Antecedents and Consequences of Temptations During Smoking Cessation:

An Ecological Momentary Assessment Study

by

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DEDICATION

This manuscript is dedicated to all members of the U.S. Armed Forces. I would not be afforded the opportunity to attend graduate school and complete this manuscript without their dedication, honor, and sacrifice.

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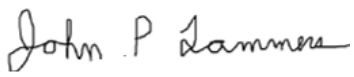

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ABSTRACT

Antecedents and Consequences of Temptations During Smoking Cessation: An Ecological Momentary Assessment Study

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Cigarette smoking is the leading cause of preventable death in the U.S. Most cigarette smokers want to quit but are unable to do so. Both theory and data suggest that stress and negative affect may elicit craving and temptations to smoke, and undermine cessation attempts. However, few studies have examined these relationships in the field and none have examined the time course of these relationships in the field. The current study used ecological momentary assessment to examine the relationship between stress/negative affect and temptations during the first week of a quit attempt. Participants (n=120) reported their level of stress and negative affect (NA) at random times up to four times per day (random assessments; RAs), and at temptation episodes (TAs). Consistent with prior data, participants reported higher levels of stress/negative affect at TAs than RAs. In addition, stress/NA were elevated in the two hours prior to a temptation episode.

However, stress/NA were not elevated following a temptation episode. Overall, the data suggest that stress/NA may provoke temptations during a quit attempt.

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CHAPTER 1: INTRODUCTION

OVERVIEW

Cigarette smoking is the leading cause of preventable death in the U.S. It has an estimated economic impact of approximately $300 billion due to medical care costs and lost productivity (Office of the Surgeon General, 2014). However, smoking cessation programs have a low rate of success and many individuals relapse within the first week of a initiating a cessation attempt (Shiffman & Waters, 2004). Therefore, more effective smoking cessation interventions are required.

There has been much interest in the psychological processes underlying nicotine addiction and relapse to smoking. Researchers believe that a better understanding of these processes will lead to more effective interventions. Many authors have argued that stress and negative affect elicit craving and temptations to smoke, and undermine cessation attempts. This study investigates the relationship between stress, negative affect, and temptations in the first week of a quit attempt.

The background section is organized as follows. First, a review of the health effects of smoking and smoking cessation will be presented. Second, there will be a brief review of the nicotine addiction literature. Third, a review of the literature on the role of stress and negative affect in smoking behavior will be presented. Fourth, the methodology used in the current study (ecological momentary assessment, EMA) will be introduced and pertinent literature reviewed. Finally, the rationale for the current study will be presented.

Smoking Prevalence and Monetary Impact

In the 40 years following the release of the surgeon general's report outlining the damaging effects of smoking in 1964, an estimated 12 million people died from smoking related illnesses (U.S. Department of Health and Human Services, 2004). Although smoking prevalence in the U.S. declined significantly from 1960 through the 1990s there has been little decline in the past decade (Office of the Surgeon General, 2014). Currently, approximately 21 percent of the US population or 43 million people smoke cigarettes in the United States with an estimated 4,000 people trying cigarettes for the first time each day (Office of the Surgeon General, 2014; U.S. Department of Health and Human Services, 2004). Annually, smoking related diseases cost nearly $170 billion in direct medical expenses and $156 billion in lost productivity (Office of the Surgeon General, 2014; Xu, Bishop, Kennedy, Simpson, & Pechacek, 2015).

Health Consequences of Smoking and Smoking Cessation

Cigarette smoking is the largest single contributor to preventable deaths in the United States with more than 443,000 people dying each year from smoking related diseases (Office of the Surgeon General, 2014). The negative effects of smoking also extend to bystanders, where it is estimated that 42,000 deaths each year in the U.S. are attributable to second-hand smoke (Centers for Disease Control and Prevention, 2016).

Cigarette smoking is linked to numerous serious diseases including multiple types of cancer, chronic obstructive pulmonary disease (COPD), coronary heart disease, emphysema, diabetes, and stroke (Novello, 1990; Office of the Surgeon General, 2014; U.S. Department of Health and Human Services, 2004, 2006, 2012). Women who smoke while pregnant have an increased risk of miscarriage, as well as low-birth weight,

stillborn or premature infants (U.S. Department of Health and Human Services, 2004). Non-smokers in contact with second-hand smoke are at an elevated risk of developing heart disease, lung cancer, and respiratory infections (U.S. Department of Health and Human Services, 2006).

Cigarette smoking in the military is of concern due to the higher smoking rate in the military compared to the general population and due to the detrimental impact on readiness (Institute of Medicine, 2009). Approximately 24 percent of active duty military members in the U.S. are current smokers (The Department of Defense, 2013). Cigarette smoking negatively affects military members' ability to perform their duties. Smoking use is associated with declines in physical performance as assessed by physical fitness tests, reduced night vision adaptation, accelerated hearing loss, and higher rates of basic training failure (Institute of Medicine, 2009).

Smoking cessation has been shown to have health benefits including reducing the risk of suffering a stroke, developing numerous types of cancers and developing coronary heart disease (U.S. Department of Health and Human Services, 2004). Overall, people who quit smoking live longer than those who continue to smoke (Centers for Disease Control and Prevention, 2016). Unfortunately, even with the development of pharmaceutical, telephone, group interventions, and online cessation resources, smoking cessation rates remain low. The majority of current smokers report wanting to quit, and approximately 70 percent of smokers report making a quit attempt in the past year (Messer, Trinidad, Al-Delaimy, & Pierce, 2008). However, less than 5 percent of people who attempt to quit smoking remain abstinent for more than 3 months (U.S. Department of Health and Human Services, 2004). It is also estimated that one third of smokers who

are able to quit for one year begin smoking again (U.S. Department of Health and Human Services, 2004).

In sum, despite the availability of smoking cessation interventions, an estimated 43 million people continue to smoke in the US. This suggests that the development of novel cessation methods, perhaps using current technology, should be pursued in order improve cessation rates and reduce smoking prevalence.

NICOTINE ADDICTION

There is a scientific consensus that smoking cessation is difficult due to the addictive nature of nicotine (U.S. Department of Health and Human Services, 2004). Out of the thousands of chemicals contained in modern cigarettes, research has implicated nicotine as the primary factor in cigarette addiction. Repeated and chronic exposure to nicotine leads to neuroadaptations that lead to dependence (Baker, Brandon, & Chassin, 2004). Simply put, individuals who have developed a nicotine addiction are dependent on this substance to function normally.

For example, studies have investigated the acute hedonic and cognitive effects of smoking of smoking and nicotine. Varying methods of nicotine administration have been studied including intravenous, transdermal, and inhalation. A meta-analysis of 41 double-blind, placebo controlled studies found that smoking improved attention and memory (Heishman, Kleykamp, & Singleton, 2010). A review of the literature on the acute subjective effects of nicotine and smoking and has reported that nicotine and smoking have acute pleasurable effects (Kalman, 2002). Smokers often report relief of negative symptoms, particular negative affect, as a positive outcome associated with smoking

(Baker et al., 2004). In sum, smoking is reinforced by the acute hedonic and/or cognitive effects of nicotine, and this reinforcement may underlie dependence.

Nicotine Withdrawal

Tolerance to and withdrawal from nicotine are hallmark criteria of nicotine dependence (American Psychiatric Association, 2013). If individuals do not take in the required level of nicotine, they will experience nicotine withdrawal. The symptoms of nicotine withdrawal vary depending on the individual but are characterized by negative changes in mood, cognition, and physical symptoms (American Psychiatric Association, 2013). Individuals may experience one or more of the following symptoms during nicotine withdrawal: dysphoria, anxiety, difficulty concentrating, increased appetite, weight gain, sleep disruptions, and increased cravings which may last for weeks or months following cessation (Baker et al., 2004). These negative symptoms have been theorized to be a major factor in maintaining smoking. Avoidance of withdrawal symptoms (negative reinforcement) has been indicated as a reason individuals fail in a cessation attempt (Baker et al., 2004).

ROLE OF NEGATIVE AFFECT & STRESS IN MAINTAINING ADDICTION

As noted earlier, the current study focuses on the role of negative affect and stress. Baker and colleagues (2004) reviewed relevant literature and succinctly outlined major theories underlying smoking dependence. They described several theories outlining the relationship between social and cognitive factors related to addiction to cigarettes that are beyond the scope of this study. Negative affect and stress have been identified as major factors contributing to relapse (Shiffman & Waters, 2004), and are of particular interest to this study.

The definitions of stress and negative affect can differ depending on the context in which they are used. For the purposes of this paper, stress and negative affect are defined below. If "stressors" consists of situations that that exert demands on an individual threatening homeostasis, then "stress" is the experience of cognitive, emotional, and physiological changes in response to these "stressors" (Kassel, Stroud, & Paronis, 2003). Negative affect is a "a general dimension of subjective distress and unpleasurable engagement that subsumes a variety of aversive mood states, including anger, contempt, disgust, guilt, fear, and nervousness, with low NA being a state of calmness and serenity" (Watson, Clark, & Tellegen, 1988).

In the following sections, research examining the role of stress and negative affect in cigarette smoking will be reviewed. The first section will review laboratory studies, and a later section will review Ecological Momentary Assessment (EMA) studies. Illustrative studies are summarized in Tables 1A and 1B. Research studies examining cigarette smoking have contained different variables based on the research question at hand.

Research on the relationship between stress/negative affect and craving (as opposed to stress/negative and smoking) is most relevant to the current proposal. Craving is a key factor to investigate as it has been repeatedly shown to be a primary precipitant of both ad libitum smoking and relapse during a cessation attempt (Shiffman, Gnys, et al., 1996; Shiffman, Paty, Gnys, Kassel, & Hickcox, 1996). Although researchers have been most interested in the idea that negative affect increases craving, there is also the possibility that craving itself elicits negative affect. This would indicate a bidirectional relationship between negative affect and craving.

Therefore, some of the studies reviewed examine the effect of stress/negative affect on craving (Stress/NA → Craving). Other studies examine the effect of craving (or cue exposure) on stress/negative affect (Craving → Stress/NA).

Lab Studies Examining Effect of Stress/NA on Craving

The following section reports the results of studies that have manipulated stress or negative affect as an independent variable and examined the effect of this manipulation on craving (the dependent variable) (Stress/NA → Craving).

Heckman and colleagues completed a meta-analysis of 27 laboratory studies that examined the effect of negative affect (and positive affect) on subsequent craving to smoke (Heckman et al., 2013). The results of this meta-analysis showed that a negative affect manipulation increased post-manipulation craving with a medium effect size (Heckman et al., 2013). Manipulations of positive affect did not increase post-manipulation craving. This meta-analysis is important in that it supports theoretical models and participant self-report that increases in negative affect are associated with an increase in craving (Heckman et al., 2013).

An illustrative study was completed by Tiffany and Drobes (1990) (Table 1A). Participants rated their smoking craving and urges following sessions of guided imagery. The guided imagery scenarios were designed to elicit smoking urges and consisted of negative affect and smoking urges, positive affect and smoking urges, explicit smoking urges, negative affect only, and positive affect only (Tiffany & Drobes, 1990). There were significant differences in level of craving elicited depending on script type. Scripts containing smoking cues (negative affect and smoking urges, positive affect and smoking urges, and explicit smoking urges) induced significant increase in craving. While both

negative affect only and positive affect only scripts produced significant increases in urge and craving, negative affect did so at a larger magnitude (Tiffany & Drobes, 1990). This study is important in that it demonstrated that negative affect alone in a laboratory setting was capable of eliciting significant increases in smoking urge and craving (Tiffany & Drobes, 1990).

Despite the findings of Heckman et al. (2013), it should be noted that not all studies revealed that a manipulation of negative affect increased craving. Shiffman and colleagues (2013) utilized various cue sets and examined the effect on subsequent craving and smoking behavior. Participants were exposed to six cue set types (cigarettes, positive affect, negative affect, smoking prohibitions, alcohol and neutral) over six separate laboratory session (Shiffman et al., 2013). The results of this study showed significant increases in craving following exposure to the smoking and alcohol cues and a decrease in craving following the positive affect scenario (Shiffman et al., 2013). In this study, the negative affect cue set did not significantly increase craving (Shiffman et al., 2013). The authors outlined possible factors that contributed to this nonsignificant finding including decreased length of deprivation in their study and the availability of smoking following cue exposure (Shiffman et al., 2013).

Lab Studies Examining Effect of Craving on Stress/NA

The following section reports the results of studies that have manipulated craving as an independent variable and examined the effect of the manipulation on stress or negative affect (Craving → Stress/NA) (Table 1B). Craving has generally been manipulated by use of a cue exposure (imaginal or in vivo) paradigm. Participants have

been exposed to drug cues (that elicit craving) and/or neutral cues (that elicit less craving). The effect of this manipulation on stress and negative affect is then assessed.

Consistent with previous studies, participants reported significantly greater craving, as assessed with the Questionnaire of Smoking Urges (Drobes & Tiffany, 1997). There were no significant differences in subsequent craving between imaginal and in vivo scenarios. More pertinent to the current study, this study also demonstrated that manipulation of craving in a laboratory setting increased negative affect and decreased positive affect (Drobes & Tiffany, 1997). In a study by Heishman and colleagues (2010), participants were exposed to multiple cue types (neutral vs. smoking and imaginal/in-vivo) and subsequent changes in subjective and physiological variables were assessed. The smoking cue sets, both imaginal and in-vivo, resulted in significantly increased negative mood and significantly decreased positive mood, while neutral cue sets had no effect (Heishman, Lee, Taylor, & Singleton, 2010) (Table 1A).

In sum, these data demonstrate that manipulating stress/negative affect can increase craving, and manipulating craving can increase stress/negative affect, although more studies have examined the former. The studies reviewed so far have all taken place in the laboratory. A number of studies have also examined relationships between stress/negative affect and craving in the field, using EMA. These studies will be reviewed in Chapter 2. But first, an introduction to EMA will be provided.

CHAPTER 2: ECOLOGICAL MOMENTARY ASSESSMENT

INTRODUCTION TO EMA

Ecological momentary assessment can be best introduced by defining each of its terms. “Ecological” refers to the naturalistic setting in which participants complete the assessments. The term “momentary” refers to the fact that participants respond to how they are feeling at that moment. “Assessment” refers to the evaluation of subjective and objective variables that can be included in EMA studies.

When compared to laboratory studies, EMA studies have a number of strengths including the greater ecological validity resulting from the fact that participants complete the assessments in their natural environments rather than under strictly controlled laboratory settings (Shiffman, Stone, & Hufford, 2008). By assessing phenomenon in the “moment” or very recent past, data gained from EMA studies can be less subject to recall biases that can influence data in some laboratory studies. The addition of repeated sampling produces richer datasets for examining temporal sequences over a timescale of hours, days, and weeks, when compared to laboratory studies (Shiffman et al., 2008)

Tools available for EMA studies have developed over the years and consist of self-report journals and logs, electronic diaries, and specialized software programs contained on personal digital assistant (PDA), and smartphone platforms (Shiffman et al., 2008). EMA has been extensively used to identify variables related to temptations and relapse in studies of addiction. EMA methodology is appropriate for investigating addiction and relapse due its ability to capture the episodic nature of drug administration, contextual information related to drug taking, as well as changes throughout the day.

In sum, EMA studies are a useful compliment to laboratory studies because EMA studies have greater ecological validity and permit collection of richer datasets for

examination of temporal sequences (Shiffman et al., 2008). Shiffman, et al. (2008) review the history and suitability of EMA as a type of study design and the relevant background information is contained below.

ASSESSMENT SCHEDULES

EMA studies use different schedules of assessment administration depending on the hypothesis and goals of research (Shiffman, 2009). There are two main assessment schedules that allow for the participant to complete multiple measures outside of the laboratory setting (Shiffman et al., 2008). Some studies utilize an event-based schedule of reporting where the participants are instructed to complete an assessment each time a previously defined event occurs (Shiffman et al., 2008). In the case of addiction research, these events could include incidents of seeing another person use their preferred substance, when a person experiences a particular mood, or after a meal is eaten (Shiffman, 2009). Event-based assessments provide valuable information regarding the immediate internal and external factors associated with drug use or abstinence.

The second type of assessment schedule is time-based and requires participants to provide information at particular times points throughout the study. Time-based assessments can occur at either fixed intervals (e.g. every 4 hours after waking and until bedtime) or at random times (e.g. 4 assessments randomly distributed during waking hours; "random assessments") (Shiffman et al., 2008). Data from time-based assessments such as random assessments are useful when determining how changes in a variable, for example, mood or cognition, are related to subsequent behaviors (Shiffman, 2009). Studies may utilize both event-based and time-based assessments within the same study. This approach was taken in the current study.

USE OF EMA TO STUDY ADDICTION

Craving and relapse are common elements in models of addiction but can be challenging to study comprehensively in the laboratory. For example, the unusual context of a laboratory setting (vs. real-world setting) may influence craving responses. Traditional lab-based studies (as reviewed above) are generally only capable of collecting reliable information of how the participant is feeling at that moment rather than capturing changes as they occur over an extended period of time, such as during a cessation attempt (Shiffman, 2009). EMA methods allow for closer examination of factors that contribute to relapse by assessing participants multiple times in their natural environments (Serre, Fatseas, Swendsen, & Auriacombe, 2015; Shiffman, 2009). Using EMA methods, researchers can gather contextual information of drug use and relapse including mood state, stress, affect, craving, and environmental information (Shiffman, 2009).

A common concern of EMA studies is whether participants are able to adhere to the study protocol. This becomes even more of a concern when working with individuals with drug addiction who may have generally chaotic lifestyles (Shiffman, 2009). However, research conducted with separate groups of crack-cocaine, opiate, and heroine addicted participants resulted in sufficient compliance to the study protocols and demonstrated the utility of employing EMA methods and handheld technology to collect data on illicit drug use (Shiffman, 2009).

USE OF EMA TO STUDY CIGARETTE SMOKING

EMA has been widely used to study smoking cessation (Serre et al., 2015). An illustrative study was conducted by Shiffman & Waters (2004). Participants attempting to quit were instructed to complete both event based and random assessments. The event

based assessments were to be initiated during both periods of significantly heightened temptation and incidents where they lapsed. Of particular note, the researchers included a measure of negative affect that was administered during every assessment. The focus of this study was to clarify the immediate precipitants of lapse with a focus on stress and negative affect. Results showed that negative affect increased in the hours preceding a subset of lapses (those for which the participants endorsed stress or bad mood as a trigger for the lapse). In contrast, daily ratings of negative affect or stress were not prospectively associated with relapse. This suggests that rapid hour-by-hour changes in negative affect were associated with risk or relapse (Shiffman & Waters, 2004).

As noted earlier, EMA studies have also examined whether stress/negative affect is associated with craving, and whether craving is associated with stress/negative affect. Studies are reviewed below and illustrative studies are also shown in Table 1B.

EMA Studies Examining Effect of Stress/NA on Craving

Shiffman and colleagues (1996) examined negative affect at random assessments, temptation assessments, and lapse assessments in smokers attempting to quit smoking. A temptation assessment was defined as any occasion when the participant experienced "an acute rise in urge to smoke or an occasion in which they felt they had come to the brink of smoking". Participants were asked to report their level of negative affect as it was just prior to the temptation. As expected, higher levels of urge to smoke and craving were found prior to temptation assessments compared to random assessments (Shiffman, Paty, et al., 1996). More pertinent to the current paper, negative affect ratings were higher just prior to temptation episodes than at random assessments. Negative affect was highest just

prior to lapse assessments. Overall, the data suggest that negative affect provokes temptations (Shiffman, Paty, et al., 1996).

In a second study, researchers again examined data from temptation assessments and random assessments (Shiffman, Gnys, et al., 1996). The data collected from these two types of assessments were compared between participants who maintained abstinence (maintainers) and those who lapsed back to smoking (lapsers). The results of this study show that temptations assessments do not significantly differ between groups in terms of setting, frequency, intensity, and affect (Shiffman, Gnys, et al., 1996). Similar to previous findings, data showed that temptations, regardless of group, were more likely to occur when consuming alcohol or coffee, when exposed to smoking cues, and, most pertinent here, when negative affect was significantly elevated (Shiffman, Gnys, et al., 1996).

Since maintainers and lapsers did not significantly differ in how they experienced and responded to temptations, the researchers provided several suggestions that could account for why some participants successfully abstained from smoking while others did not (Shiffman, Gnys, et al., 1996). The authors suggest that situational factors contributed to lapses and that the maintainers were not exposed to these situations or were better skilled at avoiding these situations (Shiffman, Gnys, et al., 1996).

EMA Studies Examining Effect of Craving on Stress/NA

Cue-reactivity EMA (CREMA) studies have manipulated cue type (either neutral or smoking) during EMA and then measured changes in craving and changes in mood at the same time point. Data from CREMA studies provide complimentary information to that gained from laboratory cue reactivity studies in that they show that the effects of cue

exposure can be detected in the field. Initial CREMA studies were conducted to determine the feasibility of eliciting craving and mood changes following exposure to smoking-related cues in the participant's natural environment (Warthen & Tiffany, 2009). The researchers conducted both laboratory and field assessments in order to compare how location and method of administration influenced subsequent changes in mood and craving. This study utilized a 2x2 experimental design where participants were exposed to either smoking-related or neutral-related cues contained within either photographs or imagery scripts.

The results of this study showed there were significant increases in craving following exposure to smoking-related cues but not neutral cues in both presentation conditions during EMA (Warthen & Tiffany, 2009). Most pertinent to the current study, there were also significant increases in negative mood and significant decreases in positive mood following exposure to smoking-related cues with the photographs having a larger magnitude of change compared to imagery scripts. Perhaps most importantly, the data gathered from the laboratory sessions did not significantly differ from those completed in the field.

A similar CREMA design was used to investigate how craving and mood were influenced by presenting smoking and neutral cues utilizing photographic and in-vivo presentation methods (Wray, Godleski, & Tiffany, 2011). In line with the previous study, smoking cues elicited higher craving than neutral cues for both presentation types (in-vivo and photographic), and negative mood was significantly elevated following exposure to smoking cues (Wray et al., 2011).

An interesting finding was that presentation mode had a significant effect on magnitude of mood and craving with photographic presentation of cues have a larger effect than in-vivo exposure. Researchers suggested that the photographs were novel in familiarity and subsequently exerted a greater influence on craving and mood compared to the in-vivo exposures which involved exposure to the participant's own items (Wray et al., 2011). The results of this study are significant because they replicated findings from Warthen & Tiffany (2009) and generated significant results, albeit of a lessor magnitude, from an in-vivo presentation method.

In general, both lab studies (Table 1A) and EMA studies (Table 1B) have provided support for the hypotheses that stress/negative affect increases craving (or elicits temptations) and that craving increases stress/negative affect. However, there are limitations with this literature. First, relatively few studies have examined these relationships during EMA. More data are required to confirm that the findings reported from laboratory studies occur in the natural environment. Second, studies have not examined the timeline of the relationship between stress/NA and craving (or between craving and stress/NA). Stated another way, no studies have examined changes in stress/NA both before and after craving (or temptation) episodes. Third, those studies that have reported higher levels of stress/NA at temptations (vs. RAs) have relied on retrospective recall. After a temptation episode had concluded, participants were required to report their negative affect as it was just prior to a temptation episode (Shiffman, Paty, et al., 1996). Thus, data from these reports may be potentially biased by the mood state at the time of recall. The current study will add to this literature by examining the time

course of stress/NA in the hours before and after temptations using EMA in smokers attempting to quit.

CHAPTER 3: STUDY RATIONALE & SPECIFIC AIMS

STUDY RATIONALE

Overall, there is evidence that stress/NA increases craving in both laboratory and real-world settings. In the current study, both stress and negative affect are included as separate variables and referred to as stress/NA. There are relatively few studies that have examined the relationships between stress/NA and temptation episodes in a real-world context. Most importantly, there are no data on the timeline of stress/NA preceding and following temptation assessments while individuals attempt to quit. The current study examines whether stress/NA can provoke temptations during a quit attempt, and whether the experience of a temptation can increase stress/NA as it occurs during the first week following a quit attempt (see Figure 1).

These relationships were examined in smokers attempting to quit during the first week of the quit attempt. This time period was selected because many smokers relapse to smoking during this time and experience intense cravings and temptations to smoke.

Justification for Focus on First Week

The first week of a quit attempt is important to study for several reasons. First, lapses to smoking, defined as "any smoking, even a puff", often occur during the first week of a quit attempt. Therefore, smokers are most at risk of bad outcomes, such as lapses (and craving/temptations), during this period. For example, a large proportion of individuals who are motivated to quit and who seek treatment for smoking cessation report lapses very rapidly, often within one week of quitting (Garvey, Bliss, Hitchcock, Heinold, & Rosner, 1992; Hughes, Keely, & Naud, 2004). Furthermore, the vast majority of smokers attempting to quit on their own without medication report at least one lapse

within one week of a quit attempt (Hughes et al., 2004). Estimates for lapse rates during the first week of a cessation attempt range from 50% (Garvey et al., 1992) to approximately 80% (Garvey et al., 1992). Furthermore, lapses in the early stages of a quit attempt predicted future relapse status (Kenford et al., 1994). Moreover, withdrawal symptoms, including negative affect and craving are at their highest early in a quit attempt (Alessi, Badger, & Higgins, 2004). Withdrawal symptoms and craving during the first week of abstinence also predicted smoking outcomes (Piper et al., 2008).

Taken together these findings highlight the importance of assessing psychological processes in the first week of smoking cessation when quitters are at highest risk of lapse and at a time when any intervention may be most usefully deployed. For these reasons, the current study will examine stress/negative affect during the first week of an attempt to quit smoking.

Justification for Focus on Temptations

Temptation episodes, rather than lapse episodes, were the main focus in the current study. The rationale for this focus as follows. First, temptation episodes are of theoretical and clinical importance. There is likely much overlap between the psychological processes that underlie temptation episodes and those that underlie lapse episodes (Shiffman, Paty, et al., 1996). For example, as described earlier, research using EMA in smokers has shown that negative affect is elevated just prior to both lapse and temptation episodes (vs. at random assessments) (Shiffman, Paty, et al., 1996). In addition, features of temptations have been associated with subsequent relapse. For example, duration of temptations has been associated with subsequent relapse (Shiffman et al., 1997). In individuals who experienced a first lapse, the peak reported urge during

temptations significantly increased in the four days before the first lapse (Shiffman et al., 1997).

Second, the focus on temptation episodes during an attempt to maintain abstinence permits a more direct comparison with previous lab studies that examined the association between stress/negative affect and craving. Previous studies have demonstrated that craving and temptation are highly correlated, and this is further discussed below. In previous laboratory studies examining the relationship between stress/negative affect and craving, participants would generally have been required to maintain abstinence during the laboratory session, as stress/negative affect and craving were assessed. In addition, smoking behavior or relapse is rarely assessed in these studies as an outcome variable.

Third, in the dataset used for the current study, there were also several methodological challenges with using lapse episodes as an outcome of interest. Due to nature of the EMA protocol (see methods), there was difficulty verifying the specific time of lapses. That is, the precise time of first lapse was rarely known. In addition, a preliminary review of the data indicated that not all first lapse episodes were entered by participants. These considerations diminished enthusiasm for analyses involving lapses.

Relationship between Temptation Episodes and Craving

In the current study, participants were instructed to enter a temptation episode when they experienced a temptation to smoke, defined, as noted before, as "an acute rise in urge to smoke or an occasion in which they felt they had come to the brink of smoking". Using this definition, "craving", which is very highly correlated with "urge", can be seen as part of the definition of a temptation. Therefore, it is expected that

participants would report higher craving at TAs than RAs, and this has always been observed (Shiffman, Paty, et al., 1996).

Although TAs are associated with higher craving than RAs, temptations are not coterminous with high craving. Theoretically, part of the definition of temptation involves the perception that one has come to the brink of smoking without actually doing so. The sense of being ready to act may occur without craving. Berridge (2009) has argued that an addict "might urgently "want" to act". At an empirical level, some TAs are reported with low levels of craving. For example, in one large EMA study that provided data for Shiffman et al. (1996), craving of "0" or "1" (on a 0-10 scale) was endorsed on 18% of TAs (Shiffman, email communication, 9/24/16). Although it is possible that such entries are due to measurement error, it is more plausible that subjects do indeed experience some temptations when experiencing little or no craving. Relatedly, using EMA research indicates 7% of first *lapses* to smoking occurred when participants reported little or no craving (Ferguson & Shiffman, 2010). In sum, although temptations are associated with elevated craving, they are also theoretically distinct and are sometimes reported when craving levels are low.

The specific aims of the study were as follows.

STUDY AIMS

Specific Aim 1

To examine the relationship between Stress/NA & Assessment Type during attempted abstinence from smoking.

Hypothesis 1: It is expected that Stress/NA will be higher at TAs vs. RAs.

Specific Aim 2

To examine whether Stress/NA provokes temptations during attempted abstinence from smoking.

Hypothesis 2: If Stress/NA causes temptation, it is hypothesized that Stress will be higher at RAs that immediately precede TAs than at RAs distal from TAs.

Specific Aim 3

To examine whether temptations provoke Stress/NA during attempted abstinence from smoking.

Hypothesis 3: If temptations cause Stress/NA, it is hypothesized that Stress/NA will be higher at RAs that immediately follow TAs than at RAs distal from TAs.

CHAPTER 4: METHODS

PARTICIPANTS

The methods presented in this manuscript are taken from Waters et al. 2014. Participants were adult cigarette smokers (N=120) recruited from the Houston, Texas, and Washington, DC, metropolitan areas who volunteered to participate in an EMA study during a smoking cessation attempt. Participants were a subset of 268 participants who enrolled in the parent smoking cessation study. The EMA portion of the parent study was initiated midstream, so only 231 participants (of the 268 participants) were offered the opportunity to enroll in the EMA study. Of the 231 participants, 129 volunteered to enroll and 120 provided EMA data.

Inclusion and exclusion criteria are reported in Table 2 (Waters et al., 2014). All participants received the same cessation interventions (described below). The study was approved by the Institutional Review Boards of the University of Texas M. D. Anderson Cancer Center and the Uniformed Services University of the Health Sciences.

The 120 participants (43% female) were on average 43.3 years old (*SD* = 11.1), and they reported smoking an average of 19.1 (*SD* = 7.9) cigarettes per day. On a question asking participants to endorse which race they identified with, 52.9% of participants self-identified as White, 39.5% self-identified as Black or African American, and 7.6% self-identified another category. The average expired level of CO in breath at orientation was 20.1 ppm (*SD* = 8.66), the average level of cotinine (a nicotine metabolite) in saliva was 405.1 ng/ml (*SD* = 242.0), and the average score on the Fagerstrom Test of Nicotine Dependence (Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991) was 5.11 (*SD* = 2.07), indicating that the sample was comprised of medium to heavy smokers with on average moderate levels of dependence (Waters et al.,

2014). For the parent study, participants received $25 for an orientation session, and $50 for each of five laboratory sessions. Participants enrolled in the EMA portion also received $2.50 for each RA that they completed during the one week EMA phase of the study. To minimize the incentive to report "false" temptations, participants were not compensated for participant-initiated assessments.

PROCEDURE

Potential participants for the parent study were first screened by a telephone interview during which tobacco history and demographic information were obtained. Participants initially deemed eligible after the phone interview were invited to attend an orientation session, during which expired breath CO was assessed to determine final eligibility. Participants also completed the following assessments: the Patient Health Questionnaire (PHQ; (Spitzer, Kroenke, & Williams, 1999)); Section K (Non-alcohol psychoactive substance use disorders) of the Mini International Neuropsychiatric Interview (MINI; (Sheehan et al., 1998)); the Rapid Estimate of Adult Literacy in Medicine (REALM; (Davis et al., 1991)); and the Alcohol Use Disorders Identification Test (AUDIT;(Saunders, Aasland, Babor, de la Fuente, & Grant, 1993)).

Enrolled participants attended up to five additional laboratory visits consisting of two pre-quit laboratory visits, a quit day visit (Week 0), a visit one week post quit day (Week +1), and a visit at end of treatment (four weeks after Week 0) (Waters et al., 2014). On quit-day, participants could volunteer to take part in the one week EMA study. and were trained how to use the PDA. They completed an assessment on the PDA in the lab to ensure participants were able to comply with instructions contained in the assessment. They took the PDA home and completed up to four RAs on the PDA each

day. Compliance, defined as the proportion of RAs presented for which the subject initiated an assessment, was 80.1% (across all subjects and days) (Waters et al., 2014).

Participants also completed participant-initiated assessments. They initiated an assessment any time they experienced a temptation to smoke, with temptation being defined as an occasion when they "felt an acute increase in the desire to smoke, or an occasion when they felt they came to the brink of smoking without actually smoking" (Waters et al., 2014). Participants initiated this assessment by pressing a button labelled "temptation or lapse assessment" on the PDA home screen. They were also instructed to initiate this assessment if they lapsed. (As noted earlier, data from lapse assessments were not analyzed). Participants returned the PDA at Week +1.

Treatment

Participants received self-help manual containing relapse prevention/coping skills. All participants received the same treatment and treatment outcomes are not examined for the current study aims and analysis. At each laboratory visit, they also received brief (15-20 minute) individualized smoking cessation counseling from a licensed counselor based on standard approaches described in Treating Tobacco Use and Dependence Clinical Practice Guideline (U.S. Department of Health and Human Services, 2008). At Week +2 and Week +3, participants also received two brief telephone-counseling sessions.

MEASURES

EMA Measures

Participants self-reported their level of craving and stress using single items on the PDAs at both RAs and participant-initiated assessments. Craving was assessed using a 7-point as follows: "I am craving a cigarette"; 1=strongly disagree to 7=strongly agree.

Stress (“right now”) was assessed as follows: “Right now”; “I am stressed”; 1= not stressed at all to 7= extremely stressed (Waters et al., 2014).

Negative affect was measured using seven items where four items were positively oriented (relaxed, happy, enthusiastic, overall feeling (strongly negative to strongly positive)) and 3 items were negatively oriented (angry, sad, bored). The positive items were reverse scored in order to produce an overall measure of negative affect (alpha = .92). Higher scores on the negative affect composite score indicate higher levels of negative affect. Over all assessments, subjective reports of stress and negative affect correlated highly at r = .68.

Smoking Measures

Participant’s recent smoking behavior was queried at each EMA assessment. Participants indicated whether they had smoked that day (“Smoked so far today?”; 2 response options: “Yes” or “No”). A second item asked how long it had been since the last cigarette (“Time since last cigarette?”; 4 response options: “Just smoked/smoking now”, “5-30 minutes”, “31 minutes to 2 hrs”, “greater than 2 hours”). Smoking “so far that day” was also assessed at each lab visit.

To verify reports of abstinence, CO levels in exhaled breath were used using a CO monitor (Vitalograph, Lexena, KS) (SRNT Subcommittee on Biochemical Verification, 2002). A breath CO level of less than or equal to 10 parts per million (ppm) was required to be considered abstinent for post-quit visits (Week +1, Week +4).

PDA Hardware and Software

A HP iPAQ Pocket PC was used to present the assessments. The iPAQ used a pen-based, touch-screen system. Participants did not need to have any computer skills to

use the PDA or program. Participants could not access any other functions on the PDA. Participants were given a carrying case.

The software was written by Terminal C, a Houston-based company. The program was written in C#.NET. Participants were able to set a "Wake up" and "Bedtime" on each day. Using the wake-up time and bed time on each day, the program divided the day into four equal "periods", and an RA was scheduled at a random time during each period. As described earlier, participants could also self-initiate assessments. Participants could prevent the PDA from presenting RAs for up to 2 hours using a "suspend" function, and they could delay RAs by 5 minutes (up to three times per RA). The delay function was incorporated to allow participants to briefly delay an assessment if they were busy at that moment but would be available in the near future.

DATA ANALYSIS

Data presented in this paper were gathered as part of the parent study (Waters et al., 2014). Of the 231 participants who had the opportunity to participate in the EMA study 129 volunteered for the EMA study, and 120 provided data. Two PDAs were reported by participants as being stolen, and data from seven participants were lost due to participant error (failure to charge the PDA) or due to researcher error (Figure 2).

The primary analyses focused on assessments that occurred on days in which there was no reported smoking. A day was designated as an "abstinent day" if the participant reported that 1) they had not smoked so far that day on the "Smoked so far today" item, and 2) they endorsed "> 2 hours" on the "Time since last cigarette" item. Data were excluded if participants reported smoking so far that day at lab visits occurring

on the Quit Day visit. Similarly, data on quit day were excluded if CO level were high on Quit Day (> 11 ppm).

Using the above criteria, a total of 105 participants reported at least 1 day of abstinence, and these 105 participants completed 1377 RAs and 266 TAs. Linear mixed models (LMM) were used for analyses using SAS PROC MIXED. LMM analyses account for the dependence between assessments due to clustering of data by subjects, and LMMs also allow subjects to have different numbers of assessments (Waters et al., 2014). As is common in EMA analyses, we used a random (subject-specific) intercept and a first order autoregressive model for the errors (residuals) within subjects. For all models, we used a random (subject-specific) intercept and an autoregressive model of order 1 for the residuals within subjects. Day in study (continuous variable) was included in all models as a covariate. For all hypotheses, the two dependent variables, stress and negative affect, were tested in separate models. Parameter estimates were reported as an (unstandardized) measure of effect size (Wilkinson, 1999). Standardized effect sizes were computed as r (computed from t value (Kashdan & Steger, 2006)).

For Aim 1, the primary independent variable was Assessment Type (TA vs. RA; a within-subject variable) which was allowed to vary across subjects (random slope). Following Hedeker et al. (2009), a term capturing the proportion of completed assessments that were TAs (i.e., no. of TAs divided by total number of assessments, a subject-level variable) was included in these models. This ensures that the parameter estimate for Assessment Type provides the within-subject effect (Hedeker & Gibbons, 2006).

For Aim 2, the primary independent variable was Time before TAs (a categorical variable), which was divided into three bins: RAs occurring within 2 hrs before a TA (n=48 RAs); RAs occurring 2-4 hrs before a TA (n=34 RAs); and RAs occurring more than 4 hrs before a TA (henceforth referred to as "Control RAs"). (Assessment Type was not included as an independent variable in this analysis, because all data derive from RAs.) LMMs compared stress/negative affect for the following comparisons: RAs < 2 hrs vs. Control RAs; RAs 2-4 hours before a TA vs. Control RAs. Two-hour bins (vs. 1 hour bins) were used to increase the number of available RAs for analysis in each time bin. Time (binary variable) was treated as a fixed effect in these analyses; results did not differ if it was treated as a random effect.

For Aim 3, the primary independent variable was Time after TAs (a categorical variable), which was divided into three bins: RAs occurring within 2 hrs following a TA (n=69 RAs); RAs occurring 2-4 hrs following a TA (n=55 RAs); and RAs occurring more than 4 hrs following a TA ("Control RAs"). LMMs compared stress/negative affect for the following comparisons: RAs < 2 hrs vs. Control RAs; RAs 2-4 hours after a TA vs. Control RAs. Time was treated as a fixed effect in these analyses; results did not differ if it was treated as a random effect.

CHAPTER 5: RESULTS

MANIPULATION CHECK

First, a manipulation check was performed to examine whether reported craving was higher at TAs than at RAs. Reported craving was higher at TAs vs. RAs, *PE*=1.10, *SE*=0.15, $p<.001$, $r=.66$ (Figure 3).

Aim 1

Using LMM, both stress and negative affect were elevated at TAs (vs. RAs) with moderate-to-large effect sizes (see Table 3, Figures 4-5).

Aim 2

Using LMM, stress at RAs occurring less than 2 hours prior to a TA was compared to stress at Control RAs (Table 3, Figure 6). Stress at RAs < 2 hours before a TA was higher than stress at Control RAs. Stress at RAs occurring 2-4 hours prior to a TA was also compared to stress at Control TAs. In contrast to the prior analysis, stress at RAs occurring 2-4 hours prior to a TA was not higher than at Control RAs.

The results were similar when using negative affect as the dependent variable (Table 3, Figure 7). That is, negative affect at RAs < 2 hours before a TA was higher than negative affect at Control RAs. Negative affect at RAs occurring 2-4 hours prior to a TA was also compared to negative affect at Control TAs. Negative affect at RAs occurring 2-4 hours prior to a TA was not higher than negative affect at Control RAs.

Aim 3

Using LMM, stress at RAs occurring less than 2 hours following a TA was compared to stress at Control RAs (Table 3). Stress at RAs < 2 hours following a TA was not higher than at Control RAs. Stress at RAs occurring 2-4 hours following a TA was

also compared to stress at Control TAs. Stress at RAs occurring 2-4 hours following a TA was not higher than at Control RAs.

The results were similar when using negative affect as the dependent variable (Table 3, Figure 8). Negative affect at RAs < 2 hours following a TA was not higher than negative affect at Control RAs. Negative affect at RAs occurring 2-4 hours following a TA was also compared to negative affect at Control TAs. Negative affect at RAs occurring 2-4 hours following a TA was not higher than negative affect at Control RAs.

CHAPTER 6: DISCUSSION

The main findings of this study were as follows. First, as expected, reported stress and negative affect were higher at temptation episodes than at random assessments. Second, stress and negative affect were elevated in the 2-hr period prior to temptation episodes, suggesting that elevated stress and negative affect may predate and precipitate temptation episodes. Third, there was no evidence that stress and negative affect were elevated after a temptation episode. Each of these findings is discussed further below.

The results of Aim 1 provide strong evidence that participants experience elevated stress/NA at temptation assessments compared to random assessments. This finding is consistent with previous literature reviewed earlier where participants reported elevated stress/NA at temptation assessments compared to random assessments (Heckman et al., 2013; Shiffman, Gnys, et al., 1996).

The results for Aim 1 indicate there is an association between stress/NA and assessment type but they do not reveal the direction of the relationships. That is, they do not reveal whether stress/NA provoke temptations, or whether temptations provoke stress/NA.

The results of the analyses examining Aim 2 indicate that stress/NA were elevated in the hours immediately preceding a temptation episode during periods of attempted abstinence, which indicates that the elevations in stress/NA may provoke temptations. These results indicate increases in stress/NA over the timescale of a couple of hours may increase the likelihood of experiencing a temptation to smoke.

These results suggest it may be useful to monitor stress/NA during EMA in a cessation attempt. As stress/NA increase, it may then be possible to intervene in that

moment ("ecological momentary intervention") to reduce the stress/NA. Interventions that reduce stress/NA may improve cessation rates by reducing the likelihood of experiencing temptation episodes.

Aim 3 examined whether temptation episodes provoke stress/NA during periods of attempted abstinence. The results did not support the hypothesis that episodes of temptation result in increased levels of stress/NA. These results therefore run counter to those from laboratory and EMA studies noted earlier that suggest that the induction of craving can increase negative affect (Drobes & Tiffany, 1997; Warthen & Tiffany, 2009).

A number of factors may account for the non-significant results for Aim 3. First, participants undergoing this cessation attempt were receiving clinician support in learning skills and developing strategies on how to handle periods of temptation and craving. While the results indicate that periods of temptation are not associated with subsequent increases in stress/NA, this may be the result of participants being able to successful deploy coping strategies in the midst of a temptation episodes. In other words, the therapy that participants received may have attenuated the ability of temptation episodes to elicit stress and negative affect.

Second, temptation episodes may acutely increase negative affect, but the effect dissipates quickly over time, making it difficult to detect an effect in the two hours following a temptation episode. In contrast, in laboratory studies the effect of the craving manipulation on reported negative affect is typically assessed fairly soon after the manipulation, i.e., in the timescale of minutes rather than hours. This was also true for the CREMA studies reviewed earlier (Warthen & Tiffany, 2009), and suggests one reason for why the results from the current study may differ from these earlier EMA studies.

Moreover, the effect of (participant-initiated) temptations on negative affect may differ from that of cue-induced craving, which is induced by the experimenter. Future research could investigate this issue by combining the CREMA methodology with that used in current study.

Third, participants in the current study were motivated to quit smoking. Motivation level of participants may have significant impact on how craving/temptations influence stress/negative affect (and vice versa). In contrast, in the laboratory studies reviewed earlier, participants were generally not motivated to quit.

LIMITATIONS

The study has a number of limitations. Because biological measures of smoke exposure were not taken each day it is difficult to verify reported abstinence. We relied on participant self-report in order to verify abstinence and to subset to days with no reported smoking. Without biological data, there is therefore some uncertainty as to whether participants were truly abstinent on all the days analyzed.

Second, there was a relatively small number of RAs occurring before and after a temptation. This limited the power to detect differences over time. Therefore, results from all Aims, and Aim 3 in particular, should be treated with caution.

Third, to reduce burden, data were not collected on the "start time" and "end time" of temptations. Thus, there is some uncertainty as to when a temptation episode actually started, meaning that its onset could have occurred prior to the subject entry, potentially complicating interpretation. This point notwithstanding, in previous studies the average duration of temptations has been fairly brief. For example, Shiffman et al. (1996) reported a mean temptation duration of around 16 minutes, and the median

duration is likely to be briefer than this value (which is likely inflated by a few long temptation episodes).

Fourth, the study focused on temptation episodes and did not examine relationships with specific relapse episodes. As noted earlier, this focus was in part due to the fact that laboratory studies have mainly focused on craving as an outcome variable. In addition, as noted earlier, temptations are an important outcome in their own right.

Fifth, as noted earlier some participants did not report any temptations. The results therefore only generalize to participants who report temptations during the first week of a quit attempt.

Sixth, the study had a number of limitations shared by all EMA studies. There is the possibility that the act of assessment itself causes changes in the processes being measured, a phenomenon known as "reactivity." As described elsewhere, reactivity could potentially complicate data interpretation (Shiffman et al., 2008). Futhermore, EMA data are correlational. That is, although stress/NA precede temptations, the study does not demonstrate a causal relationship between stress/NA and temptations. A third variable may be causing both stress/NA and, somewhat later, temptation episodes. That said, data from experimental studies conducted in the laboratory reviewed earlier bolster confidence that the association between stress/NA and temptations is causal. In common with all EMA studies, given that participants did not respond to all RAs, there is potential for bias in the analyses. For example, participants may be less likely to respond to RAs when feeling stressed (i.e., non-response to RAs is related to the value of the dependent variable at the time of non-response). If this were true, this effect would tend to reduce

levels of stress/NA at RAs. However, it is not clear why non-response should influence patterns of stress/NA over time.

Last, in common with all studies using temptation episodes, it is difficult to validate reports of these self-initiated assessments. It is not known how many times the participants consciously felt tempted, but elected not to enter a TA. Therefore, there is uncertainty whether the number of TAs reported during EMA reflect the "true" number of temptation episodes. There is also uncertainty as to whether self-reported TAs in the field are truly representative of tempted moments. It might be useful to consider the number of temptation episodes as a lower bound estimate of the "true" number of temptation episodes.

STRENGTHS

The study also had strengths. The study examined precipitants of temptation episodes during a highly vulnerable period (the first week during smoking cessation) using EMA. As noted earlier, the majority of individuals attempting to quit experience some kind of lapse in the first week of a quit attempt. Participants were also trying to quit without using medication, which is the case for the majority of attempts to quit smoking.

Moreover, although previous studies have reported that negative affect is higher just before a temptation episode than at random assessments (e.g., Shiffman et al., 1996), this study is the first to provide a timeline of antecedents and consequences of temptation episodes by assessing negative affect "right now". This methodology thereby minimized the role of recall bias meaning that the assessment method (assessing "right now") was the same for random assessments and temptation assessments. This study also provided a

complimentary approach to previous lab studies by investigating subjective experiences of stress/NA before and after temptations episodes in the field.

CONCLUSION

The results of this study indicated that elevated stress/NA affect could result in subsequent periods of temptation. In contrast, there was no evidence that temptation results in increases in stress/NA over the timescale of a few hours. However, it is still possible that temptation acutely increases stress/NA during the temptation episode itself, or for a brief period thereafter.

The results have clinical implications. First, it would mean that cessation programs that focus on reducing affect/stress management may reduce the occurrence of temptations, and, perhaps, improve cessation rates. Second, as noted earlier, interventions could be administered "just in time" (ecological momentary intervention) when stress/NA are elevated. Third, there is no evidence to suggest that interventions that reduce the occurrence of temptations will reduce stress/NA over the timescale of a few hours.

FUTURE DIRECTIONS

Future studies should continue to investigate how changes in stress/NA during a cessation attempt predict subsequent temptations. Other variables which are theoretically related to temptations could also be examined. For example, in the current dataset, attentional bias was assessed during EMA and researchers could examine whether it is elevated before and after temptations. Future studies could also assess self-reported exposure to smoking cues (such as the presence of other smokers), and examine if cue exposure is elevated prior to temptations. Research could also examine the joint influence of smoking and affective cues.

Future studies with more intensive or targeted assessment schedules and/or more subjects could examine the time course of changes in stress/negative affect with greater granularity (e.g., hour-by-hour, or in 30-min blocks). Future studies using more assessments should also examine the psychological mechanisms underlying the association between stress/NA and temptations and relapse. For example, stress and negative affect may deplete resources and undermine other adaptive coping mechanisms (Shiffman & Waters, 2004).

Researchers of the current study chose to subset to days where there were no reported lapses and only conducted analysis using temptations. It may be useful to utilize lapses in future analyses using other, larger, datasets since relapse is the occurrence of most importance in cessation studies. Ultimately, further research of variables that are predictive of temptations and relapse can help researchers develop a predictive algorithm capable of identifying periods of heightened relapse risk. This algorithm could be applied to real life situations to shift to provide ecological momentary interventions to improve cessation rates.

Table 1A: Lab Studies

Author/Year	**IV→ DV**	**Participants**	**IV**	**DV**	**Results**	**Discussion**
Tiffany and Drobes (1990)	NA → Craving	60 smokers, 37 male and 23 female	Imagery scripts: 5 types (positive affect-urge, negative affect-urge, positive affect, negative affect, and neutral affect)	Vividness, Urge/craving	Negative affect, positive affect-urge, negative affect-urge increased levels of urge/craving.	Scripts with smoking/urge cues exerted highest influence-regardless of affect type. NA scripts elicited higher craving than PA or neutral scripts
Shiffman et al. (2013)	NA → Craving	207 smokers (57% men), no intention of quitting	Cue set (6-levels: cigarettes, PA, NA, alcohol, smoking prohibitions, and neutral)	Craving (QSU), smoking behavior, Affect Mood Form	NA cue set did not increase craving. Smoking cues significantly increased craving. PA cue set decreased craving.	Proximal smoking cues increased craving. NA had no significant effect on smoking behavior.
Heckman et al. (2013)	NA → Craving (Meta-analysis)	27 studies: average of 31.30 y/o, 57% male, smoked 20.60 CPD, FTND=5.26	Manipulation of PA and NA	Post-manipulation craving	NA manipulations yielded medium effects for inducing cravings to smoke. No effect was observed for PA inductions.	NA manipulation increased craving, but at a smaller magnitude than smoking cues.

Drobes and Tiffany (1997)	Craving → NA	100 smokers, 50 men and 50 women	Imaginal exposure: urge and neutral scrips In-vivo exposure: urge and neutral	Urge rating scale- 11 items. PA and NA - 1 item, 100 pt scale	Urge trials associated with significantly greater urge ratings. Sig. main effect for urge content on NA and PA.	Abstinence increased urge across both urge and neutral conditions.
Heishman, Lee, Taylor, and Singleton (2010)	Craving → NA	60 smokers, 30 men and 30 women	Imaginal exposure: urge and neutral scrips In-vivo exposure: urge and neutral	Tobacco craving questionnaire-SF, Visual Analog Scales for mood/ craving,	Smoking imagery/ exposure increased craving and negative mood (> magnitude with in-vivo).	Manipulating craving resulted in increase of negative mood and decrease in positive mood.

Note: Selected laboratory studies that have examined the relationship between Stress/NA and Craving. NA = Negative Affect.

Table 1B: EMA Studies

Author/Year	IV→ DV	Participants	IV	DV	Results	Discussion
Shiffman et al. (1996a)	NA → Craving	108 who quit smoking for 24 hours	Assessment Type (temptation vs. random assessment)	Subjective states: NA, attention, arousal, restless, hunger Social setting, location, activities	NA higher just prior to temptation episodes than at random assessments	NA elevated just prior to temptation episode during quit attempt, but data are slightly retrospective
Shiffman et al. (1996b)	NA → Craving	151 who quit in another study: 116 lapsed and 35 maintained abstinence; 88 women, 63 men	Assessment Type (temptation vs. random assessment) by Relapse Status (maintainer vs. relapse)	Subjective states: NA, attention, arousal, restless, hunger Social setting, location, activities,	Temptation and random assessments differed on urge, NA, restlessness, environmental smoking, and consumption of food/drink	Temptation vs. random assessment difference does not differ between lapsers and maintainers.
Warthen and Tiffany (2009)	Craving → NA (CREMA)	43 (24 men/19 women) regular smokers	2 (neutral and smoking cues) x 2 (photographs and imagery scripts) x 2 (before and after cue presentation)	Craving: Questionnaire of Smoking Urges. Single-item PA & NA	Smoking stimuli produced significantly stronger craving than neutral stimuli. NA was higher and PA was lower on smoking trials than on neutral trials.	Proof of concept of CREMA procedures. Cue-elicited craving similar in magnitude between lab and field assessments. .

Wray, Godleski, and Tiffany (2011)	Craving → NA (CREMA)	68 (27 male/ 41 female) regular smokers	2 (neutral and smoking cues) x 2 (photographs and in-vivo cues)	Craving: QSU. Single item PA & NA	NA ratings were significantly higher after smoking cues than after neutral cues. PA did not differ as a function of cue type or mode of presentation	CREMA results mirrored findings of previous lab studies. Magnitude of cue-reactivity effects at least as great as the effects generated in the laboratory.

Note: Selected EMA studies that have examined the relationship between Stress/NA and Craving. NA = Negative Affect.

Table 2. Inclusion and Exclusion Criteria

Inclusion	Exclusion
Age 18-65	Active substance abuse or dependence (other than nicotine)
Smoke at least 10 cigarettes per day	Regular use of tobacco products other than cigarettes
Have a home address	Use of nicotine replacement products or smoking cessation medication
Have a functioning home telephone	Live with another person enrolled in the study
Be able to speak, read, and write in English at an eighth-grade level	Self-reported color-blindness
Report English is the first language	Expired breath carbon monoxide <10ppm
	Pregnant or breast feeding
	Current suicidal ideation or depression

Table 3. Results of Linear Mixed Models of Study Aims 1, 2, and 3.

Aim	DV → IV ↓	H	n_1	n_2	Stress *df*	Stress *PE*	Stress *SE*	Stress *F*	Stress *p*	Stress *r*	Negative Affect *df*	Negative Affect *PE*	Negative Affect *SE*	Negative Affect *F*	Negative Affect *p*	Negative Affect *r*
1	TA vs. RA	1	1638	105	1, 70	0.47	0.12	15.1	<.01	.42	1, 70	0.32	0.08	17.0	<.01	.44
2	Proximal vs. Control	2	1341	105	1, 1234	0.40	0.16	5.97	<.05	.28	1, 1235	0.20	0.10	4.03	<.05	.23
	Distal vs. Control	2	1327	104	1, 1221	0.05	0.19	0.08	*Ns*		1, 1222	-0.11	0.11	1.04	*ns*	
3	Proximal vs. Control	3	1317	105	1, 1210	-0.07	0.13	0.32	*Ns*		1, 1211	-0.06	0.09	0.65	*ns*	
	Distal vs. Control	3	1031	104	1, 1195	0.16	0.14	1.07	*Ns*		1, 1196	0.08	0.09	0.97	*ns*	

Table Note: Data are results of linear mixed models. n_1 = no. assessments; n_2 = number of subjects. H = Hypothesis; *PE* = parameter estimate; *SE* = standard error; *F* = F value from LMM; *r* = measure of effect size (computed using methods of Kashdan and Steger, 2006, for significant effects, with *df*=70); *ns* = non-significant. Data shown reflect analyses using all subjects (*N*=105); results are similar when subsetting to participants who complete at least one TA (*n*=70).

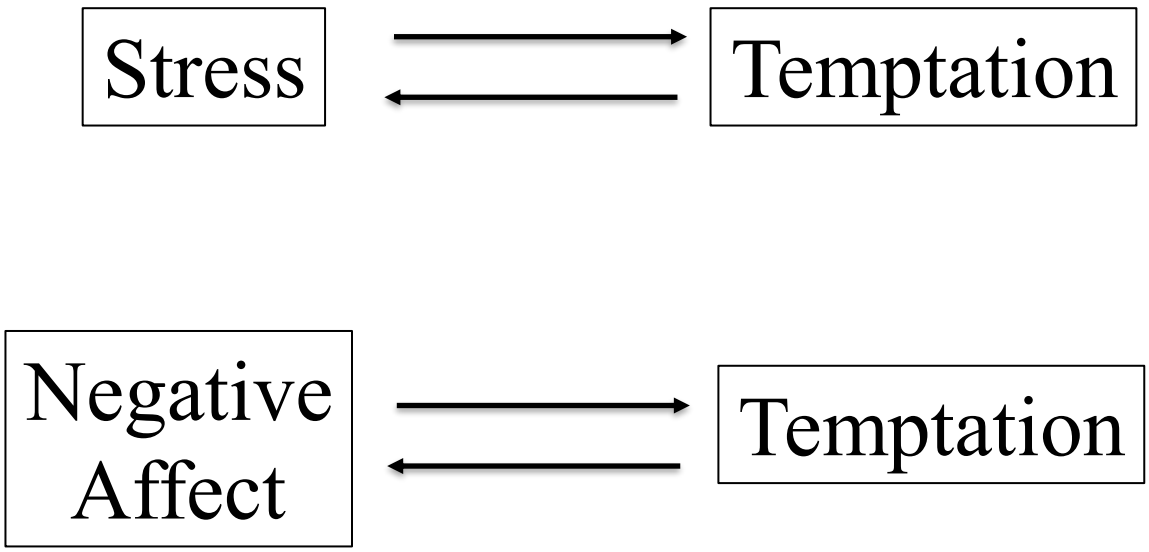

Figure 1. Conceptual model displaying theorized relationship between temptation and stress/NA.

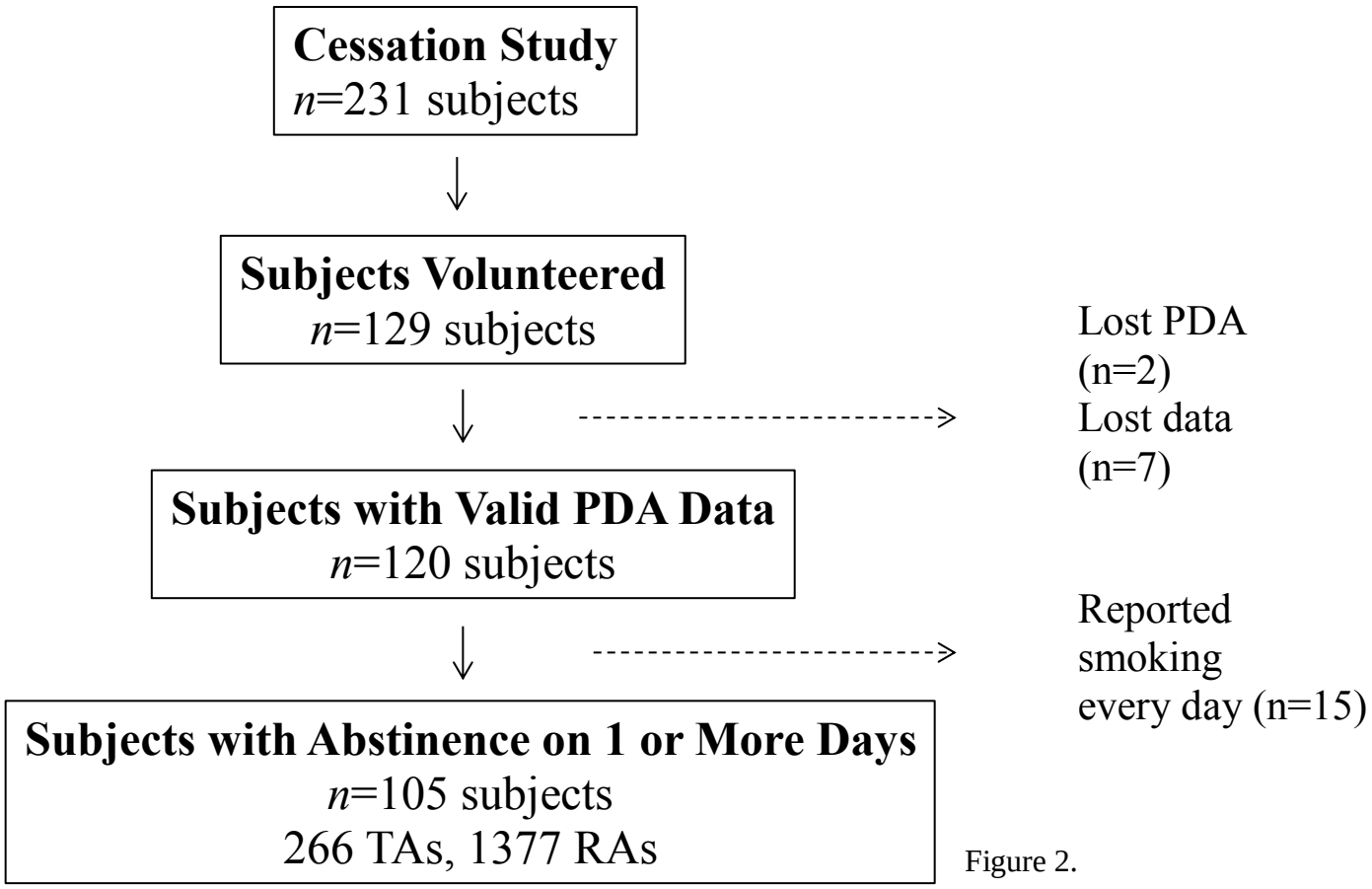

Figure 2.

Consort chart

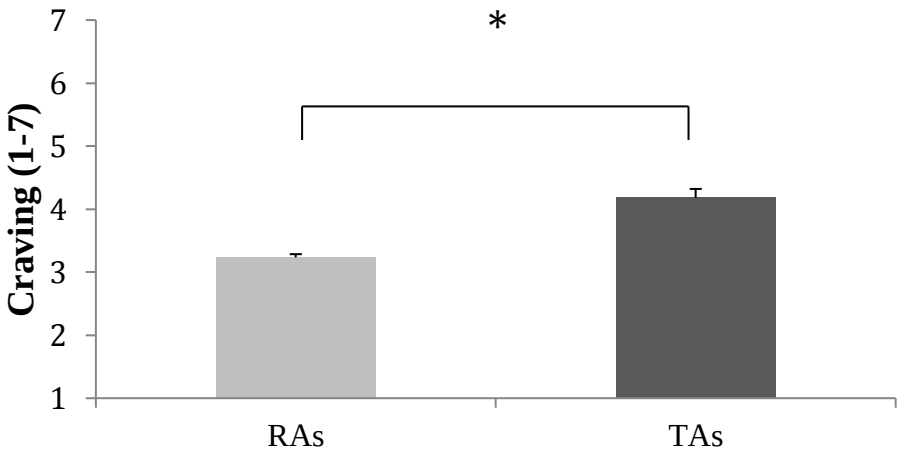

Figure 3. Effect of Assessment Type on Craving. Data are Mean (± 1 S.E.), *p < .01

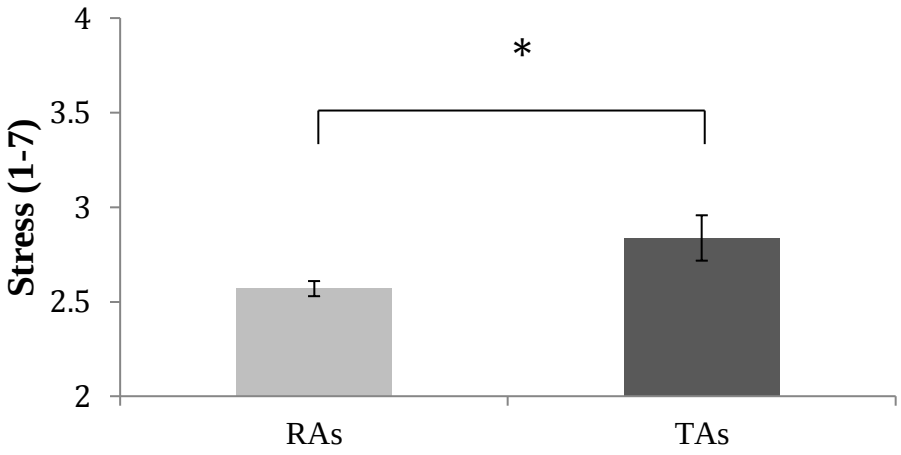

Figure 4. Stress at RAs compared to stress at TAs. Data are Mean (± 1 S.E.), *p < .01

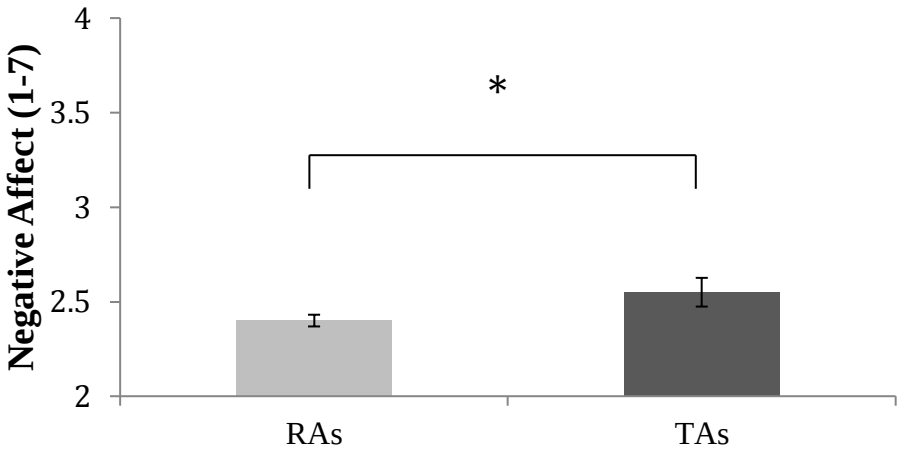

Figure 5. Negative affect at RAs compared to negative affect at TAs. Data are Mean (± 1 S.E.), *p < .01

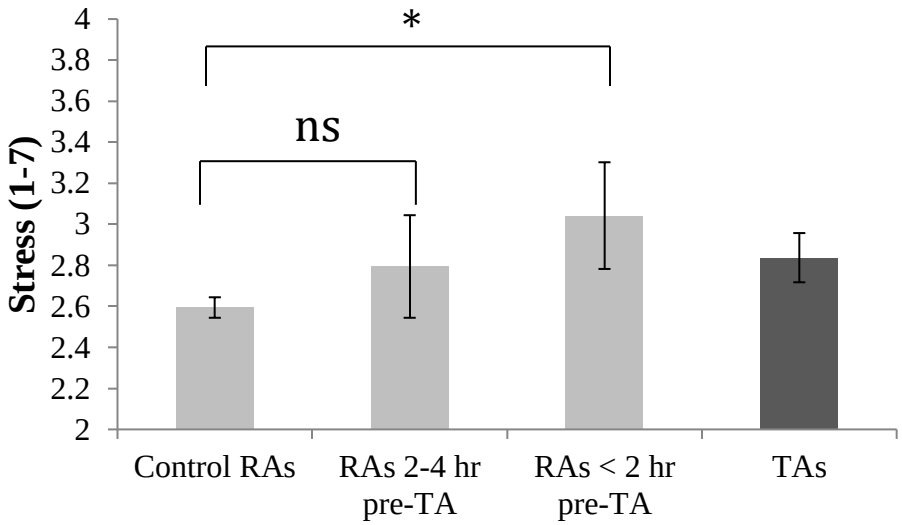

Figure 6. Stress before TAs. Data are Mean (± 1 S.E.), *p < .05

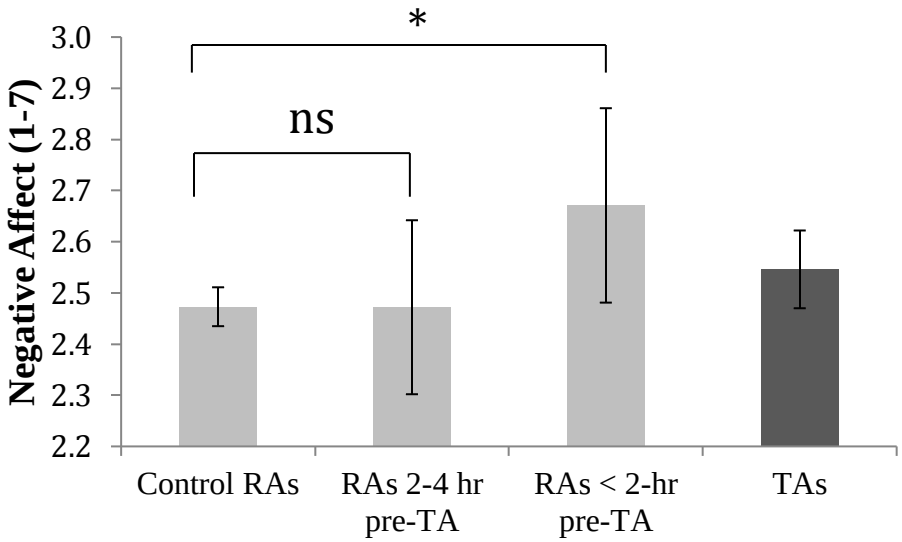

Figure 7. Negative affect before TAs. Data are Mean (± 1 S.E.), *p < .05

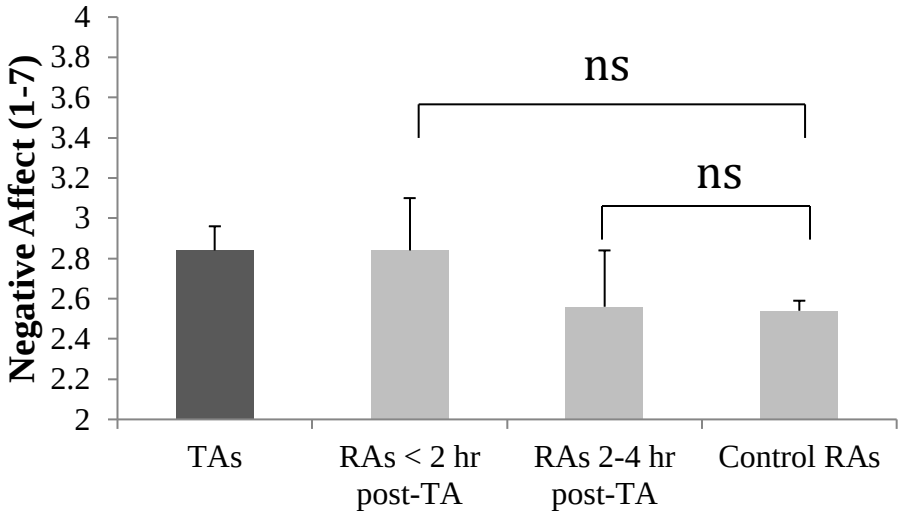

Figure 8. Negative affect after TAs. Data are Mean (± 1 S.E.).

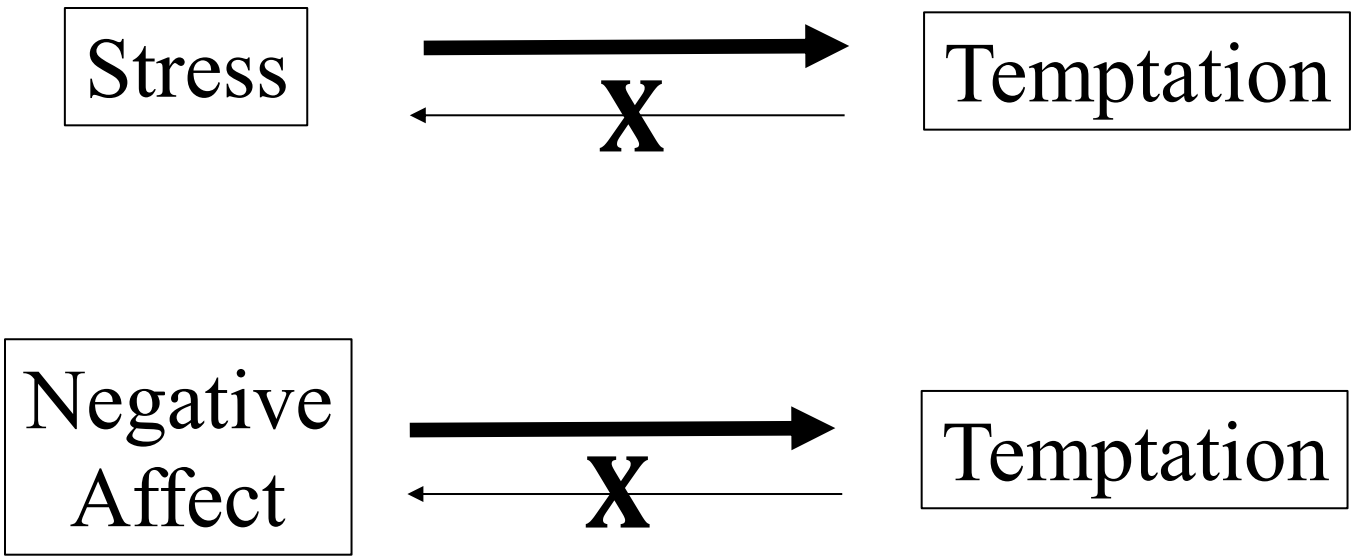

Figure 9. Conceptual model depicting relationship supported from this study

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Appendix A: USUHS IRB Approval

UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES
4301 JONES BRIDGE ROAD
BETHESDA, MARYLAND 20814-4799

September 8, 2009

MEMORANDUM FOR DR. ANDREW WATERS, PH.D., MEDICAL AND CLINICAL PSYCHOLOGY

SUBJECT: Uniformed Services University Institutional Review Board (FWA 00001628; DoD Assurance P60001) Approval regarding Human Subjects Research Protocol G172JY.

Congratulations! The amendment for your No More Than Minimal Risk human subjects research protocol G172JY, entitled "*Cognitive Processes in Smoking Cessation,*" was reviewed and approved for execution on Tuesday, September 8, 2009 by Edmund G. Howe III, M.D., J.D., Chairperson, Uniformed Services University IRB, under the provisions of 32 CFR 219.110(b)(2). This approval will be reported to the full Uniformed Services University IRB scheduled to meet on Thursday, October 15, 2009.

The purpose of this behavioral research study is to find out which types of smokers are in need of more help with quitting smoking.

This action approves amendment #5 that: (1) adds two study personnel (CITI complete 7/18/09 and 8/13/09); (2) revises recruitment numbers up to 250 to account for participants who sign the ICD but are later deemed ineligible; (3) makes minor revisions to the ICD regarding compensation; and (4) adds venues for study advertisements (utilizing the previously approved advertisements).

Authorization to conduct protocol G172JY will automatically terminate on Tuesday, January 5, 2010. You are authorized to enroll up to 250 subjects in this study. If you plan to continue data collection or analysis beyond this date, IRB approval for continuation is required. Please submit a USU Form 3204A/B (application for continuing approval) to the IRB Office 60 days prior to the termination date. The IRB Office will attempt to assist you by sending you a reminder; however, submission of an application for continuation is your responsibility. Please note the termination date and the date for submission of your USU Form 3204A/B in your calendar!

You are required to submit amendments to this protocol, changes to the informed consent document (if applicable), adverse event reports, and other information pertinent to human research for this project to this office for review. No changes to this protocol may be implemented prior to IRB approval. If you have questions regarding this IRB action, or questions of a more general nature concerning human participation in research, please contact the undersigned at mstretch@usuhs.mil or (301) 295-0819.

Micah Stretch, M.A., J.D.
IRB Coordinator

cc: Chair, MPS
VPR/OSP
File

Appendix B: MDACC Approval of Data Transfer

THE UNIVERSITY OF TEXAS
MD ANDERSON
CANCER CENTER
Office of Protocol Research

Institutional Review Board (IRB)
Unit 1437
Phone 713-792-2933
Fax 713-794-4589

To: Paul Cinciripini 03/31/2009
From: Marion B. Olson
CC: Sunetra Martinez, Victoria L. Brown, Evanna L. Thompson, Veronica Roberts
MDACC Protocol ID #: 2005-0741
Protocol Title: Cognitive Processes in Smoking Cessation
Version: 13

Subject: Administrative IRB Approval – Protocol 2005-0741

On Tuesday, 03/31/2009, the Institutional Review Board (IRB) 4 chair or designee reviewed and approved your revision dated 03/27/2009 for Protocol 2005-0741

These Pages Include:

- Protocol Body – Document header Date: 03/27/2009

Revision included the following changes:
Clarifying that the de-identified data will be sent to Dr. Andrew Waters and his statistical team at the Uniformed Services University of the Health Sciences.

Additional Revision History:
Please note that along with this revision the M. D. Anderson IRB approves the transfer of de-identified study data for analysis to Dr. Andrew Waters, collaborator on this study, and his statistical team at the Uniformed Services University of the Health Sciences.

The revision can now be implemented. Please inform the appropriate individuals in your department or section and the collaborators of these changes.

Please inform the appropriate individuals in your department/section and your collaborators of these revisions.

Please Note: This approval does not alter or otherwise change the continuing review date of this protocol.

In the event of any questions or concerns, please contact the sender of this message at (713) 792-2933.

Marion B. Olson 03/31/2009 10:02:17 AM

This is a representation of an electronic record that was signed electronically and below is the manifestation of that electronic signature:

Marion B. Olson
03/31/2009 09:51:14 AM

IRB 4 Chair Designee
FWA #: IRB 4 IRB00005015

Appendix C: Study 2 - USUHS Informed Consent Form

This consent form is valid only if it contains the IRB stamped date

Consent for Voluntary Participation in a Non-Clinical Research Study

1. INTRODUCTION OF THE STUDY

You are being asked to be in a research study entitled, "Cognitive Processes in Smoking Cessation", at the Uniformed Services University (USU), Bethesda, Maryland. You have been asked to take part in this study because you are a smoker, and you want to quit smoking. Your participation is voluntary. Refusal to participate will not result in any punishment or loss of benefits to which you are otherwise permitted. Please read the information below, and ask questions about anything you do not understand, before deciding whether to take part in the study.

2. PURPOSE OF THE STUDY

The purpose of this behavioral research study is to find out which type of smokers are in need of more help with quitting smoking. This study may help researchers create more effective cessation (quitting) programs. Researchers want to learn the reasons why some smokers who quit smoking choose to start up again (relapse) more quickly than other smokers. Also, researchers want to use computerized tasks to help predict who is likely to relapse.

Other studies have shown that some computerized tasks are helpful in determining which smokers are likely to relapse more quickly. We want to carry out more research using additional tests.

3. PROCEDURES TO BE FOLLOWED

If you agree to be in this study, you will be asked to attend a total of 6 sessions at USU. At the first session (orientation), you will complete a breath test that allows the investigators to know how much you smoke. You will also complete about 7 questionnaires, which will take a total of about 1 hour to complete. The questionnaires will ask about you and your health, your smoking habits, and your drinking habits. There will also be a brief reading test, which will take about 5 minutes to complete. It will check your reading ability. The orientation will help researchers learn if you are eligible to participate in this study.

If you are found to be eligible and you wish to take part in this study, you will attend 5 laboratory sessions at USU. You will attend 2 sessions before trying to quit, 1 session on your quit day, 1 session one week after your quit day, and a final session 1 month after your quit day. At each of these laboratory sessions, you will complete a series of computerized evaluations, which will take about 90 minutes to complete. These evaluations are reaction-time tests.

At the 2 pre-quit sessions, you will be asked to smoke a cigarette (after the computerized evaluation). Before one of these pre-quit sessions, which will be picked randomly, you will be asked to stop smoking for 12 hours before the session.

During each of the laboratory sessions, you will also complete about 7 questionnaires that ask about your mood, cigarette cravings, and smoking habits. These questionnaires will take about 30 minutes in total to complete at each session. You will also be asked to complete a breath test and to provide a saliva sample. The breath test and the saliva sample will help the researchers find out how much you have smoked.

You will also be called on 2 occasions after your quit day, and you will be asked some questions about your smoking. Each phone call will last about 15 minutes. During the study, a staff member will meet with you for 10 to 20 minutes and help you to try and quit. You will meet with the staff member at each of the laboratory sessions. Every participant will receive the same help.

Some participants will be asked to carry a handheld computer (PDA) around for 1 week after their quit day. The PDA will beep randomly about 4 times a day (random assessments). Participants will answer some questions about their mood and craving, and complete a computerized reaction time task. Each assessment takes about 5 minutes.

Participation in this study will be over after your final visit to USU, which will be 4 weeks after your quit day.

4. NUMBER OF PEOPLE THAT WILL TAKE PART IN THIS STUDY

Up to 250 subjects are expected to take part in this study at USU.

5. AMOUNT OF TIME FOR YOU TO COMPLETE THE STUDY

If you are eligible, you will be part of this study for about 7 weeks.

ELIGIBILITY AND PAYMENT FOR BEING IN THIS STUDY

Civilians and military personnel may be paid for participation in this study. Payments will be made after each visit, as described above.

Civilians (non-federal). You will receive $25 for completing the orientation (the first session). You will also receive $50 for completing each laboratory session. You will receive compensation after each session. You will also receive $15 for each telephone assessment that you complete, and you will receive this at the final laboratory session. Participants who carry around the PDA for a week will receive $2.50 for each random assessment that they complete.

Civilians (federal). You will only receive compensation for laboratory sessions/telephone assessments if those sessions occur during non-duty hours. In addition, if you wish to be compensated for participation during non-duty hours, you must file a request for outside activity. If
the request is approved and the sessions occur during non-duty hours, payment will be made as follows. You will receive $25 for completing the orientation (the first session). You will also receive $50 for completing each laboratory session. You will receive compensation after each session. You will also receive $15 for each telephone assessment that you complete (if those assessments occur during non-duty hours), and you will receive this at the final laboratory session. Federal civilians may participate in the PDA part of the study, but they can only be compensated for the PDA assessments that occur during non-duty hours.

Uniformed Personnel. You will only receive compensation for laboratory sessions if those sessions occur during non-duty hours. In addition, if you wish to be compensated for participation during non-duty hours, you must file a request for outside activity. If the request is approved and the sessions occur during non-duty hours, payment will be made as follows. You will receive $25 for completing the orientation (the first session). You will also receive $50 for completing each laboratory session. You will receive compensation after each session. You will also receive $15 for each telephone assessment that you complete (if those assessments occur during non-duty hours), and you will receive this at the final laboratory session. Uniformed personnel may participate in the PDA part of the study, but they can only be compensated for the PDA assessments that occur during non-duty hours.

Please Note: Federal Civilians and Uniformed Personnel should inform their supervisors about the study for which they are volunteering whether or not they will receive compensation.

At the orientation session, if you are ineligible for the study because the breath test indicates that you have low levels of carbon monoxide in your breath, the orientation session will end right away and you will receive $10 for your time and travel expenses. If you are ineligible for another reason, the session will last for a longer duration and you will receive $25 for your time and travel expenses. Payments to ineligible participants follow the same rules as those written above for the eligible participants.

7. POSSIBLE RISKS OR DISCOMFORTS FROM BEING IN THIS STUDY

The expected risks or discomforts from being in this study are expected to be minimal. There are no known risks associated with the computerized evaluations. On 1 pre-quit session, you will arrive having not smoked on that day. You may experience symptoms of nicotine withdrawal, which include restlessness, difficulty concentrating, and/or mood changes. You will also smoke a cigarette at each of the pre-quit visits. Though smoking is considered bad for your health, your smoke intake is not likely to be increased by participating in this study. (Your smoke intake is likely to be decreased by participating in the study).

You may refuse to answer any question that makes you feel uncomfortable. If you have concerns after completing the questionnaires, you are encouraged to contact your doctor or the study chair.

If something in this research makes you uncomfortable or upset, you may choose to stop taking part in this research at any time without loss of benefits; you may contact the investigator for referral. If the investigators note any distress or anxiety associated with the research, you will receive referrals, if appropriate.

POSSIBLE BENEFITS FROM BEING IN THIS STUDY

You may benefit from this study because if you are able to quit, this may be very beneficial to your health. Future smokers may benefit from what is learned. The information we learn may help us learn to develop better smoking cessation programs.

However, no benefit can be guaranteed.

9. CONFIDENTIALITY/PRIVACY AND HOW YOUR IDENTITY AND YOUR RESEARCH RECORDS WILL BE MAINTAINED

All information you provide as part of this study will be confidential and will be protected to the fullest extent provided by law. Your responses to our interviews and questionnaires, as well as audio-taped sessions will be maintained in a locked filing cabinet in lab offices in the Department of Medical and Clinical Psychology. All records related to this study will be accessible to those persons directly involved in conducting this study and members of the USUHS Institutional Review Board (IRB), which provide oversight for protection of human research volunteers. In addition, the IRB at USUHS and other federal agencies that help protect people who are involved in research studies, may need to see the information you give us. Other than those groups, records from this study will be kept private to the fullest extent of the law. Scientific reports that come out of this study may include your ideas, but they will not use your name or identify you in any way.

10. CONDITIONS WHICH YOUR PARTICIPATION IN THIS STUDY MAY BE STOPPED WITHOUT YOUR CONSENT

The investigator may stop you from taking part in this study if being in the study is unsafe or dangerous to you or if you lose your right to receive medical care at military hospitals. The investigator may also stop you participating if you experience difficulty in following the procedures.

11. IF YOU DECIDE TO STOP TAKING PART IN THIS STUDY AND THE INSTRUCTIONS FOR STOPPING EARLY

You have the right to withdraw from this study at any time. If you decide to stop taking part in this study, you should tell the principal investigator as soon as possible; by leaving this study at any time, you in no way risk losing your right to medical care.

12. RECOURSE IN THE EVENT OF INJURY

If at any time you believe you have suffered an injury or illness as a result of participating in this research project, you should contact the Director of Human Research Protections Program at the Uniformed Services University of the Health Sciences, Bethesda, Maryland 20814-4799 at (301) 295-9534. This office can review the matter with you, can provide information about your rights as a subject, and may be able to identify resources available to you. If you believe the government or one of the government's employees (such as a military doctor) has injured you, a claim for damages (money) against the federal government (including the military) may be filed under the Federal Torts Claims Act. Information about judicial avenues of compensation is available from the University's General Counsel at (301) 295-3028.

CONTACT FOR QUESTIONS OR PROBLEMS

If you have questions about this research, you should contact Andrew J. Waters, Ph.D. the person in charge of the study. His phone number at USUHS is 301 295-9675. Even in the evening or on weekends, you can leave a message at that number. If you have questions about your rights as a research subject, you should call the Director of Human Research Protections Program at USUHS at (301) 295-9534. She is your representative and has no connection to the researcher conducting this study.

SIGNATURE OF RESEARCH PARTICIPANT OR LEGAL RESPRESENTATIVE

You have read (or someone has read to you) the information in this consent form. You have been given a chance to ask questions and all of your questions have been answered to your satisfaction.

BY SIGNING THIS CONSENT FORM, YOU FREELY AGREE TO TAKE PART IN THE RESEARCH IT DESCRIBES.

_____ _____

Participant's Signature Date

_____

Participant's Printed Name

SIGNATURE OF INVESTIGATOR/RESEARCH TEAM MEMBER

You have explained the research to the participant, or his/her legal representative, and answered all of his/her questions. You believe that the volunteer subject understands the information described in this document and freely consents to participate.

_____

Investigator's/Research Team Member's Signature Date (must be the same as the participant's)

_____

Investigator's/Research Team Member's Printed Name

SIGNATURE OF WITNESS

Your signature as witness is intended to attest that the information in the consent document and any other information was explained to and apparently understood by the participant, or the participant's legal representative, that questions and concerns were addressed and that informed consent was freely given.

_____

Witness' Signature Date (must be the same as the participant's)

_____

Witness' Printed Name