Regulation of Craving: Stress and Anxiety in Cigarette Smokers

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Abstract

Consumption behaviors, when uncontrolled, can be both costly and deleterious. Stress is thought to play a role in consumption behaviors, including drug use, such as cigarette smoking. Craving is another factor that may lead to increased consumption of food and drugs. Stress may induce craving, while craving may hinder regulation of stress. To inform existing treatments for Substance Use Disorders, the effect of stress on regulation strategies drawn from cognitive behavioral therapy will be investigated as well. Using fMRI and the Regulation of Craving task combined with a threat-of-shock (TOS) paradigm, this study investigates the degree to which regulation of craving is impaired by stress and assesses its relationship to anxiety sensitivity in cigarette-smoking individuals. In this currently ongoing study, preliminary data analysis provides evidence that, when controlling for anxiety sensitivity, cognitive regulation and TOS both have significant effects on self-reported craving for cigarettes. However, contrary to our hypothesis, higher anxiety sensitivity is negatively correlated with craving and stress ratings. This may imply that anxious individuals do not experience more stress or craving explicitly, but in anticipation of any distress engage in consumption behaviors such as smoking as a maladaptive coping mechanism.

Keywords: Craving, regulation of craving, stress, nicotine dependence, anxiety sensitivity, TOS
Introduction

Uncontrolled consumption behaviors are deleterious for one’s health. For example, cigarette smoking affects the health of an estimated 36.5 million adults in the United States (CDC 2016) and causes 5.4 million deaths annually worldwide, making it the leading preventable cause of morbidity and mortality in developing nations (CDC, 2008). Importantly, one third of individuals who smoke develop Nicotine Dependence (ND; USDHHS 1994), a chronic and relapsing condition. Despite health repercussions, and although 70% of smokers actively want to quit, only 5% are successful (CDC 2008). Additionally, not only do cigarette smokers harm their own health, they also affect the health of those around them by means of secondhand smoke. Secondhand smoke has caused the deaths of approximately 2.5 million nonsmokers in the US since 1964 (USDHHS 2014). In regard to economic burden, estimated annual healthcare spending attributed to cigarette smoking in the U.S. amount to as much as $170 billion (Xu et al., 2015).

Another common example of deleterious consumption behavior is overeating. One ensuing consequence of overeating is obesity, defined by a body mass index (BMI) of over 30. Obesity increases risk of coronary heart disease (CHD), diabetes, stroke, cancer, and further health complications (Aronne, 2002). From 2011 to 2014, approximately 36.5% of American adults were reported as obese (Ogden et al., 2014). Comparable to medical costs for smoking, a meta-analysis looking at the economic effects of obesity found that the annual medical spending attributed to obesity in the US is approximately $149.4 billion (Kim et al., 2016). Importantly, overeating can commonly occur in any healthy individual, but can also occur at a more extreme degree in individuals who suffer from binge eating disorder (BED). According to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5; APA 2013), BED is
categorized as having binge-eating episodes at least once a week for a minimum of three months, no triggering of any compensatory behaviors such as purging, and having marked distress regarding binge eating. As of 2015, 2.8% of American adults reported suffering from binge eating disorder (BED) at some point during their lifetimes (Hudson et al., 2007).

Given the prevalence and cost of problematic consumption behaviors like cigarette smoking and overeating, identifying targets for possible intervention is arguably imperative. One contributor thought to be central to consumption behavior is stress, a bodily response consisting of the physical release of hormones such as adrenaline, cortisol and norepinephrine, as well as psychological, emotional, and cognitive components. As is done colloquially, this paper uses the terms ‘stress’ and ‘distress’ seemingly interchangeably, while in fact distress is a state of experiencing unpleasantness that can be induced by stress. Undoubtedly, many people during stressful periods in their lives (e.g., rough breakup, job search, or finals) can confirm that distress can manifest through exaggerated behavior including eating, colloquially referred to as ‘stress-eating,’ or increased drug consumption, such as cigarette smoking. Indeed, studies have confirmed that during exam week, students increase their food consumption (Greeno & Wing, 1994) and that acute stress increases drug use, specifically cigarette smoking, as well as eating (McKee et al., 2011). Acute stress has also been shown to predict lower inhibitory control (Roos et al., 2017), and moreover, cigarette smokers retrospectively cite stressful events and distress as reasons for relapse (Shiffman et al., 1996).

One mechanism that may underlie the effect of stress on consumption behaviors is craving, defined as “a strong desire” (APA, 2013). Craving was added as a diagnostic criterion for SUDs in the DSM-5 (APA, 201), and can be triggered by stimuli previously associated with a formerly used substance (i.e., cue-induced craving; Kober, 2015). Data from animal and human
studies have suggested that stress can also induce craving, which may account for consumption patterns such as increased eating and cigarette smoking in times of stress. For example, exposure to stress in animal models can induce drug-seeking behavior (Erb et al., 1996). In studies with alcoholics, exposure to stress and alcohol cues significantly increases alcohol craving, anxiety, and negative emotions (Fox et al., 2007). Craving, in turn, predicts subsequent consumption of food and drugs (for review, see Kober & Mell, 2015). Higher craving has been shown to be associated with increased probability of smoking, faster progression to smoking, increased probability of lighting a second cigarette, taking more puffs, longer puffing, and greater increases in CO, which is measured using a carbon monoxide breath monitor and indicates an increase in cigarettes being smoked (Shiffman et al., 2013).

Thus far, when talking about the mechanisms involved in stress-induced consumption behaviors, research has primarily focused on pathways through which stress can increase craving. However, another potential pathway through which stress may increase consumption behaviors is reduced cognitive control. That is, stress may increase consumption behavior not only though induction of craving, but also by making craving harder to regulate. However, the relationship between stress and regulation of craving has been poorly studied, let alone in the context of ND. Many models of substance use disorders (SUDs; addictions) emphasize impaired cognitive control, including regulation of craving (Kober, Mende-Siedlecki, et al., 2010; Suzuki & Kober, in press). Importantly, we previously showed using functional magnetic resonance imaging (fMRI) that regulation of craving depends on the dorsolateral and ventrolateral prefrontal cortices (Kober 2010), which are regions implicated in cognitive control. However, evidence shows that stress may impair cognitive control and PFC function (Arnsten, 2009). Stress may thus render treatments such as Cognitive Behavioral Therapy (CBT; i.e., cognitive
reappraisal), which draws heavily on the PFC, less effective. Because cue-induced craving may contribute to the relapse of SUDs, CBT where individuals are exposed to drug cues and then learn to regulate subsequent cravings may be extremely important for future treatment of SUDs. Studies within the past decade have demonstrated that cognitive strategies such as reappraisal can be used to reduce cue-induced craving in cigarette smokers, as well as for food (Kober, 2010).

The relationship between stress and consumption behavior may be further mediated by a personality factor: anxiety sensitivity (AS). AS is an important predictor of displayed and reported anxiety, and has been reported to be more related to self-reported anxiety in stressful conditions than any actual physiological changes (Shostak & Peterson, 1990). Psychological stress has been shown to suppress immune systems, which also occurs as a result of stress-induced anxiety (Maes et al., 1998). Therefore, individual differences in AS may render some people vulnerable to the effects of stress, which, in turn, may increase craving and/or decrease individuals’ ability to regulate craving. Indeed, this prediction is consistent with a previously reported correlation between stress-induced alcohol craving and anxiety (Fox et al., 2007). Given that some people may use drugs to ameliorate anxiety, which may be related to craving and drug seeking, anxiety can also be induced by withdrawals. Anxiety-like behavior has been induced in alcoholics by substituting stress for repeated withdrawals from chronic ethanol (Breese et al., 2005). From this we can conjecture that stress in an abstinent alcoholic may be perceived as a “withdrawal-like syndrome” capable of producing anxiety-associated symptoms, consistent with reported negative affect and anxiety by abstinent alcoholics (Begleiter and Porjesz, 1979; Roelofs, 1985). Additionally, high comorbidity between BED and anxiety disorders (Ulfvebrand et al., 2015) point to a potential association between anxiety, food craving, and eating behavior.
Anxiety and sensitivity to stress can also develop during high-fat diets and may play a key role in perpetuating consumption of high-fat foods and the development of obesity (Sharma 2013).

In ND individuals, AS may mediate the relationship between stress-induced cravings that increase cigarette consumption. Smokers with high AS may be particularly motivated to smoke to avoid experiencing emotional distress or anxiety (Gregor et al., 2008). In laboratory challenge tasks such as breath holding, participants with higher AS were more likely to use an escape option when distressed, i.e. smoke (Brown et al., 2005). This suggests that higher AS may predict early smoking relapse for individuals exposed to stressful situations. In addition, studies have shown that high anxiety smokers experience a reduction in anxiety from smoking in stressful situations, but not in low stress situations (Evatt & Kassel 2010). As Pomerleau & Pomerleau (1991) said, “The relationship between stress and smoking, and a corresponding link between smoking and anxiety reduction, are so well entrenched in the lore concerning cigarette smoking that they have assumed the status of truisms.” In fact, anxiety may be a reduction in experiential distress that occurs as a result of acute nicotine withdrawal (Parrott 1999). Smoking has indeed been shown to produce symptoms similar to states of anxiety, including heart palpitations, elevations in blood pressure, and increased coronary blood flow (Pickering et al., 1995). Nonetheless, the degree to which AS plays a role in the effects of stress on craving and regulation of craving has not been rigorously investigated.

In our current study in Dr. Hedy Kober’s Clinical and Affective Neuroscience Laboratory (CAN Lab), we addressed these issues in a single study by quantifying the degree to which regulation of craving is impaired by stress, and further assessing its relationship to anxiety sensitivity. Using fMRI, we investigated how stress influences cue-induced craving as well as the regulation of craving for food and cigarettes, both behaviorally through self report and
changes in brain activity through fMRI. We recruited individuals with ND, who completed the Regulation of Craving task (ROC task; Kober, Kross, Mischel, Hart, & Ochsner, 2010) combined with a threat-of-shock (TOS) paradigm while undergoing fMRI scanning. The ROC task uses a cognitive regulation strategy drawn upon skills taught in CBT. This strategy has direct clinical implications on treatment of substance use disorders (SUDs), including ND and BED. TOS is a well-known and reliable stress-induction methodology, extensively used in models of stress (e.g., Grillon & Ameli, 1998). We hypothesized that stress would increase cue-induced craving as well as interfere with regulation of craving, and that individuals with higher Anxiety Sensitivity Index (ASI; Reiss, Peterson, Gursky, & McNally, 1986) scores would have higher self-reported craving ratings due to their potential higher stress levels.

Additionally, individuals that are highly sensitive to anxiety may report higher stress-induced craving and exhibit less capacity to regulate craving under stressful conditions. A distinction should be made between state anxiety, defined as “an unpleasant emotional arousal in face of threatening demands or dangers” and trait anxiety, which reflects the individual differences in the tendency to respond with state anxiety in anticipation of threatening situations (Spielberger, 1970). The State-Trait Anxiety Inventory (STAI; Spielberger 1983) is a questionnaire that measure both state and trait anxiety, and this study uses both STAI and ASI to measure general anxiety. Understanding how stress interacts with craving, anxiety and the use of cognitive strategies will hopefully lead to an understanding of factors that may hinder efforts at self-regulation. The role of stress on a cognitive strategy drawn from CBT will be investigated using a neuroscientific approach that could be used to further inform and expand upon existing treatments for SUDs. This investigation will help characterize individuals that are most
vulnerable to stress-induced craving and enhance our understanding of the role that stress plays in ND individuals in the hopes of aiding their treatment.

**Research Design and Methods**

**Participants**

Participants (ages 18-65) were recruited from the New Haven community. Individuals were included if they (1) smoked ≥10 cigarettes per day, (2) fulfilled criteria for ND according to the Fagerstrom Test of Nicotine Dependence (FTND; Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991), (3) scored ≥27 on the Mini-Mental State Examination (MMSE; Folstein et al., 1983), and were (4) otherwise healthy. Individuals were excluded if they (1) met criteria for any active DSM-IV Axis I diagnosis (except ND), assessed by the Mini International Neuropsychiatric Interview (MINI; Lecrubier et al., 1997), (2) currently used smoking cessation pharmacotherapies, any current psychoactive medications, recreational drugs (other than marijuana, which was not cause for exclusion if used less than twice weekly), or medications that affect blood flow, (3) had any contraindications for fMRI (e.g., claustrophobia, metal in the body, severe head trauma, pregnancy in females). The final sample included 20 participants.

**Recruitment**

Recruitment for participants was conducted via local flyering and city bus advertisements throughout the city of New Haven, television ads, and online postings on websites such as
Facebook and Craigslist. Interested individuals underwent an initial phone screening procedure for determination of initial eligibility. The phone screening included confidential questions assessing smoking status, personal medical history, familial psychiatric history, current presence of mental illness. Participants then came in for an in-person screening visit for further assessment of eligibility.

**Procedure**

**Visit 1**

During the first visit, participants were provided with a consent form approved by the Yale Institutional Review Board (IRB) to sign. Following the consent procedure, MINI, FTND, and MMSE were administered, and measures of breath alcohol content, exhaled carbon monoxide, and urine cotinine were obtained to confirm smoking status and eligibility according to study criteria. Smoking and other alcohol/drug use was assessed using the Timeline Followback (Robinson 2014), which is a quantitative tracking of drug use over the last calendar month. If eligible, participants provided information including employment, socioeconomic, and marital status. Other assessments completed during the screening visit include the Cold Pressor Task (see Cold Pressor Task below) used to measure stress sensitivity (Lovallo, 1975) and the ASI (Reiss, Peterson, Gursky, & McNally, 1986). Upon completion of the visit, participants were compensated for their participation ($15/h) and scheduled for the MRI visit.

**Cold Pressor Task**

In the Cold Pressor Task, a cold compress was placed on the participant’s right forearm, while measuring their heart rate and skin conductance. Prior to application of the cold compress,
participants were instructed to indicate the moment when they first experienced pain, as well as the moment they could no longer take the pain, at which point the experimenter removed the compress from the participant’s arm. The temperatures of the cold compress surfaces were taken before and after the procedure. The Cold Pressor Task was conducted as an independent measure of stress tolerance (Lovallo 1975).

Visit 2

During the second visit, participants underwent an fMRI scan at the Yale Magnetic Resonance Research Center. Upon arrival, participants reviewed the consent and MRI safety forms, provided breath and saliva samples, and were fit with MR-compatible shock electrodes to undergo shock calibration. Assessments for STAI were given both pre- and post-scan.

Prior to the fMRI scan, participants were trained on the ROC task (see ROC Task below) and practiced using a hand-held button box to make responses during the task. Further, they were introduced to the TOS paradigm and underwent the calibration procedure (see TOS and Calibration below). fMRI scanning started once participants demonstrated complete understanding of the task procedures.

ROC Task

In the ROC task, participants were presented with images of food and cigarettes previously shown to induce craving (Kober, Kross et al. 2010) and instructed to think about each image in one of two ways:

(1) **Craving condition**: The instruction word **POSITIVE** (POS) directed them to focus on the immediate positive effects of consuming the item presented (e.g., it will taste/feel
(2) **Regulation condition:** The instruction word **NEGATIVE** (NEG) directed them to focus on the negative consequences associated with regular consumption of the item presented (e.g., lung cancer for cigarettes; weight gain for foods).

In each trial, after the image presentation, participants provided a rating of their craving for the item on a 5-point visual analogue scale from 1 (not at all) to 5 (very much). Food images were interspersed among the cigarette image types to provide appetitive, non-addiction controls.

To implement the TOS paradigm in the ROC task, each run of the task included two blocks of trials. At the beginning of each block, participants were presented with the instructions **THREAT** or **SAFE**, which indicate whether they may experience an electric shock at any point (**THREAT**) or that no shocks will be administered (**SAFE**) during the upcoming trials. Each run included one **THREAT** block and one **SAFE** block, in randomized order. After each block, participants made ratings of their stress and craving, again on a 5-point visual analogue scale.

Importantly, a priming shock was administered on the first trial of the first **THREAT** block to increase face validity of TOS, and up to 16 shocks were administered randomly across all **THREAT** blocks.

As such, the ROC task with TOS was designed with 8 conditions (2 TOS Cues x 2 Instructions x 2 Image Types). The task was administered in 8 runs, each with of 2 blocks of 8 trials, except for the first run which included a “dummy trial” for the priming shock. Thus, participants completed a total of 129 trials.

**TOS and Calibration**
As in pilot studies run by CAN Lab, we used BIOPAC Systems for shock administration. Importantly, participants underwent shock only during calibration and the task itself, but not during task training. Participants never received more than 25 shocks throughout the visit (including the calibration).

Shock intensities were individually calibrated to a level that is “uncomfortable but tolerable,” and safe. Calibration involved two steps: (1) prior to training on the ROC task, and (2) re-calibration in the scanner suite. Participants were first affixed with MR-compatible electrodes on the left (inner) ankle, then completed other procedures, allowing the electrodes time to moisturize the skin and establish effective conductivity (≥20min). Electrodes were then connected to an STM shock-producing device, set to 0.01mA. Next, participants were informed that the shock calibration would begin, and that the shock would be increased incrementally, until they felt that it had reached the level that is “uncomfortable but tolerable,” (Choi et al., 2012). We quantify this in verbal instructions as a “7 in a 1 to 10 rating scale;” the highest level of pain that participants are willing to tolerate for the study. Participants were informed that if the shock reached a point too intense, they could request to lower it. The experimenter then increased the shock level from 0 to 35 volts, applied a shock, and asked participants if they could detect the shock. If participants felt the shock, they were asked whether or not the voltage could be increased. If they did not feel the shock, or if they agreed to the increase, the experimenter increased the level incrementally, applied another shock, and continued in this manner until participants indicated that the level of the shock was “uncomfortable but tolerable”.

Once participants were ready to be scanned in the MRI, they were taken to the MR suite and positioned on the scanner bed. At that time, the electrodes were connected to the STM shock-producing device in the MR suite, which was set 2 levels lower than the prior level set. As
needed, shock level was re-calibrated. Once participants reached levels that were “uncomfortable but tolerable,” they were asked to rate their level of stress, and to indicate that they were ready to begin the scan. Participants were also informed that they may ask for shock level to be adjusted between runs, and may ask to stop the experiment at any time.

**Data Acquisition & Analysis**

The ROC task was programmed and ran using E-Prime version 2.0 (Psychology Software Tools, Inc.). The task was presented to the participants in the MRI scanner using a back-projection mirror. During the ROC task, participants made responses using an MRI-compatible button box, through which craving ratings were collected. Stress in response to the TOS was assessed using both subjective and objective measures, including salivary cortisol and psychophysiological measurements (e.g., heart rate, galvanic skin response, respiration; BIOPAC systems).

For data analysis, craving was calculated by taking the average of the self-reported craving ratings across trials in each condition. The craving ratings from the TOS trials were removed prior to analysis. To test the effects of stress of craving and regulation of craving, we conducted a 2x2x2 repeated-measure ANOVA, with ASI scores included as a covariate, using SPSS, IBM; 2 (Instruction: Positive, Negative) x (Image Type: Cigarette, Food) x (TOS: Threat, Safe). Further, we assessed whether anxiety sensitivity correlated with regulation success, which we operationalized as the difference between craving reports in the craving condition and the regulation condition. Biological data, including MRI, will not be analyzed as part of this thesis.
Results

Self-Report Craving During ROC Task

Including ASI as a covariate, we found a significant main effect of image type ($F_{(1,18)}=7.507$, $p=.013$), with individuals reporting greater craving with images of cigarettes (CIG) than food ($t_{(19)}=3.526$, $p=.002$). We also found a significant main effect of instruction, ($F_{(1,18)}=6.589$, $p=.019$), such that individuals reported greater craving in Positive than Negative ($t_{(19)}=2.638$, $p=.016$). Craving ratings did not significantly differ between threat versus safe trials ($p=.154$). We found a significant interaction between image type and TOS ($F_{(1,18)}=4.852$, $p=.041$). Thus, we separated the analysis by image type, and found a main effect of TOS for cigarette images only ($F_{(1,18)}=5.122$, $p=.036$).

![Figure 1. Mean Craving Ratings by Trial Type. Craving ratings were significantly higher in the POS than NEG instruction trials ($t_{(19)}=3.5257$, $p=.0023$). Craving ratings were significantly higher in the CIG than FOOD image type trials ($t_{(19)}=2.6344$, $p=.0163$). The error bars indicate the standard error of the mean.](image-url)
Figure 2. Mean Craving Ratings For Cigarette Images in TOS Trials as a Function of Deviation from ASI Ratings. Individuals with ASI scores one standard deviation below the mean reported significantly higher cravings compared to those individuals with ASI scores one standard deviation above the mean ($t_{(7)}=2.3708 = .0495$). For individuals with low ASI, craving is higher during Threat than Safe blocks, but individuals with high ASI reported higher cravings during Safe blocks. The groups were divided into standard deviations of ASI because only when controlling for ASI was there an effect of TOS on craving.

**Correlation with Anxiety**

STAI is positively correlated with stress ratings in the Threat blocks ($r_{(18)}=.522, p=.018$) and in the Safe blocks ($r_{(18)}=.699, p=.001$).

Individually with higher ASI had reduced craving for cigarette images during POS trials ($r_{(18)}=-.590, p=.006$) in both Threat ($r_{(18)}=-.641, p=.002$) and Safe ($r_{(18)}=-.528, p=.017$) blocks.
Correlation with Stress

Block ratings for craving and stress were positively correlated in the Threat condition ($r_{18} = .685$, $p = .001$) but not for the Safe blocks ($p = .36$). No other factors or interactions were significant predictors.

Discussion

This paper sought to explore the relationship between stressors, regulation of craving, and anxiety in a cigarette-smoking population in the hopes of understanding what individuals are most vulnerable to stress-induced craving and how certain cognitive strategies may aide in counterbalancing its effects. The significant effect of cigarette image types and Positive instruction trials replicate our previous findings using the ROC task (Kober et al., 2010). However, contrary to our hypotheses, individuals with higher anxiety levels did not report higher stress or craving, nor exhibit less capacity to regulate craving under stressful conditions.

In threat trials for cigarette but not food image types, participants reported greater overall craving, indicating vulnerability to specific cue-induced cravings for cigarettes in ND individuals. Furthermore, this study demonstrated that cognitive strategies can be successfully used to reduce cue-induced cravings. In the Positive instruction trials, they reported higher cravings than in the Negative trials, where they were instructed to think of the negative consequences that would result from consumption of the item shown in the image type.

Individuals were more stressed during the threat blocks, indicating that the TOS paradigm was able to induce stress. When examining correlations between STAI and stress ratings during the tasks, we found that STAI was positively correlated with stress ratings in both
the Threat and Safe blocks. This indicates that highly anxious individuals did feel stressed, but did not seem to be made more vulnerable to stress-induced craving, seeing as their craving ratings were negatively correlated with ASI. Unexpectedly, individuals with higher ASI scores had reduced craving for cigarettes in the craving condition (or POS), in both Threat and Safe blocks. ASI was found to be negatively correlated to craving only in the cigarette image type and only in the instruction condition Positive (e.g., with Safe_CIG_POS and Threat_CIG_POS), but not for other conditions.

When controlling for ASI, TOS had a significant effect on craving, such that TOS increased craving for individuals with low ASI scores, but decreased craving for individuals with high anxiety sensitivity. As stated previously in this paper, although smokers with high AS may be particularly motivated to smoke to avoid experiencing emotional distress or anxiety (Gregor et al., 2008), they may be acting only to avoid potential future stress before any onslaught of stress itself. There is a general association between anxiety-related states and use of drugs (Kushner et al., 1990), but as our preliminary results indicate, anxiety does not seem to directly increase craving itself.

The negative affect of anxiety is relevant to the prediction of emotional distress (Rassovsky et al., 2000), and anxiety sensitivity levels among individuals with a history of clinical illness (i.e., past major depressive disorder) can predict relapse during the first week of attempting to quit smoking (Brown et al., 2001). However, there is no concrete understanding of how anxiety sensitivity may predict smoking cessation outcomes. People more sensitive to anxiety had less craving and stress overall, regardless of TOS trials. This is contrary to our hypothesis that high scoring ASI individuals would report higher cravings. Although these results indicate that people who are more sensitive to anxiety are potentially less prone to craving
or stress, this seems both unlikely and illogical. Alternatively, the acute stress of the TOS paradigm may have caused lack of clarity in making judgments during self-rated cravings. On the one hand, these individuals may be used to functioning at higher levels of stress and thus able to better regulate their cravings while undergoing TOS, but it is also possible that the individuals with higher anxiety levels may have been overwhelmed with the amount of stimuli and thus unable to register craving and stress or accurately report these feelings.

A study that used maximum breath-holding duration as a means to measure distress tolerance in heavy cigarette smokers found that ASI scores did not significantly differ between the groups, contrary to their hypothesis (Zvolensky et al., 2001). Similar to our results, this indicates that ASI scores do not contribute directly to increased levels of stress and craving, but may drive an individual to anticipate and attempt to proactively avoid any state of withdrawal or negative affect that may then be incurred, i.e. smoking cigarettes. In the real world, highly anxious individuals may predict their anxiety levels rising, and proactively engage in activities (such as smoking) that they believe will alleviate negative affect. To escape states of distress, individual smokers may end up relying on smoking (Kassel & Shiffman, 1997), and in high stress individuals, especially women who have experienced trauma, emotional suppression may be a related symptom (Moore et al., 2008).

Several limitations should be taken into account when considering the implications of this data, aside from the fact that the study is still ongoing. Due to strict exclusion criteria, we were so far only able to analyze the data of 20 participants. A study with a larger sample size would be able to strengthen the power of our statistical analyses. Furthermore, there may be different levels of sensitivity in regard to different kinds of stress; this study only used TOS (and a cold compress for setting baseline biological markers) as stressors. Finally, it should taken into
account that the construct validity of ASI has been proven to be more robust than STAI (Taylor et al., 1991), and that future studies should account for any discrepancies between the two assessments.

**Conclusion**

ND individuals reported craving cigarettes more than food, and were able to either regulate their cravings when instructed to do so. However, individuals with higher ASI scores actually reported less stress and craving overall compared to individuals with lower ASI scores in this TOS paradigm. When controlling ASI, the effect of TOS on craving for cigarette images was that craving ratings were higher during Threat than Safe blocks for individuals with low ASI, but individuals with high ASI reported higher cravings during Safe blocks. The findings in this paper are important empirical evidence for the need to explore how anxiety sensitivity may mediate the relationship between stress and regulation of craving. Although ASI scores were not correlated with stress and regulation of cue-induced cravings as our original hypothesis predicted, this study does establish that the relationship must be further investigated as the relationship may be mediated by other factors.

**Author Contributions**

This research was conducted through Yale’s CAN Lab. Professor Kober designed the study. The research assistants in CAN Lab and the lab’s other undergraduate students collected the data. The data was analyzed with the help of Suzuki and Rebeca Boswell. Kober, Suzuki and Nilofar Vafaie helped produce feedback for an outline and drafts of the final paper.
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