Smoking Withdrawal Dynamics:
I. Abstinence Distress in Lapsers and Abstainers

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Smoking withdrawal reports from a clinical trial ($n = 893$) were submitted to hierarchical linear modeling as a cross-method replication of a heterogeneity approach to withdrawal measurement and to clarify the influence of postcessation smoking on symptom reports. Five individual difference parameters tapping distinct facets of withdrawal were derived: intercepts (mean severity), linear slope (direction and rate of change), quadratic trend (curvature), volatility (scatter) and, among lapsers, a cigarette coefficient (smoking-related deflections of symptoms). All parameters were highly variable across persons. Lapsers had more aversive symptom patterns than abstainers, and symptoms tended to be higher than otherwise predicted on lapse days. These results reinforce the conclusion that withdrawal symptoms are highly variable and argue against discarding withdrawal data from participants who lapse.

Smoking withdrawal symptoms—aversive states that arise after abrupt cessation of smoking—became the focus of a great deal of clinical research in recent years because they are cited by smokers as barriers to cessation (Cummings, Jaen, & Giovino, 1985) and

because withdrawal is considered a hallmark of addiction (e.g., Crabbe, 2002; Kenny & Markou, 2001). As this body of research grew, it pointed to an incongruous set of conclusions. On the one hand, ample evidence documented the existence of a reliable, aversive syndrome in ex-smokers that was readily reversed by nicotine (Hughes, Higgins, & Hatsukami, 1990). On the other hand, relatively little evidence suggested that the observed symptoms were clinically important: Levels of postcessation symptoms predicted smoking relapse poorly (Patten & Martin, 1996). These discrepant findings raised serious issues for both clinical practice and theoretical conceptualizations of smoking. If withdrawal symptoms are motivationally inert, then there is little justification for treatments designed to ameliorate withdrawal or for training individuals to cope with withdrawal. Theoretically, such findings might be taken to challenge negative reinforcement models of addiction (cf. Lyvers, 1998, and Robinson & Berridge, 1993) or might be used to question whether nicotine is indeed an addictive agent.

The variability of smoking withdrawal symptoms—noted in the earliest investigations of the syndrome (e.g., Shiffman & Jarvik, 1976)—may hold the key to escaping this impasse (Piasecki, Fiore, & Baker, 1998). Numerous theoretical treatments of withdrawal symptoms emphasize their dependence on affective and associative processes that should yield variable symptom patterns within and across individuals (Baker, Morse, & Sherman, 1987; Solomon, 1977; Wikler, 1973). Moreover, the large number of mood-related items included on traditional withdrawal inventories virtually guarantees heterogeneous symptom time courses because mood is responsive to a host of nondrug influences. Traditionally, investigators have averaged over or ignored withdrawal variability, focusing instead on cross-sectional "snapshots" of withdrawal *severity* when predicting behavioral outcomes such as relapse (Piasecki et al., 1998). However, to the extent that smokers smoke

for negative reinforcement purposes (i.e., to reduce negative affect), withdrawal *variability* may be phenomenologically and motivationally important (Baker et al., 1987; Brandon, 1994; Piasecki et al., 2000). Systematic research attention to withdrawal variability may provide fresh insights into smoking motivation, relapse, and dependence.

Previous Research on Withdrawal Heterogeneity

Two recent investigations probed the potential utility of characterizing withdrawal trajectory over time in smokers trying to quit (Piasecki et al., 1998, 2000). In both investigations, dynamic cluster analysis (Prochaska, Velicer, DiClimente, Guadagnoli, & Rossi, 1991) was used to parse samples into subgroups having different withdrawal profile shapes over the course of the quit attempt. These preliminary investigations suggested that individual differences in withdrawal shape have clinical and research implications. For instance, in each sample, smokers displayed diverse withdrawal profiles, including trajectories involving sustained or exacerbating symptoms. Moreover, prediction models showed that trajectory information was related to relapse likelihood; quitters with "atypical" withdrawal patterns (e.g., increasing symptoms) were found to be at especially high risk for relapse (Piasecki et al., 1998, 2000).

This research was limited by the shortcomings inherent in cluster analysis. For instance, clustering creates potentially artificial categories that can convey only a portion of the complexity in withdrawal experience. The coarse nature of clustering also prevents sensitive tests of any interplay between time-varying postcessation events and withdrawal reports, precluding analysis of the context of symptom fluctuations. Finally, the recovered clusters are heavily dependent on sample-specific features of the data; it is difficult to foster comparability across investigations if the number and nature of particular withdrawal clusters represent the only available descriptive indices.

In the present article, we improved on earlier clustering research by using hierarchical linear models (HLM; Bryk & Raudenbush, 1992) to characterize withdrawal variability. Five symptom parameters, hypothesized to provide a reasonably comprehensive picture of withdrawal dynamics, are introduced: an *intercept* measure describing mean symptom severity; a *linear slope* measure that captures the direction and rate of symptom change; a *quadratic* component that captures any curvature or deceleration in symptoms; a *volatility* index that describes the lability in withdrawal, corrected for systematic trends; and (in lapsers) a *cigarette coefficient* that captures features of the withdrawal profile reliably associated with smoking days.

Understanding Intratreatment Smoking and Withdrawal Variability

Although lapse occurrence is a potent predictor of outcome in smoking cessation attempts (e.g., Kenford et al., 1994), little is known about its influence on withdrawal symptom severity or trajectory. In theory, postcessation smoking might precipitate either increased or decreased symptoms; increased symptoms could be due to mechanisms such as priming (Stewart, deWit, & Eikelboom, 1984), and decreased symptoms could be due to the supression of withdrawal by the direct pharmacologic actions of nicotine. Because of uncertainty as to how aperiodic smoking affects withdrawal, most investigators have opted to restrict analyses of withdrawal reports to subjects who maintain continuous abstinence over the period of interest (e.g., Gottlieb, Killen, Marlatt, & Taylor, 1987; Hatsukami, Skoog, Allen, & Bliss, 1995; Levin et al., 1994; West, Hajek, & Belcher, 1989). If withdrawal plays a causal role in lapses and relapse, however, excluding individuals who are found to have smoked may eliminate from consideration precisely those subjects with the most severe and motivationally relevant withdrawal symptoms (Gilbert et al., 1998; Hughes et al., 1990; Jorenby et al., 1996; Patten & Martin, 1996; Piasecki et al., 1998). Thus, it is possible that investigators' frequent failure to find prospective connections between withdrawal and relapse may in part be attributable to this restriction of range (Patten & Martin, 1996; Piasecki et al., 1998).

In this research, we explored the interplay between lapses and withdrawal using two complementary strategies. First, differences between lapsers and abstainers in modeled withdrawal parameters are explicitly tested. If postcessation smoking strongly distorts withdrawal profiles by alleviating symptoms, we would expect lapsers to show patterns on each parameter that are less extreme than those of abstainers. A second approach uses smoking reports as time-varying covariates within the subgroup of lapsers, allowing quantification of the linkages between day-to-day fluctuations in smoking and withdrawal. If lapses alleviate symptoms, cigarettes should be reliably associated with downward deflections of the withdrawal profile. On the other hand, if smoking occurs in response to exacerbating symptoms, cigarettes should be associated with acute increases in symptom reports. This procedure also yields an additional individual difference parameter, the cigarette coefficient, that complements other withdrawal parameters in characterizing the withdrawal experiences of lapsers.

In sum, the present study was designed to assess individual differences in distinct dimensions of withdrawal (e.g., elevation, trajectory, volatility) and determine how withdrawal is related to postcessation smoking. A companion article (Piasecki, Jorenby, Smith, Fiore, & Baker, 2003) assesses connections between withdrawal patterning and relapse, using additional data from this sample.

Method

Parent Trial Participants and Design

Data were drawn from a four-center, double-blind, fully factorial clinical trial evaluating the 21-mg nicotine patch and bupropion for smoking cessation (Jorenby et al., 1999). A total of 893 smokers enrolled in the trial and were randomly assigned to one of four treatment groups, with preferential assignment to treatments involving active medication: placebo patch + placebo pill ($n = 160$); nicotine patch + placebo pill ($n = 244$), bupropion + placebo patch ($n = 244$), and bupropion + nicotine patch ($n = 245$). The design and primary outcomes of the parent trial are provided in greater detail by Jorenby et al. (1999).

Measures

Daily diary measures. Smoking withdrawal symptoms and smoking behavior were assessed with a daily diary. Each diary page contained a modification of the Minnesota Nicotine Withdrawal Scale (MNWS; Hughes & Hatsukami, 1986) that asked respondents to rate the following nine symptoms on a scale from 0 to 4 (0 = *absent,* 1 = *slight,* 2 = *mild,* 3 = *moderate,* 4 = *severe*): craving for cigarettes, depressed mood, difficulty falling asleep, awakening at night, irritability/frustration/anger,

anxiety, difficulty concentrating, restlessness, and increased appetite. Each diary page also contained a space for participants to record the number of cigarettes smoked that day. Participants were instructed to enter a value of zero on days they did not smoke. Participants were instructed to complete a diary page just before going to bed each night so that they could reflect on the entire day's experience when providing their responses. At each weekly study visit, participants returned completed diaries from the past week and received blank diaries to be completed each day between visits.

Participants completed the diaries daily for 11 weeks after the quit date. Daily withdrawal and smoking data from the first 8 postcessation weeks were the focus of the present research for three reasons: (a) provision of active pharmacotherapy lasted 8 weeks, and termination of medication could have a major influence on reported symptoms; (b) the 8-week window is consistent with prior research on withdrawal heterogeneity (e.g., Piasecki et al., 1998); and (c) we wanted to strike a balance between describing a long-run course of symptoms and maintaining prospective prediction of short-term clinical outcomes from growth model parameters (see companion article; Piasecki et al., 2003).

In all growth models, the raw sum of withdrawal item scores was used as the repeated dependent measure. The withdrawal metric was therefore similar in range to daily cigarette counts used as covariates (the resulting score could range from 0 to 36). Scores from all withdrawal items were combined rather than examining individual symptoms or families of items. Some research suggests that classes of withdrawal symptoms may differ in trajectory and motivational importance (Piasecki et al., 2000). However, these findings were derived in research using multiple-item scales tapping individual symptom domains. Omnibus scores were used in the present research for two reasons. First, the MNWS contains only single items to assess each domain, and modeling them separately courts problems with reliability. Second, preliminary analyses indicated positive correlations among all withdrawal items (including craving) when either scores at a single point in time or rates of linear change were considered.

Lapser–abstainer split. Before modeling differences in withdrawal trajectory between lapsers and abstainers, it was necessary to allocate participants to subgroups on the basis of smoking behavior. This split of the sample was determined using data from daily cigarette tallies from the first 8 weeks of the cessation attempt. Although 893 subjects were randomized to a treatment, 4 failed to report to any postscreening study visits and did not complete any withdrawal or smoking ratings. Of the remaining 889, only 418 participants provided a complete series of cigarette tallies, with 194 of these reporting complete abstinence and 224 reporting at least one smoking event. Of the 471 subjects with one or more missing cigarette tally in their diaries, 318 reported smoking at least one postcessation cigarette in the completed ratings. This left 153 participants with an incomplete series of cigarette reports, with all completed reports indicating zero smoking. Following the spirit of intent-to-treat conventions, these individuals were assigned to the lapsed or abstinent groups according to the extensity of missing data; participants with three or fewer missing ratings were deemed abstainers, and those with four or more missing values were assigned to the smoking group. This rule assigned 63 participants to the abstinent group and 90 to the lapse group. In practice, individuals classified as lapsed according to this rule were missing an average of 41 withdrawal reports; most of these missing values were massed at the end of the trial—the missing values seemed attributable to attrition and/or relapse. In sum, 257 (29%) participants were counted as continuously abstinent over the first 8 weeks of cessation, and 632 (71%) participants were counted as lapsers.

Statistical Analyses

Hierarchical linear modeling of withdrawal. HLMs assess change using a strategy that can be loosely described as performing "regressions of regressions." At Level 1, a regression equation is written that describes the shape of *a single individual's pattern of change* on the repeated measure as a function of time. A set of Level 2 models is then specified, with each model attempting to account for *individual differences across Level 1 models* as a function of other measured variables. That is, Level 1 equa-

tions describe a single person's withdrawal experience, and the Level 2 models attempt to organize and explain the differences among the hundreds of individually modeled withdrawal profiles. In actual practice, the two steps are estimated simultaneously through restricted maximum likelihood (Bryk & Raudenbush, 1992). In this article, estimated Level 1 coefficients are used to plot illustrative predicted profiles for individual participants and as a baseline for computing an ancillary measure of symptomatic volatility for each smoker. Level 2 coefficients are used to test omnibus effects and differences between lapsers and abstainers.

Individual-level (Level 1) growth functions: Form and interpretation. A quadratic function was specified in Level 1 equations to model withdrawal trajectory across days. Given that we had 56 repeated measures, we had the degrees of freedom to "spend" on estimating a large number of high-order polynomial trend components. However, plots of withdrawal data suggested that a quadratic function was adequate. Higher order trend information, when it exists in a participant's symptom profile, is captured by an additional volatility statistic (see below).

Limiting the analyses to a quadratic function also enhances interpretability of the findings. The growth models yield three interpretable parameters: (a) the intercept term yields an estimate of each participant's mean withdrawal severity over the 8-week period of interest; (b) the linear trend coefficient indexes direction and rate of change in symptoms across the 8-week period (a positive linear coefficient indicates that symptoms became more severe over time, and a negative coefficient describes symptoms that diminish over time); and (c) the quadratic coefficient, which represents more complex curvature. Positive quadratic coefficients indicate a U-shaped symptom pattern, and a negative coefficient indicates a symptom profile with a middle "hump." These three coefficients are fundamental indices of symptomatic experience that are common to all models; they are supplemented with additional withdrawal measures (i.e., volatility, cigarette coefficients) as described below.

Missing data. HLM allows for flexible handling of cases with missing withdrawal ratings (Bryk & Raudenbush, 1992). Random effects models do not require that all subjects provide complete data. Where missing data exist, the modeling assumes the completed ratings are representative of each subject's deviation from the modal trend line, and available data are augmented with reference to the whole-sample trend (Hedeker & Gibbons, 1997; Laird, 1988).

Growth Model 1: Contrasting withdrawal in lapsers and abstainers. At Level 1, each individual's symptom growth was modeled as a function of the three parameters described above (intercept, linear trend, and quadratic trend) plus random error.[1] At Level 2, lapse status was represented using a dummy code, with abstainers coded as 0 and lapsers coded as 1.

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[1] Specifically, the Level 1 model was a regression equation of the form:

$$Y_{ti} = \beta_{0i} + \beta_{1i}(L_t) + \beta_{2i}(Q_t) + r_{ti},$$

where Y_{ti} is the withdrawal score of individual i at time t, the βs are estimated coefficients that describe the growth of individual i's withdrawal across the window, L_t and Q_t are the linear and quadratic trend functions for time t, and r_{ti} is a random error term. Orthogonal polynomials were used to construct L_t and Q_t values; linear values ranged from $-.23$ (Day, 1) to $+.23$ (Day 56); quadratic values were $+.28$ at both tails, with the reversal at $-.15$.

The Level 2 model apportioning variance in the intercept term was:

$$\beta_{0i} = \gamma_{00} + \gamma_{01}(LAP) + u_{0i},$$

where β_{0i} is the withdrawal intercept estimated for individual i at Level 1, γ_{00} is an estimate of the average intercept for all subjects conditioned on lapse status, γ_{01} is an estimate of the separation of lapsers and abstainers, LAP is the lapser–abstainer dummy code, and u_{0i} is a residual term representing individual i's deviation from the value predicted by the fixed effects. Analogous equations were constructed at Level 2 for each of the βs in the Level 1 model.

Growth Model 2: Cigarette effects in lapsers. Including cigarette tallies as time-varying covariates in the Level 1 model of withdrawal growth allows an estimation of the size and direction of *deflections from the predicted withdrawal function.* Because the model required variance in smoking records at the individual level in order to be estimated, this analysis was limited to lapsers. The Level 1 model in this analysis was a simple elaboration of the quadratic function described above to include a time-varying cigarette term.[2] The Level 2 models in this analysis were analogous to those described for the lapser–abstainer model, with the exception that the lapse status variable was omitted (because only lapsers were included in this model).

Symptomatic volatility. The configural features of withdrawal may have motivational significance that is distinct from the elevation and trajectory components (Piasecki et al., 2000). If increases in withdrawal spur motivation to smoke, then acute increases seen from one day to the next should be associated with relapse. Therefore, in theory, to the extent that a person shows day-to-day changes or volatility in withdrawal, he or she should be at greater risk for relapse.

To capture this phenomenon, volatility indices were computed for each of the two growth models. The volatility index was defined as the average squared deviation (per day) between a participant's observed or raw withdrawal profile and his/her HLM-predicted withdrawal function (i.e., around the composite function formed by, at a minimum, subject-specific intercept, linear, and quadratic terms). Average squared deviation was selected in preference to the sum of squared deviations so that participants with complete or missing withdrawal data could be assessed on a common metric. The volatility statistic is related to the growth models insofar as it requires Level 1 ordinary least squares (OLS) estimates for its computation, and it is conceptually linked to the residual variance around the prediction function. However, the volatility index is computed separately, not estimated as part of the growth curve modeling. Note that there is no clear-cut conceptual dividing line that separates volatility from a higher order function. That is, variance that could be accounted for by, for example, a quintic function, will add to volatility variance in the present analyses because no supraquadratic functions were modeled. Of course, measurement error will also be captured to some extent by the volatility metric. Nevertheless, it seemed important to capture this information because of volatility's theoretical connection to relapse.

Exemplar profiles. For each major growth model, raw withdrawal profiles for 4 exemplar participants are overlaid on their Level 1 prediction functions. Each individual's growth coefficients are also presented in the figures. These plots are presented for two reasons. First, they help to convey what is being modeled at the individual level; this will be helpful in interpreting the meaning of the growth parameters and volatility. Second, raw profiles from individual participants help to convey the diversity of withdrawal experiences in the sample, which might not be intuitively appreciated from aggregate profiles and prediction functions.

Results

Contrasting Withdrawal in Lapsers and Abstainers

Table 1 summarizes the results of the model. A total of 836 subjects (257 abstainers, 579 lapsers) provided sufficient data to be included in this model. Each of the estimated effects was significantly different from zero. Abstainers were characterized by a mean symptom severity of 6.8, a downward linear trend over time, and a tendency toward a U-shaped profile of symptoms. In contrast to the abstainers, lapsers had more severe average symptoms (+3.3 intercept effect relative to the abstainer estimate), had smaller linear decreases in symptoms (+3.7 linear effect relative to the abstainer slope), and tended to have diminished U-shaped curvature in their profiles (−1.5 quadratic effect relative to abstainer estimate). The parameters were estimated with good pre-

Table 1

Summary of the Growth Model Contrasting Lapsers and Abstainers (N = 836)

Fixed effect	Coefficient
Intercept	6.75
Lapser increment	3.26
Linear slope	−9.07
Lapser increment	3.67
Quadratic	4.15
Lapser increment	−1.51

Note. "Lapser increment" connotes that the coefficient must be summed with the corresponding estimate to yield the predicted effect for the lapser subgroup. The listed estimate represents the separation between the abstainer and lapser group fixed effects. For example, the intercept lapser increment of 3.26 suggests that lapsers had an average intercept of 10.01 (3.26 points higher than the abstainer intercept of 6.75). Tests evaluating whether the listed coefficients were significantly different than zero were uniformly significant; for all coefficients, $p < .01$. Thus, abstainers had nonzero intercepts, slopes, and quadratic trends; lapsers' intercepts, slopes, and quadratic coefficients differed significantly from those of abstainers.

cision, reliability estimates for the intercept, linear, and quadratic coefficients were .99, .91, and .84, respectively. Tests of random effects (not shown) revealed that significant heterogeneity in all growth parameters was observed after accounting for the lapser–abstainer differences ($ps < .001$). Figure 1 depicts the predicted trend functions for each group, overlaid with the groups' raw means. Note that the lapsers' predicted trend diverges from the raw means late in the quit period in Figure 1. This reflects the accumulation of missing data among lapsers; the modeling compensates to some extent for the dwindling sample sizes by using the available data to estimate the likely pattern of outcomes if all withdrawal data were completed. Withdrawal data from a 1-week baseline period are included in Figure 1 for comparison; these data were not explicitly modeled with HLM. The baseline data demonstrate that both groups showed cessation-contingent changes in symptoms. A post hoc repeated measures ANOVA showed that lapsers reported higher symptoms than abstainers, even prior to the cessation attempt, $F(1, 743) = 6.57, p = .01$.

Symptomatic volatility In the lapser–abstainer model, volatility indices for the whole sample ranged from 0.0 (1 participant) to 275.3 ($M = 12.1, SD = 14.8$). Mean volatility among complete abstainers was 7.9 ($SD = 7.6$), whereas lapsers had a mean volatility index of 13.9 ($SD = 16.7$). A planned, two-tailed t test comparing volatility estimates between lapsers and abstainers showed that lapsers had significantly higher volatility scores across the 8 weeks, $t(834) = −5.49, p < .001$. This result is consistent with the hypothesis that greater symptom fluctuation is associated with postcessation smoking. However, it is possible the increased volatility in lapsers reflects the symptomatic consequences of smoking events rather than naturally arising symptom variability that predisposes to later smoking. Metric factors (e.g., a floor effect) might also contribute to lowered volatility in abstainers.

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[2] Formally, the Level 1 model was expanded as:

$$Y_{ti} = \beta_{0i} + \beta_{1i}(L_t) + \beta_{2i}(Q_t) + \beta_{3i}(C_{ti}) + r_{ti},$$

where the new term (C_{ti}) is the number of cigarettes individual i reported smoking at time t.
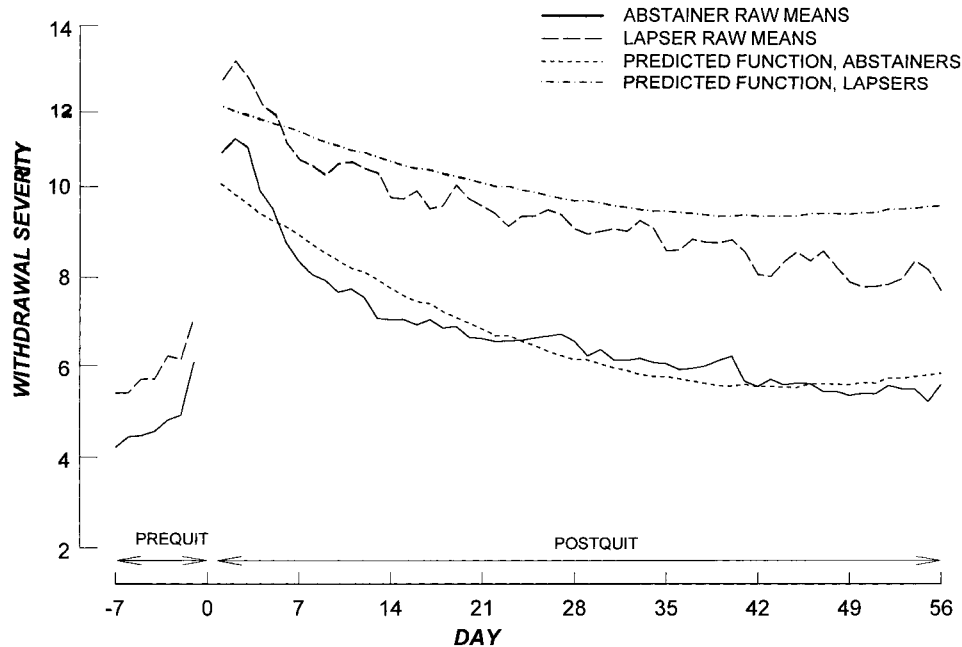
Figure 1. Predicted withdrawal growth models compared with raw pre- and postquit means for lapsers and abstainers.

Exemplar profile. The four panels of Figure 2 display both raw symptom profiles and predicted Level 1 OLS growth functions, along with raw symptom data from 1 pre-quit week, for a handful of individual participants. These particular participants were selected from the first five lapsers in the data set with enough data to fit Level 1 OLS models. Only lapsers were selected so that the same individuals could be used to illustrate the meaning of cigarette coefficients in subsequent models. Thus, there is no special significance to these particular 4 individuals, nor were they selected in a random fashion. However, they nicely depict the range of withdrawal patterns in the sample as well as differing slopes and diverse covariate effects. Moreover, they are fairly representative of the patterns in the data set as a whole. For instance, approximately 23% of the analyzed sample ($n = 194$) had positive linear slopes, as seen prominently in the profile of Participant 1001. Nearly 70% of the sample ($n = 583$) had the U-shaped quadratic trend seen in Participants 1003, 1004, and 1010.

The raw profiles themselves are noteworthy for their complexity. The figures nicely summarize the cross-subjects' heterogeneity and intrasubject variability in withdrawal experiences. Overlaying the prediction functions and the raw profiles conveys both what is and is not captured by the linear models at Level 1. The relevance of the volatility index is apparent when scrutinizing these plots. For instance, Participant 1003 reported symptoms that generally declined across 8 weeks of cessation but reported several large-magnitude spikes in symptoms, especially early in the quit attempt; these are poorly captured by the prediction function.

Modeling Cigarette Effects in Lapsers

We examined lapsers separately because this would provide not only the most informative estimate of the impact of smoking on

symptoms but also illustrate how accounting for cigarette-related variance affects other model components (e.g., volatility). A total of 578 lapsers provided sufficient data to be included in this model. Table 2 summarizes the results of this model. As can be seen from the table, the fixed effects suggested a mean symptom severity of 9.99, a linear decline in symptoms, and a U-shaped symptom pattern. The fixed effect associated with the cigarette covariate was 0.22, suggesting that symptom reports tended to be higher than those predicted by the intercept, linear, and quadratic terms on days when smoking occurred. Although the estimate of the fixed cigarette effect was small in magnitude, remember that it is interpreted as the predicted effect per cigarette and that this could translate to large modulations in symptomatology at the individual level. All fixed effects were significantly different from zero, and significant samplewide heterogeneity was found for each parameter, as indicated by tests of the random effects (not shown; $ps < .001$). The intercept, linear, and quadratic effects were estimated reliably (.99, .91, and .83, respectively), but the cigarette effect was estimated with somewhat less precision (0.60).

Symptomatic volatility in lapsers. It is possible that much of the volatility among lapsers could be accounted for by the impact of smoking on withdrawal symptoms. Therefore, we examined the level of symptom volatility when cigarette-related fluctuations were controlled. Volatility coefficients for the smoking-covaried model ranged from 0.6 to 242.2 ($M = 12.6$, $SD = 14.6$). These descriptive statistics are broadly similar to those found among lapsers in the lapser–abstainer model. Therefore, one implication is that, samplewide, dispersion of withdrawal reports around the prediction function are not eliminated by accounting for cigarette-related fluctuations. Volatility in lapsers likely reflects a mixture of smoking-attributable distortions of withdrawal experience and naturally arising variability in symptoms.
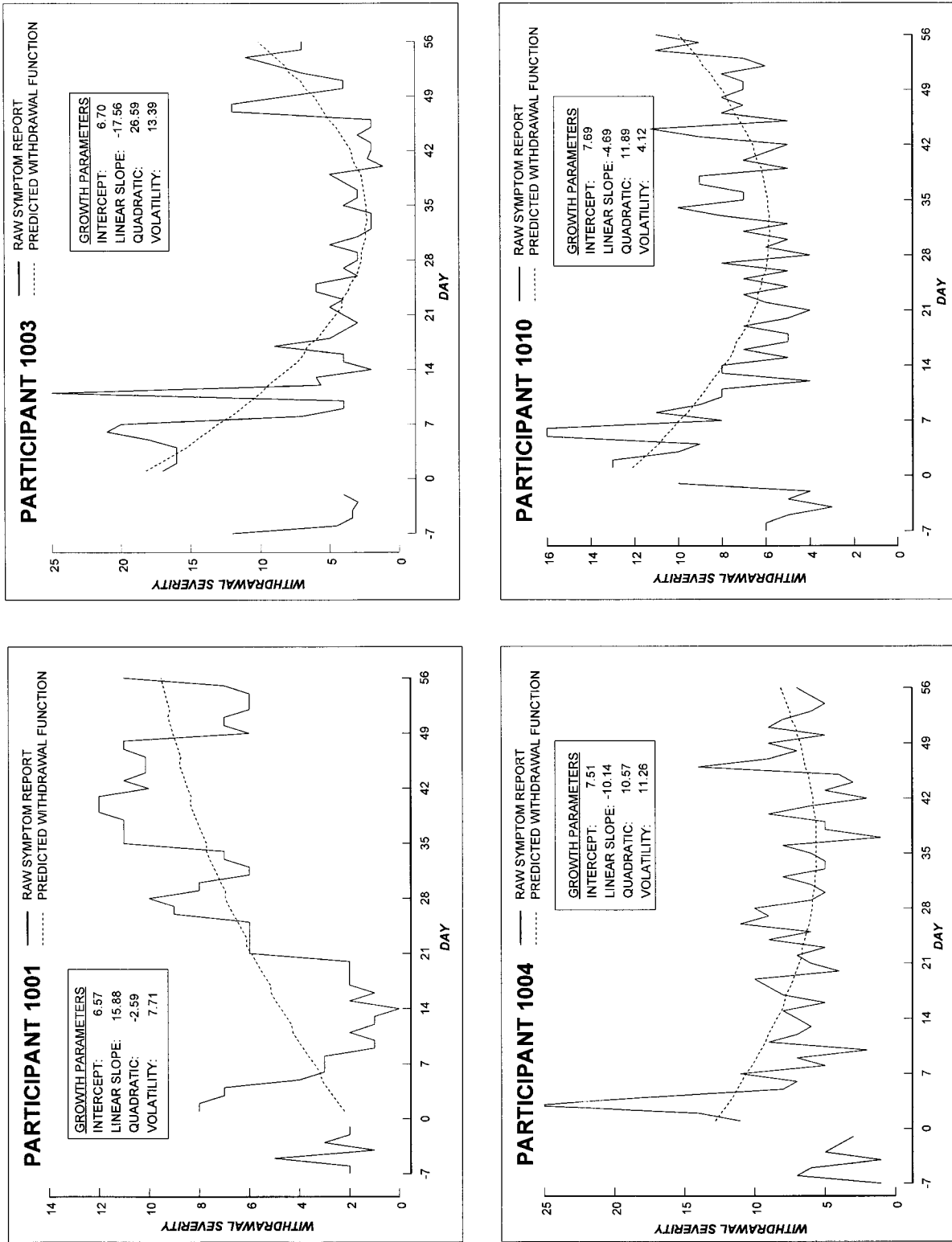
Figure 2. Predicted withdrawal growth functions, raw withdrawal profiles, and estimated growth parameters from the lapser–abstainer model for the four exemplar participants.

Table 2
Summary of the Smoking-Covaried Growth Model Limited to Lapsers (N = 578)

Fixed effect	Coefficient
Intercept	9.99
Cigarette effect	0.22
Linear slope	−5.81
Quadratic	2.65

Note. For all values, $p < .01$.

Exemplar profiles. The four panels of Figure 3 display the raw withdrawal profiles, raw smoking tallies, and OLS smoking-adjusted prediction functions for the same 4 participants shown in Figure 2. These plots are helpful for appreciating the meaning of the cigarette-related growth term and illustrate the heterogeneity in cigarette effects. For instance, Participants 1001 and 1004 were characterized by very small, positive cigarette coefficients. Including this term in the plotting of each of these participants' Level 1 OLS regression line made nearly imperceptible modifications to the function derived in the lapser–abstainer analysis. Each of these individuals smoked on several occasions, so the small modifications to the predicted function may be attributed to the fact that neither participant reported a reliable or consistent association between withdrawal change and smoking extensity. For instance, Participant 1001 smoked between 2 and 5 cigarettes on eight occasions, all between Days 42 and 56. Four smoking occasions were reported prior to the large downturn in symptoms on Day 50, whereas 4 occurred after this event. Because the raw symptom reports fall on either side of the regression function, the deviations from the predicted values on smoking days tend to cancel one another out, producing a small cigarette coefficient and a small ripple in the regression line.

Contrast this with the findings for Participants 1003 and 1010. Participant 1003 smoked on only seven occasions postcessation but, in each case, smoking was accompanied by high or worsening symptoms. Therefore, Participant 1003 has a large, positive cigarette coefficient. Moreover, superimposing the cigarette-related deflections on Participant 1003's prediction function accounts for several of the large spikes that characterize the raw profile. Notably, this individual's estimated volatility index was substantially reduced (9.7 vs. 13.4) once smoking was taken into account. Participant 1010 had a negative cigarette coefficient. The deflection from this individual's prediction line generally coincided with reported dips in symptomatology, although many fluctuations in symptomatology were not tied to smoking events.

Post hoc examination of cigarette effects. The diverse cigarette coefficients found in the foregoing analyses have, to our knowledge, never been described; further data are needed to understand their meaning. Smoking variables, especially the frequency and extensity of postcessation smoking, might plausibly be related to the magnitude and direction of individuals' cigarette coefficients. For instance, individuals might end up with positive cigarette coefficients because they smoked at low levels, priming withdrawal symptoms, or because high or rapidly rising symptoms produced a momentary breakdown in resolve. Symptom relief, and thus negative cigarette coefficients, might be expected to be associated with higher levels of smoking.

To test these ideas, the sample was split according to the direction of the cigarette effect (positive vs. negative). These groups were then compared on three smoking parameters using *t* tests: total number of cigarettes in the time frame, number of smoking occasions in the time frame, and the average number of cigarettes per occasion during the first 8 postcessation weeks. Table 3 contains the results of these comparisons. Groups defined on the basis of the direction of the cigarette effect differed significantly on all smoking-related measures. All effects were in the hypothesized direction, with individuals assigned negative smoking coefficients (smoking was associated with decreased symptoms) reporting more smoking occasions, more total cigarettes, and more cigarettes per occasion.

Discussion

The subjective effects of smoking follow a time course that can be described as either remarkably stereotyped or strikingly variable, depending on one's level of analysis. In the aggregate, smoking withdrawal symptoms seem to be highly stereotyped. When symptom ratings are averaged across subjects and plotted against time, a consistent pattern is observed (see Figure 1; Hughes, 1992; Jorenby et al., 1996). This occurs, no doubt, because averaging amplifies the reliable "signal" in withdrawal profiles and "washes out" idiosyncrasies not related to common experiences. It is plausible that aggregate plots accurately reflect the "true" time course of abstinence-primed withdrawal (at least as it is reflected in the sorts of measures used in the present research). The variability in individual profiles, however, illustrates that it may be quite inappropriate to assume that the aggregate pattern is applicable to any given quitter (Figures 2 and 3). The complex ups and downs of individual profiles may reflect nonpharmacologic "noise," which could influence smoking behavior but is not "withdrawal" in the classic sense.

This simple account of withdrawal patterning might be clinically useful, but it contains some as-yet-unverified assumptions. In fact, the causal pathway could be more complex. Consider the possibility that nicotine removal might result in a long-lasting state of heightened reactivity to stressors. Such reactivity could be an important piece of the withdrawal syndrome but would remain latent when not activated by provocative environmental events. A latent symptom of this sort would manifest itself as aperiodic spikes in the symptom profile. Under this scenario, the magnitude of situationally provoked symptoms may depend on the contribution of a subtle but important component of abstinence-primed withdrawal. It is also possible that symptom spikes in withdrawal are enhanced not because of any enhanced latent affect reactance but because smokers are denied their most effective affect-amelioration response.

It remains an open question as to when an affective response is withdrawal and when it is merely affect (e.g., Gilbert & McClernon, 2000; Kassel, 2000; Parrott, 1999; Piasecki & Baker, 2000). How future research deals with this thorny issue may depend on the goals of particular projects. Investigators interested in using withdrawal measures to understand individual differences in smoking motivation (e.g., predicting relapse, correlates of symptoms) should use data analytic methods that are sensitive to the individual-level variability in symptom expression. Such analyses give smokers "full credit" for the extent of their distress and may be more likely to reveal systematic associations with nonwith-
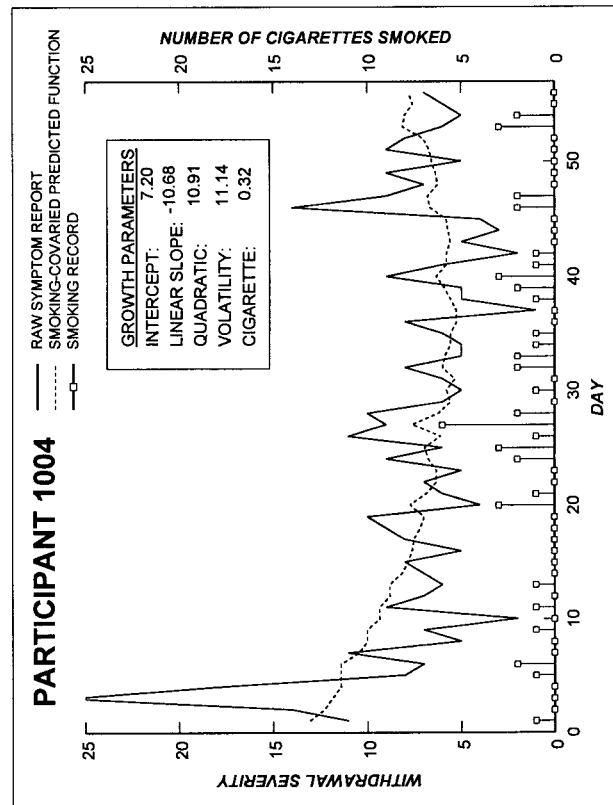
PARTICIPANT 1003

RAW SYMPTOM REPORT
SMOKING-COVARIED PREDICTED FUNCTION
SMOKING RECORD

GROWTH PARAMETERS
INTERCEPT: 5.98
LINEAR SLOPE: -19.63
QUADRATIC: 20.66
VOLATILITY: 9.74
CIGARETTE: 0.96

NUMBER OF CIGARETTES SMOKED
WITHDRAWAL SEVERITY
DAY

PARTICIPANT 1010

RAW SYMPTOM REPORT
SMOKING-COVARIED PREDICTED FUNCTION
SMOKING RECORD

GROWTH PARAMETERS
INTERCEPT: 7.92
LINEAR SLOPE: -4.11
QUADRATIC: 11.81
VOLATILITY: 3.94
CIGARETTE: -0.17

NUMBER OF CIGARETTES SMOKED
WITHDRAWAL SEVERITY
DAY

PARTICIPANT 1001

RAW SYMPTOM REPORT
SMOKING-COVARIED PREDICTED FUNCTION
SMOKING RECORD

GROWTH PARAMETERS
INTERCEPT: 6.54
LINEAR SLOPE: 15.77
QUADRATIC: -2.40
VOLATILITY: 7.69
CIGARETTE: 0.12

NUMBER OF CIGARETTES SMOKED
WITHDRAWAL SEVERITY
DAY

PARTICIPANT 1004

RAW SYMPTOM REPORT
SMOKING-COVARIED PREDICTED FUNCTION
SMOKING RECORD

GROWTH PARAMETERS
INTERCEPT: 7.20
LINEAR SLOPE: -10.68
QUADRATIC: 10.91
VOLATILITY: 11.14
CIGARETTE: 0.32
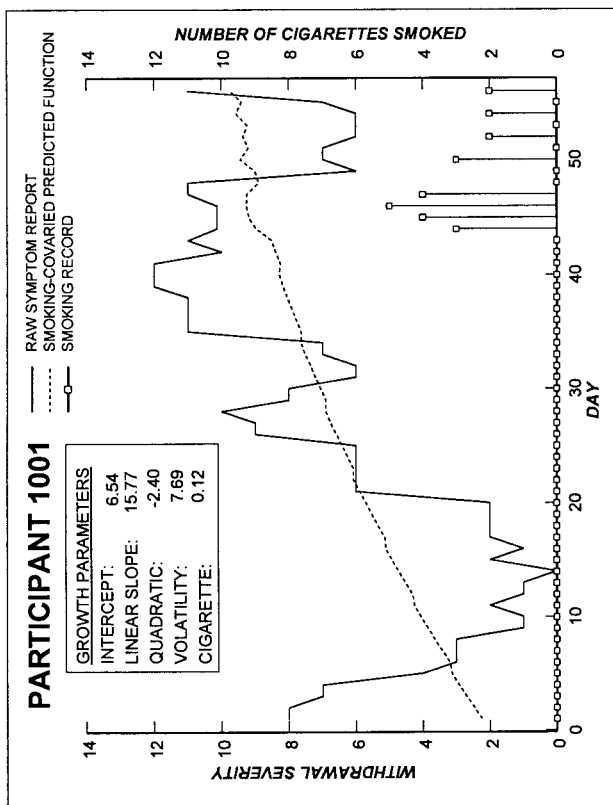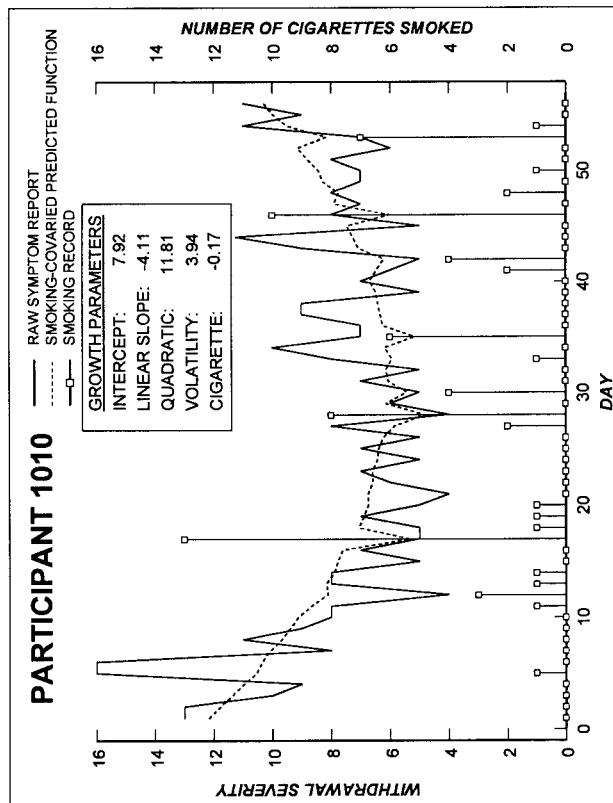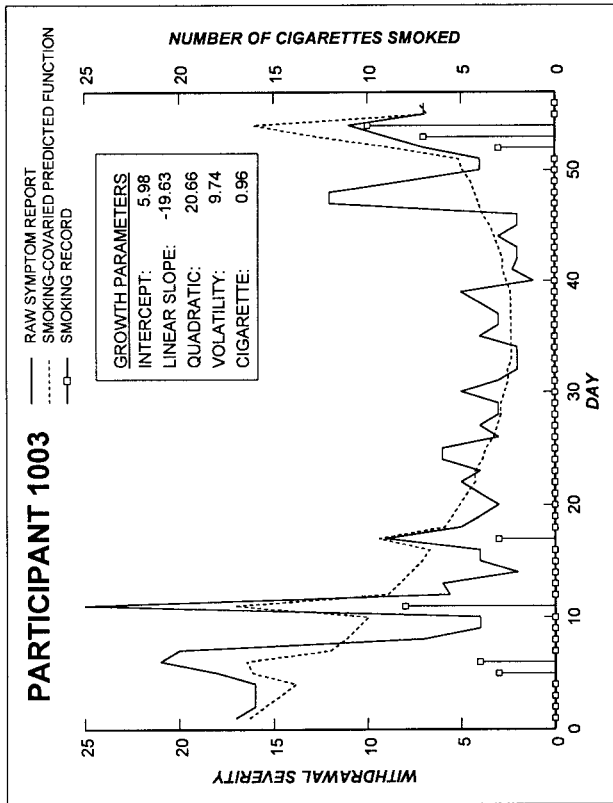
NUMBER OF CIGARETTES SMOKED
WITHDRAWAL SEVERITY
DAY

Table 3

Post Hoc Tests Examining Relations Between Postcessation Smoking Behavior and Direction of the Cigarette Coefficient

Smoking variable	NEG mean	POS mean	t	df	p
Smoking occasions	14.18	11.31	2.41	537	<.05
Total reported cigarettes	100.48	56.33	4.04	537	<.001
Average per occasion	6.17	4.31	3.82	537	<.001

Note. POS n = 211, NEG n = 328. NEG = subgroup with negative cigarette coefficients; POS = subgroup with positive cigarette coefficients. Analyses were limited to participants for whom Level 1 ordinary least squares (OLS) coefficients could be computed. Of the 632 participants counted in the lapsed group, 54 had no valid entries in their smoking diaries and thus could not be included in the model, yielding an effective sample size of 578 for lapser analyses. An additional 39 participants had no variance in their smoking tallies (i.e., either a vector of zeros and missing values or single nonzero values); they provided enough data to contribute to the estimation of the modal trend but insufficient data for OLS estimates to be computed.

drawal variables. On the other hand, researchers interested in elucidating the nature and time course of abstinence-primed withdrawal per se (the withdrawal signal ostensibly due to physical dependence) may need to consider developing measures that have less potential for "cross-talk" with naturally occurring variability in persons and the environment.

The present research was primarily descriptive in nature, but the findings have some basic clinical implications. Clinicians may need to educate smokers preparing to quit about the variability in withdrawal symptoms and to convey clearly the expectation that a "bumpy ride" is common. In clinical settings, we have noticed that smokers preparing to quit ask about the duration of withdrawal symptoms frequently and seriously. Although we know of no research on this phenomenon, our impression is that smokers use the answer to such questions to set benchmark dates that acquire motivational importance (i.e., "If I can just get through the 10 days of withdrawal, I'll be nearly out of the woods"). If this sort of process is common, a mismatch between the withdrawal expectations created by clinicians and actual withdrawal experiences may have a toxic effect on the motivation to quit. We suspect that most clinicians underestimate the duration and variability of withdrawal symptoms when discussing the issue with their patients.

The analyses presented here were designed not only to yield interpretable facets of withdrawal distress but also to scrutinize the influence of postcessation smoking on withdrawal reports. One clear finding was that eliminating lapsers from descriptive studies of smoking withdrawal does tend to exclude patients reporting more severe and/or unremitting withdrawal symptomatology. For instance, the lapser–abstainer model revealed that lapsing was associated with significant increments in the fixed intercept, linear slope, and quadratic effects, with lapsers tending to report more severe patterns of symptomatology. Planned comparisons also revealed that lapsers' profiles were characterized by higher degrees of volatility than were those of abstainers.

Investigators' decisions to eliminate lapsers from descriptive analyses are usually predicated on the notion that smoking will reduce withdrawal scores and therefore undercut the demonstration that smoking is associated with severe withdrawal symptoms (e.g., Hatsukami et al., 1995; Jorenby et al., 1996). The findings of lapser–abstainer differences in withdrawal growth question these assumptions. The results were more consistent with an explanatory account in which high and variable withdrawal motivates the reuptake of smoking rather than one in which smoking distorts or reduces rated symptoms. This is because lapsers were found to have consistently higher withdrawal reports and slower improvement over 8 weeks of cessation. Even if these effects were wholly attributable to distortion of withdrawal ratings by cigarette smoking, this distortion seems to have the effect of marking rather than masking relapse risk and would seem to do little violence to the hypothesis that high, unremitting symptoms are indicators of relapse likelihood. In other words, lapsers as a group do not masquerade as individuals who are relatively untroubled by withdrawal symptoms.

However, the lapser–abstainer findings are also consistent with plausible alternative hypotheses. For instance, high withdrawal among lapsers might reflect an upward distortion of withdrawal reports due to priming effects from low-level smoking. As smoking rate accelerates after a lapse, participants might be more likely to show downward symptom deflections (i.e., self-medication effects), but these effects might be selectively missing from the data record because the pattern of accelerating smoking that produces them also leads to attrition from the trial. Alternatively, high symptoms among lapsers might reflect a self-presentation bias on symptom recall (e.g., Shiffman, Paty, Gnys, Kassel, & Hickcox, 1996), with individuals who smoked justifying this behavior through inflated reports of distress. In any event, the present findings should encourage the inclusion of lapsers in subsequent withdrawal research and stimulate a search for a deeper understanding of smoking-withdrawal covariance in the context of real-world cessation attempts.

Modeling smoking events as time-varying covariates within the subsample of lapsers provided a complementary view of the interplay between smoking and withdrawal symptomatology. Findings indicated that, samplewide, smoking days tended to be associated with withdrawal reports that were higher than those predicted by a simple quadratic prediction function. This accords with the findings of the lapser–abstainer model in suggesting that increased withdrawal tends to mark lapse events.

This inference must be tempered by the significant variability in the size and direction of cigarette coefficients across individuals. Post hoc tests suggested that the direction of the cigarette coefficients was related to the quantity and frequency of smoking after the quit date. Although the determinants of the size and direction of individuals' cigarette coefficients are almost certainly complex and multivariate, these findings suggest a plausible working hypothesis: Positive cigarette coefficients may represent instances in which high or volatile withdrawal provokes a momentary slip, whereas negative coefficients may mark a self-medication/relapse

Figure 3. Predicted smoking-covaried withdrawal growth functions, raw profiles, smoking tallies, and estimated growth parameters for the four exemplar participants.

process whereby smokers actively drive down their symptoms through more intense smoking. In this research, the cigarette coefficient was designed to capture basic smoking-related distortions of the withdrawal profile and quantify any stable effects of smoking withdrawal covariance at the individual level. More complex analyses would be possible in principle and might shed additional light on the relapse process. For instance, the cigarette coefficient could be computed for successive, smaller time intervals (e.g., weekly) to determine whether a shift from positive to negative coefficients marks the transition from lapses to full-blown relapse, and lag effects could be tested to further characterize smoking withdrawal dependencies.

Limitations

A number of limitations in the present study need to borne in mind when considering the results. Many variables that might help researchers better understand the mechanisms of withdrawal heterogeneity were not collected in the parent trial. For instance, we lack repeated measures of potentially important nonnicotine environmental events (e.g., stressors), measures of personality variables that might moderate reactivity to environmental stressors, and objective (non-self-report) measures of withdrawal symptomatology. Without such variables, we cannot probe important hypotheses regarding the observed variability in withdrawal symptoms. We strongly suspect that vicissitudes in withdrawal symptomatology reflect the impact of abstinence-primed processes as well as idiosyncratic environmental and person variables that are more generally related to the expression of mood. However, the available data do not allow us to describe what proportion of variance in withdrawal scores is derived from these sources, to specify the most important classes of environmental and person variables, or to characterize any change in the composition of symptom elicitors over time.

Another potential limitation was the fact that three quarters of the sample was using some form of active pharmacotherapy during the period when withdrawal scores were collected. There is evidence that both the nicotine patch and bupropion reduce the symptoms of smoking withdrawal (Jorenby et al., 1996; Shiffman et al., 2000); thus, their use could have affected the obtained results. In the analyses reported here, we did not control for pharmacotherapy assignment when estimating withdrawal parameters because pharmacotherapy was a Level 2 variable: It might explain some intersubject variance in withdrawal dynamics, but including it in the models would not affect estimation of Level 1 coefficients. Previous research has shown that withdrawal heterogeneity does not depend on the use of pharmacotherapy (Piasecki et al., 2000).

The use of daily self-report diaries to measure withdrawal symptomatology and postcessation smoking also poses some potential interpretive problems. Whenever diaries are used, there is the potential that forgetting or retrospective biases may affect the findings. Diary data are also limited with regard to their temporal resolution; this complicates the interpretation of time-varying effects of cigarette tallies and withdrawal reports. Thus, individuals who smoked early and often on a given day may end up with negative cigarette coefficients because they are reflecting on a day that was dominated by the aftereffects of smoking. Positive cigarette coefficients might arise from lapses that occur late in the day when bedtime symptom ratings focus on the unpleasant anteced-

ents of the smoking occurrence. Such processes might vary across subjects or across occasions in the same subject. An additional problem with diary methods is that some participants may back-fill them, completing several days worth of ratings just prior to a study visit to avoid the embarrassment of admitting they neglected to make the ratings on the designated days. We have no way of knowing whether this occurred in the present trial or, if so, how extensively it was done. Nonetheless, data from this and other studies using diary techniques (e.g., Piasecki et al., 1998) have yielded findings consistent enough to suggest that any back-filling does not completely obscure motivational signal in the withdrawal data. Research using experience-sampling methods (Shiffman et al., 1996; Stone & Shiffman, 1994), with enhanced temporal resolution and safeguards against back-filling, is under way and should help tease apart these alternative explanations.

A final limitation was that the analyses used data collected only during the post-quit period. A full understanding of the meaning of postcessation symptom dynamics will require systematic comparisons with symptom data collected during ongoing smoking.

Such limitations notwithstanding, our findings illustrate that withdrawal experiences are rich, complex, and varied at the individual level. Further research designed to sensitively model this variability, its causes, and consequences may enrich our understanding of smoking motivation, dependence, and relapse.

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