BEHAVIORAL ECONOMIC ANALYSIS OF CUE-ELICITED CRAVING FOR TOBACCO:
A VIRTUAL REALITY STUDY

by

JOHN DANIEL ACKER
(Under the direction of James MacKillop)

ABSTRACT

Behavioral economics in psychology affords the ability to gauge drug consumption as a function of escalating drug prices. The present study tested two hypotheses: (i) the presentation of virtual reality-based tobacco cues would result in significant increases in subjective tobacco craving and tobacco demand, and, (ii) aspects of tobacco demand would be significantly associated with smoking behavior during a self-administration paradigm. Following the presentation of tobacco cues, statistically significant changes in tobacco craving and the tobacco demand indices of $O_{\text{max}}$ (i.e., maximum expenditure), Elasticity (i.e., price sensitivity), and Breakpoint (i.e., price at which consumption is suppressed) were observed. Statistically significant positive associations were observed between number of cigarettes purchased and the indices of $O_{\text{max}}$ and Elasticity. Regression analyses revealed the index of Elasticity to incrementally predict number of cigarettes purchased, above and beyond subjective tobacco craving. The results are discussed in relation to previous investigations and recommendations for future studies.

INDEX WORDS: Tobacco, Nicotine, Behavioral Economics, Craving, Demand, Motivation
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DEDICATION

To Grace.
I would like to express my appreciation to my major professor, Dr. James MacKillop, for his continuous support and guidance throughout this project. I would also like to thank members of my committee, Dr. Joshua Miller and Dr. Sarah Fischer, for their ongoing support and guidance. I am also very grateful for the contributions of the following research assistants: Stephanie Adrean, Jared Bollinger, Carl Edge, Megan Parrish, Melanie Nembhard, Alex Rothbaum, Alex Speer, and Obioma Ekeledo.
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CHAPTER 1
INTRODUCTION

Cigarette smoking continues to be a health crisis in the United States. According to the Centers for Disease Control and Prevention (CDC; 2002), an estimated 440,000 annual deaths and more than $150 billion in annual health care expenditures can be directly attributed to smoking-related morbidity in the US. Nicotine is a highly-addictive substance, with lifetime prevalence rates of nicotine dependence in the US estimated at 24.1% (Kandel & Chen, 2000). Given such staggering statistics, clearer conceptualizations of factors related to nicotine use and smoking cessation are a health care priority.

An integral concept in investigations of tobacco use and drug use in general has been the construct of subjective craving (for a review, see Tiffany, Carter, & Singleton, 2000; Tiffany & Wray, 2012). Subjective craving is a multifaceted construct, but is commonly primarily conceptualized as consisting of a salient desire to consume a specific substance (Sayette et al., 2000). The recurrent desire to consume a substance (e.g., tobacco) is widely theorized as a consequence of neuroanatomical alterations due to repeated substance use (Robinson & Berridge, 1993; Skinner & Aubin, 2010), resulting in widespread conscious and unconscious changes in domains of cognitive, autonomic, and emotional functioning (Franken, 2003; Shiffman, West, & Gilbert, 2004; Skinner & Aubin, 2010). In the context of tobacco use, subjective craving is a prominent predictor of both nicotine addiction (Tiffany, Warthen, & Goedeker, 2009) and likelihood of smoking cessation failure (Shiffman, 1991; Shiffman et al., 2007; Shiffman, West, & Gilbert, 2004).
Although subjective craving is a central construct in empirical investigations of addictive behavior, a precise measurement of the construct poses several difficulties. First, there exist widespread inconsistencies across empirical investigations in terms of the conceptualization, time course, and definition of subjective craving (Rosenberg, 2009; Sayette et al., 2000). Related, craving is highly-subjective and can be conceptualized, experienced, and rated very differently across participants. For example, two individual’s self-ratings of “seven” on a 10-point Likert scale may not reflect the same motivational state. This subjectivity is due to the fact that there is no objective criterion with which to compare subjective levels of craving across participants, and as a result, differences in ratings of craving across individuals may not reflect true differences in the actual experience of craving. Second, subjective craving has been largely studied using one item measurements, which are inherently lacking in terms of both reliability and validity; scales with one item preclude the ability to measure internal consistency, and, the degree to which one item accurately measures a construct is highly-questionable (Rosenberg, 2009; Sayette et al., 2000; Shiffman et al., 2004; Tiffany, 1992; Tiffany et al., 2000). Third, the measurement of subjective craving may actually increase it (Rosenberg, 2009; Sayette et al., 2000; Tiffany et al., 2000). Finally, the subjective experience of craving may occur outside of awareness, which may impede one’s ability to rate accurately current or historic levels of craving (Sayette et al., 2000). Given such complexities and inconsistencies across empirical investigations of the subjective experience of craving, increased clarity of this notoriously challenging, yet highly-relevant construct remains an emphasis in the addiction literature.

The field of behavioral economics in psychology unites concepts from microeconomic theory and operant conditioning to explain human behavior in a variety of contexts (Vuchinich & Heather, 2003). Particularly relevant in the context of assessing motivational aspects of addictive
behavior are behavioral economic assays of substance demand, as such paradigms provide objective, meaningful indices of an individual’s relative value of (i.e., demand for) an addictive substance in the presence of an alternative reinforcer (e.g., money) (for a review, see Hursh, Galuska, Winger, & Woods, 2005). Typically, substance demand is quantified either through the incorporation of self-administration protocols (Perkins, Ciccocioppo, Jacobs, Doyle, & Caggiula, 2003; Willner, Hardman, & Eaton, 1995) or alternatively, through the administration of hypothetical purchase tasks (e.g., Jacobs & Bickel, 1999). The use of hypothetical purchase tasks in studies of demand in substance use populations avoids the inherent difficulties involved in self-administration paradigms (e.g., experimental burden, timing issues, and ethical issues; see also Higgins, Bickel, & Hughes, 1994), and have been increasingly used as comparable, effective measurements of substance demand. The construct of substance demand is putatively multidimensional in nature (Bickel, Marsch, & Carrol, 2000; Hursh et al., 2005), consisting of five, lower-order facets: Intensity (i.e., consumption at zero-cost); Breakpoint, (i.e., first price at which consumption is completely suppressed); Elasticity (i.e., $\alpha$; the proportionate slope of the demand curve); $O_{\text{max}}$ (i.e., maximum expenditure); and, $P_{\text{max}}$ (i.e., maximum inelastic price; price associated with $O_{\text{max}}$). These lower order facets are conceptualized as loading differentially onto two subsumed latent factors, namely, volumetric consumption, and price sensitivity (MacKillop et al., 2009).

Behavioral economic purchase tasks that measure substance demand have been profitably used to study addictive behavior, including nicotine dependence. Specifically, initial demand (i.e., Intensity) for cigarettes has been found to be significantly greater for cigarettes when compared with heroin (Jacobs & Bickel, 1999). Moreover, the facets of breakpoint (i.e., price at which consumption is completely suppressed), $O_{\text{max}}$ (i.e., maximum expenditure), $P_{\text{max}}$ (i.e.,...
maximum inelastic price), and Intensity have been found to be positively, significantly related to both nicotine use and symptoms of nicotine dependence (MacKillop et al., 2008). Similarly, the demand facets of Intensity, Breakpoint, and $O_{\text{max}}$ have been found to positively significantly relate to nicotine use and nicotine dependence in a sample of adolescent smokers (Murphy et al., 2011). Comparable results have been observed using similar behavioral economic paradigms in empirical investigations of other addictive behaviors, such as alcohol use (MacKillop & Murphy, 2007; MacKillop et al., 2010a, 2010b; Murphy & MacKillop, 2006; Murphy, MacKillop, Skidmore, & Pederson, 2009; Smith et al., 2010), and illicit drug use (Jacobs & Bickel, 1999).

Such studies of behavioral economic demand in relation to substance use are both clinically and conceptually relevant in terms of their ability to provide more objective and potentially unique measurements of specific facets of drug-related reinforcement than traditional measures of subjective craving. Empirical investigations of trait-based behavioral economic demand in substance use populations have found significant relationships between subjective reports of craving and specific facets of substance demand. The Intensity facet of demand has been found to positively, significantly relate to subjective, self-reported alcohol craving and alcohol use disorder severity (MacKillop et al., 2010a). Interestingly, a recent investigation demonstrated incremental validity of specific facets of alcohol demand, in terms of weekly alcohol consumption and levels of problematic alcohol use, when contextualized with other salient motivational factors, including subjective alcohol craving (Acker, Amlung, Stojek, Murphy, & MacKillop, in press).

The preceding studies, however, were observational investigations that cross-sectionally examined self-report measures of craving and demand. In addition, several studies have used *de facto* behavioral economic tasks in correlational laboratory designs and found significant
associations between subjective craving and the relative value of psychoactive drugs (e.g., O’Malley et al., 2002; Leeman et al., 2010). Only two laboratory studies to date have systematically used behavioral economics to improve the measurement of craving. First, MacKillop et al. (2010b) found that an acute alcohol cue exposure was associated with increases in Intensity, $O_{\text{max}}$, $P_{\text{max}}$, and breakpoint using a hypothetical alcohol purchase task. More recently, MacKillop et al. (in press) found that nicotine withdrawal induced a significant increase in Breakpoint and $P_{\text{max}}$, and trend-level effects on $O_{\text{max}}$ and Intensity, whereas cigarette cues elicited lower elasticity (greater price insensitivity) (MacKillop et al., in press). However, this study also had a number of limitations, including a constrained demand paradigm that resulted in ceiling effects for some indices. In addition, the purchase task used in that study was the basis for cigarette access, creating a redundancy between the choices made and cigarette self-administration. Importantly, across both the preceding studies, variable associations have been present between craving and indices of demand, suggesting that demand is not collinear with subjective craving.

Taken together, although the literature supporting the use of behavioral economics to improve the assessment of subjective craving is promising and growing, there remain only a small number of studies to date. The goal of the current study was to extend the existing findings by addressing a number of previous limitations. Specifically, the study is a further examination of the effects of tobacco cues on demand for cigarettes and complements the previous study in two ways. First, given the methodological limitations in the previous study, the current study used both hypothetical estimates for the behavioral economic purchase task and a dual component self-administration procedure, comprising both a delay period and a self-administration period. As the alternative reinforcer for delaying and smoking were de facto
behavioral economic measures, this permitted the study to triangulate craving using both concurrent indices of incentive value and also a behavioral economic self-administration paradigm. In addition, a second strategy for enhancing the study was elaboration of the smoking cues involved. Specifically, rather than simply using the participants preferred cigarettes, the study leveraged the substantial emerging evidence supporting virtual reality (VR) simulations as highly-effective and ecologically-valid cue exposure techniques in cigarette smokers (Baumann & Sayette, 2006; Bordnick, Graap, Copp, Brooks, & Ferrer, 2005; Lee et al., 2003, 2004; Moon & Lee, 2009; Traylor, Bordnick, & Carter, 2008, 2009). The cue reactivity paradigm has been widely validated for acutely increasing craving for addictive drugs (Carter & Tiffany, 1999), but VR cue reactivity permits a greater diversity and more immersive stimulus environment.

The primary hypothesis was that, relative to the presentation of neutral cues, the presentation of tobacco cues would result in significant increases in subjective tobacco craving and the relative value of cigarettes (i.e., indices of tobacco demand). A secondary aim of the present study was to investigate the interrelationships between subjective craving and behavioral economic indices, both following the cue exposures and in relation to subsequent smoking behavior during a dual component tobacco self-administration condition consisting of the opportunity to delay smoking and purchase cigarettes (Leeman, O’Malley, White, & McKee, 2010; McKee, 2009). We hypothesized that, when contextualized with subjective tobacco craving, specific facets of the relative value of nicotine would demonstrate significant associations with both the amount of time a participant was willing to delay smoking, and the subsequent number of cigarettes participants purchased to smoke over the course of an hour-long tobacco self-administration condition (described in detail below). In other words, the study
examined the incremental validity of the facets of demand for tobacco in relation to subjective tobacco craving in the context of the dual-component paradigm.
CHAPTER 2

METHOD

Participants

Participant characteristics (N = 47) are depicted in Table 1. Prospective participants were recruited from the Athens, GA community via newspaper advertisements, bus transit advertisements, and flyers distributed throughout the community soliciting regular smokers. Prospective participants completed a brief telephone screening to determine study eligibility. Individuals that satisfied the inclusion criteria were invited to attend an in-person experimental session. For inclusion in the present study, participants were required to: (i) be of at least 18 years of age; (ii) currently smoke ≥ 10 cigarettes per day; (iii) test negative for current pregnancy (females only); (iv) not be currently seeking nor sought-out treatment during the preceding three-months for smoking cessation, other drug problems, or psychiatric illness, including the current use of any psychotropic medications, and, (v) endorse regular computer usage (i.e., ≥ four days per week). This last criterion was implemented to ensure adequate competency with the extensive array of computerized assessments. Each participant received monetary compensation in the amount of $32 for the four-hour session, in addition to up to an additional $18 in monetary compensation earned during the dual component self-administration period (see below).
Assessment

**Baseline Assessment.** Baseline level of carbon monoxide (CO) expenditure was assessed using the piCO\textsuperscript{+} Smokerlyzer\textsuperscript{®} device (Bedfont Scientific Ltd.), a device which measures CO breath expenditure in terms of parts per million (ppm) units of concentration. A comprehensive demographics questionnaire was incorporated to assess relevant demographic variables, such as ethnicity, gender, and income. Nicotine dependence was assessed using the Fagerstrom Test for Nicotine Dependence (FTND; Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991). The FTND is a highly reliable, psychometrically-validated self-report instrument with six-items measuring current level of nicotine dependence, based on a combination of behavioral and quantitative indices.

**State-based Outcome Measures.** Subjective tobacco craving was measured using a brief, five-item visual analog scale (VAS; Schuh & Stitzer, 1995). Each item of the VAS pertains to different facets of tobacco craving (e.g., “All I want is a cigarette right now”). Participants were instructed to demarcate their current level of craving on a 100mm line for each item, with corresponding numeric values ranging from 0 (*not at all*) - 100 (*strongest feeling possible*). Cronbach’s alpha (α) coefficients for the VAS as assessed following post-neutral cues and post-tobacco cues were .94 and .96, respectively.

A state-based hypothetical Cigarette Purchase Task (CPT; e.g., MacKillop & Tidey, 2011) was incorporated to assess for the relative value of tobacco. Participants were given the following directions: “*Imagine you could smoke RIGHT NOW. The following questions ask how many cigarettes you would consume if they cost various amounts of money. The available cigarettes are your favorite brand. Assume that you have the same income/savings that you have*...
now and NO ACCESS to any cigarettes or nicotine products other than those offered at these prices. In addition, assume that you would consume cigarettes that you request today that is, you cannot save or stockpile cigarettes for a later date. Please respond to these questions honestly.”

Subsequently, participants were asked to estimate how many cigarettes they would consume at 18 different price intervals: $0 (free), 2¢, 5¢, 10¢, 20¢, 30¢, 40¢, 50¢, 60¢, 70¢, 80¢, 90¢, $1, $2, $3, $4, and, $5. Each price interval was supplemented with corresponding pack prices.

Although the primary foci were subjective craving and tobacco demand, state affect was assessed for descriptive purposes with six 100-point circumplex items (Posner, Russell, & Peterson, 2005), each ranging from -50 to +50, with negative values indicating higher levels of the affect item listed to the left; positive values indicating higher levels of the affect item listed to the right. State affect circumplex items included: Tense↔Calm, Sad↔Happy, Nervous↔Relaxed, Bored↔Excited, Stressed↔Serene, and, Depressed↔Elated.

**Virtual Reality Parameters**

The cue exposure conditions were administered using virtual reality (VR) technology. Virtual reality environments (VREs) were simulated using a dual monitor Dell 1500 computer system in conjunction with a head mounted display device (HMD; Z800 3D Visor, eMagin Corporation). The dual monitor setup allowed for the experimenter to directly observe the participant’s trajectory on one screen, while simultaneously manipulating the specific environmental parameters (e.g., paths, timing, olfactory stimuli) via an experimenter interface located on the adjacent screen. The HMD was comprised of a pair of adjustable eye goggles which were positioned comfortably over the participant’s face. Participants also wore a pair of headphones in conjunction with the HMD to simulate environmental sounds. Olfactory scents
were generated using a smell machine and an accompanying air compressor (Scent Palette, Headhunter 2000).

The VREs were preprogrammed environments obtained from a local company specializing in virtual reality technology (Virtually Better Inc., Decatur, GA). Before the administration of the neutral and tobacco cue exposures, participants underwent a brief VR acclimation condition, which consisted of an outdoor city environment. This was done to ensure familiarity and comfort with the VR setting before the initiation of the cue exposure conditions. The neutral and tobacco cue exposure conditions were experimenter-directed and approximately three minutes in duration, and consistent across participants in terms of both content and duration. The neutral cue environment consisted of two narrated nature scenes (i.e., buffaloes, flamingoes) presented on flat screen TVs on opposite sides of a neutral room. The tobacco cue environment consisted of a smoking paraphernalia room comprised of ashtrays, burning cigarettes, lighters, brand-specific cigarette packs, and alcoholic beverages, with intermittent tobacco olfactory cues (i.e., raw tobacco, cigarette smoke) administered at standardized time points (see Figure 1 for screen shots of the VR environments). Imaginal cues were also administered during the tobacco cue exposure, during which the experimenter asked the participant to imagine what it would be like to smoke – the way it would smell, taste, and feel. Participants were each given a total of five imaginal cue prompts during the tobacco cue exposure. Each cue exposure condition was approximately three minutes in duration.

**Dual-Component Self-Administration Protocol**

A dual-component tobacco self-administration paradigm (Sayette et al., 2000, 2001; Leeman, O’Malley, White, & McKee, 2010; McKee, 2009) took place following the tobacco cue.
exposure condition. The first component of the self-administration protocol consisted of the opportunity to delay smoking in exchange for money. Specifically, participants were presented with eight of their preferred brand of cigarettes and informed that they could immediately smoke and initiate the hour-long tobacco self-administration period, or, delay smoking in exchange for one dollar for every five minute increment of delay. The minimum amount of delay allowed was zero minutes; the maximum amount of delay allowed was 50 minutes. Thus, participants received between 0 - $10 during this portion of the protocol (i.e., a minimum of zero dollars for no delay; a maximum of $10 for foregoing smoking for the full 50 minute period). The primary dependent variable during the delay portion of the self-administration paradigm was amount of delay (i.e., 0-50 minutes) until participants indicated that they wanted to smoke, and thus, begin the self-administration portion of the paradigm.

Once participants indicated that they could no longer delay smoking, or after delaying for the entire 50-minute delay period, they were given a lighter and an $8 “cigarette tab” with which to purchase cigarettes at a cost of one dollar per cigarette to smoke over the course of an hour long tobacco self-administration period. Participants were informed that $1 would be subtracted from their “tab” for each cigarette that they smoke, and that any remaining, unused money from their tab will be given to them at the end of the session in the form of cash. The primary dependent measure during the self-administration period was number of cigarettes purchased. All monetary compensation earned during the delay period, in addition to any unused money left over from the cigarette tab, was given to the participant at the end of the experimental session (i.e., maximum additional monetary compensation = $18).
Procedure

All study procedures were approved by the University of Georgia Institutional Review Board. The present study began with informed consent. To equate nicotine exposure, all participants were required to have smoked within 15 minutes of the beginning of the session; those whom reported smoking ≥ 15 minutes before the session were escorted outside to smoke one cigarette ad libitum before the session began. Participants then provided a baseline carbon monoxide (CO) reading to measure level of breath CO expenditure parts per million (ppm). Participants then completed a battery of baseline assessment measures, including the FTND and comprehensive demographics assessment. Upon completion of all baseline measures, the VR acclimation condition took place to ensure participant viability for VR cue exposures (i.e., to screen for VR-related dizziness, nausea, discomfort). The VR acclimation was immediately followed by the administration of the cue reactivity conditions; the neutral cue condition was administered before the tobacco cue condition in order to control for carryover influences of the tobacco cues (Sayette et al., 2000). Primary state outcome measures (i.e., CPT-State, VAS), were administered immediately following both of the cue exposures. After the completion of the cue exposures, participants were escorted to a separate room for the dual component self-administration protocol. At the completion of the self-administration period, participants were appropriately debriefed and compensated in the amount of $32 for their participation in the study, in addition to any extra monetary compensation earned as a result of delaying, or, leftover from their “cigarette tab” (i.e., total compensation range = $32 - $50).
Data Analysis

All variables were screened for outliers through the utilization of a $Z = +/- 3.29$ cutoff score (Tabachnick & Fidell, 2004). Outliers were addressed across variables by transforming respective cases to the next highest non-outlying value. An iterative process was utilized for the CPT assessments at both a price and index level. Participant CPT performance was also initially examined for evidence of low effort or persistent task inattention, using a criterion of $\geq 2$ contradictions at escalating prices. The elasticity index of tobacco demand was derived using the non-linear exponential demand curve model (Hursh & Silberberg, 2008) equation: $\log_{10}Q = \log_{10}Q_0 + k(e^{-\alpha Q_0 C} - 1)$, where $Q$ = consumption at a given price; $Q_0$ = consumption intercept/derived intensity, $k$ = range of the dependent variable (i.e., number of cigarettes) in logarithmic units, and, $\alpha$ = rate of decline in consumption as a function of escalating price. Overall mean consumption was first analyzed to determine the best-fitting $k$ parameter, which was determined to be 2.0 across both time points (i.e., PNC, PTC; overall PNC CPT $R^2 = 0.98$; overall PTC CPT $R^2 = 0.97$). For ease of interpretation, the inverse value (i.e., $1/\alpha$) was calculated for elasticity, such that greater $\alpha$ values indicate greater price insensitivity (Banks, Roma, Folk, Rice, & Negus, 2011). The other generated CPT indices were operationalized as follows: Intensity was defined as consumption at zero cost; $O_{max}$ was defined as maximum expenditure across prices; $P_{max}$ was defined as the price corresponding with $O_{max}$; and, Breakpoint was defined as the first price at which consumption is completely suppressed.

Primary analyses were conducted using a series of repeated measures ANOVAs to determine the impact of tobacco cues relative to neutral cues on CPT demand indices, tobacco craving, and affect. For purposes of secondary analyses, an omnibus correlation matrix using Pearson’s zero-order correlations was generated to determine the interrelationships between
relevant variables within and across assessment time points, as well as in relation to smoking behavior during the dual component tobacco self-administration protocol. Subsequently, in order to determine the unique relationships between the motivational variables (i.e., craving, indices of tobacco demand) and the self-administration outcomes (i.e., delay duration, # of cigarettes purchased), a series of hierarchical regressions were performed using the former as independent variables and the latter as dependent variables. Specifically, regressions included variables that demonstrated significant zero-order correlations with the target smoking behavior outcomes following the tobacco cue exposure condition, with subjective tobacco craving entered first in each model. The order in which the behavioral economic variables were entered in each of the respective hierarchical regression analyses was based on the correlational magnitude between the predictor of interest and the relevant smoking behavior criterion; those exhibiting the strongest statistical associations were entered first, ending with those exhibiting the weakest correlational associations. During the addition of variables in each regression model, those variables that demonstrated significant incremental variance were kept in the model, whereas variables not contributing significant incremental variance were excluded from further consideration. All analyses were conducted using SPSS version 16.0 and GraphPad Prism software.
CHAPTER 3

RESULTS

Preliminary Analyses

Initial examination of the CPT data across both time points suggested low effort responding in three individuals, who were excluded from all further analyses. A total of five individuals did not reach breakpoint during the PNC CPT assessment, rendering breakpoint analysis impossible for these individuals due to ceiling effects. One individual reported a non-numeric value for the free price interval across both CPT assessments, thus precluding this individual from intensity analyses. Across the CPT assessments, a total of 7.89% of price-level responses were identified as outliers, which were each subsequently coded as the next highest non-outlying value. One index level outlier was observed for the PTC CPT assessment (i.e., elasticity), which was transformed to the next highest, non-outlying value. One outlier was observed in the depressed↔elated affect circumplex, as well as one outlier in terms of number of cigarettes purchased, both of which were transformed as the next highest non-outlying value. Individual $R^2$ values using the aforementioned demand curve model equation were acceptable across participants and time points (PNC median $R^2 = 0.78$; interquartile range [IQR] = 0.68 – 0.88; PTC median $R^2 = 0.82$; IQR = 0.70 – 0.88). In terms of behavioral performance on the self-administration paradigm, participants were willing to delay access to cigarettes an average of 36.5 minutes (SD = 15.9) and, following the delay period, 91.5% purchased at least one cigarette; participants smoked on average 1.9 cigarettes (SD = 1.0). Of those whom
purchased cigarettes, the correlation between number of cigarettes purchased and the number consumed was .94.

**Primary Analyses**

Demand and expenditure curves generated from each of the CPT assessments are depicted in Figure 2. A series of repeated measures ANOVAs revealed statistically significant increases in several indices of demand, as well as tobacco craving, and (Table 2; Figure 3). Specifically, statistically significant increases were observed in the demand indices of Elasticity, $O_{max}$, and Breakpoint, indicating that the presentation of tobacco cues resulted in significantly greater price insensitivity for cigarettes, significantly greater maximum expenditure for cigarettes, as well as significantly higher price at which consumption for cigarettes was completely suppressed, respectively (Figure 3). A significant increase in the affect circumplex vector of “Tense” to “Calm” was also observed, indicating that exposure to tobacco cues resulted in a statistically significant increase in perceived tenseness. In addition, a statistical trend was evident reflecting a reduction in relaxation. All significant effects are depicted in Figure 3.

**Zero-Order Correlations & Exploratory Analyses**

Zero-order (Pearson’s $r$) correlations between all primary outcome measures assessed following the presentation of both cue reactivity conditions and during the dual component self-administration condition are presented in Table 3. In summary, the demand indices exhibited variable associations within assessment time points, ranging from moderate inverse associations to very high positive associations ($rs = -0.26 - 0.88$). Specifically, the associations between the CPT indices assessed following each cue reactivity condition were highly variable, ranging from negligible negative correlational magnitude, to highly significant positive associations (PNC
range = -0.10 – 0.88; PTC range = -0.26 – 0.88) Subjective tobacco craving was modestly associated with the CPT indices across both time points ($rs = .13-.36$).

Variable associations were observed between the amount of time participants were willing to delay smoking (i.e., delay duration) and the primary outcomes assessed following both cue reactivity conditions. Notably, the strongest associations, albeit at only trend levels of statistical significance, were observed between delay duration and the CPT indices of Intensity and $O_{\text{max}}$. Across time points, the relationship between delay duration and subjective tobacco craving was not statistically significant ($rs = -.12, -.02$, respectively). Number of cigarettes purchased during the self-administration period was significantly associated with subjective tobacco craving, $O_{\text{max}}$, and Elasticity, and exhibited a trend-level association with Intensity and the affect circumplex item of “Nervous $\leftrightarrow$ Relaxed,” such that lower levels of relaxation and corresponding increasing levels of nervousness were associated with a larger number of cigarettes purchased.

**Hierarchical Regressions on Target Smoking Behavior Outcomes**

Hierarchical regression analyses were not conducted between delay duration and the motivational variables because there were no statistically significant zero-order correlations. For number of cigarettes purchased, the first addition to the model was subjective tobacco craving, which was significantly associated with the number of cigarettes purchased, $R^2 = .18, F (1, 45) = 10.05, p = .003$ (See Table 4). The CPT index of Elasticity was entered in a second hierarchical block, which also revealed a statistically significant contribution of predicted variance in the model, $\Delta R^2 = .11$ [overall model: $R^2 = .29, F (1, 44) = 6.93, p = .012$]. Subsequently, the demand index of $O_{\text{max}}$ was entered into the model, which did not yield additional incremental variance,
and was not retained. In summary, Elasticity and subjective tobacco craving were significantly and independently associated with number of cigarettes purchased. See Table 4 for all relevant regression coefficients pertaining to the final model with both variables (i.e., Craving, Elasticity).
CHAPTER 4

DISCUSSION

Based on the existing measurement challenges, the primary goal of the present study was to further investigate the utility of applying a behavioral economic approach to understand craving for cigarettes. More specifically, the study tested the hypothesis that tobacco-related cues, presented in an immersive virtual reality environment, would significantly increase both craving and behavioral economic indices of demand for tobacco. A secondary aim was to determine the incremental contribution of the facets of demand in relation to subsequent smoking behavior assessed during a dual component self-administration paradigm. The results from the present study largely support the first hypothesis that the presentation of tobacco cues would result in significant increases in specific elements of demand for tobacco and subjective tobacco craving. More specifically, the presentation of tobacco cues resulted in significant increases in inelastic demand, $O_{\text{max}}$, and Breakpoint, indicating that relative to the presentation of neutral cues, participants were less sensitive to increases in cigarette prices (i.e., Elasticity), reported greater overall hypothetical expenditure toward cigarettes (i.e., $O_{\text{max}}$), and, indicated that they would continue to consume at least one cigarette at higher price intervals before reporting a complete suppression of tobacco consumption (i.e., Breakpoint), as a result of the presentation of tobacco cues. Although no statistically significant associations were observed between any of the primary outcome variables and the amount of time participants delayed smoking, trend level zero-order associations were observed between delay duration and the CPT indices of Intensity and $O_{\text{max}}$, whereas no such relationship was observed between delay duration and subjective
tobacco craving. Furthermore, regression analyses revealed a significant unique incremental contribution of the demand index of Elasticity, relative to subjective tobacco craving, in relation to the number of cigarettes purchased by participants during the self-administration period. Considered together, the results from the present study provide further evidence for the utility and incremental contributions of behavioral economics to measuring acute motivation for tobacco.

Of note, the pattern of findings from the current study both overlap and contrast with findings from previous investigations, both in terms of the impact of substance specific cues on behavioral economic demand in substance using populations endorsing addictive behavior (Amlung et al., 2012; MacKillop et al., 2010b; MacKillop et al., in press), as well as in relation to previous investigations incorporating the dual component self-administration paradigm in cigarette smokers (Leeman et al., 2010; McKee et al., 2006; McKee et al., 2011; Sayette et al., 2001). The findings from the present study are largely consistent with previous investigations of the effects of substance-specific cue reactivity conditions on indices of substance demand. Specifically, the significant effects of the tobacco cue reactivity condition on the demand indices of Breakpoint and \( O_{\text{max}} \) in the present study were also observed in a recent investigation of the effects of alcohol cues on behavioral economic demand for alcohol (MacKillop et al., 2010b). Furthermore, the finding of significant increases in Elasticity as a result of the presentation of tobacco cues parallels that of a recent investigation of the effects of tobacco cues and tobacco withdrawal on demand for tobacco (MacKillop et al., in press). Thus, this pattern of results across studies provides evidence of consistency in terms of demonstrating specific facets of demand as sensitive to the presentation of substance-specific cues. Most notably, this pattern of results across studies also suggests generalizability of cue effects on specific facets of demand.
across different drug categories and substance use populations, providing further support for the importance of assessing behavioral economic demand for substances in relation to acute drug motivation in a variety of populations.

Results from the present study are somewhat consistent with previous investigations of smoking behavior during a dual component self-administration condition, but also contrast with previous investigations in important ways. Consistent with a recent study in this domain (Leeman et al., 2010), the current study suggests that subjective tobacco craving is a salient predictor of cigarette consumption during the self-administration period. This is the first study to date to examine behavioral economic demand for tobacco in the context of a subsequent dual component self-administration paradigm, and the results from the current study indicate that higher levels of price insensitivity (i.e., Elasticity) are uniquely related to number of cigarettes purchased when contextualized with subjective tobacco craving. Therefore, the present study provides proof of concept of specific elements of demand for tobacco as being particularly relevant in predicting unique aspects of subsequent smoking behavior that cannot be gleaned using self-report measurements of subjective tobacco craving.

Surprisingly, the pattern of results observed between the primary state-based measures assessed following the tobacco cue exposure and the amount of time participants were willing to forego smoking in the present study are largely discrepant from other studies that have incorporated this paradigm. Most notably, the pattern of associations observed in the present study did not reveal significant zero-order correlations between subjective tobacco craving and the amount of time participants were willing to delay smoking, which is in direct contrast with studies that have demonstrated significant associations between delay duration and tobacco craving (Leeman et al., 2010; Sayette et al., 2001; McKee et al., 2011). The lack of
correspondence between the results from the present study and the aforementioned investigations may be partially due to differences in measurements of craving utilized across investigations. More specifically, the present study utilized a five-item visual analog scale of craving, whereas the aforementioned studies utilized either a one item measure of craving (Sayette et al., 2001), or, a 10-item measurement encapsulating positive and negative reinforcing aspects of craving (Leeman et al., 2010; McKee et al., 2011). An additional possibility for the lack of association between subjective craving and delay duration is the relatively lower levels of cigarette consumption in the present sample relative to the aforementioned studies.

There were also noteworthy differences between the present study and other previous studies investigating the impact of substance cues on behavioral economic demand which are potentially meaningful. First, the additional demand indices of \( P_{\text{max}} \) and Intensity exhibited significant increases in response to alcohol cues in MacKillop et al. (2010b), whereas these indices did not reach the level of statistical significance in response to tobacco cues in the present study. Moreover, findings from the present study partially contrast with those from another previous investigation of behavioral economic demand for tobacco in relation to the effects of tobacco cues and nicotine deprivation (MacKillop et al., in press), wherein the sole effect of tobacco cues on demand was confined to the demand index of Elasticity. However, it is important to note that the differences observed in the present study may be partially attributed to factors such as study-specific task parameters and sample composition. First, the present study utilized an open-ended choice format for the CPT; that is, participants were not given a specific monetary tab from which to estimate their consumption at each price interval, a feature which has been utilized in previous investigations that have utilized purchased task methodologies (e.g., Amlung et al., 2012; MacKillop et al., in press). Relatedly, the price intervals utilized in the
present study differ somewhat from those utilized in the aforementioned studies and variations in task parameters may be responsible for variations in findings across studies. Second, on the whole, the level of nicotine dependence reported by participants in the present study sample was relatively low compared with MacKillop et al. (in press). Thus, it is possible that the observation of relatively greater number of significant increases in state-based tobacco demand indices in the present study compared with previous investigations is partially due to lower levels of nicotine dependence, arguably rendering individuals more susceptible to cue-induced increases in specific facets of demand for tobacco. A parallel argument could also be made that individuals at higher levels of nicotine dependence are already at ceiling in terms of demand for tobacco before the presentation of tobacco cues, which would preclude the ability to discern any true cue reactivity effects on tobacco demand. However, this is speculative at this time and future studies are clearly needed in this domain in order to test this notion and, more generally, clarify the pattern of cue effects on behavioral economic demand indices.

Taken together, the pattern of results from the current study provides additional support for a behavioral economic approach to acute drug motivation. More specifically, the pattern of results in the present study suggests that specific aspects of acute drug motivation are gleaned from facets of behavioral economic demand that cannot be readily captured via self-report measurements of other salient motivational factors (i.e., subjective tobacco craving, affect). The findings should be considered in the context of the study's strengths and limitations. Strengths include the use of an immersive VR-based cue exposure protocol (Baumann & Sayette, 2006; Bordnick, Graap, Copp, Brooks, & Ferrer, 2005; Lee et al., 2003, 2004; Moon & Lee, 2009; Traylor, Bordnick, & Carter, 2008, 2009), which provoked significant increases in craving and the demand indices. The present study provides further support for the utilization of VR-based
techniques in investigations of acute drug motivation in cigarette smokers. Furthermore, the current study is the first to incorporate a dual component self-administration paradigm in relation to behavioral economic demand for tobacco, which permitted multiple perspectives on motivation for tobacco.

The aforementioned strengths of the study should be considered in conjunction with respective limitations. First, the present study utilized a hypothetical purchase task for the purpose of reducing the limitations of utilizing an actual purchase task, such as ceiling effects and restriction in range. Although estimations for hypothetical rewards were deliberately used to avoid redundancy and have been found to correspond well with estimations toward actual rewards (e.g., Amlung et al., 2012), it is possible that the hypothetical format affected the outcomes. Second, it is important to recognize that the incorporation of both components of the self-administration paradigm used in previous investigations of smoking behavior (Leeman et al., 2010; McKee et al., 2006; McKee et al., 2011), may have confounding effects of one component on the other. That is, the amount of time an individual is willing to delay smoking may be inherently confounded with number of cigarettes purchased, resulting in a potential lack of internal validity as a result of using both components of the self-administration paradigm. That is, increasing levels of delay duration may diminish the impact of the tobacco cue exposure and craving due to the passage of time, and thus reduce the number of cigarettes purchased. Alternatively, the reverse may also be true – that individuals who delay longer may be more likely to purchase more cigarettes due to an incubation of increased tobacco craving over the course of the delay duration. Thus, future investigations may profit from the utilization of either the delay or the self-administration condition in order to reduce the potentially confounding synergistic effects of the combined conditions. Related to that, however, a further limitation of
the present study was the utilization of a single monetary amount in relation to both the delay and the self-administration portions of the study. A recent investigation which utilized varying levels of monetary reinforcement in conjunction with the dual-component self-administration paradigm found significantly lower levels of delay duration as a function of lower monetary reinforcement for delaying smoking (McKee, Weinberger, Shi, Tetrault, & Coppola, in press). Future investigations may consider utilizing several different price increments when incorporating elements of the dual component self-administration paradigm, as differing levels of monetary reinforcement and cigarette costs will likely impact decisions as to how long to forego smoking and how many cigarettes to purchase. Finally, due to issues of inconsistent responding (i.e., low effort), ceiling effects (i.e., participants not reaching break point following neutral cues), and non-numeric responding on the CPT, several participants’ data were necessarily removed from analyses, resulting in a reduced sample size.

In addition to the aforementioned suggestions for future studies, there are additional considerations for future empirical investigations in this domain. Subsumed under the broad category of negative affect, the subjective experiences of stress and tobacco withdrawal are highly-relevant aspects of acute tobacco motivation (Kassel et al., 2007; Baker, Brandon, & Chassin, 2004) and should therefore be considered both directly and interactively in future investigations of demand for tobacco. Future research is also needed in terms of the predictive utility of substance-specific behavioral economic demand in relation to treatment outcome. A recent study found a significant relationship between baseline levels of impulsive decision-making (i.e., delayed-reward discounting – a behavioral economic assay of impulsivity) and treatment outcome status (MacKillop & Kahler, 2009), but as of yet, no such investigations have
been conducted to date in relation to substance-specific behavioral economic demand and likelihood of successful treatment outcome.

To summarize, the aim of the present study was to further apply a behavioral economic approach to craving using a VR methodology. Results from the present study largely support the hypotheses that the presentation of tobacco cues would result in significant increases in indices of demand for tobacco, and, that specific indices of demand would provide unique, incremental variance in terms of predicting subsequent smoking behavior. It is certainly worth acknowledging that not all hypotheses were supported and some of the findings contrasted with those from other recent investigations using the dual-component tobacco self-administration paradigm. Nonetheless, overall, the pattern of results supports the utility of incorporating behavioral economic assays of demand for tobacco as measurements of acute drug motivation and, given the discrepancies and the recency of this domain of inquiry, further applications are warranted.
REFERENCES


The acute effects of nicotine on positive and negative affect in adolescent smokers.


### Participant Characteristics (N=47)

<table>
<thead>
<tr>
<th>Variable</th>
<th>%/M (SD)</th>
</tr>
</thead>
<tbody>
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<td>Gender (% Female)</td>
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</tr>
<tr>
<td>Age (SD)</td>
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<tr>
<td>Ethnicity (%)</td>
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<tr>
<td>Black/African-American</td>
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<td>Asian</td>
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<td>Income</td>
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<td>&lt; $15,000</td>
<td>39.13</td>
</tr>
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<td>$15,000 - $30,000</td>
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<td>$105,000 - $120,000</td>
<td>4.35</td>
</tr>
<tr>
<td>&gt; $120,000</td>
<td>4.35</td>
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<tr>
<td>Cigarettes per Day (SD)</td>
<td>14.9 (7.2)</td>
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<td>Baseline CO ppm (SD)</td>
<td>17.3 (10.5)</td>
</tr>
<tr>
<td>FTND (SD)</td>
<td>4.1 (2.2)</td>
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</table>

*Note.* Baseline CO ppm = Baseline breath carbon monoxide expenditure, parts per million; FTND = Fagerstrom Test for Nicotine Dependence.
Table 2.

Repeating Measures ANOVAs demonstrating effects of virtual reality-based tobacco cue reactivity condition on demand indices, tobacco craving, and affect.

<table>
<thead>
<tr>
<th>Primary Outcome Variables</th>
<th>N</th>
<th>PNC M (SE)</th>
<th>PTC M (SE)</th>
<th>F</th>
<th>p</th>
<th>η²p</th>
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<tr>
<td>Elasticity</td>
<td>47</td>
<td>12.6 (1.84)</td>
<td>20.9 (4.03)</td>
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<td>.18</td>
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<tr>
<td>Intensity</td>
<td>46</td>
<td>13.5 (2.36)</td>
<td>13.8 (2.17)</td>
<td>0.33</td>
<td>.57</td>
<td>.00</td>
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<tr>
<td>$O_{\text{max}}$</td>
<td>47</td>
<td>$3.12 (0.45)$</td>
<td>$4.08 (0.64)$</td>
<td>8.86</td>
<td>.01</td>
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<td>$P_{\text{max}}$</td>
<td>47</td>
<td>$0.91 (0.19)$</td>
<td>$0.96 (0.18)$</td>
<td>0.10</td>
<td>.76</td>
<td>.00</td>
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<td>Breakpoint</td>
<td>42</td>
<td>$1.12 (0.15)$</td>
<td>$1.52 (0.22)$</td>
<td>4.23</td>
<td>.05</td>
<td>.09</td>
</tr>
<tr>
<td>Craving</td>
<td>47</td>
<td>52.0 (3.56)</td>
<td>62.0 (3.90)</td>
<td>26.16</td>
<td>&lt;.01</td>
<td>.36</td>
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<table>
<thead>
<tr>
<th>Secondary Outcome Variables</th>
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<tr>
<td>Affect Tense-Calm</td>
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<tr>
<td>Affect Sad-Happy</td>
</tr>
<tr>
<td>Affect Nervous-Relaxed</td>
</tr>
<tr>
<td>Affect Bored-Excited</td>
</tr>
<tr>
<td>Affect Stressed-Serene</td>
</tr>
<tr>
<td>Affect Depressed-Elated</td>
</tr>
</tbody>
</table>

Note. SE= Standard Error of the Mean; PNC = Post-Neutral Cues; PTC = Post-Tobacco Cues; Elasticity, Intensity, $O_{\text{max}}, P_{\text{max}},$ Breakpoint = Demand indices generated from State-based CPT.
Table 3.
Zero-order Pearson correlations amongst the primary state outcome measures, delay duration, and cigarettes purchased following both cue reactivity conditions. Correlation coefficients listed above the diagonal pertain to associations among variables assessed following the post-neutral cue reactivity condition; values listed below the diagonal pertain to associations among variables assessed following the post-tobacco cue reactivity condition.

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<th>Variable</th>
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<td>-</td>
<td>.67**</td>
<td>.63**</td>
<td>.49**</td>
<td>.79**</td>
<td>.28†</td>
<td>.11</td>
<td>.28†</td>
<td>.17</td>
<td>.24</td>
<td>.01</td>
<td>.21</td>
<td>-1.11</td>
<td>.29</td>
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<td>-</td>
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<td>-10</td>
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<td>.27†</td>
<td>.20</td>
<td>.16</td>
<td>.30*</td>
<td>.00</td>
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<td>3. Onset</td>
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<td>-</td>
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<td>.09</td>
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<td>-</td>
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<td>.05</td>
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<td>-.60**</td>
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<td>12. Affect Depressed-Relaxed</td>
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<td>-.75**</td>
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<td>.35*</td>
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<td>13. Delay Duration</td>
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<tr>
<td>14. # cigs purchased</td>
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<td></td>
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</table>

Note: Delay Duration = amount of delay (mins.) during the delay period; # cigs purchased = number of cigarettes purchased during the self-administration period; † = p < .10; * = p < .05; ** = p < .01
Table 4.

Hierarchical regression analyses with PTC variables exhibiting statistically significant associations with number of cigarettes purchased. Regression coefficients reflect final model values with both variables.

<table>
<thead>
<tr>
<th>Variable</th>
<th>$R^2/\Delta R^2$</th>
<th>$B$</th>
<th>SE</th>
<th>$\beta$</th>
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<td>Craving</td>
<td>.18</td>
<td>.02</td>
<td>.01</td>
<td>.31</td>
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<tr>
<td>Elasticity</td>
<td>.11</td>
<td>.02</td>
<td>.01</td>
<td>.35</td>
</tr>
</tbody>
</table>

*Note. $B$ = unstandardized beta coefficient; $SE$ = standard error of the mean; $\beta$ = standardized beta coefficient; $^* = p < .05; \dagger = p < .10$*
Figure Captions

Figure 1. Black and white screen shots of the virtual reality (VR) environments. Panels A and B depict screenshots of the neutral VR environment; Panels C and D depict screenshots of the tobacco VR environment.

Figure 2. Hypothetical state-based tobacco demand and expenditure curves generated from the cigarette purchase task (CPT) assessed following the presentation of neutral and tobacco cues. Panel A depicts overlapping demand curves, with corresponding estimated consumption plotted with price per cigarette, generated across both time points, with circles and dashed lines depicting the PNC demand curve; diamonds and dotted lines depicting the PTC demand curve. Panel B depicts overlapping expenditure curves, with corresponding maximum expenditure plotted with price per cigarette, generated across both time points, with circles and dash lines depicting the PNC expenditure curve; diamonds and dotted lines depicting the PTC expenditure curve. Intensity refers to consumption at zero cost; Elasticity refers to the slope of the demand curve; Breakpoint refers to the price at which consumption is completed suppressed (depicted in Panel A); $O_{\text{max}}$ refers to maximum expenditure; and, $P_{\text{max}}$ refers to the price associated with $O_{\text{max}}$ (depicted in Panel B).

Figure 3. Bar graphs depicting significant tobacco cue effects on target variables of interest; each panel depicts mean levels of each variable at each time point. Panel A depicts the CPT index of Elasticity (i.e., slope in the demand curve). Panel B depicts the CPT index of $O_{\text{max}}$ (i.e., maximum expenditure toward cigarettes). Panel C depicts the CPT index of Breakpoint (i.e., price at which consumption is completely suppressed). Panel D depicts subjective tobacco craving. Panel E depicts the affect circumplex vector of “Tense $\leftrightarrow$ Calm.”

40
Figure 1.
Figure 2.

A

B
Figure 3.