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Evaluating the effect of smoking cessation treatment on a complex dynamical system

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A R T I C L E I N F O

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A B S T R A C T

Objective: To understand the dynamic relations among tobacco withdrawal symptoms to inform the development of effective smoking cessation treatments. Dynamical system models from control engineering are introduced and utilized to evaluate complex treatment effects. We demonstrate how dynamical models can be used to examine how distinct withdrawal-related processes are related over time and how treatment influences these relations.

Method: Intensive longitudinal data from a randomized placebo-controlled smoking cessation trial (N = 1504) are used to estimate a dynamical model of withdrawal-related processes including momentary craving, negative affect, quitting self-efficacy, and cessation fatigue for each of six treatment conditions (nicotine patch, nicotine lozenge, bupropion, patch + lozenge, bupropion + lozenge, and placebo).

Results: Estimation and simulation results show that (1) withdrawal measurements are interrelated over time, (2) nicotine patch + nicotine lozenge showed reduced cessation fatigue and enhanced self-efficacy in the long-term while bupropion + nicotine lozenge was more effective at reducing negative affect and craving, and (3) although nicotine patch + nicotine lozenge had a better initial effect on cessation fatigue and self-efficacy, nicotine lozenge had a stronger effect on negative affect and nicotine patch had a stronger impact on craving.

Conclusions: This approach can be used to provide new evidence illustrating (a) the total impact of treatment conditions (via steady state values) and (b) the total initial impact (via rate of initial change values) on smoking-related outcomes for separate treatment conditions, noting that the conditions that produce the largest change may be different than the conditions that produce the fastest change.

1. Introduction

Cigarette smoking and other forms of tobacco use remain one of the leading causes of illness and preventable death (United States Department of Health and Human Services et al., 2014). Despite these negative health consequences, many continue to smoke. This is due, in large part to tobacco dependence, which produces aversive withdrawal symptoms when dependent smokers abstain. Withdrawal symptoms include increased nicotine craving and negative affect (irritability, sadness, worry) and motivate smokers to return to smoking (Hughes and Hatsukami, 2007; Welsch et al., 1999). These symptoms may also decrease a smokers' self-efficacy (belief that he or she can successfully quit) and increase cessation fatigue or tiredness of trying to quit smoking (Liu et al., 2013; Piper, 2015). Successful medical and behavioral interventions have been shown to work, in part, by reducing craving, negative affect, and cessation fatigue (Lerman et al., 2002; McCarthy et al., 2008; Piper et al., 2008), suggesting these withdrawal symptoms are promising targets for interventions aimed at helping smokers quit. However, withdrawal symptoms tend to be analyzed as a unified syndrome or in isolation, when in fact, all may be interrelated in a dynamic system that changes throughout the duration of the quit attempt (Piper, 2015; Piper et al., 2016). Further, withdrawal-related cognitive processes such as self-efficacy and cessation fatigue and their relations with withdrawal symptoms have not been well studied (Piper, 2015). A better understanding of these dynamics may provide insight into the constructs of dependence and withdrawal and inform the development of more effective smoking interventions.

The dynamics of smoking cessation, including features such as

Abbreviations: ILD, intensive longitudinal data; EMA, ecological momentary assessment

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withdrawal, cessation fatigue, and self-efficacy, have been studied previously (Lagoa et al., 2014; Lanza et al., 2013; Liu et al., 2013; Piper, 2015), yet precise descriptions of the complex processes underlying withdrawal dynamics are still limited. The recent shift toward collecting intensive longitudinal data (ILD) via ecological momentary assessment (EMA) presents new opportunities to use tools from control engineering, such as dynamical systems models. These tools allow researchers to efficiently characterize dynamic phenomena pertinent to social, public health, and behavioral health problems (Ashour et al., 2016; Boker, 2012; Boker and Graham, 1998; Lagoa et al., 2014; Rivera et al., 2007; Timms et al., 2014).

Linear dynamical system models are commonly used in the engineering field, and are typical tools for characterizing the relations among two or more constructs. The dynamical model describes not only how these constructs change over time in response to each other, but also how these constructs change in response to their previous values. In research with physical systems, this is typically done using differential equations (Ogunnaike and Ray, 1994). As has been shown in previous research (Boker, 2012; Chow et al., 2005), dynamical systems models can be applied to study change in social and psychological systems as well, such as the process by which smokers cease their use of cigarettes. Although dynamical systems models share a number of features with multilevel modeling (MLM), a popular method for studying change processes in the behavioral sciences, as well as with time-series analysis, dynamical systems models offer a unique perspective on the analysis of such data.

For example, dynamical systems models permit modeling of multiple constructs that constitute the smoking cessation process as an interrelated system; that is, interrelations among these variables can be estimated simultaneously, in real time. This is traditionally not done in a multilevel modeling framework, which is typically used to model relationships between two constructs, forcing the analyst to choose one as the outcome and one as the predictor. Therefore, instead of analyzing single outcomes, such as craving (Lanza et al., 2013) or cessation fatigue (Liu et al., 2013) as a function of other variables (e.g., negative affect, self-efficacy), dynamical models allow a more comprehensive analysis of the dynamic relations among all key constructs (e.g., negative affect, craving, self-efficacy, cessation fatigue), which may facilitate more accurate long-term predictions of cessation success. This is important because cessation fatigue, negative affect, nicotine craving, and self-efficacy are highly related to each other and together influence the success of a smoking cessation attempt (Baker et al., 2004; Lanza et al., 2013; Liu et al., 2013; Shadel and Cervone, 2006; Shiffman et al., 1997). Moreover, the model does not assume that these processes will change at the same rate. Additionally, dynamical systems approaches readily allow the analyst to characterize change processes in terms of system dynamics, facilitating an understanding of dynamic descriptors such as the *steady state*, which describes where (and when) a particular change process will come to rest, and the *rate of initial change*, which describes the onset and speed of a change process in the early moments of, for example, smoking cessation. With a better understanding of these parameters, we may be able to manipulate the dynamics of smoking cessation through a carefully designed intervention aimed at cessation success. In other words, understanding of the interrelations of these key cessation process variables over time could provide insight that could be used to tailor or adapt treatment, including the use of just-in-time interventions (Nahum-Shani et al., 2014). Lastly, dynamical models can accommodate the effects of exogenous events or “shocks”, both measured and unmeasured, that may interrupt or alter the observed change process.

1.1. The current study

The current study applies a dynamical systems approach to understanding the interrelations among craving, negative affect, self-efficacy, and cessation fatigue in a sample of smokers participating in a smoking cessation trial. Ecological momentary assessment (EMA) was used to measure these process variables intensively over time. Results of the dynamic systems model are briefly divided into two sections.

1 The first section characterizes the interrelations among withdrawal symptoms and withdrawal-related cognitive factors over time during a quit attempt, showing how each dynamically influences the others from moment to moment.
2 The second section demonstrates how dynamical system models can be used to evaluate smoking cessation treatments by using the model results to
   a Estimate the treatment effect on each outcome to analyze the total treatment effect on long term,
   b Determine the expected speed of initial change to analyze the total treatment effect on short term.

In this study, we show that the treatment might have different impact on different measurements and these impacts differ in short term and long term. Further, linear relations among multiple aspects of smoking cessation dynamics can be explicitly described using these models. For example, researchers can interpret the expected effects of increasing negative affect on craving. Understanding the interrelations among features of smoking dynamics is important for developing new and efficient treatment methods to treat smoking behavior in time and in context (Lagoa et al., 2014; Timms et al., 2013).

2. Methods

2.1. Study and participants

The EMA data analyzed in this study are derived from a randomized, placebo-controlled clinical trial N = 1504; 42% male; 17% Black (Piper et al., 2009). All study participants smoked more than 10 cigarettes per day for six months and were motivated to quit smoking (≥ 8 on a 1–10 scale where 10 is highly motivated to quit). Study participants received six smoking cessation counseling sessions and were randomly assigned to one of the six following treatment groups: [1] bupropion (n = 264), [2] nicotine lozenge (n = 260), [3] nicotine patch (n = 262), [4] nicotine patch + nicotine lozenge (n = 267), [5] bupropion + nicotine lozenge (n = 262), and [6] placebo (n = 189). To explore potentially complex effects of pharmacotherapy, we estimated the dynamical model separately for each treatment group.

Participants carried palmtop devices to respond to EMA prompts four times per day (wake-up, 2 random prompts, before bed) for the one week before and two weeks after the target quit day (TQD). Data from the two weeks after the TQD is used to identify the dynamical model. To ensure sufficient density of data to estimate the model, participants were included in our models if they provided data at three or more assessments per day, and none of these reports could be spaced farther than 12 h. Thus, 1100 participants were included in the analyses: 197 in the bupropion group, 185 in the nicotine lozenge group, 191 in the nicotine patch group, 206 in the nicotine patch + nicotine lozenge group, 193 in the bupropion + nicotine lozenge group, and 128 in the placebo group. To assess the potential for differential attrition, we compared included versus excluded individuals on key characteristics including age, sex, and number of cigarettes smoked per day. In each of the groups, we found little evidence for differences in these characteristics.

2.2. Measures

The dynamical model for each treatment group included *cessation fatigue*, *negative affect*, *craving*, and *self-efficacy* as the outcomes (referred to as “states” in the engineering literature), each measured intensively over the 2 weeks post-TQD. *Negative affect* was calculated as the mean of six items from the Wisconsin Smoking Withdrawal Scale