, effect size estimates indicate a small effect (r=.15), indicating that a 1 unit increase in fatigue severity indicates a 1.97 unit increase in smoking urges. The addition of the smoking deprivation condition in model 3 was not statistically significant (b=6.07, se=4.22, p=.162), yet a medium effect (r=.27) was observed suggesting that those that were smoking abstinent evinced a 6.07 unit increase in smoking urges. The fully conditional model, including the fixed effect of fatigue severity, deprivation condition, and the interaction term, suggest that within each individual, fatigue severity was not a statistically significant predictor of smoking urges (b=3.26, se=2.23, p= .149, r=.20). In addition, smoking deprivation condition (b=16.13, se=12.12, p=.193, r=.23) nor the interaction term (b=-2.66, se=2.98, p=.378, r=-.15) were statistically significant predictors of smoking urges. Lastly, the model with covariates did not exhibit statistically significant results.

Smoking Withdrawal. Inspection of data distribution, skewness (1.25), kurtosis (1.14), Kolmogorov-Smirnov (.17, p < .05) and Shapiro-Wilk (.88, p < .01) test statistics indicated a non-normal distribution for smoking withdrawal in the smoking as usual condition, and a normal distribution in the smoking deprivation condition (skewness (0.32), kurtosis (0.16), Kolmogorov-Smirnov (.13, p =.200) and Shapiro-Wilk (.96, p =.305)).

Results from the empty model suggest that 62% of the variance in withdrawal is at the between-subjects level. For a full breakdown of parameter estimates for each step of the model, see Table 4.5. In model 2, fatigue severity was a statistically significant predictor of withdrawal (b=0.16, se=0.08, p<.05, r=.26), such that a 1 unit increase in fatigue severity scores evinced an increase in smoking withdrawal symptoms by 0.16. In model 3, the addition of smoking deprivation condition was not statistically significant (b=0.13, se=0.18, p=.485, r=.14). The fully conditional model, including the fixed effect of fatigue severity, deprivation condition, and the interaction term, suggest that within each individual, fatigue severity was not a statistically significant predictor of withdrawal (b=0.15, se=0.10, p= .148, r=.20). In addition, smoking deprivation condition (b=0.01, se=0.52, p=.992, r=.001) nor the interaction term (b=0.03 se=0.13, p=.797, r=.05) were statistically significant predictors of withdrawal. Lastly, the model with covariates did not exhibit statistically significant results (see Table 8).

Post Hoc Tests

Due to lack of statistically significant effects for the hypotheses, as well as lack of significant effects in general, a series of theoretically-driven exploratory analyses were conducted to better understand whether study results reflected experimental limitations (e.g., limited power due to the sample size). The data collected from participants at the baseline appointment was utilized for the post hoc tests. First, bi-variate correlations between baseline fatigue severity and smoking outcomes were examined. Results for the correlations are presented in Table 5.1. Specifically, fatigue severity was statistically significantly and robustly correlated with severity of quit problems ($r = .45$, $p < .01$), negative consequences ($r = .52$, $p < .01$), positive reinforcement ($r = .39$, $p < .05$), and negative reinforcement ($r = .50$, $p < .01$) outcome expectancies (See Appendix 1 for description of measures).

To more thoroughly examine the relation between fatigue severity and smoking outcomes, four separate linear regression models were then conducted with the following smoking criterion variables: quit problems, negative consequences, positive reinforcement, and negative reinforcement outcome expectancies. Covariates were entered in the first step of each model and included baseline CO and sleepiness. Fatigue severity was entered in step 2 of each model. Model fit for each of the steps was evaluated with the F statistic and an increase in variance accounted for as evidenced by a change in R^2. Squared semi-partial correlations (sr^2) were used as measures of effect size (interpreted as .01 = small, .09 = moderate, and .25 = large; Cohen, 1988).

Quit Problems. In terms of severity of symptoms when trying to quit, step one of the model with covariates was not statistically significant ($R^2 = .09$, $F(2, 30) = 1.46$, p =.250; See Table 6.1). In step two, the addition of fatigue severity resulted in a statistically significant model ($\Delta R^2 = .18$, $p < .05$), with fatigue severity emerging as a statistically significant predictor (p<.05).

Negative Consequences. In terms of negative consequences from smoking outcome expectancies, step one of the model with covariates was not statistically significant (R^2 = .05, $F(2, 31)$ = 0.82, p =.452). In step two, the addition of fatigue severity resulted in a statistically significant model (ΔR^2 = .22, $p < .05$), with fatigue severity emerging as a statistically significant predictor ($p<.01$).

Positive Reinforcement. In terms of positive reinforcement outcome expectancies, step one of the model with covariates was not statistically significant (R^2 = .09, $F(2, 30)$ = 1.36, p =.272). In step two, the addition of fatigue severity did not yield a statistically significant model (ΔR^2 = .05, p=.236).

Negative Reinforcement. In terms of negative reinforcement outcome expectancies, step one of the model with covariates was not statistically significant (R^2 = .12, $F(2, 29)$ = 1.92, p =.167). In step two, the addition of fatigue severity did not yield a statistically significant model (ΔR^2 = .13, p =.055), however, fatigue severity emerged as a statistically significant predictor ($p<.05$).

DISCUSSION

The purpose of the present study was to examine fatigue severity on smoking behavior across periods of abstinence and non-abstinence among daily adult combustible cigarette smokers. Specifically, the relation between fatigue severity and latency to smoking initiation, number of cigarettes smoked, average puff velocity, average inter-puff interval, smoking urges, and smoking withdrawal, were examined. Next, the main and interactive effects of fatigue severity and deprivation condition on smoking outcomes were examined. Key findings from primary aims are discussed, as well as the results from exploratory analyses.

Latency to First Cigarette

Latency to smoking initiation has been conceptualized as a behavioral indicator of craving (McKee et al., 2006), with shorter latency to initiation indicative of strong craving for smoking. It was hypothesized that fatigue severity would be significantly associated with shorter latency to smoking initiation, and that the deprivation condition would moderate this relation. First, given that the convergence criteria of the multi-level model could not be met, the main effects could not be examined. Examination of the correlation between fatigue severity and latency to smoke did not yield significant results in either smoking condition. Further, the paired samples t-test revealed that there was not a significant difference in the mean of latency to smoke between the two conditions. There was also no significant interactive effect between fatigue severity and smoking deprivation condition. It is perhaps surprising that there was no significant main effect of smoking deprivation condition on latency to smoke, as past work suggests that smokers exhibit significantly shorter latency to smoke after smoking deprivation periods as low as 30 minutes (McKee et al., 2006; Zacny & Stitzer, 1985). However, it is important to note that the number of seconds to smoke, on average, in the abstinent condition (M=599.29) was lower than in the non-abstinent condition (M=917.91). Such results indicate that participants smoked, on average, more quickly when smoking deprived. Although no work to date has examined fatigue severity in the context of smoking deprivation manipulation, past work suggests that fatigue is sensitive to experimentally aversive/stressful contexts (Brower et al., 1988; Grillon et al., 2015; Lukkahatai & Saligan, 2013; Tran et al., 2009). Further, McKee and colleagues (2006 & 2011) have demonstrated that laboratory induced stress significantly relates to reduced latency to smoke, however, in addition to smoking deprivation, participants received additional experimental manipulation (i.e. consumed alcohol or viewed stressful images). It may be the case that short term smoking deprivation alone is not enough to induce significant fatigue that would impact smoking behavior. Indeed, one study found no statistically significant differences in fatigue scores among smokers that were both abstinent and non-abstinent (Pang & Leventhal, 2013).

It is also likely that measurement of latency to smoking initiation was subject to confounding factors in the current study. First, based on study design, all smokers were taken outside to smoke, after they completed the brief experimental survey. Therefore, for all participants, latency to smoking initiation was measured once individuals were outside. Depending on how long it took participants to complete the survey, or the time they initially arrived to the lab for their appointment, they may inadvertently feel smoking deprived, even during the non-abstinent appointment. In order to minimize the impact of such effects, participants smoked a "control" cigarette prior to the initiation of the McKee task during the non-abstinent appointment, however, there may still be unaccounted for deprivation effects on latency to smoking initiation.

Second, to measure latency to smoking initiation, a timer was used, and was started as soon as the instructions to the McKee task were provided. Many factors could have artificially impacted this window. A research assistant may have dropped the stopwatch, or a participant may have asked a question, dropped their lighter, or knocked the cigarette out of the CReSS device, all prior to actually initiating smoking/timing.

Number of Cigarettes

It was hypothesized that there would be a significant main effect of fatigue severity on number of cigarettes smoked, however, results were inconsistent with hypothesis, with small effects observed (r=.06). Past work examining the impact of smoking deprivation on smoking behavior found no significant differences in fatigue level between those that were smoking deprived and those that were smoking as usual (Pang & Leventhal, 2013). Such findings may suggest that it is necessary to more directly manipulate fatigue severity, such as through sleep deprivation, or laboratory based behavioral tasks while smoking deprived, to more directly examine the fatigue-smoking relationship. Notably, past work has found that sleep deprived smokers with greater fatigue symptoms were more likely to smoke more cigarettes during a relapse analog task (Hamidovic & de Wit, 2009).

However, partially consistent with hypothesis, the interaction of fatigue severity and smoking deprivation significantly predicted the number of cigarettes smoked. Examination of the interaction plot (see Figure 2.1) suggests a negative relation between fatigue severity and number of cigarettes smoked in the smoking deprivation group, such that those with greater self-reported fatigue smoked fewer cigarettes. A negative, medium effect was found (r=-.38). Although inconsistent with prediction, it is noteworthy that those with greater fatigue smoked more cigarettes in the non-abstinent condition. In addition, it may be the case that number of cigarettes smoked is not a robust indicator of lapse behavior, as those in the abstinent condition, on average, smoked a cigarette more quickly and took deeper puffs. Nonetheless, the mean differences were not statistically significant. This may account for the negative relation between fatigue and number of cigarettes smoked, as individuals were more intent on smoking sooner, rather than smoking more to cope with fatigue. More work is needed to elucidate such findings.

Of note, smoking deprivation condition, after accounting for fatigue severity, did significantly relate to number of cigarettes smoked, indicating that those that were smoking deprived were more likely to smoke more cigarettes. Such results are consistent with past work (Pang & Leventhal, 2013), and add to the growing literature around the importance of examining lapse behavior among adult smokers (Roche et al., 2014).

Smoking Topography

Two smoking topography variables were examined to explore the role of fatigue severity and smoking deprivation: puff volume and inter-puff interval. First, the correlations between these two variables were not statistically significant across both conditions. Examination of the correlation in the non-abstinent condition revealed that puff volume and inter-puff interval were positively but modestly correlated (r=.15), suggesting that as participants took deeper puffs, they waited longer to smoke in between puffs. In contrast, in the abstinent condition, puff volume and inter-puff interval were negatively correlated (r=-.08), suggesting that as participants took deeper puffs, the time in between puffs decreased. Although the correlations are not statistically significant, the direction of the associations are as expected for the smoking deprivation manipulation. While there was no statistically significant main effect of fatigue severity for either topography outcome found, effect size estimates do indicate a small effect for both puff velocity and inter-puff interval (r=-.16 and .11, respectively). Due to sample size limitations, such effects are meaningful and may indicate that fatigue severity is an important individual difference factor to consider when examining smoking behavior. Of note, estimates indicate a negative relation between fatigue severity and puff velocity. This is the first study to examine the relation between fatigue severity and smoking behavior, and therefore, more work is needed to elucidate the role of fatigue as a mechanism of change in smoking.

There was a main effect for smoking deprivation condition on puff velocity, after controlling for fatigue severity. Effect size estimates indicates a medium effect of condition on puff velocity (r=.38). This finding is consistent with the majority of past work (McKee et al., 2006; McKee et al., 2011). While statistically significant results were not observed for inter-puff interval, effect size estimates indicate a small effect (r=.17), which may be statistically meaningful given the small sample size. Further, the interaction between fatigue severity and smoking deprivation was not statistically significant. To date, this is the first study to examine the interactive effects of fatigue severity and smoking deprivation on smoking topography outcomes. As noted previously, it may be the case that deprivation manipulation alone is not sufficient in inducing significant fatigue symptoms that would impact smoking topography outcomes (Pang & Leventhal, 2013).

It is important to note that smoking topography variables were averaged across the cigarettes smoked (Burling et al., 1985; De Jesus et al., 2015), or, in the case of puff velocity, averaged across the first cigarette smoked (Kassel et al., 2007; Perkins et al., 2010), consistent with past work. However, it may be the case that puff behavior changes occur over the course of smoking a single cigarette (Collins et al., 2010; Guyatt et al., 1989). Specifically, one study found that smokers decreased the magnitude of puff volume during the course of a single cigarette by 33% and increased inter-puff interval by 75% (Guyatt et al., 1989). It is possible that by averaging topography variables, linear changes in puffing behavior over the course of a single cigarette are missed. It may be the case that early topography data is more indicative of smoking deprivation behavior.

Smoking Urges/Withdrawal

Smoking urges and withdrawal include a range of adverse symptoms that typically emerge within hours of abstaining from smoking (Pang & Leventhal, 2013). It was hypothesized that fatigue severity would significantly relate to both smoking urges and withdrawal, as past work suggest that fatigue is a common adverse symptom associated with smoking deprivation. Results were partially consistent with prediction, as fatigue severity statistically significantly predicted smoking withdrawal, but not smoking urges. Despite the non-significant findings for smoking urges, effect size estimates suggest a small to medium effect (r=.15). Given that the current study is underpowered, such effects may suggest that there is a meaningful relation between fatigue severity and smoking urges. Little work has examined the relation between fatigue and smoking withdrawal symptoms. The current findings are important and indicate that fatigue severity is an important individual difference factor in better understanding smoking withdrawal symptoms and smoking urges. More work is warranted to determine the pattern of the observed effects for those attempting to quit smoking. It may be the case that fatigue severity is a risk factor for early lapse or relapse, due to an increase in withdrawal symptoms. Similarly, little work has examined the relation between fatigue severity and smoking urges. One study examined smoking urges among smokers that were sleep deprived and posited that sleep deprivation may increase cravings to smoke, with the goal of reducing overall sleepiness (Hamidovic & de Wit, 2009). Such results may suggest, as noted previously, that further manipulation of fatigue severity is needed to fully elucidate this relationship.

One potential underlying factor in the fatigue-smoking urges relationship may be caffeine consumption. While limited in scope, research suggests that smokers in deprivation periods are more likely to increase their caffeine consumption to combat deprivation induced fatigue (Swanson et al., 1997). Caffeine use in the current sample was not measured, and may be a potential confounding factor. Future work would benefit from controlling for the effects of caffeine, to increase the interpretability of the relation between fatigue severity and smoking urges.

In addition, the main effects of smoking deprivation condition, after accounting for the effects of fatigue, were examined, and while they yielded no statistically significant effects, effect size estimates indicate small to medium effects for smoking urges (r=.27) and smoking withdrawal (r=.14). Further, as mentioned previously, there was a statistically significant mean difference observed in smoking urges between the non-abstinent and abstinent appointment, such that participants reported statistically significantly greater smoking urges when smoking deprived and the interactive effects of smoking deprivation condition and fatigue severity on smoking urges and withdrawal (p<.05). This finding is consistent with past work suggesting that smokers report greater smoking urges when smoking deprived, compared to smoking as usual (Pang & Leventhal, 2013; Wong et al., 2014). Sample size limitations may help explain why significant findings were not observed for smoking withdrawal, as past work indicates that smokers in deprivation report greater withdrawal symptoms (Pang & Leventhal, 2013; Wong et al., 2014). Interpretation of the effect size estimate for this model suggests that there may be a meaningful difference in smoking withdrawal by condition.

Post Hoc Tests

Due to the lack of empirical support for the primary study aims and concerns about statistical power given the sample size, post hoc tests were conducted to more thoroughly examine the fatigue-smoking relation. As previously mentioned, past work indicates that cigarette smokers report greater levels of fatigue when compared to non-smokers (Corwin et al., 2002), and cigarettes may be utilized as a tool to reduce fatigue symptoms (Hamidovic & de Wit, 2009). Further, while work among combustible cigarette smokers is limited, work to date among electronic cigarette users indicates that fatigue severity is significantly related to greater perceived barriers for quitting, greater dependence, greater perceived risks and benefits of use, and greater cravings (Manning, Garey, Mayorga, et al., 2020; Manning, Garey, Viana, et al., 2020; Manning et al., 2021). As such, it was important to the current investigation to explore the importance of fatigue severity as it relates to smoking outcomes indicative of smoking behavior and potential quit success. Therefore, a series of linear regressions were conducted with severity of symptoms when trying to quit, negative consequences, positive reinforcement, and negative reinforcement outcome expectancies included as criterion variables. Results indicate that fatigue severity was a statistically significant predictor of severity of symptoms when trying to quit and negative consequences outcome expectancies, over and above the effects of CO and sleepiness. Effect size estimates indicate moderate to large effects (.18 and .22 respectively). Such results may suggest that smokers with elevated fatigue experience a greater number of negative symptoms when trying to quit (i.e. irritability, headaches) and more expected negative consequences from smoking (i.e. greater health concerns). In addition, the models predicting positive reinforcement and negative reinforcement did not yield significant results. However, fatigue severity did emerge as a significant predictor of negative reinforcement, with moderate effects (.13). As outlined previously, it is theorized that cigarette smokers with elevated fatigue may smoke more to combat unpleasant fatigue symptoms and acute withdrawal, consistent with the negative reinforcement model of addiction (Baker et al., 2004). Such results should be interpreted with caution as they are exploratory and cross-sectional in nature. Future work would benefit from examining the above relations in a longitudinal design in order to establish the temporal nature of fatigue and smoking outcomes.

Clinical Implications

Based upon the current findings, it appears that fatigue severity is not sensitive to smoking deprivation, indicating that, while smokers may experience greater rates of fatigue compared to non-smokers (Corwin et al., 2002), this may not be a relevant factor to consider regarding smoking lapse. However, the results from the current study indicate that fatigue severity is significantly related to smoking withdrawal, quit problems, negative consequences, and negative reinforcement outcome expectancies. While it is difficult to draw specific conclusions based upon the contradictory results, future research is warranted to more comprehensively test the role of fatigue across a range of smoking processes. This work will be most impactful when a larger sample size is utilized than that in the present study, which is perhaps the chief methodological concern underlying the interpretation of the data. If fatigue states change based upon smoking deprivation, it may be the case that smokers with greater fatigue symptoms are more likely to encounter barriers to being able to quit successfully, and, in fact, may hinder one's ability to engage in a quit attempt at all. From an intervention perspective, it may ultimately be useful to utilize evidenced-based fatigue-related treatments, such as cognitive-behavior therapy (Wiborg et al., 2015) or physical exercise (White et al., 2011), or their combination (McCrone et al., 2012), to help adult smokers better manage their fatigue symptoms and decrease their perceived dependence on cigarettes and/or facilitate quit attempts.

Limitations

Several limitations warrant further discussion. First, the sample size was small (N=36), yielding about 45% power to detect moderate associations between fatigue severity and smoking outcomes. As such, the sample size limits the interpretability of the current results, as the analyses may have been underpowered to detect significant effects. Future work would benefit from recruiting a larger sample, or employing a less advanced modeling approach, such as linear regression. Second, the current sample consisted of community-recruited daily adult combustible cigarette smokers. Future work may benefit from conducting similar work among a sample of treatment-seeking smokers to better understand smoking behavior among those motivated to engage in a quit attempt. Third, although the average number of cigarettes per day was 16.25 (*SD* = 9.01), which is characteristic of 'heavy smoking' (e.g., at least 10 cigarettes per day; Ameringer et al., 2015), future work may benefit from recruiting light and moderate smokers to generalize the findings to the smoking population in general. Fourth, the use of electronic cigarettes (e-cigarettes) has risen dramatically in the United States (Boakye et al., 2022; Dai & Leventhal, 2019). As such, there would be benefit to extending the current model beyond just combustible cigarette users to determine the impact of smoking deprivation among e-cigarette users.

Fifth, while the FTCD was only used to describe the level of cigarette dependence in the current sample, it does warrant comment that the measure demonstrated fair internal consistency, which is a well-established concern with this measure (Berlin et al., 2015; Korte et al., 2013). Sixth, because fatigue is a multi-dimensional experience (Chen, 1986) that often co-occurs with mental and physical health concerns (Hudson et al., 1993), the unique impact of severe fatigue among a non-clinical population is difficult to determine. While efforts were employed to control for extraneous factors (i.e. restricting time of day of experimental appointments, controlling for similar constructs such as sleepiness, examining relations with potential confounding variables including sleep, BMI, and health conditions), more work is needed to better understand severe fatigue as it relates to combustible cigarette use. Seventh, the majority of the sample identified as African American (56.8%). While research among diverse racial populations is important, past research indicates that African Americans are a unique subset of the cigarette smoking population. Indeed, the majority of African Americans smoke menthol cigarettes, 74%-88% as compared to 26% of their White counterparts, which provide cooling and anesthetic properties, making it easier to inhale (Alexander et al., 2016; Prochaska et al., 2017). Menthol cigarette use is associated with increased smoking initiation and progression to regular use, as well as greater cigarette dependence (Alexander et al., 2016). Further, a greater proportion of menthol cigarette users experience mental illness compared to non-menthol cigarette smokers (Prochaska et al., 2017). In addition, African Americans experience more difficulty quitting smoking, and cigarette smoking is a disproportionate cause of disease and death among this population (Alexander et al., 2016; Lawless et al., 2015; Prochaska et al., 2017). Therefore, the current results may not be generalizable to the general smoking population. Future work would benefit from conducting the current study among different racial/ethnic groups in order to determine whether and if differences in fatigue severity and smoking behavior are significant and meaningful.

Conclusions

The present study explored fatigue severity in the context of cigarette use and smoking deprivation. Based upon available data, it appears that fatigue is an important individual difference factor in better understanding cigarette use (Corwin et al., 2002; Hamidovic & de Wit, 2009), yet the current study yielded few statistically significant results to bolster such findings. However, the present study was subject to a number of limitations, including a small sample size that may have impacted the ability to uncover statistically significant effects. Indeed, post hoc tests revealed that fatigue severity is a statistically significant predictor of severity of symptoms when trying to quit, negative consequences, and negative reinforcement outcome expectancies. Such findings, although explanatory, establish the importance of continuing to investigate the explanatory role of fatigue severity in the context of cigarette use (i.e. smoking behaviors, smoking withdrawal, lapse/relapse). Future work would benefit from replicating the current study among a larger and more diverse sample of cigarette smokers in order to derive more concrete conclusions regarding the importance of fatigue as a predictor, or perhaps a symptom, of more problematic cigarette use.

Table 1.1 List of Measures Included in Analyses

Measure	Use	Assessment Point
Carbon Monoxide	Covariate	Experimental Sessions
Sleepiness	Covariate	Experimental Sessions
Fatigue Severity	Predictor	Experimental Sessions
Smoking Topography	Criterion	Experimental Sessions
Smoking Urges	Criterion	Experimental Sessions
Smoking Withdrawal	Criterion	Experimental Sessions

Note. Carbon Monoxide=CO level; Sleepiness=Epworth Sleepiness Scale (Johns, 1991); Fatigue Severity=Fatigue Severity Scale (Krupp et al., 1989); Smoking Topography=Latency to Cigarette, Number of Cigarettes, Puff Velocity, Inter-Puff-Interval; Smoking Urges=Questionnaire of Smoking Urges-Brief (Cox et al., 2001); Smoking Withdrawal= Minnesota Nicotine Withdrawal Scale (Hughes & Hatsukami, 1986).

Table 2.1 Non-Abstinent Bi-Variate Correlations and Descriptives.

	1.	2.	3.	4.	5.	6.	7.	8.	Mean (SD)/N (%)
1. CO PPM	1								19.31 (10.37)
2. Sleepiness	-.02	1							9.11 (6.01)
3. Fatigue Severity	.39*	.28	1						3.95 (1.64)
4. Latency to cigarette	.06	.26	-.05	1					917.91 (1299.00)
5. Number of Cigarettes	.21	-.27	.23	-.40*	1				2.26 (1.48)
6. Puff Velocity	-.36*	.11	-.17	-.06	.05	1			60.66 (41.91)
7. Inter-Puff Interval	-.02	-.11	-.06	-.14	.32	.17	1		24.10 (18.78)
8. Urges	-.04	.08	.34	-.23	.15	-.29	.06	1	31.82 (19.98)
9. Withdrawal	.17	.12	.27	-.15	.07	-.26	-.04	.71***	1.21 (1.10)

Note. N=36. **p*<.05, ***p*<.01, ****p*<.001. CO PPM=CO level during non-abstinent session; Sleepiness=Epworth Sleepiness Scale (Johns, 1991); Fatigue Severity=Fatigue Severity Scale (Krupp et al., 1989); Urges=Questionnaire of Smoking Urges-Brief (Cox et al., 2001); Withdrawal= Minnesota Nicotine Withdrawal Scale (Hughes & Hatsukami, 1986).

Table 2.2 Abstinent Bi-Variate Correlations and Descriptives.

	1.	2.	3.	4.	5.	6.	7.	8.	Mean (SD)/N (%)
1. CO PPM	1								5.31 (3.02)
2. Sleepiness	-.23	1							8.00 (5.19)
3. Fatigue Severity	.13	-.21	1						3.88 (1.56)
4. Latency to cigarette	-.14	.03	.09	1					599.29 (1196.22)
5. Number of Cigarettes	-.01	.09	-.06	-.28	1				2.40 (1.06)
6. Puff Velocity	-.09	-.15	-.14	.18	-.07	1			83.24 (62.59)
7. Inter-Puff Interval	.04	.01	.11	.01	.15	-.07	1		28.75 (35.45)
8. Urges	-.12	.06	-.03	.01	.03	-.01	-.16	1	38.85 (21.60)
9. Withdrawal	-.39*	-.13	.37*	.03	.20	-.03	.91	.52**	1.39 (.84)

Note. N=35. **p*<.05, ***p*<.01, ****p*<.001. CO PPM=CO level during abstinent session; Sleepiness=Epworth Sleepiness Scale (Johns, 1991); Fatigue Severity=Fatigue Severity Scale (Krupp et al., 1989); Urges=Questionnaire of Smoking Urges-Brief (Cox et al., 2001); Withdrawal= Minnesota Nicotine Withdrawal Scale (Hughes & Hatsukami, 1986).

Table 3.1. Paired Samples T-Test Results.

Condition	*M*	*SD*	*t*	*df*	*p*	*d*	LLCI	ULCI
Fatigue Severity								
Abstinent	3.79	1.48	-0.06	26	.952	-.01	-0.39	0.37
Non-abstinent	3.81	1.56						
Latency to Cigarette								
Abstinent	599.29	1196.22	-1.61	30	.255	-.21	-0.56	0.15
Non-abstinent	970.81	1323.45						
Num. of Cigarettes								
Abstinent	2.40	1.06	0.76	34	.454	0.13	-0.21	0.46
Non-abstinent	2.26	1.48						
Puff Velocity								
Abstinent	82.38	63.40	1.98	31	.057	.35	-0.01	.0.71
Non-abstinent	60.08	39.35						
Inter-Puff Interval								
Abstinent	28.75	35.45	0.73	34	.473	.12	-0.21	0.45
Non-abstinent	24.10	18.78						
Smoking Urges								
Abstinent	38.74	20.96	2.52	30	$<.05^{*}$	.45	0.08	0.82
Non-abstinent	28.77	18.11						
Smoking Withdrawal								
Abstinent	1.36	0.83	0.68	27	.503	.13	-0.25	0.50
Non-abstinent	1.25	1.06						

Note. N=36. **p*<.05. Abstinent= Smoking deprivation experimental session; Non-abstinent= Smoking as usual experimental session; Sleepiness=Epworth Sleepiness Scale (Johns, 1991); Fatigue Severity=Fatigue Severity Scale (Krupp et al., 1989); Smoking Urges=Questionnaire of Smoking Urges-Brief (Cox et al., 2001); Smoking Withdrawal= Minnesota Nicotine Withdrawal Scale (Hughes & Hatsukami, 1986); LLCI=Lower Level of the 95% Confidence Interval; ULCI=Upper Level of the 95% Confidence Interval.

Table 4.1. Solutions for Fixed Effects in Models 1-5 for Number of Cigarettes.

Effect	*b*	*SE*	*df*	*t*	*p*	LLCI	ULCI	*r*
Model 1								
Intercept	2.32	0.20	34	11.85	<.001	1.93	2.73	
Model 2								
Intercept	2.06	0.42	57.16	4.93	<.001	1.22	2.90	.55
Fatigue	0.04	0.10	58.99	0.44	.663	-0.15	0.23	.06
Model 3								
Intercept	1.95	0.43	57.39	4.55	<.001	1.09	2.81	.51
Fatigue	0.04	0.10	57.93	0.44	.665	-0.15	0.23	.06
Condition	0.22	0.19	28.32	1.16	.256	-0.17	0.61	.22
Model 4								
Intercept	1.42	0.48	53.95	2.94	<.01	0.45	2.38	.37
Fatigue	0.18	0.11	48.48	1.64	.108	-0.04	0.40	.23
Condition	1.35	0.52	30.88	2.58	<.05	0.28	2.42	.42
FatigueXCondition	-0.29	0.13	32.02	-2.29	<.05	-0.56	-0.03	-.38
Model 5								
Intercept	1.34	0.62	49.92	2.18	<.05	0.10	2.58	.29
Fatigue	0.13	0.13	50.41	1.00	.322	-0.13	0.38	.14
Condition	1.53	0.58	32.92	2.65	<.05	0.36	2.70	.42
FatigueXCondition	-0.28	0.14	31.83	-2.00	.054	-0.56	0.01	-.33
Sleepiness	-0.01	0.03	51.48	-0.39	.698	-0.08	0.05	-.05
CO	0.02	0.02	42.50	0.97	.337	-0.02	0.06	.02

Note. Fatigue=Fatigue Severity Scale (Krupp et al., 1989); Condition coded non-abstinent=0/abstinent=1; CO PPM=CO level during abstinent session; Sleepiness=Epworth Sleepiness Scale (Johns, 1991); LLCI=Lower Level of the 95% Confidence Interval; ULCI=Upper Level of the 95% Confidence Interval.

Table 4.2. Solutions for Fixed Effects in Models 1-5 for Puff Velocity.

Effect	*b*	*SE*	*df*	*t*	*p*	LLCI	ULCI	*r*
Model 1								
Intercept	71.90	7.29	33.11	9.86	<.001	57.07	86.74	
Model 2								
Intercept	92.86	20.32	46.09	4.57	<.001	51.97	133.75	.56
Fatigue	-5.64	4.76	50.63	-1.19	.242	-15.21	3.92	-.16
Model 3								
Intercept	79.21	20.84	50.45	3.80	<.001	37.35	121.07	.47
Fatigue	-5.79	4.64	51.12	-1.24	.218	-15.12	3.53	-.17
Condition	28.24	12.43	30.86	2.27	<.05	2.88	53.61	.38
Model 4								
Intercept	79.60	25.95	53.90	3.07	<.01	27.57	131.62	.39
Fatigue	-5.89	6.14	53.51	-0.96	.342	-18.21	6.42	-.13
Condition	27.27	34.16	37.38	0.80	.430	-41.92	96.45	.13
FatigueXCondition	0.25	8.28	41.22	0.03	.976	-16.47	16.98	.001
Model 5								
Intercept	90.41	29.72	49.63	3.04	<.01	30.70	150.12	.40
Fatigue	-2.02	7.17	49.85	-0.28	.780	-16.42	12.39	-.04
Condition	20.05	36.26	38.52	0.55	.584	-53.33	93.42	.09
FatigueXCondition	-2.34	9.17	37.34	-0.26	.800	-20.93	16.23	-.04
Sleepiness	-0.02	1.55	43.37	-0.01	.990	-3.15	3.10	-.002
CO	-1.34	1.11	49.84	-1.21	.233	-3.56	0.89	-.17

Note. Fatigue=Fatigue Severity Scale (Krupp et al., 1989); Condition coded non-abstinent=0/abstinent=1; CO PPM=CO level during abstinent session; Sleepiness=Epworth Sleepiness Scale (Johns, 1991); LLCI=Lower Level of the 95% Confidence Interval; ULCI=Upper Level of the 95% Confidence Interval.

Table 4.3. Solutions for Fixed Effects in Models 1-5 for Inter-Puff Interval.

Effect	*b*	*SE*	*df*	*t*	*p*	LLCI	ULCI	*r*
Model 1								
Intercept	26.42	3.57	34	7.41	<.001	19.17	33.67	
Model 2								
Intercept	19.01	10.91	45.88	1.75	.087	-2.87	41.07	.25
Fatigue	1.98	2.60	49.90	0.76	.449	-3.24	7.21	.11
Model 3								
Intercept	15.82	11.50	50.54	1.38	.175	-7.27	38.91	.19
Fatigue	2.00	2.61	49.66	0.77	.446	-3.24	7.24	.11
Condition	6.32	7.04	28.89	0.90	.377	-8.08	20.71	.17
Model 4								
Intercept	20.47	14.87	56.85	1.38	.174	-9.31	50.25	.18
Fatigue	0.79	3.58	56.58	0.22	.826	-6.38	7.97	.03
Condition	-1.35	19.98	36.50	-0.07	.947	-41.84	39.15	-.001
FatigueXCondition	1.97	4.83	39.52	0.41	.686	-7.80	11.73	.07
Model 5								
Intercept	27.78	8.76	51.78	3.17	<.01	10.20	45.36	.40
Fatigue	-1.21	1.78	51.65	-0.68	.501	-4.78	2.36	-.09
Condition	-1.84	8.88	36.60	-0.21	.837	-19.83	16.16	-.03
FatigueXCondition	0.65	2.14	35.20	0.31	.762	-3.69	5.00	.05
Sleepiness	-0.09	0.44	47.90	-0.21	.836	-0.97	0.79	-.03
CO	-0.04	0.29	49.84	-0.14	.893	-0.63	0.55	-.02

Note. Fatigue=Fatigue Severity Scale (Krupp et al., 1989); Condition coded non-abstinent=0/abstinent=1; CO PPM=CO level during abstinent session; Sleepiness=Epworth Sleepiness Scale (Johns, 1991); LLCI=Lower Level of the 95% Confidence Interval; ULCI=Upper Level of the 95% Confidence Interval.

Table 4.4. Solutions for Fixed Effects in Models 1-5 for Smoking Urges

Effect	*b*	*SE*	*df*	*t*	*p*	LLCI	ULCI	*r*
Model 1								
Intercept	35.73	2.93	32.10	12.21	<.001	29.77	41.69	
Model 2								
Intercept	28.02	7.69	49.25	3.64	<.001	12.56	43.47	.46
Fatigue	1.97	1.79	54.34	1.10	.277	-1.62	5.55	.15
Model 3								
Intercept	24.56	8.03	52.60	3.06	<.01	8.45	40.67	.39
Fatigue	2.06	1.78	54.21	1.16	.252	-1.51	5.63	.16
Condition	6.07	4.22	25.96	1.44	.162	-2.60	14.74	.27
Model 4								
Intercept	19.94	9.52	54.44	2.10	<.05	0.86	39.01	.27
Fatigue	3.26	2.22	53.02	1.46	.149	-1.21	7.73	.20
Condition	16.13	12.12	31.16	1.33	.193	-8.59	40.85	.23
FatigueXCondition	-2.66	2.98	35.12	-0.89	.378	-8.72	3.39	-.15
Model 5								
Intercept	19.29	10.88	50.58	1.77	.082	-2.56	41.14	.24
Fatigue	4.15	2.54	50.58	1.64	.108	-0.94	9.25	.22
Condition	13.88	12.80	32.88	1.08	.286	-12.17	39.92	.19
FatigueXCondition	-2.77	3.21	31.34	-0.86	.396	-9.32	3.79	-.15
Sleepiness	0.13	0.57	43.47	0.23	.823	-1.02	1.28	.03
CO	-0.23	0.38	51.00	-0.61	.550	-0.98	0.53	-.09

Note. Fatigue=Fatigue Severity Scale (Krupp et al., 1989); Condition coded non-abstinent=0/abstinent=1; CO PPM=CO level during abstinent session; Sleepiness=Epworth Sleepiness Scale (Johns, 1991); LLCI=Lower Level of the 95% Confidence Interval; ULCI=Upper Level of the 95% Confidence Interval.

Table 4.5. Solutions for Fixed Effects in Models 1-5 for Smoking Withdrawal

Effect	*b*	*SE*	*df*	*t*	*p*	LLCI	ULCI	*r*
Model 1								
Intercept	1.30	0.16	31.55	8.31	<.001	0.98	1.61	
Model 2								
Intercept	0.65	0.36	50.17	1.82	.074	-0.07	1.37	.25
Fatigue	0.16	0.08	54.30	2.02	<.05	0.01	0.33	.26
Model 3								
Intercept	0.58	0.37	52.39	1.57	.122	-0.16	1.33	.22
Fatigue	0.16	0.08	53.38	2.03	<.05	0.01	0.33	.27
Condition	0.13	0.18	26.38	0.71	.485	-0.25	0.51	.14
Model 4								
Intercept	0.64	0.44	53.70	1.45	.153	-0.25	1.53	.19
Fatigue	0.15	0.10	52.77	1.47	.148	-0.05	0.36	.20
Condition	0.01	0.52	30.14	0.01	.992	-1.05	1.06	.001
FatigueXCondition	0.03	0.13	33.01	0.26	.797	-0.22	0.29	.05
Model 5								
Intercept	0.37	0.53	49.09	0.71	.484	-0.69	1.43	.10
Fatigue	0.13	0.12	49.56	1.12	.268	-0.10	0.37	.16
Condition	0.12	0.54	30.92	0.22	.825	-0.98	1.23	.04
FatigueXCondition	0.06	0.13	28.38	0.46	.646	-0.21	0.33	.09
Sleepiness	0.01	0.02	46.99	0.23	.82	-0.05	0.06	.03
CO	0.01	0.02	47.20	0.83	.409	-0.02	0.05	.12

Note. Fatigue=Fatigue Severity Scale (Krupp et al., 1989); Condition coded non-abstinent=0/abstinent=1; CO PPM=CO level during abstinent session; Sleepiness=Epworth Sleepiness Scale (Johns, 1991); LLCI=Lower Level of the 95% Confidence Interval; ULCI=Upper Level of the 95% Confidence Interval.

Table 5.1 Baseline Bi-Variate Correlations and Descriptives for Post Hoc Tests.

	1.	2.	3.	4.	5.	6.	Mean (SD)/N (%)
1. CO PPM	1						17.69 (8.83)
2. Sleepiness	-.04*	1					9.45 (5.57)
3. Fatigue Severity	.06	.23	1				4.69 (1.70)
4. Quit Problems	-.27	.24	.45**	1			2.15 (0.89)
5. Negative Consequences	.09	.13	.52**	.41*	1		5.54 (2.25)
6. Positive Reinforcement	.09	.15	.39*	.43*	.78***	1	6.10 (1.96)
7. Negative Reinforcement	.19	.16	.50**	.48**	.65***	.81***	6.23 (2.22)

Note. N=36. *p<.05, **p<.01, ***p<.001. CO PPM=CO level during baseline session; Sleepiness=Epworth Sleepiness Scale (Johns, 1991); Fatigue Severity=Fatigue Severity Scale (Krupp et al., 1989); Quit Problems=Smoking History Questionnaire-Problems Quitting Subscale (Brown et al., 2002); Negative Consequences=Smoking Consequences Questionnaire-Negative Consequences Subscale (Brandon & Baker, 1991); Positive Reinforcement= Smoking Consequences Questionnaire-Positive Reinforcement/Sensory Satisfaction Subscale (Brandon & Baker, 1991); Negative Reinforcement= Smoking Consequences Questionnaire-Negative Reinforcement/Negative Affect Reduction Subscale (Brandon & Baker, 1991).

Table 6.1. Linear Regression Results for Post Hoc Tests.

Step		ΔR^2	*b*	*SE*	*t*	*p*	sr^2
			Quit Problems				
1	Sleepiness	.09	0.02	0.42	0.68	.505	.01
	CO		-0.02	0.01	-1.10	.280	.04
2	Fatigue Severity	.18	0.17	0.06	2.61	<.05	.18
			Negative Consequences				
1	Sleepiness	.05	0.09	0.08	1.10	.282	.04
	CO		0.06	0.05	1.08	.291	.04
2	Fatigue Severity	.22	0.65	0.23	2.88	<.01	.22
			Positive Reinforcement				
1	Sleepiness	.09	0.09	0.07	1.38	.179	.06
	CO		0.06	0.05	1.42	.167	.07
2	Fatigue Severity	.05	0.31	0.24	1.31	.202	.05
			Negative Reinforcement				
1	Sleepiness	.12	0.11	0.08	1.53	.139	.08
	CO		0.09	0.05	1.75	.091	.10
2	Fatigue Severity	.13	0.51	0.25	2.08	<.05	.13

Note. CO PPM=CO level during baseline session; Sleepiness=Epworth Sleepiness Scale (Johns, 1991); Fatigue Severity=Fatigue Severity Scale (Krupp et al., 1989); Quit Problems=Smoking History Questionnaire-Problems Quitting Subscale (Brown et al., 2002); Negative Consequences=Smoking Consequences Questionnaire-Negative Consequences Subscale (Brandon & Baker, 1991); Positive Reinforcement= Smoking Consequences Questionnaire-Positive Reinforcement/Sensory Satisfaction Subscale (Brandon & Baker, 1991); Negative Reinforcement= Smoking Consequences Questionnaire-Negative Reinforcement/Negative Affect Reduction Subscale (Brandon & Baker, 1991).

Figure 1.1. Consort Diagram.

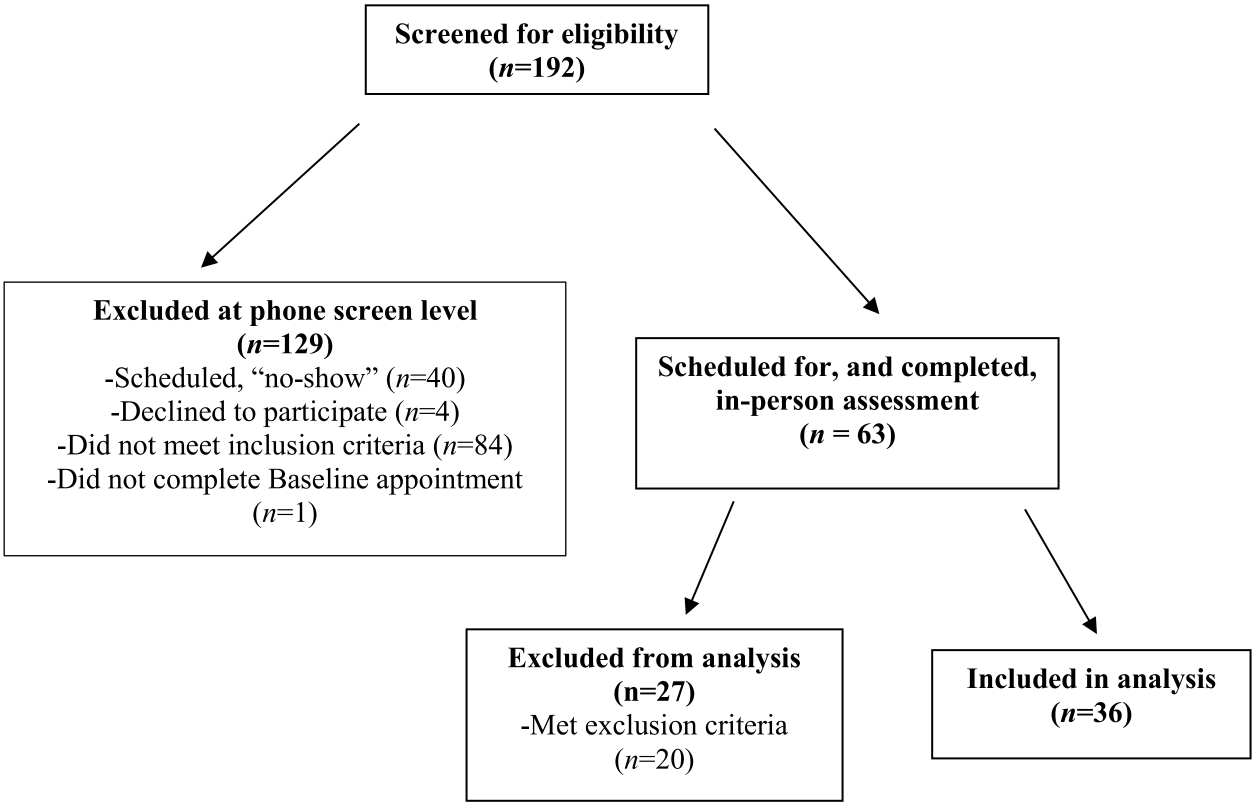
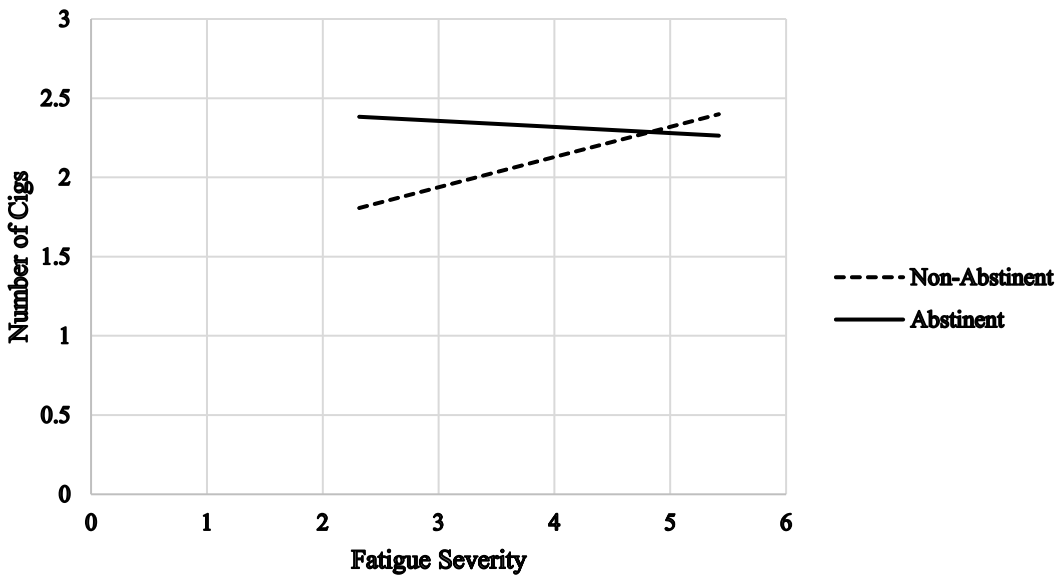


Figure 2.1. Interaction between Fatigue Severity and Smoking Condition Predicting Number of Cigarettes Smoked.



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APPENDICES

Appendix 1. Descriptions of Additional Measures for Post Hoc Tests

Smoking History Questionnaire (SHQ; Brown et al., 2002). The SHQ is a self-report questionnaire used to assess smoking history and patterns of smoking (e.g. smoking rate, age of onset, number of years smoking). The SHQ also contains a 17 item quit problems subscale. Items on this subscale are rated on a 5-point Likert-type scale ranging from 1 (not at all) to 5 (extremely). The quit problems subscale has been used successfully in previous smoking research (Rogers et al., 2018), and demonstrated excellent internal consistency ($\alpha = .94$). The subscale was utilized as a criterion variable in the post hoc tests.

Smoking Consequences Questionnaire (SCQ; Brandon & Baker, 1991). The SCQ is a 50-item measure that assesses smoking expectancies on a 10-point Likert type scale for likelihood of occurrence, ranging from 0 (completely unlikely) to 9 (completely likely). The measure consists of four subscales: Negative Consequences (18 items), Positive Reinforcement/Sensory Satisfaction (15 items), Negative Reinforcement/Negative Affect Reduction (12 items), and Appetite-Weight Control (5 items). Specifically, the Negative Consequences (e.g., The more I smoke, the more I risk my health), Positive Reinforcement/Sensory Satisfaction (e.g., I enjoy the taste sensations while smoking), and Negative Reinforcement/Negative Affect Reduction (e.g., Smoking helps me calm down when I feel nervous), subscales were utilized as criterion variables. Consistent with past work (Brandon & Baker, 1991; Zvolensky et al., 2004), the Negative Consequences, Positive Reinforcement, and Negative

Reinforcement subscales demonstrated excellent internal consistency ($\alpha = .95, .92, .96$ respectively).