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Authors

Bujarski, Spencer
Roche, Daniel J O
Sheets, Erin S
et al.

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Modeling naturalistic craving, withdrawal, and affect during early nicotine abstinence: a pilot EMA study

Spencer Bujarski[1], **Daniel J.O. Roche**[1], **Erin S. Sheets**[2], **Jennifer L. Krull**[1], **Iris Guzman**[1], and **Lara A. Ray**[1,3]

[1]University of California Los Angeles, Department of Psychology, Los Angeles, CA, USA

[2]Colby College, Department of Psychology, Waterville, ME, USA

[3]University of California, Los Angeles, Department of Psychiatry and Biobehavioral Sciences, United States, Los Angeles, CA, USA

Abstract

Despite the critical role of withdrawal, craving, and positive (PA) and negative affect (NA) in smoking relapse, relatively little is known about the temporal and predictive relationship between these constructs within the first day of abstinence. This pilot study aims to characterize dynamic changes in withdrawal, craving and affect over the course of early abstinence using ecological momentary assessment. Beginning immediately after smoking, moderate and heavy smoking participants (n = 15 per group) responded to hourly surveys assessing craving, withdrawal, NA, and PA. Univariate and multivariate multilevel random coefficient modeling was used to describe the progression of craving, withdrawal/NA and PA and to test correlations between these constructs at the subject-level over the course of early abstinence. Heavy smokers reported greater craving from 1–4 hours of abstinence and greater withdrawal/NA after 3 or more hours as compared to moderate smokers. Level of withdrawal/NA was strongly positively associated with craving, and PA was negatively correlated with craving, however the temporal dynamics of these correlations differed substantially. The association between withdrawal/NA and craving decreased over early abstinence, whereas the reverse was observed for PA. These findings can inform experimental studies of nicotine abstinence as well as their clinical applications to smoking cessation efforts. In particular, these results help to elucidate the role of PA in nicotine abstinence by demonstrating its independent association with nicotine craving over and above withdrawal/NA. If supported by future studies, these findings can refine experimental methods and clinical approaches for smoking cessation.

Keywords

Smoking; Craving; Withdrawal; Affect; Ecological Momentary Assessment

Correspondence concerning this article should be addressed to: Lara A. Ray, Ph.D., Associate Professor, University of California, Los Angeles, Psychology Department, 1285 Franz Hall, Box 951563, Los Angeles, CA 90095-1563; Phone: 310-794-5383; Fax: 310-206-5895; lararay@psych.ucla.edu.

Introduction

Nicotine abstinence has been associated with symptoms of both increased negative affect (NA) and smoking urge/craving (Chandra, Scharf, & Shiffman, 2011; Zhou et al., 2009). In studies using Ecological Momentary Assessment (EMA) to measure real-time data in the natural environment, the severity of NA and craving are highly predictive of smoking lapse and relapse during abstinence (McCarthy, Piasecki, Fiore, & Baker, 2006; Piasecki et al., 2000; Piasecki, Fiore, & Baker, 1998; Piper, Loh, Smith, Japuntich, & Baker, 2011; Shiffman, 2005; Shiffman et al., 1997, 2007). While withdrawal, craving, and negative affect may each predict one's ability to remain abstinent, the temporal and directional relationships between these constructs at the micro-longitudinal level remains unclear. For example, in both the laboratory and natural environment, NA is highly predictive of cigarette craving (Dunbar, Scharf, Kirchner, & Shiffman, 2010; Heckman et al., 2013; Shiyko, Naab, Shiffman, & Li, 2014). However, NA, withdrawal, and craving also appear to be dissociable, as they can display different temporal patterns within and across days (Chandra et al., 2011; Vasilenko et al., 2014) and their predictive relationship may vary depending on the context (e.g., abstinence vs. ad libitum smoking; Dunbar et al., 2010; Teneggi et al., 2002) and population being studied (e.g., high vs. low nicotine dependence, daily vs. non-daily smoker; Chandra et al., 2011; Dunbar et al., 2010; Shiffman et al., 2002, 2014). Therefore, using EMA to provide a more precise characterization of the relationship between withdrawal components across different populations of smokers and under different smoking conditions may refine our understanding of how these factors contribute to the maintenance of nicotine addiction.

Current theories of the role of affect in addiction suggest that NA is predictive of craving and lapse/relapse during smoking abstinence, but that positive affect (PA) is predominantly related to craving and motivation to smoke during *ad libitum* smoking (Baker, Morse, & Sherman, 1987; Baker, Piper, McCarthy, Majeskie, & Fiore, 2004; Carmody, Vieten, & Astin, 2007). While the results of several studies provide support for this theorized role of NA (Piasecki, 2006; Shiffman, 2005; Shiffman, Paty, Gnys, Kassel, & Hickcox, 1996; Shiffman & Waters, 2004), the contribution of PA to *ad libitum* smoking behavior, as well as to craving, withdrawal, and relapse during abstinence is less well understood. A recent meta-analysis indicated that in the laboratory, only manipulations of NA, but not PA, were directly related to cigarette craving (Heckman et al., 2013). In the natural environment, support for PA contributing to *ad libitum* smoking behavior has been mixed, with some EMA studies reporting a positive association with cigarette craving and smoking (Dunbar et al., 2010; Shiffman et al., 2014; Shiffman & Paty, 2006) and others finding no relationship (Shiffman et al., 2002; Shiffman & Waters, 2004). Conversely, increases in PA have been associated with decreased risk for smoking lapse, suggesting a protective role of PA in early nicotine abstinence (Ferguson, Shiffman, & Gwaltney, 2006). One factor that has undoubtedly contributed to the poor characterization of PA's role in smoking behavior and abstinence is that many EMA studies examining affect as a predictor of craving or smoking behavior subscribed to the circumplex model of emotion, which suggests that NA and PA are not independent factors of emotion and are, in fact, bipolar ends of the same affective dimension (Russell, 1980; Russell & Carroll, 1999; Shiffman, 2013). Consistent with this

model, many studies have only examined NA as a predictor or have used a single factor to account for both NA and PA. However, a sizeable body of evidence suggests that PA and NA are indeed independent dimensions with distinct underlying neurological and psychological constructs, and an individual can concurrently experience, for example, heightened PA and NA (Cacioppo, Gardner, & Berntson, 1999; Cook et al., 2004; Watson, Clark, & Tellegen, 1988; Watson & Tellegen, 1985). Thus, an EMA study examining both PA and NA as independent predictors may provide clarification on PA's role in nicotine withdrawal and smoking behavior.

The frequency and quantity of cigarette smoking is highly related to nicotine dependence level, the severity of withdrawal during abstinence, and numerous other smoking-related variables. For example, heavy daily smokers have demonstrated greater nicotine dependence, withdrawal symptoms, cigarette craving, difficulty quitting smoking (Dale et al., 2001; Killen, Fortmann, Telch, & Newman, 1988; Nides et al., 1995), tolerance to nicotine's subjective and cardiovascular effects (Perkins, 1995; Perkins, Epstein, Stiller, Marks, & Jacob, 1989), and more health-related problems than light daily smokers (Wilson, Parsons, & Wakefield, 1999). Non-daily smokers often do not display signs of nicotine dependence or report symptoms of withdrawal after prolonged abstinence (Shiffman, Dunbar, Scholl, & Tindle, 2012; Shiffman, Paty, Gnys, Kassel, & Elash, 1995); yet, their *ad libitum* smoking behavior, as measured by EMA, has been positively associated with NA (Shiffman et al., 2012; Shiffman & Paty, 2006), which is contrary to findings in heavy daily smokers (Chandra et al., 2011; Shiffman et al., 2002; Shiffman & Waters, 2004). In both daily and non-daily smokers, cigarette-related cues increase craving in the laboratory (Shiffman et al., 2013) and PA appears to be positively associated with smoking behavior in *ad libitum* conditions in the natural environment (Shiffman et al., 2014).

In sum, despite the critical role of withdrawal, craving, PA, and NA in the dynamic process of smoking lapse and relapse, little is known about 1) the temporal and predictive relationship between these withdrawal-related constructs during early abstinence and 2) how smoking heaviness affect the trajectories and relationships between these key psychological constructs. Furthermore, EMA studies have typically employed either a multilevel modeling (MLM) framework to examine within-person associations between variables at a defined moment in time or, more recently, time-varying effect models to understand the pattern of within-person association between variables over time (e.g. Shiyko, Lanza, Tan, Li, & Shiffman, 2012; Shiyko et al., 2014). However, using such EMA analytical techniques cannot examine whether the rates of change or trajectories of craving, withdrawal, NA, and PA are associated over the course of abstinence. The present pilot study aimed to address these gaps in the literature by using both MLM and a series of multivariate random coefficient models (MRM) to elucidate the interplay between craving, withdrawal, PA, and NA trajectories in early smoking abstinence.

Method

Participants

Participants were 32 non-treatment seeking adults (11 female) recruited from the community into two groups based on smoking status, hereafter termed moderate or heavy smokers (n =

16 per smoking group). Moderate smokers were required to smoke between 5 and 14 cigarettes per day and heavy smokers were required to smoke 15 to 24 cigarettes per day. Additional inclusion criteria included: (1) age between 18 and 55, and (2) no smoking abstinence lasting 3 months or more in the past year. Exclusion criteria were (1) currently taking psychoactive medications, (2) history of major psychiatric disorders, (3) current use of nonprescription drugs (other than alcohol and marijuana), and (4) if female, pregnant or planning to get pregnant.

Study Procedures

Study procedures were approved by the Institutional Review Board at the University of California, Los Angeles and all participants provided written informed consent after receiving a full explanation of the study. Following telephone screening, participants completed a 1-hour in-person assessment visit. Prior to assessment completion, participants had to produce a BrAC of 0.000 g/dl on a breathalyzer, a negative urine toxicology screen (except for marijuana), and a negative pregnancy test (if female). Current smoking status was also verified by a cotinine test ($\geq$ 100ng/ml of cotinine) and participant's expired carbon monoxide (CO) reading level was recorded at baseline. All participants completed a number of interviews and questionnaires assessing cigarette smoking, nicotine dependence (Fagerstrom Test for Nicotine Dependence (FTND): Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991), alcohol, and drug use. Eligible participants were enrolled in the EMA portion of the study described below.

EMA Procedures

EMA data were collected on a Samsung i200 smart phone using the open source EMA tool MyExperience (Froehlich, Chen, Consolvo, Harrison, & Landay, 2007). Immediately after smoking the last cigarette of the day, participants were trained in the EMA protocol and completed the first momentary assessment. Participants completed 1 additional survey (5 minutes after the last cigarette) in the lab and then carried the device for one day. Participants responded to survey prompts until midnight. At each prompt, current craving, withdrawal, NA, and PA were assessed. All EMA data were time-stamped relative to the last cigarette or waking and were analyzed with respect to the time of assessment. Target assessment points were 0, 5, 15, 30 minutes and then hourly after participants smoked their last cigarette. Upon returning to the laboratory 24 hours later, expired CO readings were collected to verify smoking abstinence and only those with verified abstinence were included in the analyses.

EMA Measures

Items for EMA assessment were selected from well validated scales (e.g., the Questionnaire of Smoking Urges, the Minnesota Withdrawal Symptom Scale and the Profile of Mood States). Item selection was informed by a principal component analysis on data collected during overnight abstinence from a similar sample (i.e., daily non-treatment seeking smokers) recruited for a human laboratory study (Ray et al., 2013).

Cigarette Craving—Participants rated craving by responding on a scale of 1 (*strongly disagree*) to 7 (*strongly agree*) to two sentences from the Questionnaire of Smoking Urges –

Brief scale: "I have an urge for a cigarette" and "All I want right now is a cigarette" (Cox, Tiffany, & Christen, 2001; Toll, Katulak, & McKee, 2006). Factor loading for these two items from the item selection sample were 0.91 and 0.91 respectively. Ratings were summed to form the Craving scale.

Nicotine Withdrawal/Negative Affect—Participants rated three items from the Minnesota Nicotine Withdrawal Scale from 1 (*none*) to 5 (*severe*) (Etter & Hughes, 2006; Hughes & Hatsukami, 1986). Specific items were "irritability/frustration," "difficulty concentrating," and "impatience" and their factor loadings were 0.90, 0.81 and 0.89 respectively. Participants also rated four items taken from the Profile of Mood States (POMS) on a scale of 1 (*not at all*) to 5 (*extremely*) (McNair, Lorr, & Droppleman, 1971). The POMS Negative Affect items were downhearted (loading = 0.69), discouraged (loading = 0.76), uneasy (loading = 0.73), and anxious (loading = 0.79). Sum scores from the three withdrawal questions and four POMS Negative Affect items were correlated 0.79 and were thus summed to produce a single withdrawal/NA scale (Piasecki, Kenford, Smith, Fiore, & Baker, 1997).

Positive Affect—Participants rated four items from the POMS on a scale of 1 (*not at all*) to 5 (*extremely*) (McNair et al., 1971). Two items, joyful and cheerful, were from the happiness subscale (loadings = 0.86, and 0.88 respectively) and two items, energetic and lively, were from the vigor subscale (loadings = 0.82, and 0.82 respectively). The four items were summed to form the PA subscale.

Data Analytic Strategy

In order to describe the progression of nicotine craving and withdrawal over the course of 24 hours of abstinence, a series of polynomial mixed effects random coefficient models were analyzed with observations (level 1) nested within subjects (level 2). These models included a polynomial function of hours since last cigarette (Hours, a level 1 predictor), smoking group (Group: a level 2 predictor coded moderate smoker = 0, heavy smoker = 1) as well as their interactions. Prior to model estimation, intraclass correlations (ICC) were calculated for each dependent variable. ICCs for craving, withdrawal/NA and PA were 0.44, 0.62, and 0.62 respectively, suggesting substantial between-subjects variation in addition to a large proportion of within subject variability.

Mixed effects models were estimated in the R statistical package version 2.13.1 using the **lme** function in the multilevel package (Bliese, 2008). Models were estimated using full information maximum likelihood estimation to allow for comparison of models with different fixed and random effects. In order to improve the stability of model estimation all outcome variables were centered. The best fitting model was determined via -2 log-likelihood change tests using the **anova** function with nested models. Estimated models took the form of:

Level 1: $Craving = \beta_{0i} + \beta_{1i}(Hours) + \beta_{2i}(Hours^2) + \beta_{3i}(Hours^3) + e_{it}$

Level 2: $\beta_{0i} = \gamma_{00} + \gamma_{01}(Group) + u_{0i}$

$\beta_{1i} = \gamma_{10} + \gamma_{11}(Group) + u_{1i}$

$\beta_{2i} = \gamma_{20} + \gamma_{21}(Group) + u_{2i}$

$\beta_{3i} = \gamma_{30} + \gamma_{31}(Group) + u_{3i}$

When a significant interaction between Group and one or more growth parameters was observed, a series of post-hoc tests were conducted wherein Hours was successively re-centered at different values to determine the regions of time where moderate smoking and heavy smoking groups significantly differed on the outcome variable (i.e. regions where a significant simple effect of Group was observed at $p < 0.05$).

Subsequently a series of multivariate random coefficient models (MRM) are conducted to examine the between-person correlations among craving, withdrawal/NA and PA growth parameters (i.e. intercept and instantaneous rate of change) at particular time points during the nicotine deprivation. These models tested, for example, whether level of withdrawal or affect at a given time point was significantly correlated with level of craving at the same time (i.e., correlation of intercept terms) and whether the instantaneous linear rate of change in the various domains were correlated at particular time points (i.e., correlations of linear slope terms). Thus these analyses addressed the question of whether subjects' rate of change of withdrawal at a particular point in time was correlated with rate of change for craving. This sort of analytical approach is more commonly applied to long-term longitudinal data; however given that this particular EMA dataset has a very clear time origin (i.e., finishing the last cigarette) and a focus on how individual experience changes over time relative to that point, such an approach is well-suited to address the questions of interest.

Results

Assessment Completion

Of the initial sample of 32, a large percentage (N=30) provided sufficient data for statistical analysis (4 observations; n=15 per group), from which we collected 309 complete observations. Participants received an average of 11.97 prompts (SD = 3.32) and completed an average of 10.37 assessments per person (SD = 2.31, range = 7–16). The mean time between consecutive assessments was 57.27 min (SD = 17.02). Moderate and heavy smoking groups were not found to differ in terms of either number of subjects or observations in hourly bins (Table S1; p's 0.61). Substantial variability was observed on all EMA variables on Day 1 (Craving: SD = 4.13, Withdrawal/NA SD = 6.00, PA SD = 3.66).

Sample Characteristics

Moderate and heavy smoking groups were not found to differ from each other in terms of demographic factors including age, sex and education (Table 1). As intended by the participant selection procedures, moderate and heavy smokers significantly differed in terms of average cigarettes per day (p < 0.001), severity of nicotine dependence on the FTND (p = 0.001), and time to first cigarette in the morning (FTND item 1: $p = 0.01$).

Progression of Craving, Withdrawal/NA, and PA on Day 1

The first aim was to characterize progression of craving, withdrawal/NA, and PA over the course of 24 hours of abstinence in moderate and heavy smokers. The final model with regions of significant group difference is shown in Figure 1A. The best fitting model describing the progression of craving over the course of Day 1 was a cubic polynomial. All growth parameters were found to significantly vary across individuals (p's < 0.001) and were estimated as random effects. Further, group was found to moderate all growth parameters (Group × Hours: B = 1.83, p < 0.01; Group × Hours^2: B = –0.51, p < 0.01, and Group × Hours^3: B = 0.03, p < 0.01). Post-hoc tests revealed significant group differences in craving between 1 and 4 hours after the last cigarette (simple effect of Group: p's < 0.05) such that heavy smokers had significantly greater craving as compared to moderate smokers only for the period of 1 to 4 hours of abstinence. In sum, craving was found to increase more quickly in heavy smokers such that heavy smokers reported greater craving 1–4 hours after the last cigarette.

Similarly the best fitting model of progression of withdrawal/NA over Day 1 was a cubic polynomial with all growth parameters found to vary significantly between subjects (p's < 0.05) shown in Figure 1B. A trend towards a significant interaction was observed between linear hours since last cigarette and smoking group (Group × Hours: B = 0.38, p = 0.06). Post-hoc tests revealed significant group difference beginning 3 hours after the last cigarette (simple effect of Group: p's < 0.05) such that heavy smokers had significantly greater withdrawal/NA as compared to moderate smokers starting 3 hours after the last cigarette and lasting until the end of the day.

In terms of PA, the best fitting model was a cubic polynomial with all growth parameters varying across individuals (p's < 0.01) presented in Figure 1C. Smoking group was not found to predict progression of PA either as a main effect or as a moderator of growth parameters (p's > 0.24). While PA was found to decrease over time, this pattern did not differ between moderate and heavy smokers.

Between-Subjects Growth Parameter Correlations

After these growth curves were described, we examined the subject level correlations between random growth parameters to determine whether levels (i.e., intercepts) of craving, withdrawal/NA and PA were correlated (e.g., are subjects' reported levels of withdrawal/NA and craving correlated?) and whether instantaneous rates of change in these variables (i.e., linear slopes) were correlated (e.g., are subjects' rates of change for withdrawal/NA and craving correlated?) at hourly time points after the last cigarette.

Intercept correlation magnitudes over time are presented in Figure 2. Withdrawal/NA and craving intercepts were significantly and positively correlated at all time points (r range: 0.47 – 0.75, all p's < 0.01). To test time trends in the magnitude of the between-subject correlations, a series of regressions were run predicting Fisher transformed correlation coefficients over time. Magnitude of correlation between craving and withdrawal/NA generally decreased over time (B = –0.058, t = –7.66, p < 0.001) such that a person's level of withdrawal/NA was a stronger predictor of that person's level of craving early after the

last cigarette as compared to later in the night. This result may be due to relatively stable levels of withdrawal/NA and craving several hours after the last cigarette. Further, between-subject intercept growth parameters for PA and craving were significantly and negatively correlated at time points 2 hours or more after the last cigarette (r range: $-0.362 - -0.423$, p's< 0.05). Overall, the association between a person's level of craving and that person's level of PA was found to increase in magnitude over the time period examined (B = -0.01, t = -2.45, $p< 0.05$), yet the increase in magnitude was decelerating (Hours2: B = 0.006, t = 9.61, $p < 0.001$). Intercepts for PA and withdrawal/NA were significantly and negatively correlated 1 or more hours after participants last cigarette (r-range: $-.387 - -0.576$, p's < 0.05, Figure 2). These correlations increased in magnitude over Day 1 (B = -0.042, t = -6.38, $p < 0.001$), yet this magnitude increase was decelerating (Hours^2: B = 0.007, t = 9.76, $p < 0.001$). In sum, levels of withdrawal/NA were correlated with craving, yet this correlation decreased over time. Conversely, level of PA was negatively correlated with levels of craving and withdrawal/NA and these correlations increased in magnitude over time.

Correlation magnitudes of slopes over time are presented in Figure 3. Subject-level instantaneous trajectories for withdrawal/NA and craving were significantly and positively correlated only 6 – 8 hours after participants' last cigarette (r range: 0.44 – 0.77, all p's < 0.05). Over the course of Day 1 the magnitude of correlation rose over time (B = 0.097, t = 3.79, $p < 0.01$) and was accelerating (Hours^2: B = 0.029, t = 8.31, $p < 0.001$; Figure 3). These results suggest that participants who experienced greater increases in withdrawal later in the day also experienced concurrent increases in craving. The associations between subject-level instantaneous slopes for craving and PA were statistically significant and negative at all time points (r-range: $-0.37 - -0.70$, p's < 0.05) suggesting that participants who experienced greater decrease in PA were concurrently experiencing greater increase in craving. These correlations decreased in magnitude from 0 to 5 hours after participant's last cigarette (B = 0.066, t = 9.54, $p < 0.001$) and then proceeded to increase thereafter (B = -0.24, t = 12.69, $p = 0.05$, correlation magnitudes shown in Figure 3). Subject-level withdrawal/NA and PA slopes were significantly and negatively correlated at all time points (r-range: -0.444, -0.800, p's < 0.05, Figure 3) suggesting that those participants who experienced greater increases in withdrawal/NA also experienced greater decreases in PA. This correlation was found to increase in magnitude over time (B = -0.087, t =-6.38, $p < 0.001$). In sum, participants' rates of change in withdrawal/NA and craving were only observed to be correlated late in the day whereas participants' rates of change in positive affect were negatively correlated with rates of change in craving and withdrawal/NA throughout the day.

Discussion

Craving, withdrawal, and negative affect have been associated with risk for relapse in smoking cessation trials (McCarthy et al., 2006; Piper et al., 2011; Shiffman, 2005; Shiffman et al., 1997), yet relatively few studies have utilized rapid sampling procedures to precisely model the time course of these constructs (Brown et al., 2013; Hendricks, Ditre, Drobes, & Brandon, 2006). This study used a high-frequency EMA approach to characterize the dynamic interplay between withdrawal/NA, craving, and PA in moderate and heavy

daily smokers during early nicotine abstinence. The first set of analyses sought to characterize the progression of craving, withdrawal/NA, and PA over early abstinence and to detect periods of nicotine deprivation where smoking groups significantly differed from one another. These data suggested that heavy smokers reported greater cigarette craving in very early abstinence (e.g. 1 to 4 hours), but that this initial group difference diminished over time. Heavy smokers were found to reach an early plateau, whereas the craving of moderate smokers steadily increased over the course of the day. A different pattern emerged for withdrawal/NA, such that in our data heavy smokers reported significantly greater withdrawal/NA than moderate smokers beginning 3 hours into abstinence. On the other hand, PA decreased over early abstinence and did not differ between groups. Together, these preliminary results suggest that the effects of smoking pattern (heavy vs. moderate) differ over the course of early abstinence and based on the construct of interest.

If replicated in a larger sample, these results would suggest several methodological recommendations for future smoking studies. For example, studies interested in detecting smoking group differences in abstinence-related constructs may consider abstinence requirements of 3–4 hours. It is worth noting however, that more highly powered studies may be more sensitive to detecting smoking group differences (e.g. differences in withdrawal/NA may be detectable sooner than 3 hours of abstinence).

This study also examined whether levels of craving, withdrawal/NA and PA were correlated (intercepts) and whether the trajectories of these variables were correlated (slopes) over early abstinence. These data suggested that levels of withdrawal/NA and craving were strongly and positively correlated and that this relationship decreased over time. These results are concordant with the finding that abstinence-induced NA was most sensitive to alleviation by nicotine administration (Perkins, Karelitz, Conklin, Sayette, & Giedgowd, 2010). Furthermore, levels of PA and craving were negatively correlated and contrary to the effect of withdrawal/NA, this association increased in magnitude over time. Of note, in spite of these divergent time trends, withdrawal/NA was found to be a stronger predictor of craving than PA at all time points assessed.

In these data the magnitude of anticorrelation between withdrawal/NA and PA was only moderate, suggesting that these variables may not be at the opposite ends of a single affect dimension. In other words, these pilot data were not consistent with the circumplex model of emotion often utilized in EMA smoking studies which posits that NA and PA represent opposing ends of the same affective dimension (Russell, 1980; Russell & Carroll, 1999; Shiffman, 2013) and provide further evidence that these two variables should be examined as separate constructs (Watson & Tellegen, 1985).

As compared to NA, PA has been relatively under-represented as an independent predictor in EMA studies with mixed results when it is examined (e.g. Dunbar et al., 2010; Shiffman et al., 2002, 2014; Shiffman & Waters, 2004). These preliminary data indicated that the rate of change in PA was stably and negatively correlated with craving, suggesting the subjects experiencing acute decreases in PA was related to the observed increases in craving. Conversely, withdrawal/NA and craving trajectories were only significantly correlated late

in the day. These findings should be considered preliminary and require replication in future studies.

Clinically, these results suggest that interventions such as pleasurable activity scheduling, that target PA could effectively target craving for nicotine during abstinence (Kanter et al., 2010; MacPherson et al., 2010). They also suggest that within the first day of a quit attempt, withdrawal/NA may be a primary factors differentiating moderate from heavy smokers. These findings are consistent with the use of nicotine replacement therapies targeting withdrawal (Silagy, Mant, Fowler, & Lodge, 1994; Stead et al., 1996; Wu, Wilson, Dimoulas, & Mills, 2006) and antidepressants such as bupropion (Dale et al., 2001; Eisenberg et al., 2008) among heavy smokers. Conversely, light or moderate smokers who did not report substantial withdrawal and NA, may benefit more from other intervention strategies such as Varenicline (de Dios, Anderson, Stanton, Audet, & Stein, 2012), although treatment efficacy among lighter smokers is under studied (Husten, 2009; Okuyemi et al., 2002).

These findings must be interpreted in the context of study strengths and limitations. The primary limitation in this study is the small sample size and relatively narrow range of smoking heaviness (e.g. no "chippers"; Shiffman & Paty, 2006). The sample size limitation is partially mitigated by the intensive nature of the assessment battery and the high compliance rates which resulted in over 309 complete observations. The study is limited by the fact that participants were not actively trying to quit smoking. Biological verification of abstinence, via CO, strengthens the inferences drawn from this study as only individuals who successfully abstained where included in the analyses. The lack of a non-abstinence control condition is an additional limitation as it is possible that diurnal rhythms partially account for the observed changes in affective dimensions, particularly in terms of NA and PA which do not explicitly assess nicotine-related effects. The potential for diurnal rhythms to fully account for the observed effects involving craving and withdrawal is, in our opinion, modest as our findings are largely consistent with prior studies examining short term abstinence effects as compared to non-abstinence ad-libitum smoking (Hendricks et al., 2006). Ecological momentary assessment studies have typically adopted a random assessment design; in order to model longer term abstinence on the order of days to weeks. This study used a fixed-interval rapid assessment design to accurately model short term abstinence, thus this should be noted when comparing findings with other studies. Lastly, environmental stimuli have been shown to be significant drivers of craving, which we were not able to adequately model in our data.

In conclusion, this pilot EMA study provides a unique characterization of the dynamic interplay between cigarette craving, withdrawal/NA, and PA during early nicotine abstinence. Results can inform experimental studies of these constructs, for example by suggesting that studies investigating the role of smoking heaviness should consider requiring 3–4 hours of abstinence, when group differences in both craving and withdrawal/NA were observed. Furthermore, by demonstrating robust associations between PA and craving in nicotine abstinence and the modest anticorrelation between NA and PA, the present study underlines the necessity of addressing both NA and PA independently in both etiological research and in treatment development efforts. Future studies with larger samples are

required to properly validate and extend these findings, which in turn can (a) inform patterns of vulnerability during early quit attempts, thus informing early cessation treatment targets, and (b) refine assessment methods used for treatment development.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

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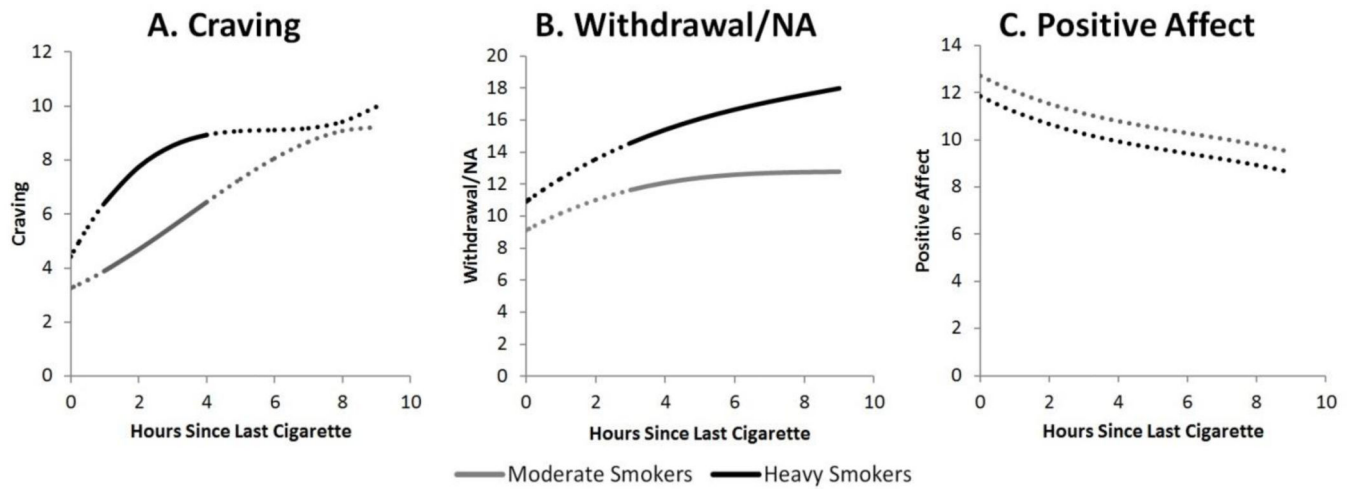
Figure 1.
Time course of craving, withdrawal/negative affect and positive affect during initial abstinence. Predicted values from the best fitting multilevel model are presented based on hours since last cigarette and smoking group. Significant smoking group differences are represented by solid lines. N = 15 per smoking group.

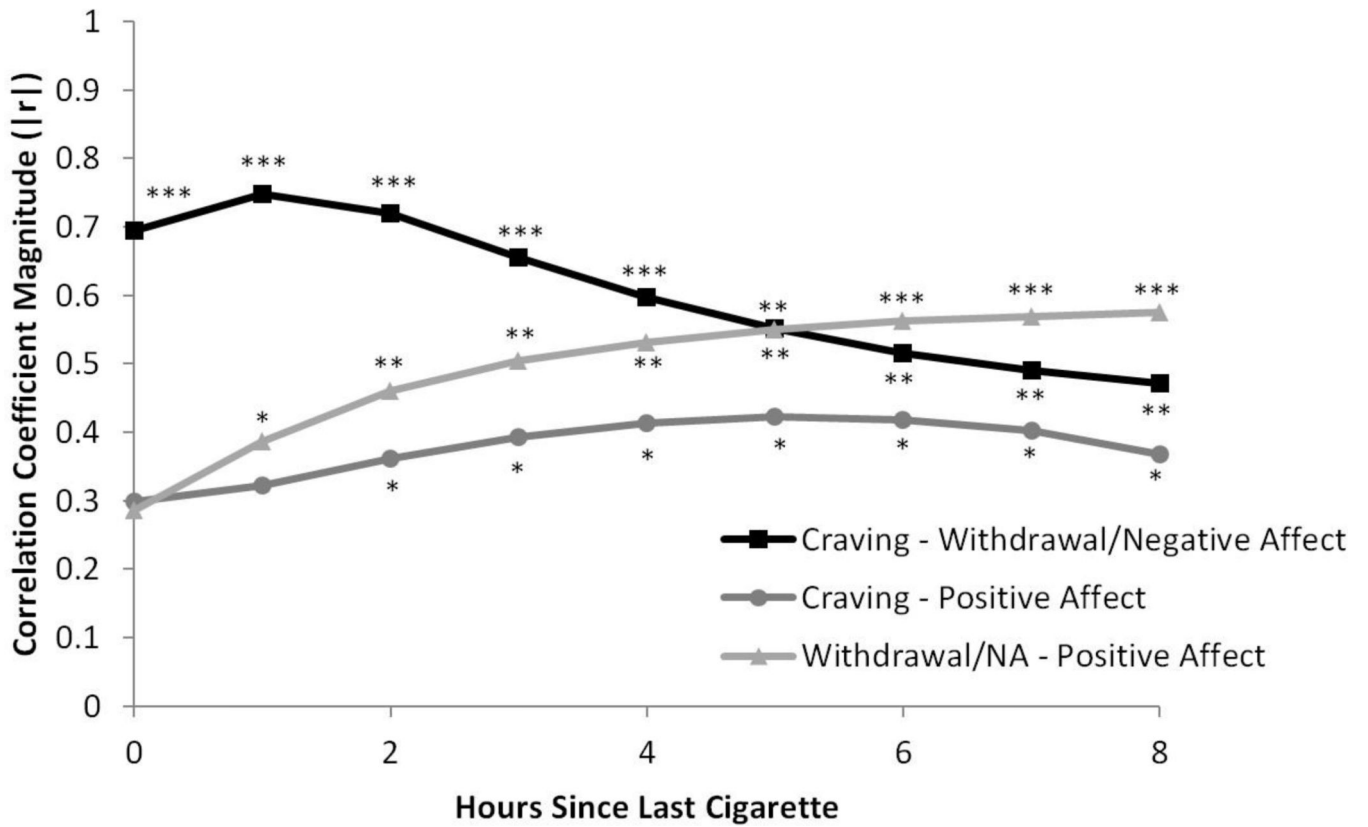# Between-Subjects Intercept Correlation Magnitudes

Figure 2.
Magnitude of between-subject intercept correlations for craving, withdrawal/negative affect and positive affect. Correlation coefficients are plotted hourly relative to the last cigarette of the day. N = 30. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Note: The correlations between withdrawal/NA and PA and between PA and craving are negative but the absolute magnitude of these correlations has been presented to aid interpretability.

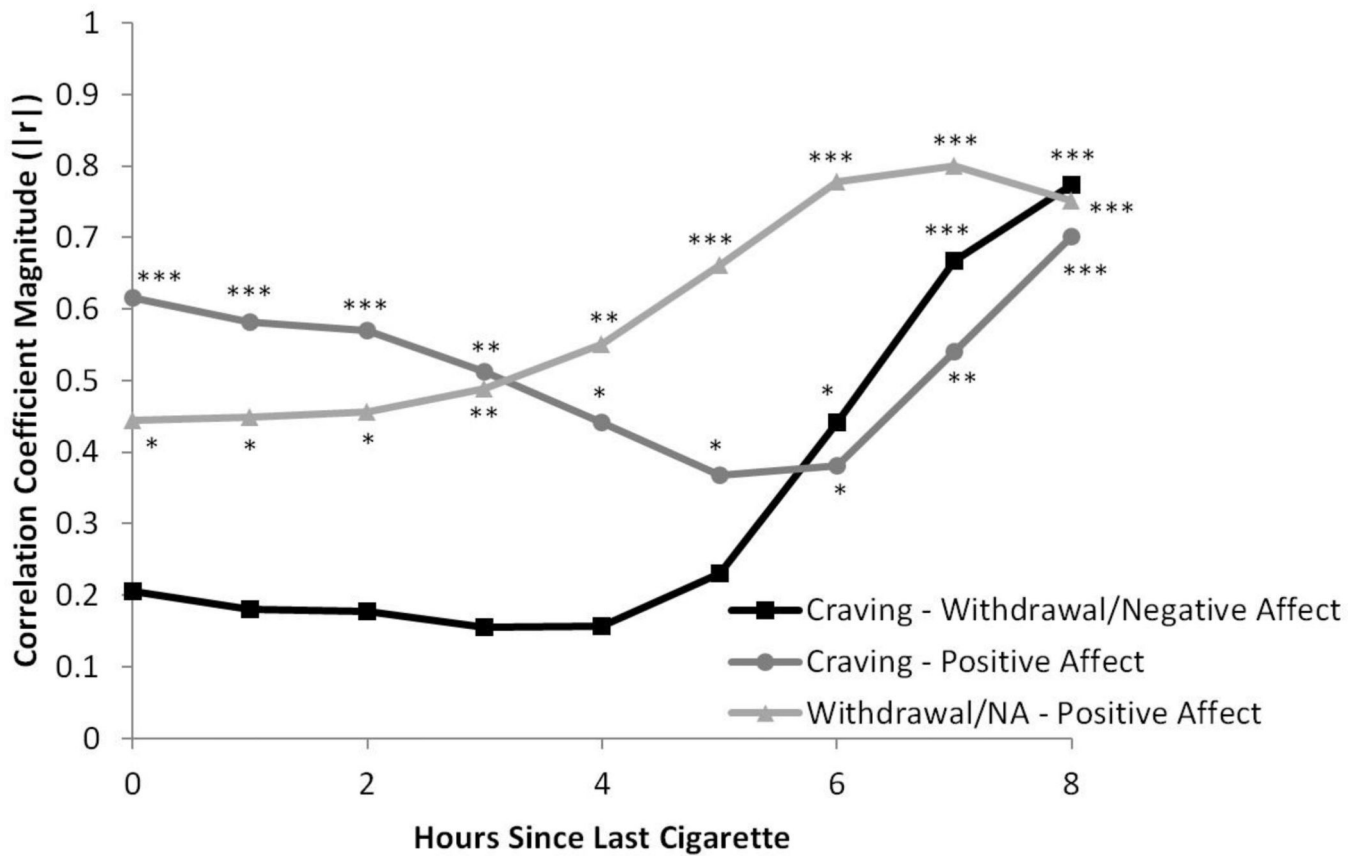# Between-Subjects Slope Correlation Magnitudes

Figure 3.

Magnitude of between-subject slope correlations for craving, withdrawal/negative affect and positive affect. Correlation coefficients are plotted hourly relative to the last cigarette of the day. N = 30. * $p < 0.05$, ** $p < 0.01$, ***$p < 0.001$

Note: The correlations between withdrawal/NA and PA and between PA and craving are negative but the absolute magnitude of correlations has been presented to aid interpretability.

Table 1

Sample characteristics and tests of group mean differences. (CPD = cigarettes per day from a 30-day timeline follow-back; FTND = Fagerstrom Test for Nicotine Dependence; time to first cigarette taken from item 1 on the FTND scale)

	Moderate Smokers (N = 15)	Heavy Smokers (N = 15)	Statistical Test
Age	36.67 (11.65)	38.27 (13.11)	t=−0.35, p = 0.73
Education*	93% HS or above	93% HS or above	Fisher exact p = 0.64
Sex (%female)	40%	20%	Fisher exact p = 0.39
Ethnicity (% white)*	33%	20%	Fisher exact p = 0.83
CPD	9.48 (2.42)	19.11 (2.70)	t = 10.30, $p < 0.001$
FTND	5.6 (2.50)	8.33 (1.35)	t = −3.73, $p = 0.001$
Time to 1st Cig	1.80 (1.08)	2.67 (0.49)	t = −2.83, $p = 0.01$
Baseline CO	11.87 (7.28)	15.53 (5.62)	t = −1.54, p= 0.13

*
Note: Education and Ethnicity were both collected and analyzed as categorical variables with 4 and 5 levels respectively. For ease of presentation, proportion of subjects who graduated high school and proportion reporting white ethnicity are reported.