Special Section

LISTENING TO NICOTINE: Negative Affect and the Smoking Withdrawal Conundrum

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Abstract—*In recent years, theoretical models of drug motivation and drug dependence have downplayed the role of withdrawal symptoms in the maintenance of addiction During this same period, strong links between drug use and measures of negative affect have been uncovered in empirical research In this article we examine these trends in the context of research on smoking Evidence is presented from two recent studies on smoking relapse that highlight the intimate connection between withdrawal symptomatology and negative affect Specifically, these studies reveal that (a) single-occasion measures of withdrawal symptoms or other markers of physical dependence do not contribute incremental validity in predicting relapse relative to measures of negative affect, (b) the trajectory of withdrawal symptoms is highly idiosyncratic, (c) exacerbations cannot be tightly coupled with pharmacological events, (d) the temporal dynamics of withdrawal reflect fluctuations in negative affect, and (e) differences in the trajectory of withdrawal symptoms index relapse vulnerability We conclude that a broadened view of withdrawal recognizing its probable affective bases will enhance its explanatory power and suggest new treatment strategies*

Over the past two decades, most accounts of drug dependence and drug motivation have deemphasized the role of withdrawal symptoms (e g , Robinson & Berridge, 1993, Stewart, deWit, & Eikelboom, 1984) Withdrawal has been downplayed for various reasons For example, relapse sometimes occurs well after withdrawal symptoms should be abating Additionally, relieving withdrawal does not, by itself, constitute a very effective treatment strategy Moreover, drugs that produce physiologically serious withdrawal syndromes do not necessarily support the strongest or most refractory self-administration patterns (e g , Jaffe, 1992, Robinson & Berridge, 1993) Finally, some recent evidence suggests that relapse to drug use may be initiated by phasic, situational precipitants, not tonic, internal events such as homeostatic withdrawal processes (Shiffman, Paty, Gnys, Kassel, & Hickcox, 1996)

At the same time that withdrawal models of drug dependence have been deemphasized, researchers have generated new research and theory that implicate affect in drug motivation and dependence This trend is apparent in the research literature on smoking Leventhal and Cleary (1980), for instance, argued that the regulation of emotions is a core element in smoking motivation Another theory (Baker, Morse, & Sherman, 1987) proposes that motivational states associated with smoking urges and self-administration are affective phenomena and that affective response systems serve as readouts of the intensity of drug motivation Considerable recent research supports an intimate link between affect and smoking motivation–tobacco dependence (Brandon, 1994) For example

1 Self-reported urges to smoke are reliably correlated with affect across response domains (e g , Sayette & Hufford, 1995, Zinser, Baker, Sherman, & Cannon, 1992)

2 Affect is linked to smoking motivation–tobacco dependence through epidemiological research In population-based samples, smoking status is positively related to symptoms of affective disorders such as anxiety and depression (Anda et al , 1990) Within smokers, symptoms of nicotine dependence are directly related to the magnitude of affective symptomatology (Breslau, 1995) Smokers with high levels of negative affect are less likely to quit smoking (e g , Anda et al , 1990)

3 High levels of negative affect, or personality dispositions fostering negative affect, predict the initiation of smoking (Kandel & Davies, 1986) For instance, Lipkus, Barefoot, Williams, and Siegler (1994) found that trait hostility predicted both smoking initiation and an inability to quit smoking Tschann et al (1994) found that a composite measure of emotional distress prospectively predicted substance abuse behaviors that included cigarette smoking

4 Perhaps the most strongly held and frequently endorsed expectation that smokers have about smoking is that it will ameliorate negative affect (Brandon & Baker, 1991) Such expectations prospectively predict both the withdrawal experienced when smokers attempt to quit smoking and smokers' likelihood of quitting successfully (Wetter et al , 1994) These expectations pertain to negative affect generated by smoking withdrawal as well as by nonpharmacological instigators (Wetter, Brandon, & Baker, 1992)

5 Not only do smokers expect cigarettes to ameliorate negative affect, but there is copious evidence that these expectancies are valid, that is, that smoking produces a rapid and significant reduction in negative affect (e g , Gilbert, 1995, Zinser et al , 1992)

6 Relapse to smoking typically occurs in a situation or context characterized by negative affect (Brandon, Tiffany, Obremski, & Baker, 1990) Shiffman et al (1996) recently found that negative affect seems linearly related to the severity of the lapse-relapse crisis This research revealed that when smokers were tempted to smoke, they reported stronger negative affect than when they were not tempted, when smokers actually lapsed to smoking, they reported stronger negative affect than when they were merely tempted

The evidence linking affect with smoking is remarkable not only because affect is associated with so many important markers of smoking motivation, but also because the relations obtained are so often

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linear, suggesting an intimate causal relation, not just a co-occurrence produced by lifestyle or other indirect mediators. Also, it is notable that the affect-smoking link cuts across a broad range of affective phenomena and dispositions. It cannot be attributed to a subset of negative affects or diagnostic classes.

RELATIVE VALIDITY: THE PREDICTION OF SMOKING RELAPSE

Because the regular, dependent use of tobacco may be influenced by a host of factors and may effect outcomes that range from acute physiological and social impacts to premature morbidity and mortality, it is reasonable to believe that measures of smoking and nicotine dependence will be associated with numerous characteristics of the individual. Therefore, explanatory models gain credence to the extent that they demonstrate incremental validity relative to other explanatory accounts of the essential features of nicotine dependence. In this section, we report on an investigation (Kenford, Smith, Wetter, Fiore, & Baker, 1996) that explored whether relapse to smoking, the sine qua non of dependence, would be better predicted by a model comprising affective measures (affect model) or a model comprising frequently used and validated measures of nicotine dependence (physical dependence model).

This study compared the ability of the physical dependence and affect models to predict 6-month relapse in 632 smokers who participated in clinical trials using the nicotine patch. This sample was first randomly split into two halves, with one half serving as a derivation sample and the other half serving as a validation sample. Logistic regression model-building procedures of Hosmer and Lemeshow (1989) were used to build the two models in the derivation sample. Table 1 displays the variables that were candidates for inclusion in the models. The variables in the physical dependence model were measures of either nicotine-tobacco exposure, patterns of compulsive use of tobacco, or withdrawal severity. The measures in the affect model were designed to assess either magnitude of negative affect, susceptibility to experience negative affect, or a disposition to use smoking for affective coping. After models were built in the derivation sample, the retained model elements were tested in the validation sample.

Only one variable in the physical dependence model predicted 6-month abstinence across both the derivation and the validation samples: postcessation withdrawal severity. Only two variables in the affect model predicted 6-month abstinence across both samples: history of depression and postcessation negative affect. Although withdrawal severity did predict 6-month outcome, this measure proved to yield a rather unsatisfactory account of the forces leading to relapse. First, withdrawal severity, along with control variables such as gender and nicotine patch status (active patch vs. placebo), did not produce a good-fitting model (as revealed by a significant test value for Hosmer and Lemeshow's fit index). Second, withdrawal severity failed to improve model fit once postcessation negative affect was entered into the logistic model. In other words, the measure of withdrawal severity had no incremental validity after accounting for postcessation negative affect. Conversely, the measure of negative affect significantly improved model fit when withdrawal severity had previously been entered in the model. In short, the predictive validity of withdrawal severity depended on its assessment of negative affect. The statistical redundancy of the two measures is understandable from an inspection of the content of the Minnesota Nicotine Withdrawal Scale (MNWS; Table 2) (Hughes & Hatsukami, 1986). The overlap in well-validated withdrawal and affect items is why the two types of items typically load on the same factor in factor analyses (e.g., Kenford et al., 1996; Shiffman et al., 1996).

Thus, in this research, a set of affective measures was superior to a collection of widely used dependence measures in terms of generating a good-fitting model of relapse. Moreover, this research reveals that measures of withdrawal and affect are similar, but more important, that the motivational significance of withdrawal depends on its sensitivity to affect. These results might be used to argue against the significance of withdrawal. Conversely, we believe that the results help confirm the hypothesis that nicotine dependence arises largely from affective processing systems (Baker et al., 1987), and that awareness of the relation between nicotine dependence and affect can illuminate the important role of withdrawal in addictive phenomena.

Table 1. *Candidate variables for model building in Kenford, Smith, Wetter, Fiore, and Baker (1996)*

Physical dependence model	Affect model
Precessation variables	
Breath carbon monoxide	Negative affect[c]
Serum cotinine	Perceived stress[d]
Serum nicotine	History of depression[e]
Smoking rate[a]	Negative reinforcement[f]
Fagerstrom Tolerance Questionnaire[b]	Coping style[g]
Postcessation variables	
Withdrawal severity[h]	Negative affect[c]
	Perceived stress[d]

[a]Smoking rate was assessed via self-report of number of cigarettes smoked per day. [b]Fagerstrom (1978). [c]Negative affect was assessed using the negative affect items of the Positive and Negative Affect Scale (Watson, Clark, & Tellegen, 1988). [d]Perceived stress was assessed using the Perceived Stress Scale (Cohen, Kamarck, & Mermelstein, 1983). [e]History of depression was assessed with a single item asking about prior depression. [f]Expectancies about negative reinforcement were assessed with the first scale of the Smoking Consequences Questionnaire (Brandon & Baker, 1991). [g]Coping style was assessed with the Three Factor Coping Scale (Rohde, Lewinsohn, & Tilson, 1990). [h]Withdrawal severity was assessed using the Minnesota Nicotine Withdrawal Scale (Hughes & Hatsukami, 1986).

Table 2. *Items on the Minnesota Nicotine Withdrawal Scale that sensitively reflect tobacco withdrawal (Hughes & Hatsukami, 1986)*

Desire to smoke
Anger, irritability, frustration
Anxiety, nervousness
Difficulty concentrating
Impatience, restlessness
Hunger
Awakening at night
Depression

A REVAMPED VIEW OF WITHDRAWAL: IMPROVING PREDICTION OF SMOKING RELAPSE

The finding that the motivationally prepotent elements of the withdrawal syndrome depend on affective processing systems has implications for the way withdrawal is conceptualized and assessed One fundamental insight suggested by this finding is that withdrawal is likely not a phenomenon sui generis driven exclusively by pharmacological factors Although pharmacological instigators are undoubtedly involved in the expression of smoking withdrawal symptoms, the overlap of smoking withdrawal and negative affect suggests that the current view of withdrawal needs to be broadened to encompass affect-relevant nonpharmacological instigators Sensitivities to negative affect, stressors, and the impact of declining levels of nicotine in the blood may represent fungible precipitants of the phenomenological experience of smoking withdrawal, or these variables may interact to produce the motivationally significant elements of withdrawal

Even in the absence of a detailed theory regarding the interplay among affective processing, pharmacological events, and expression of withdrawal symptoms, a broadened view of withdrawal suggests new strategies for assessing it For example, recognition of the affect-laden nature of self-reported smoking withdrawal (Table 2) suggests that traditional ideas regarding the time course of smoking withdrawal symptoms may require revision

In prior research, the time course of various smoking withdrawal symptoms has been characterized by averaging withdrawal ratings from all abstinent smokers at each point in time then plotting these means against time (e g , Cummings, Giovino, Jaen, & Emrich, 1985 Gritz, Carr, & Marcus, 1991, West, Hajek, & Belcher, 1989) The implicit assumption underlying this practice is apparently that only pharmacological events common to all smokers drive the expression of withdrawal symptoms If this is true, then averaging data from all subjects should produce the most accurate possible estimate of the time course of the various withdrawal symptoms These efforts have converged on a common finding When ratings are averaged across subjects, most individual symptoms on the MNWS show a characteristic transient time course, in which symptoms appear within 24 hr of cessation, peak within 1 to 2 weeks, and decrease in a linear fashion before disappearing by 4 to 6 weeks postcessation

An implicit corollary of the view that withdrawal symptoms have characteristic time courses is that severity is the critical dimension of individual differences in withdrawal If this premise is accepted, single-occasion measures of withdrawal should be sufficient to capture all of the motivationally significant variance in withdrawal This is the most common approach used for prediction in the literature on smoking withdrawal

A broadened view of withdrawal, one allowing for affective influences on its expression, implies that diversity, rather than uniformity, should characterize the time course of individual withdrawal symptoms An affective account assumes that the substrates of withdrawal (i e , affective processing systems) persist after cessation, and may be responsive to a wide array of inputs (e g , stressors, decreased blood levels of drug, smoking-related cues, psychiatric disorders) that need not be temporally contingent with initial abstinence According to this perspective, the apparent uniformity in the time course of withdrawal found in the literature may result from indiscriminate averaging that masks crucial individual differences in the temporal pattern of withdrawal symptoms Individual differences in the trajectory of withdrawal distress over time may hold important information regarding the motivational significance of withdrawal These trajectory differences are ignored by single-occasion measurements

We recently examined withdrawal data from two clinical trials of the nicotine patch in order to evaluate some of the implications of an affective model of expression of withdrawal symptoms (Piasecki, Fiore, & Baker, in press) In both studies, subjects were given diaries that contained multiple copies of the MNWS (Hughes & Hatsukami, 1986) and were asked to rate the severity of symptoms daily for 8 weeks following their quit date Withdrawal ratings were averaged across symptoms to yield a measure of global distress, and ratings from the first 55 days of treatment were used to construct a temporal withdrawal profile for each subject These profiles were equated for elevation and scatter (Cronbach & Gleser, 1953) and then clustered to form groups that were homogeneous with respect to the shape of their withdrawal profiles (i e , with respect to time course) Relations between withdrawal and relapse at both end-of-treatment and 6-month follow-ups were evaluated via hierarchical logistic regression Two withdrawal variables were entered in these analyses cluster membership (based on withdrawal trajectory) and average severity during the first week after quitting

Initial examination of the withdrawal profiles of individual subjects clearly confirmed that many did not resemble the transient pattern commonly reported in the literature However, the transient pattern was readily produced by averaging across subjects The top panel of Figure 1 depicts the withdrawal profiles of 50 randomly selected patients from one of the patch studies These profiles have been converted to z scores on a case-by-case basis, in order to equate them for elevation and scatter the heterogeneity in time course of withdrawal is even more striking when raw scores are used The bottom panel of Figure 1 shows the results of averaging these standardized profiles across these 50 subjects

Cluster analyses in both studies yielded three clusters with satisfactory internal consistency and markedly different trajectories of withdrawal distress The cluster solution for one of the studies, a multisite, double-blind, randomized, placebo-controlled trial of the 22-mg nicotine patch, is depicted in Figure 2, along with the average profile of all subjects included In this sample of 224 smokers, 71 (31 7%) were assigned to Cluster I, which most closely resembles the transient pattern described in the majority of smoking withdrawal research Cluster II, characterized by an increase in severity of withdrawal over time, contained 31 individuals (13 8%) Cluster III included 122 individuals (54 5%) These subjects reported a small improvement in severity of withdrawal during the first 2 weeks of the trial, but no improvement thereafter In all three clusters, profiles constructed on the basis of the negative affect items of the Positive and Negative Affect Scale (Watson, Clark, & Tellegen, 1988) were highly correlated with the withdrawal profiles, suggesting that the negative affective symptoms on the MNWS were largely responsible for the temporal withdrawal patterns

In these studies, withdrawal measures were significant predictors of relapse at both end-of-treatment (Week 8) and 6-month follow-up Cluster membership, a proxy for the time course of withdrawal, was a significant predictor in all models, despite being entered after the severity measure and control variables such as patch dose This finding suggests that the trajectory per se is motivationally significant, and the importance of withdrawal in the relapse process may be underestimated by conventional analytic approaches that consider information about severity only

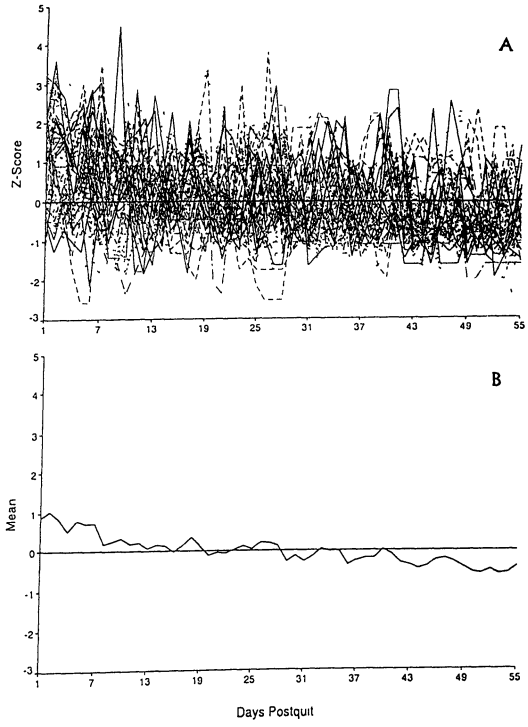

Fig 1 Withdrawal profiles from a nicotine patch study (Piasecki, Fiore, & Baker, in press, Study 2) Standardized withdrawal profiles for 50 randomly selected patients are shown in (a) Each profile has a mean of 0 and standard deviation of 1 The average of all 50 profiles is plotted in (b)

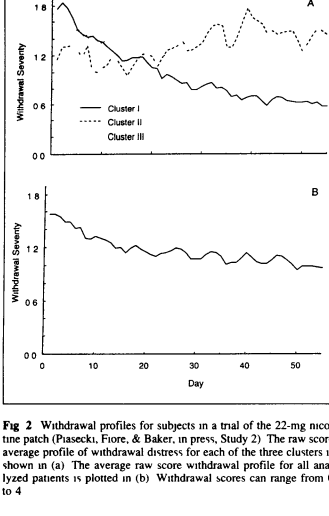

Fig 2 Withdrawal profiles for subjects in a trial of the 22-mg nicotine patch (Piasecki, Fiore, & Baker, in press, Study 2) The raw score average profile of withdrawal distress for each of the three clusters is shown in (a) The average raw score withdrawal profile for all analyzed patients is plotted in (b) Withdrawal scores can range from 0 to 4

CONCLUSIONS AND IMPLICATIONS

The data presented here suggest that measures of postcessation negative affect and smoking withdrawal symptoms are highly redundant Moreover, our data demonstrate that a view of withdrawal that assumes such redundancy, and allows for idiosyncratic, nonpharmacological influences on expression of withdrawal symptoms, can improve the prediction of relapse compared with traditional assessment approaches Our research does not indicate that affective systems underlie all withdrawal phenomena However, our findings do suggest that a motivationally significant element of withdrawal is reflected in affective outputs, and that this knowledge can be useful in crafting more sensitive assessments of withdrawal

In sum, we espouse the view that withdrawal is much like bereavement (Gilbert, 1995) in that in both phenomena a relatively discrete class of events activates or stokes negative affect, yet myriad other factors may affect the shape, intensity, and duration of withdrawal by modulating affective processing This view raises an interesting question about when an affect in a smoker or drug user is really an affect and when it is withdrawal Such a question may lead to no fruitful or satisfactory distinction "The fish is in the water, and the water is in the fish " At present, we conceptualize the withdrawal syndrome a an affective disorder having a variable course that is observed only in drug-deprived, dependent individuals Theory and methodology commonly used to study affective disorders might profitably be applied to the study of the withdrawal syndrome, and its relation to other affective phenomena

The present research underscores the heterogeneity of smokers, the persistence or reemergence of withdrawal in some smokers, and the role of affect in vulnerability to relapse These results may prove useful in crafting new treatments for smoking cessation

REFERENCES

Anda, R F Williamson D F Escobedo L G Mast E E Giovino G A & Remington P L (1990) Depression and the dynamics of smoking A national perspective *Journal of the American Medical Association, 264* 1541–1545

Baker T B Morse E & Sherman J E (1987) The motivation to use drugs A psychobiological analysis of urges In C Rivers (Ed) *Nebraska Symposium on Motivation. Vol 34 Alcohol use and abuse* (pp 257–323) Lincoln University of Nebraska Press

Brandon T H (1994) Negative affect as motivation to smoke *Current Directions in Psychological Science 3* 33–37

Brandon T H & Baker T B (1991) The Smoking Consequences Questionnaire The subjective expected utility of smoking in college students *Psychological Assessment 3* 484–491

Brandon T H Tiffany S T Obremski K M & Baker T B (1990) Postcessation cigarette use The process of relapse *Addictive Behaviors 15* 105–114

Breslau N (1995) Psychiatric comorbidity of smoking and nicotine dependence *Behavior Genetics 25* 95–101

Cohen S Kamarck T & Mermelstein R (1983) A global measure of perceived stress *Journal of Health and Social Behavior 24* 385–396

Cronbach, L J & Gleser G C (1953) Assessing similarity between profiles *Psychological Bulletin 50* 456–473

Cummings K M Giovino G Jaen C & Emrich L J (1985) Reports of smoking withdrawal symptoms over a 21 day period of abstinence *Addictive Behaviors 10* 373–381

Fagerstrom K O (1978) Measuring degree of physical dependence to tobacco smoking with reference to individualization of treatment *Addictive Behaviors 3* 235–241

Gilbert D G (1995) *Smoking Individual differences, psychopathology, and emotion.* Washington DC Taylor & Francis

Gritz E R Carr C R & Marcus A C (1991) The tobacco withdrawal syndrome in unaided quitters *British Journal of Addiction 86* 57–69

Hosmer D W & Lemeshow S (1989) *Applied logistic regression.* New York John Wiley & Sons

Hughes J R & Hatsukami D K (1986) Signs and symptoms of tobacco withdrawal *Archives of General Psychiatry 43* 289–294

Jaffe J H (1992) Current concepts of addiction In C P O Brien & J H Jaffe (Eds) *Addictive states* (pp 1–21) New York Raven Press

Kandel D S & Davies M (1986) Adult sequelae of adolescent depressive symptoms *Archives of General Psychiatry 43* 255–262

Kenford S L Smith S S Wetter D W Fiore M C & Baker T B (1996) *Tests of two models of nicotine dependence* Unpublished manuscript University of Wisconsin-Madison Madison

Leventhal H & Cleary P D (1980) The smoking problem A review of the research and theory in behavioral risk modification *Psychological Bulletin 88* 370–405

Lipkus I S M Barefoot J C Williams R B & Siegler I C (1994) Personality measures as predictors of smoking initiation and cessation in the UNC Alumni Heart Study *Health Psychology, 13* 149–155

Piasecki T M Fiore M C & Baker T B (in press) Profiles in discouragement Two studies of variability in the timecourse of smoking withdrawal symptoms *Journal of Abnormal Psychology*

Robinson T E & Berridge K C (1993) The neural basis of drug craving An incentive sensitization theory of addiction *Brain Research Reviews 18* 247–291

Rohde P Lewinsohn P M & Tilson M (1990) Dimensionality of coping and its relation to coping *Journal of Personality and Social Psychology 58* 499–511

Sayette M A & Hufford M R (1995) Urge and affect A facial coding analysis of smokers *Experimental and Clinical Psychopharmacology 3* 417–423

Shiffman S Paty J A Gnys M Kassel J A & Hickcox M (1996) First lapses to smoking Within-subjects analysis of real-time reports *Journal of Consulting and Clinical Psychology 64* 366–379

Stewart, J deWit H & Eikelboom R (1984) The role of unconditioned and conditioned drug effects in the self administration of opiates and stimulants *Psychological Review 91* 251–268

schann, J M Adler N E Irwin, C E Jr , Millstein, S G Turner R.A. & Kegeler S M (1994) Initiation of substance use in early adolescence The role of pubertal timing and emotional distress *Health Psychology 13* 326–333

Watson D Clark L.A & Tellegen A (1988) Development and validation of brief measures of positive and negative affect The PANAS scales *Journal of Personality and Social Psychology 54* 1063–1070

West, R Hajek P & Belcher M (1989) Time-course of cigarette withdrawal symptoms *Psychopharmacology* 99 143–145

Wetter D W Brandon, T H & Baker T B (1992) The relation of affective processing measures and smoking motivation indices among college-age smokers *Advances in Behavior Research & Therapy 14* 169–193

Wetter D W Smith, S S Kenford, S.L. Jorenby D E. Fiore, M C Hurt, R.D Offord, K P & Baker T B (1994) Smoking outcome expectancies Factor structure, predictive validity and discriminant validity *Journal of Abnormal Psychology 103* 801–811

Zinser M C Baker T B Sherman, J E. & Cannon, D S (1992) Relations between self-reported affect and drug urges and cravings in continuing and withdrawing smokers *Journal of Abnormal Psychology 101* 617–629