

Original Investigation

Behavioral Economic Analysis of Withdrawal- and Cue-Elicited Craving for Tobacco: An Initial Investigation

James MacKillop, Ph.D.,^{1,2} Courtney L. Brown, M.S.,¹ Monika K. Stojek, M.S.,¹ Cara M. Murphy, B.S.,¹ Lawrence Sweet, Ph.D.,³ & Ray S. Niaura, Ph.D.^{4,5}

¹ Department of Psychology, University of Georgia, Athens, GA

² Center for Alcohol and Addiction Studies, Brown University, Providence, RI

³ Department of Psychiatry and Human Behavior, Brown University, Providence, RI

⁴ Schroeder Institute for Tobacco Research and Policy Studies, American Legacy Foundation, Washington, DC

⁵ Department of Health, Behavior and Society, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

Corresponding Author: James MacKillop, Ph.D., Department of Psychology, University of Georgia, Athens, GA 30602, USA.
Telephone: 706-542-3033; Fax: 706-542-8048; E-mail: jmackill@uga.edu

Received November 22, 2011; accepted January 9, 2012

Abstract

Introduction: The role of craving in nicotine dependence remains controversial and may be a function of measurement challenges. The current study used behavioral economic approach to test the hypotheses that subjective craving from acute withdrawal and exposure to tobacco cues dynamically increases the relative value of cigarettes.

Methods: Using a 2 (1-hr/12-hr deprivation) × 2 (neutral/tobacco cues) within-subjects design, 33 nicotine dependent adults completed 2 laboratory sessions. Assessment included subjective craving and behavioral economic indices of cigarette demand, namely Intensity (i.e., cigarette consumption at zero cost), O_{\max} (i.e., maximum total expenditure), Breakpoint (i.e., highest acceptable price for cigarettes), P_{\max} (i.e., price at which consumption becomes sensitive to price), and elasticity (i.e., price sensitivity). Behavioral economic indices were generated using a Cigarette Purchase Task in which participants selected between cigarettes for a subsequent 2-hr self-administration period and money.

Results: Main effects of deprivation and tobacco cues were present for subjective craving and multiple behavioral economic indices of cigarette demand. Interestingly, deprivation significantly increased Breakpoint ($p \leq .01$) and P_{\max} ($p \leq .05$) and had trend-level effects on Intensity and O_{\max} ($p \leq .10$); whereas cues significantly reduced elasticity ($p \leq .01$), reflecting lower sensitivity to increasing prices. Heterogeneous associations were evident among the motivational variables but with aggregations suggesting variably overlapping motivational channels.

Conclusions: These findings further support a behavioral economic approach to craving and a multidimensional conception of acute motivation for addictive drugs. Methodological considerations, including potential order effects, and the need for further refinement of these findings are discussed.

doi:10.1093/ntr/nts006

Advance Access published on March 13, 2012

© The Author 2012. Published by Oxford University Press on behalf of the Society for Research on Nicotine and Tobacco. All rights reserved. For permissions, please e-mail: journals.permissions@oup.com

Introduction

Despite a long history of study, the role of subjective craving in nicotine dependence remains a matter of considerable controversy (MacKillop & Monti, 2007; Perkins, 2009; Sayette et al., 2000). This is largely because of substantial variability in the empirical findings. On one hand, cravings are widely reported and can be readily assessed (Cox, Tiffany, & Christen, 2001; Schuh & Stitzer, 1995), but on the other, the associations between craving and actual tobacco use have been highly variable in human laboratory studies (Dallery, Houtsmuller, Pickworth, & Stitzer, 2003; Houtsmuller & Stitzer, 1999; Tiffany & Carter, 1998) and clinical studies (Killen & Fortmann, 1997; Niaura, Abrams, Monti, & Pedraza, 1989; Perkins, 2009). Some of this variability may be related to measurement limitations. The most common method of assessing craving is via subjective self-report, which may be influenced by number of biases (Sayette et al., 2000; Tiffany, Carter, & Singleton, 2000). For example, individuals may vary in their semantic construal of the term “craving” as well as in their positive and negative attributions about the term. Furthermore, there is considerable variability in the elicitation and magnitude of subjective craving across individuals (Niaura et al., 1998; Shiffman et al., 2003), suggesting that its role may vary substantially. Finally, the role of subjective craving may be further obscured by more general limitations of memory and introspection (Hammersley, 1994; Wilson & Dunn, 2004).

The field of behavioral economics integrates principles from psychology and economics and has been extensively applied to the study of addictive behavior (Bickel & Vuchinich, 2000; MacKillop, Amlung, Murphy, Acker, & Ray, 2011). Behavioral economics can also be applied to understanding subjective craving for tobacco and other drugs, proposing that craving reflects an acute increase in the relative value of a commodity and is most meaningfully understood when measured in terms of incentive

value (Loewenstein, 1999; MacKillop & Monti, 2007). As such, behavioral economics may improve the measurement of craving by translating subjective desire into more objective measures of value, such as units consumed or dollars spent. Several previous studies, albeit in investigations that were not explicitly applying a behavioral economic approach, have found that experimental manipulations that typically increase craving also increased effort expended on operant tasks for cigarettes (Perkins, Epstein, Grobe, & Fonte, 1994; Perkins, Grobe, Weiss, Fonte, & Caggiola, 1996; Willner, Hardman, & Eaton, 1995). However, these studies have had various limitations, such as not always concurrently assessing subjective craving. In addition, a number of laboratory studies have found that subjective craving for cigarettes is significantly positively correlated with behavioral economic measures of relative value (Leeman, O'Malley, White, & McKee, 2010; McKee et al., 2011; Perkins, Grobe, & Fonte, 1997; Sayette, Martin, Wertz, Shiffman, & Perrott, 2001), but the relationships reported were cross-sectional. One study examined the effect of deprivation on behavioral economic indices of impulsivity and value but used a suboptimal measure of relative value (Field, Santarcangelo, Sumnall, Goudie, & Cole, 2006). Thus, the studies to date have incompletely addressed this question.

Furthermore, no studies in this area have applied what is arguably the most comprehensive methodology for quantifying value in behavioral economics, demand curve analysis (Hursh, Galuska, Winger, & Woods, 2005). Demand is an essential concept in economics and can be succinctly defined as the actual or preferred consumption of a commodity at a given price. Considered across multiple levels of price, demand curve analysis refers to the quantification of the relationship between consumption of the commodity and its cost. Demand curve analysis characterizes five different facets of the curve, each reflecting indices of motivation. These are (a) Intensity (i.e., consumption under zero or minimal price); (b) O_{\max} (i.e., maximum money allocated to the commodity across prices); (c) P_{\max} (i.e., the price at which demand becomes elastic); (d) Breakpoint (i.e., the first price that completely suppresses consumption to zero); and (e) elasticity (i.e., the proportionate slope of the overall curve). A prototypic demand curve and the indices are presented in Figure 1. Theoretically, the indices are related to one another, but nonetheless represent distinct facets of motivation (Bickel, Marsch, & Carroll, 2000). Taken together, demand curve analysis comprehensively fractionates the relative value of a commodity into multiple motivational indices of consumption, expenditure, and price sensitivity.

In applying behavioral economics to subjective craving, several previous studies on alcohol largely parallel the tobacco studies. Survey and laboratory studies have similarly reported significant associations between subjective craving and behavioral economic indices of value (MacKillop, Menges, McGeary, & Lisman, 2007; MacKillop, Miranda, et al., 2010). Moreover, in a recent cue reactivity study that also used demand curve analysis, alcohol cues dynamically increased both craving and alcohol demand (MacKillop, O'Hagen, et al., 2010). Specifically, compared with neutral cues, alcohol cues significantly increased Intensity, O_{\max} , P_{\max} , and Breakpoint and significantly decreased elasticity. Importantly, craving and behavioral economic indices of value appeared to provide complementary motivational information.

The current study sought to apply a behavioral economic approach to subjective craving for tobacco in two domains,

withdrawal-elicited craving and cue-elicited craving. Among nicotine dependent individuals, a period of mandatory nicotine abstinence acutely induces withdrawal, including increasing subjective craving (e.g., Sayette et al., 2001). Equally, the presence of tobacco cues, such as cigarettes and smoking paraphernalia, has consistently been shown to elicit acute increases in subjective craving (Carter & Tiffany, 1999). Using two extended laboratory sessions, this study used a 2×2 factorial design to examine the main effects and interactions of a 12-hr deprivation period and tobacco cues on subjective craving and cigarette demand. The a priori hypotheses were that tobacco cues and deprivation would significantly increase both subjective craving and the relative value of cigarettes according to the indices of demand. Given mixed previous findings (Bailey, Goedecker, & Tiffany, 2010; Sayette et al., 2001), no specific interaction hypotheses were made. Similarly, affect and arousal were assessed, but no specific hypotheses were made based on mixed previous findings (Carter & Tiffany, 1999).

Methods

Design

The study employed a 2 (1-hr deprivation/12-hr deprivation) \times 2 (neutral cues/tobacco cues) within-subjects design during two extended laboratory sessions.

Participants

Study participants were recruited from the community using advertisements. Inclusion criteria were (a) 18–65 years of age, (b) self-reported smoking 15 or more cigarettes/day, (c) nontreatment seeking, and (d) computer usage 4+ days/week. Exclusion criteria were (a) living with someone who participated in the study, (b) being enrolled in smoking cessation treatment (current or past 90 days), (c) pregnancy/actively seeking to conceive (female participants only), and (d) University of Georgia employee/retiree or non-U.S. citizen without a social security number (required for participant compensation). Forty-one participants met criteria and completed the protocol, but four exhibited unacceptably low effort or poor compliance (e.g., random responding during assessments, smoking the cigarette during the cue exposure) and four were noncompliant with the deprivation manipulation, providing either expired-air carbon monoxide (CO) samples more than 10 ppm or a comparative increase in CO, resulting in a final sample of 33. The participants were predominantly male (70%), White (82%, 9% Black, 9% mixed race), and of relatively low income (55% <\$15,000; 12% \$15,000–\$35,000, 6% \$30,000–\$45,000, 9% \$45,000–\$60,000; 6% \$75,000–\$90,000, 3% \$90,000–\$105,000; 0% \$105,000–\$120,000, 9% >\$120,000). Average age was 30.85 ($SD = 12.80$) and average years of education was 14.03 ($SD = 1.98$). In terms of smoking characteristics, average cigarettes per day was 19.81 ($SD = 5.69$) and average score on the Fagerström Test for Nicotine Dependence (FTND) was 5.10 ($SD = 2.18$).

Procedure

The study comprised a telephone screen and two extended laboratory sessions (4 hr and 3 hr, respectively). The two sessions were procedurally similar insofar as each comprised a check-in, a smoking cue reactivity paradigm, and a 2-hr ad libitum cigarette self-administration period (see Supplementary Figure 1). However, for the first session, participants smoked a cigarette at

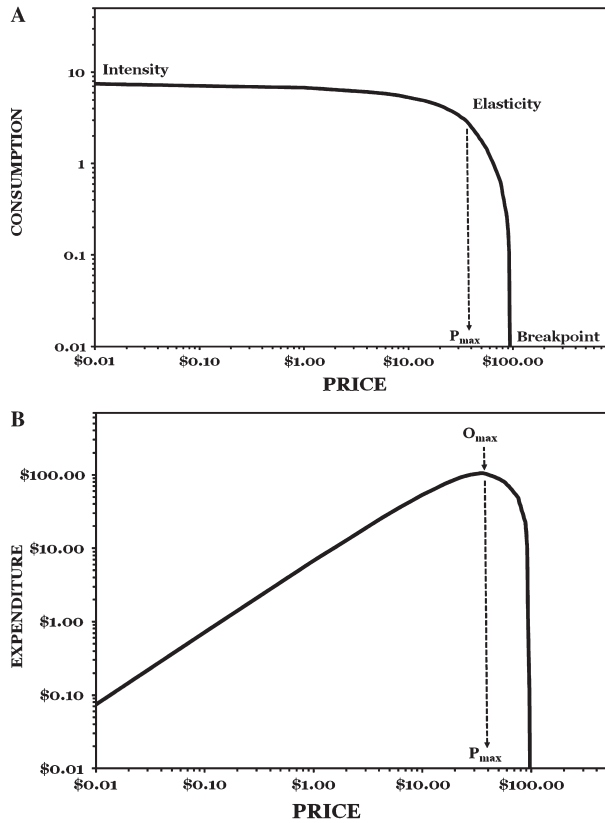


Figure 1. Prototypic behavioral economic demand and expenditure curves with the associated indices of relative value. Panel A depicts the demand curve and Panel B depicts the expenditure curve. Intensity of demand refers to consumption under conditions of zero or minimal cost; elasticity refers to the proportionate slope of either a portion or the overall demand curve; Breakpoint refers to the first price to suppress consumption to zero; O_{max} refers to the maximum total monetary allocation to consumption; P_{max} refers to the first price at which demand becomes elastic (i.e., decreases in consumption are proportionately greater than increases in price) and is also the price at which O_{max} is reached.

the outset of the session, creating a 1-hr deprivation period, and for the second session, participants were asked to abstain from smoking for at least 12 hr, which was verified using CO (≤ 10 ppm). The first session was longer because it included informed consent, orientation to the study procedures, and a collateral descriptive assessment (e.g., demographics), which together lasted 1 hr. Of note, the deprivation session order was always second because of possible interference with the study orientation and Institutional Review Board (IRB) concerns about attempting to implement experimental manipulations prior to enrollment.

The cue reactivity paradigm used previously established practices (Niaura et al., 1989, 1998, 2005). Specifically, exposure to tobacco cues comprised the participant opening an unopened pack of their preferred cigarettes, removing the insert and one cigarette, lighting the cigarette with a plastic lighter, and holding the lit cigarette without smoking it. Exposure to neutral cues comprised the participant taking a small golf pencil out of a box of pencils and manipulating it, specifically holding and writing with the pencil on a small pad of paper. Assessments were conducted following both the neutral cues and tobacco cues, with the relevant

cues and money available (\$10 in single dollar bills) placed adjacent to the computer monitor displaying the questions. Thus, stimuli associated with both outcomes were equally present. Postcue assessments comprised subjective craving and affect, psychophysiological arousal, and the behavioral economic Cigarette Purchase Task (CPT) that determined subsequent access to cigarettes during the 2-hr self-administration period. Neutral cues were always presented prior to tobacco cues based on evidence of carryover effects (Monti et al., 1987; Sayette, Griffin, & Sayers, 2010).

Of note, during orientation, participants were informed that the self-administration period was required and the only cigarettes available would come from decisions they made during preceding assessments (e.g., participants would not conclude the study sooner if they elected not to smoke). Compensation for 7 hr of participation was \$105, mailed as a check, and up to \$20 from the behavioral economic task (\$10/session), available immediately in cash. All procedures were approved by the University of Georgia IRB.

Assessments

The assessment chronology is also provided in Figure 2. Nicotine dependence was assessed using the FTND (Heatherton, Kozlowski, Frecker, & Fagerström, 1991), which exhibited adequate internal reliability ($\alpha = .75$). Withdrawal was assessed with the Minnesota Nicotine Withdrawal Scale-Revised (MNWS; Hughes & Hatsukami, 1986), which uses item-level analysis. CO was assessed via a breath sample (piCO+ Smokerlyzer, Bedfont Scientific Ltd.). Pregnancy status was verified via commercially available pregnancy tests.

During the cue reactivity paradigm, participants were assessed for subjective craving, affect, psychophysiological arousal, and behavioral economic demand for cigarettes. Craving was assessed using a five-item, 100-point Likert-type self-report measure (Shiffman et al., 2003), which exhibited high internal reliability ($\alpha = .93$). Affect was assessed using six Likert-type items (-50 to +50) from the affect circumplex (Posner, Russell, & Peterson, 2005): Tense \leftrightarrow Calm, Sad \leftrightarrow Happy, Nervous \leftrightarrow Relaxed, Bored \leftrightarrow Excited, Stressed \leftrightarrow Serene, Depressed \leftrightarrow Elated. Psychophysiological arousal was assessed as heart rate (DRE Waveline Nano Handheld Pulse Oximeter). Behavioral economic demand for cigarettes was assessed using a CPT, which assesses preferred cigarette consumption at an array of prices. Unlike previous studies (Hitsman et al., 2008; Jacobs & Bickel, 1999; MacKillop et al., 2008; Murphy, MacKillop, Tidey, Brazil, & Colby, 2011). A notable feature of the study was that the CPT was for actual cigarette and money. Specifically, participants were informed that they had a \$10 “tab” that they could either keep as cash or allocate toward up to 10 cigarettes during the self-administration period. Participants were also informed that the actual amount of cash and/or cigarettes they would receive would be determined by randomly selecting a poker chip from a fishbowl containing poker chips that each pertained to one of the CPT items, a common strategy in behavioral economic studies (e.g., Kirby, Petry, & Bickel, 1999). To ensure no confusion, the study orientation provided detailed information about all the parameters of the CPT, including a practice purchase task using hypothetical cans of soda in an identical format. The 22 specific prices on the CPT were \$0, 2¢, 5¢, 10¢, 20¢, 30¢, 40¢, 50¢, 60¢, 70¢, 80¢, 90¢, \$1, \$2, \$3, \$4, \$5, \$6, \$7, \$8, \$9, and \$10. At each price, participants selected their preferred number of cigarettes. The task automatically generated

the amount of remaining money to eliminate any potential influence of an information deficit, and responses could be amended. Above \$1, only the number of cigarettes available within the tab served as the maximum. With regard to the task outcome, after a poker chip was selected, participants were immediately given the cigarettes and money that corresponded to their response. The number of cigarettes smoked during the self-administration period was recorded.

Data Analysis

The data were initially examined for distribution abnormalities and outliers. Distributions were adequate, but two outliers, defined as $Z > 3.29$ (Tabachnick & Fidell, 2004), were identified for elasticity and were recoded as one unit above the next highest nonoutlying value at the second decimal (Tabachnick & Fidell, 2004). Indices of demand were generated using an observed values approach (Murphy & MacKillop, 2006). Specifically, Intensity was defined as consumption at zero price; O_{max} was defined as the maximum amount of money allocated to cigarettes; P_{max} was defined as the price at which O_{max} was achieved; and Breakpoint was defined as the first price that suppressed consumption to zero. In addition to observed values, elasticity was derived using nonlinear regression as the α parameter from the recently developed exponential demand equation (Hursh & Silberberg, 2008):

$$\log_{10} Q = \log_{10} Q_0 + k(e^{-\alpha Q_0 C} - 1),$$

where Q = consumption at a given price; Q_0 = maximum consumption (consumption at zero or minimal price); k = a constant

across individuals that denotes the range of consumption values in \log_{10} , in this case, a constant of 2; C = the cost of the commodity (price); and α = the derived demand parameter reflecting a standardized rate of decline of consumption.

Effects of deprivation were assessed using one-way within-subjects analyses of variance (ANOVAs; 1-hr deprivation/12-hr deprivation). The primary analyses of effects of cues and deprivation used 2 (1-hr deprivation/12-hr deprivation) \times 2 (neutral cues/tobacco cues) within-subjects ANOVAs. Income was a candidate covariate of the demand indices but was not included because of nonsignificant associations ($p > .31$). To avoid ceiling effects, participants were excluded from subjective craving and demand analyses if they were at scale maximum prior to any manipulation (i.e., neutral cue exposure during the first session) because this necessarily prevented detecting effects of cues or deprivation. This was a significant issue for Intensity and a minor issue for craving, Breakpoint, O_{max} , and P_{max} . Continuous analyses used Pearson's product-moment correlations (r).

A small number of data points were missing. One participant had one missing item on the FTND, which was imputed via mean imputation; two participants only completed the first craving item for neutral cues at Session 2, which in both cases was treated as the mean value. Two participants were missing affect values for one assessment, but no imputation was made because of the single item format.

Statistical significance was set at the conventional two-tailed $\alpha \leq .05$, with statistical trends defined as $p \leq .10$. All analyses were conducted using GraphPad Prism and SPSS 16.0.

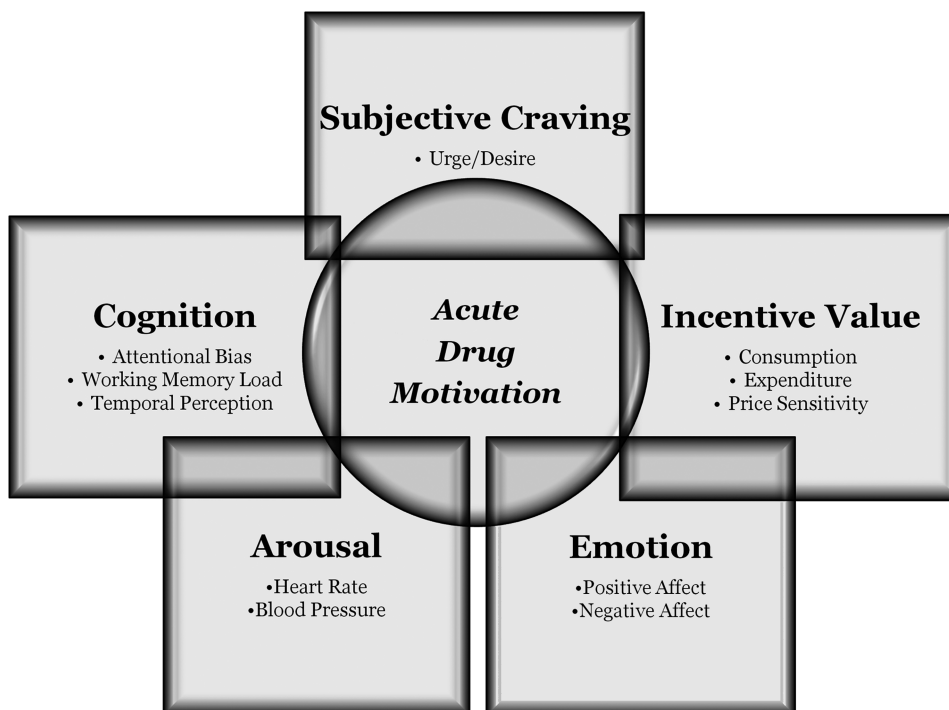


Figure 2. A multidimensional conception of acute drug motivation. Each domain has been implicated in an individual's dynamic motivational state in relation to drug acquisition and consumption. Importantly, although overlapping relationships exist to an extent, especially within domains, acute motivation is fundamentally multidimensional, not unidimensional.

Results

Manipulation Checks and Preliminary Analyses

The 12-hr deprivation significantly reduced CO and significantly increased craving, anger/irritability/frustration, anxiety, difficulty concentrating, restlessness, and impatience on the MNWS (Supplementary Material). Exponential modeling ($k = 2$) provided an excellent fit to the data for overall mean values ($R^2 = .99$) and a very good fit for individual values across CPTs (mean $R^2 = .88$). During Session 1 (S1), 67% of participants received at least one cigarette ($M = 5.18$, range = 1–10); during Session 2 (S2), 70% received at least one cigarette ($M = 4.83$, range = 1–10). Participants smoked 83% and 86% of the cigarettes available in S1 and S2, respectively, and the number of cigarettes available was significantly correlated with cigarettes smoked (S1 $r = .79$, S2 $r = .82$; $p < .001$).

Effects of Deprivation and Tobacco Cues

Main effects and interaction effects of deprivation and tobacco cues are presented in Table 1. Deprivation significantly increased craving, nervousness, stress, and two of the behavioral economic indices of demand and significantly decreased heart rate. Deprivation also increased Intensity and O_{max} at the level of statistical trends. Tobacco cues significantly increased craving, tension, nervousness, and stress but significantly decreased price elasticity. Deprivation and cues interacted with regard to Sadness ↔ Happiness, reflecting a positive mood state following neutral cues with no deprivation ($M = 10.45$, $SEM = 3.42$) but significantly lower in all other conditions (No Deprivation + Tobacco: $M = 1.77$,

$SEM = 2.21$; Deprivation + Neutral: $M = 2.13$, $SEM = 2.74$; Deprivation + Tobacco: $M = 1.61$, $SEM = 2.33$).

Associations Among Motivational Variables

Correlations among the variables that were significantly affected by either manipulation are presented in Table 2. With regard to deprivation, it was notable that craving was consistently associated with Intensity and that O_{max} , P_{max} , and Breakpoint substantially overlapped, approaching collinearity. Heart rate was uncorrelated with the other indices. With regard to cues, craving and elasticity were inversely correlated at each cross-sectional assessment, as expected (i.e., greater craving reflects lower price sensitivity).

Discussion

The goal of the current study was to apply a behavioral economic approach to understanding subjective craving for tobacco. As predicted, in addition to significantly increasing craving, both deprivation and tobacco cues significantly increased the relative value of cigarettes according to several indices. Specifically, deprivation significantly increased the maximum amount participants were willing to pay for cigarettes (Breakpoint) and the price at which they become sensitive to the price of cigarettes (P_{max}), and deprivation also exerted trend-level increases for how many cigarettes participants wanted at minimal price (Intensity) and the total amount of money they would pay for cigarettes (O_{max}). In contrast, for tobacco cues, a significant decrease in

Table 1. Means, SEs, F Ratios, Statistical Significance, and Effect Sizes (η_p^2) for 2 × 2 Within-Subjects Factorial Analyses of Variance for the Main Effects and Interaction Effect of 1-hr/12-hr Cigarette Deprivation and Neutral/Smoking Cues on Craving, Behavioral Economic Indices of Demand, Affect, and Heart Rate

	df	Deprivation level (DEP)				Cue type (CUE)				DEP × CUE		
		ND (SE)	D (SE)	F	η_p^2	NC (SE)	SC (SE)	F	η_p^2	F	p	η_p^2
Primary												
Craving	1, 31	65.58 (4.28)	75.30 (4.15)	8.63**	0.22	64.79 (4.12)	76.09 (3.77)	53.90***	0.64	2.45	.13	0.07
Intensity	1, 10	4.96 (56)	6.00 (0.70)	4.26†	0.30	5.50 (0.58)	5.46 (0.59)	0.19	0.02	1.96	.19	0.16
O_{max}	1, 25	3.55 (0.45)	4.51 (.61)	2.94†	0.11	4.13 (0.54)	3.93 (0.46)	2.82	0.10	0.87	.36	0.03
P_{max}	1, 26	2.20 (0.39)	3.79 (0.61)	6.08*	0.19	3.03 (0.38)	3.95 (0.43)	0.24	0.01	0.27	.61	0.01
BP	1, 25	3.49 (0.37)	4.88 (0.58)	7.91**	0.24	4.27 (0.40)	4.10 (0.44)	2.11	0.08	1.21	.28	0.05
α	1, 32	.03 (0.004)	.02 (0.004)	1.84	0.05	.04 (0.005)	.02 (0.002)	57.93***	0.64	1.55	.22	0.05
Secondary												
$S \leftrightarrow H$	1, 30	6.11 (2.40)	1.87 (2.24)	2.50	0.08	6.29 (2.60)	1.69 (1.69)	4.39*	0.13	5.38	.03	0.15
$N \leftrightarrow R$	1, 30	2.82 (2.60)	-2.42 (2.55)	6.06	0.17	3.34 (2.43)	-2.94 (2.49)	16.99***	0.36	2.62	.12	0.08
$B \leftrightarrow E$	1, 30	-5.63 (3.08)	-5.61 (2.96)	0.00	0.00	-6.37 (2.61)	-4.87 (2.94)	0.46	0.01	3.10	.09	0.09
$S \leftrightarrow S$	1, 30	.65 (2.71)	-8.50 (2.62)	12.02**	0.29	-1.13 (2.29)	-6.73 (2.60)	12.18**	0.29	3.11	.09	0.09
$D \leftrightarrow E$	1, 30	-.39 (1.86)	-1.58 (2.84)	0.31	0.01	-.71 (2.33)	-1.26 (2.04)	0.41	0.01	0.02	.90	0.01
$T \leftrightarrow C$	1, 30	-.74 (2.81)	-5.61 (3.50)	2.02	0.06	1.61 (3.24)	-7.97 (2.59)	16.03***	0.35	0.76	.39	0.03
HR	1, 32	74.56 (2.16)	70.15 (2.10)	5.79*	0.15	72.12 (2.14)	72.59 (1.95)	0.12	0.01	1.57	.22	0.05

Note. Interaction means are not presented. ND = nondeprived; D = deprived; NC = neutral cues; SC = smoking cues; BP = Breakpoint; $T \leftrightarrow C$ = Tense/Calm; $S \leftrightarrow H$ = Sad/Happy; $N \leftrightarrow R$ = Nervous/Relaxed; $B \leftrightarrow E$ = Bored/Excited; $S \leftrightarrow S$ = Stressed ↔ Serene; $D \leftrightarrow E$ = Depressed/Elated.

† $p \leq .10$. * $p \leq .05$. ** $p \leq .01$. *** $p \leq .001$.

Table 2. Associations Among Motivational Dependent Variables Based on Main Effects of Deprivation and Cues

Variable	Main effect: deprivation							
	1	2	3	4	5	6	7	8
1. Craving	1.00	-0.02	-0.22	0.69*	0.24	0.23	0.18	0.12
2. Nervous ↔ Relaxed	-0.12	1.00	0.61***	-0.41	-0.26	-0.35	-0.30	-0.12
3. Stressed ↔ Serene	-0.39	0.57***	1.00	-0.44	-0.26	-0.32	-0.29	-0.34
4. Intensity	0.68*	-0.26	-0.51	1.00	-0.06	-0.16	-0.06	0.05
5. O_{max}	0.41*	0.00	-0.32	0.18	1.00	0.93***	0.95***	0.26
6. P_{max}	0.10	-0.05	-0.14	-0.04	0.78***	1.00	0.98***	0.20
7. Breakpoint	0.22	-0.26	-0.18	0.11	0.83***	0.90***	1.00	0.21
8. HR	0.08	0.05	-0.06	-0.13	0.25	0.11	0.13	1.00

Variable	Main effect: cues				
	1	2	3	4	5
1. Craving	1.00	-0.26	0.00	-0.35	-0.38*
2. Tense ↔ Calm	-0.27	1.00	0.77***	0.68***	0.20
3. Nervous ↔ Relaxed	0.01	0.76***	1.00	0.55***	0.25
4. Stressed ↔ Serene	-0.20	0.45**	0.58***	1.00	0.18
5. Elasticity (α)	-0.46**	0.11	-0.05	0.15	1.00

Note. For deprivation, correlations below the intercepts (1.0) are for the satiation condition (no deprivation) and correlations above the intercepts are for 12-hr deprivation. For cues, correlations below the intercepts are for the neutral cues and correlations above are for smoking cues. Although the associations are provided for descriptive purposes, note that correlations denoted as $p < .001$ survive a Bonferroni correction.

* $p \leq .05$. ** $p \leq .01$. *** $p \leq .001$.

elasticity was present, meaning that the presence of tobacco cues made participants generally less sensitive to the price of cigarettes. This is the first study (to our knowledge) to apply a demand curve analysis approach to understanding the effects of deprivation and cues on the relative value of tobacco. In demonstrating that deprivation and tobacco cues dynamically increase the value of cigarettes, these findings reveal behavioral economic dimensions of subjective craving and extend the results of several previous associations between craving for tobacco and its relative value (Field et al., 2006; Perkins et al., 1994, 1996; Sayette et al., 2001).

Concurrent with testing the primary hypotheses, this study examined the associations among the motivational variables to understand their interrelationships. Here, a number of interesting patterns emerged. With regard to the effects of deprivation, there were essentially three aggregations among variables or what could be considered variably overlapping motivational “channels.” The first comprised significant associations among subjective craving, Intensity, nervousness, and stress; the second comprised the substantial associations among O_{max} , P_{max} , and Breakpoint, which essentially converged during the deprivation condition; and the third comprised heart rate, which was independent of the other variables. With regard to the effects of cues, two aggregations were present. The first channel comprised significant cross-sectional associations between craving and elasticity, albeit of modest magnitude, and the second comprised significant associations among tension, nervousness, and stress—a negative affect channel—of moderate magnitudes. These correlational findings are consistent with the heterogeneous relationships previously observed among dependent variables in cue reactivity studies (Carter & Tiffany, 1999). Interestingly, based on the associations for several variables, the current findings support

the notion that motivational indices are more strongly interrelated during acute drive states (Sayette, Martin, Hull, Wertz, & Perrott, 2003), albeit with modestly greater coherence observed.

Importantly, however, some caution should be applied to interpreting these findings and several limitations are worthy of consideration. First, not all of the demand indices were sensitive to the effects of deprivation or tobacco cues, which is in contrast to the earlier alcohol cue reactivity study in which alcohol cues uniformly affected demand for alcohol (MacKillop, O’Hagen, et al. 2010). This could be a valid reflection of differences between the two drugs or it may be function of methodological differences between the studies. For example, the current sample size was considerably smaller, and more participants would be likely to have brought the relationships into sharper relief, such as the statistical trends observed. In addition, this was the first study to link CPT choices to actual outcomes, necessarily constraining the price and consumption within practical experimental parameters, but also restricting the range and potentially truncating meaningful variability. The most obvious instance of this was baseline ceiling effects, which had major effects on Intensity. A final consideration is that the design did not counterbalance the order of deprivation, meaning that the effects cannot readily be disentangled from possible order effects. Although it seems improbable that all the significant deprivation effects are attributable to the passage of time or repeated assessment instead of the deprivation manipulation itself, it is nonetheless possible. This could be addressed in future studies by separating the consent and initial orientation from the experimental procedures. Taken together, for these reasons, the current study should be considered an initial study and not conclusive. Replicating the observed significant effects and directly addressing these issues will be critical in future studies.

Acknowledging these considerations, these results and the findings from previous investigations nonetheless suggest an important evolution in the measurement and understanding of subjective craving for addictive drugs. First, there is consistent evidence that experimental manipulations that increasing subjective craving also dynamically affect diverse other processes, such as cognitive processing (e.g., Field, Munafò, & Franken, 2009), approach–avoidance inclinations (e.g., Curtin, Barnett, Colby, Rohsenow, & Monti, 2005), automaticity (e.g., Houben & Wiers, 2008), and incentive value, as in the current study. Importantly, these findings do not suggest that subjective craving is simply a readily accessible part of a monolithic whole. Rather, it is often only modestly related or unrelated to other these indicators. In this way, these alternative indicators do not “translate” subjective desire into more objective measures but capture separate motivational channels concurrently. As such, they support the notion that subjective desire is but one indicator of “acute drug motivation,” a superordinate construct defined as an individual’s state-level drive for the drug that is multidimensional in nature. In other words, subjective craving may reflect an experiential dimension of acute drug motivation, demand indices may reflect an incentive value dimension, attentional bias may represent a cognitive dimension, and so on. This is illustrated in Figure 2. The typical amount of overlap among domains remains an open question, but may emerge across studies (e.g., Field et al., 2009), and the relative theoretical and clinical importance of different indicators is by no means established. Nonetheless, a shift in focus to acute drug motivation as a multidimensional construct may stimulate progress and reduce the ambiguity by emphasizing the importance of diverse psychological processes beyond subjective craving.

Finally, the current findings may also have important applications. For example, behavioral economic indices may be useful in clinical research, where the predictive validity of cue-elicited subjective craving has been actively debated (Munafò & Hitsman, 2010; Perkins, 2009; Tiffany & Wray, 2009). Supporting this notion, several recent studies have found delayed reward discounting, a behavioral economic index of impulsivity, predicts smoking cessation outcomes (e.g., MacKillop & Kahler, 2009), and there is some initial evidence that indices of demand might also be clinically informative (MacKillop & Murphy, 2007; Madden & Kalman, 2010). In addition, craving is a common target of pharmacotherapy mechanism studies (e.g., Niaura et al., 2005; Shiffman et al., 2003), and behavioral economic indices of demand may be useful in that domain or for understanding behavioral interventions. Finally, functional magnetic resonance imaging studies have used these manipulations to investigate the neural basis for craving (e.g., David et al., 2007) and integrating behavioral economic concepts to develop a neuroeconomic understanding of craving also has significant potential. Although clearly further study is necessary to confirm and refine these relationships, these findings nonetheless suggest a number of promising future directions in both basic and clinical research.

Supplementary Material

Supplementary Figure 1 and Table 1 can be found online at <http://www.ntr.oxfordjournals.org>

Funding

This study was supported by a grant from the Global Research Awards for Nicotine Dependence, an extramural peer-reviewed funding program sponsored by Pfizer, Inc., and National Institutes of Health grants K23 AA016936 and P30 DA027827. The funding bodies played no role in the study’s design, data collection, analysis, or interpretation.

Declaration of Interests

The authors have no conflicts of interest with regard to the findings in this study.

Acknowledgments

The authors would like to gratefully acknowledge the assistance of a number of undergraduate Research Assistants at the University of Georgia: Chris Bower, Whitney Adams, Stephanie Adrean, Patricia Hatcher, Katie Hebrank, Casey Howard, John Knopf, and Spencer Speagle.

References

- Bailey, S. R., Goedecker, K. C., & Tiffany, S. T. (2010). The impact of cigarette deprivation and cigarette availability on cue-reactivity in smokers. *Addiction, 105*, 364–372. doi:10.1111/j.1360-0443.2009.02760.x
- Bickel, W. K., Marsch, L. A., & Carroll, M. E. (2000). Deconstructing relative reinforcing efficacy and situating the measures of pharmacological reinforcement with behavioral economics: A theoretical proposal. *Psychopharmacology (Berlin), 153*, 44–56. doi:10.1007/s002130000589
- Bickel, W. K., & Vuchinich, R. E. (Eds.) (2000). *Reframing health behavior change with behavioral economics*. Mahwah, NJ: Lawrence Erlbaum.
- Carter, B. L., & Tiffany, S. T. (1999). Meta-analysis of cue-reactivity in addiction research. *Addiction, 94*, 327–340. doi:10.1046/j.1360-0443.1999.9433273.x
- Cox, L. S., Tiffany, S. T., & Christen, A. G. (2001). Evaluation of the brief questionnaire of smoking urges (QSU-brief) in laboratory and clinical settings. *Nicotine & Tobacco Research, 3*, 7–16. doi:10.1080/14622200020032051
- Curtin, J. J., Barnett, N. P., Colby, S. M., Rohsenow, D. J., & Monti, P. M. (2005). Cue reactivity in adolescents: Measurement of separate approach and avoidance reactions. *Journal of Studies on Alcohol, 66*, 332–343.
- Dallery, J., Houtsmuller, E. J., Pickworth, W. B., & Stitzer, M. L. (2003). Effects of cigarette nicotine content and smoking pace on subsequent craving and smoking. *Psychopharmacology (Berlin), 165*, 172–180. doi:10.1007/s00213-002-1242-8
- David, S. P., Munafò, M. R., Johansen-Berg, H., Mackillop, J., Sweet, L. H., Cohen, R. A., et al. (2007). Effects of acute nicotine abstinence on cue-elicited ventral striatum/nucleus accumbens

- activation in female cigarette smokers: A functional magnetic resonance imaging study. *Brain Imaging and Behavior*, 1, 43–57. doi:10.1007/s11682-007-9004-1
- Field, M., Munafò, M. R., & Franken, I. H. (2009). A meta-analytic investigation of the relationship between attentional bias and subjective craving in substance abuse. *Psychological Bulletin*, 135, 589–607. doi:10.1037/a0015843
- Field, M., Santarcangelo, M., Sumnall, H., Goudie, A., & Cole, J. (2006). Delay discounting and the behavioural economics of cigarette purchases in smokers: The effects of nicotine deprivation. *Psychopharmacology (Berlin)*, 186, 255–263. doi:10.1007/s00213-006-0385-4
- Hammersley, R. (1994). A digest of memory phenomena for addiction research. *Addiction*, 89, 283–293. doi:10.1111/j.1360-0443.1994.tb00890.x
- Heatherington, T. F., Kozlowski, L. T., Frecker, R. C., & Fagerström, K.-O. (1991). The Fagerström Test for Nicotine Dependence: A revision of the Fagerström Tolerance Questionnaire. *British Journal of Addiction*, 86, 1119–1127. doi:10.1111/j.1360-0443.1991.tb01879.x
- Hitsman, B., MacKillop, J., Lingford-Hughes, A., Williams, T. M., Ahmad, F., Adams, S., et al. (2008). Effects of acute tyrosine/phenylalanine depletion on the selective processing of smoking-related cues and the relative value of cigarettes in smokers. *Psychopharmacology (Berlin)*, 196, 611–621. doi:10.1007/s00213-007-0995-5
- Houben, K., & Wiers, R. W. (2008). Implicitly positive about alcohol? Implicit positive associations predict drinking behavior. *Addictive Behaviors*, 33, 979–986. doi:10.1016/j.addbeh.2008.03.002
- Houtsmuller, E. J., & Stitzer, M. L. (1999). Manipulation of cigarette craving through rapid smoking: Efficacy and effects on smoking behavior. *Psychopharmacology (Berlin)*, 142, 149–157. doi:10.1007/s002130050874
- Hughes, J. R., & Hatsukami, D. (1986). Signs and symptoms of tobacco withdrawal. *Archives of General Psychiatry*, 43, 289–294.
- Hursh, S. R., Galuska, C. M., Winger, G., & Woods, J. H. (2005). The economics of drug abuse: A quantitative assessment of drug demand. *Molecular Interventions*, 5, 20–28. doi:10.1124/mi.5.1.6
- Hursh, S. R., & Silberberg, A. (2008). Economic demand and essential value. *Psychological Review*, 115, 186–198. doi:10.1037/0033-295X.115.1.186
- Jacobs, E. A., & Bickel, W. K. (1999). Modeling drug consumption in the clinic using simulation procedures: Demand for heroin and cigarettes in opioid-dependent outpatients. *Experimental and Clinical Psychopharmacology*, 7, 412–426. doi:10.1037/1064-1297.7.4.412
- Killen, J. D., & Fortmann, S. P. (1997). Craving is associated with smoking relapse: Findings from three prospective studies. *Experimental and Clinical Psychopharmacology*, 5, 137–142. doi:10.1037/1064-1297.5.2.137
- Kirby, K. N., Petry, N. M., & Bickel, W. K. (1999). Heroin addicts have higher discount rates for delayed rewards than non-drug-using controls. *Journal of Experimental Psychology: General*, 128, 78–87. doi:10.1037/0096-3445.128.1.78
- Leeman, R. F., O'Malley, S. S., White, M. A., & McKee, S. A. (2010). Nicotine and food deprivation decrease the ability to resist smoking. *Psychopharmacology (Berlin)*, 212, 25–32. doi:10.1007/s00213-010-1902-z
- Loewenstein, G. (1999). A visceral account of addiction. In J. Elster & O. J. Skog (Eds.), *Getting hooked: Rationality and addiction* (pp. 188–213). Cambridge, UK: Cambridge University Press.
- MacKillop, J., Amlung, M. T., Murphy, C. M., Acker, J. T., & Ray, L. A. (2011). The behavioral economics of health behavior. In R. DiClemente, L. F. Salazar, & R. A. Crosby (Eds.), *Health behavior theory for public health: Principles, foundations, and applications* (pp. 131–162). Burlington, MA: Jones and Bartlett.
- MacKillop, J., & Kahler, C. W. (2009). Delayed reward discounting predicts treatment response for heavy drinkers receiving smoking cessation treatment. *Drug and Alcohol Dependence*, 104, 197–203. doi:10.1016/j.drugalcdep.2009.04.020
- MacKillop, J., Menges, D. P., McGeary, J. E., & Lisman, S. A. (2007). Effects of craving and DRD4 VNTR genotype on the relative value of alcohol: An initial human laboratory study. *Behavioral and Brain Functions*, 3, 11. doi:10.1186/1744-9081-3-11
- MacKillop, J., Miranda, R., Jr., Monti, P. M., Ray, L. A., Murphy, J. G., Rohsenow, D. J., et al. (2010). Alcohol demand, delayed reward discounting, and craving in relation to drinking and alcohol use disorders. *Journal of Abnormal Psychology*, 119, 106–114. doi:10.1037/a0017513
- MacKillop, J., & Monti, P. M. (2007). Advances in the scientific study of craving for alcohol and tobacco: From scientific study to clinical practice. In P. M. Miller, & D. J. Kavanagh (Eds.), *Translation of addictions sciences into practice*. Amsterdam: Elsevier.
- MacKillop, J., & Murphy, J. G. (2007). A behavioral economic measure of demand for alcohol predicts brief intervention outcomes. *Drug and Alcohol Dependence*, 89, 227–233. doi:10.1016/j.drugalcdep.2007.01.002
- MacKillop, J., Murphy, J. G., Ray, L. A., Eisenberg, D. T., Lisman, S. A., Lum, J. K., et al. (2008). Further validation of a cigarette purchase task for assessing the relative reinforcing efficacy of nicotine in college smokers. *Experimental and Clinical Psychopharmacology*, 16, 57–65. doi:10.1037/1064-1297.16.1.57
- MacKillop, J., O'Hagen, S., Lisman, S. A., Murphy, J. G., Ray, L. A., Tidey, J. W., et al. (2010). Behavioral economic analysis of cue-elicited craving for alcohol. *Addiction*, 105, 1599–1607. doi:10.1111/j.1360-0443.2010.03004.x
- Madden, G. J., & Kalman, D. (2010). Effects of bupropion on simulated demand for cigarettes and the subjective effects of

- smoking. *Nicotine & Tobacco Research*, 12, 416–422. doi:10.1093/ntr/ntq018
- McKee, S. A., Sinha, R., Weinberger, A. H., Sofuoglu, M., Harrison, E. L., Lavery, M., et al. (2011). Stress decreases the ability to resist smoking and potentiates smoking intensity and reward. *Journal of Psychopharmacology*, 25, 490–502. doi:10.1177/02698811110376694
- Monti, P. M., Binkoff, J. A., Abrams, D. B., Zwick, W. R., Nirenberg, T. D., & Liepman, M. R. (1987). Reactivity of alcoholics and nonalcoholics to drinking cues. *Journal of Abnormal Psychology*, 96, 122–126. doi:10.1037//0021-843X.96.2.122
- Munafò, M. R., & Hitsman, B. (2010). What's the matter with cue-induced craving? A commentary on Perkins. *Addiction*, 105, 1860–1861. doi:10.1111/j.1360-0443.2010.03127.x
- Murphy, J. G., & MacKillop, J. (2006). Relative reinforcing efficacy of alcohol among college student drinkers. *Experimental and Clinical Psychopharmacology*, 14, 219–227. doi:10.1037/1064-1297.14.2.219
- Murphy, J. G., MacKillop, J., Tidey, J. W., Brazil, L. A., & Colby, S. M. (2011). Validity of a demand curve measure of nicotine reinforcement with adolescent smokers. *Drug and Alcohol Dependence*, 113, 207–214. doi:10.1016/j.drugalcdep.2010.08.004
- Niaura, R., Abrams, D. B., Monti, P. M., & Pedraza, M. (1989). Reactivity to high risk situations and smoking cessation outcome. *Journal of Substance Abuse*, 1, 393–405.
- Niaura, R., Sayette, M., Shiffman, S., Glover, E. D., Nides, M., Shelanski, M., et al. (2005). Comparative efficacy of rapid-release nicotine gum versus nicotine polacrilex gum in relieving smoking cue-provoked craving. *Addiction*, 100, 1720–1730. doi:10.1111/j.1360-0443.2005.01218.x
- Niaura, R., Shadel, W. G., Abrams, D. B., Monti, P. M., Rohsenow, D. J., & Sirota, A. (1998). Individual differences in cue reactivity among smokers trying to quit: Effects of gender and cue type. *Addictive Behaviors*, 23, 209–224. doi:10.1016/S0306-4603(97)00043-9
- Perkins, K. A. (2009). Does smoking cue-induced craving tell us anything important about nicotine dependence? *Addiction*, 104, 1610–1616. doi:10.1111/j.1360-0443.2009.02550.x
- Perkins, K. A., Epstein, L. H., Grobe, J., & Fonte, C. (1994). Tobacco abstinence, smoking cues, and the reinforcing value of smoking. *Pharmacology, Biochemistry, and Behavior*, 47, 107–112. doi:10.1016/S0091-3057(96)00079-2
- Perkins, K. A., Grobe, J., & Fonte, C. (1997). Influence of acute smoking exposure on the subsequent reinforcing value of smoking. *Experimental and Clinical Psychopharmacology*, 5, 277–285.
- Perkins, K. A., Grobe, J. E., Weiss, D., Fonte, C., & Caggiula, A. (1996). Nicotine preference in smokers as a function of smoking abstinence. *Pharmacology, Biochemistry, and Behavior*, 55, 257–263.
- Posner, J., Russell, J. A., & Peterson, B. S. (2005). The circumplex model of affect: An integrative approach to affective neuroscience, cognitive development, and psychopathology. *Developmental Psychopathology*, 17, 715–734. doi:10.1017/S0954579405050340
- Sayette, M. A., Griffin, K. M., & Sayers, W. M. (2010). Counterbalancing in smoking cue research: A critical analysis. *Nicotine & Tobacco Research*, 12, 1068–1079. doi:10.1093/ntr/ntq159
- Sayette, M. A., Martin, C. S., Hull, J. G., Wertz, J. M., & Perrott, M. A. (2003). Effects of nicotine deprivation on craving response covariation in smokers. *Journal of Abnormal Psychology*, 112, 110–118. doi:10.1037/0021-843X.112.1.110
- Sayette, M. A., Martin, C. S., Wertz, J. M., Shiffman, S., & Perrott, M. A. (2001). A multi-dimensional analysis of cue-elicited craving in heavy smokers and tobacco chippers. *Addiction*, 96, 1419–1432. doi:10.1080/09652140120075152
- Sayette, M. A., Shiffman, S., Tiffany, S. T., Niaura, R. S., Martin, C. S., & Shadel, W. G. (2000). The measurement of drug craving. *Addiction*, 95(Suppl. 2), S189–S210.
- Schuh, K. J., & Stitzer, M. L. (1995). Desire to smoke during spaced smoking intervals. *Psychopharmacology (Berlin)*, 120, 289–295. doi:10.1007/BF02311176
- Shiffman, S., Shadel, W. G., Niaura, R., Khayrallah, M. A., Jorenby, D. E., Ryan, C. F., et al. (2003). Efficacy of acute administration of nicotine gum in relief of cue-provoked cigarette craving. *Psychopharmacology (Berlin)*, 166, 343–350. doi:10.1007/s00213-002-1338-1
- Tabachnick, B. G., & Fidell, L. S. (2004). *Using multivariate statistics*. (5th ed.). Needham Heights, MA: Allyn & Bacon.
- Tiffany, S. T., & Carter, B. L. (1998). Is craving the source of compulsive drug use? *Journal of Psychopharmacology*, 12, 23–30. doi:10.1177/026988119801200104
- Tiffany, S. T., Carter, B. L., & Singleton, E. G. (2000). Challenges in the manipulation, assessment and interpretation of craving relevant variables. *Addiction*, 95(Suppl. 2), S177–S187. doi:10.1046/j.1360-0443.95.8s2.7.x
- Tiffany, S. T., & Wray, J. (2009). The continuing conundrum of craving. *Addiction*, 104, 1618–1619. doi:10.1111/j.1360-0443.2009.02588.x
- Willner, P., Hardman, S., & Eaton, G. (1995). Subjective and behavioural evaluation of cigarette cravings. *Psychopharmacology (Berlin)*, 118, 171–177. doi:10.1007/BF02245836
- Wilson, T. D., & Dunn, E. W. (2004). Self-knowledge: Its limits, value, and potential for improvement. *Annual Review of Psychology*, 55, 493–518. doi:10.1146/annurev.psych.55.090902.141954