REVIEW

Integrating Ecological Momentary Assessment and Functional Brain Imaging Methods: New Avenues for Studying and Treating Tobacco Dependence

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ABSTRACT

Introduction: Ecological momentary assessment (EMA) and related methods typically entail repeatedly and intensively sampling behavior as it occurs over time and under naturalistic conditions. Although the methodological features of EMA make it a highly valuable research technique in its own right, EMA can also be a potent counterpart to other approaches. One methodological partnership with substantial yet largely untapped potential for the study of tobacco dependence is the pairing of EMA with functional brain imaging.

Methods: The goal of this review is to outline the promise of this approach, with a focus on the combined use of EMA and functional magnetic resonance imaging (fMRI). Due to the unique and complementary strengths of each method, the merger of EMA and fMRI methods has the potential to advance the understanding of tobacco dependence in ways difficult or impossible to achieve through the use of either method in isolation.

Results: In addition to describing a conceptual basis for combining EMA with fMRI, we provide a preliminary empirical illustration of this integrative approach using data from an ongoing study.

Conclusions: EMA and fMRI have independently yielded important findings regarding the nature and treatment of tobacco dependence. The integration of these powerful research methods, however, holds even greater potential for the field of tobacco research. Additionally, recent advances are paving the way for the synergistic use of fMRI and EMA-based methods to develop innovative approaches to tobacco cessation.

INTRODUCTION

Ecological momentary assessment (EMA) and related methods typically entail repeatedly and intensively sampling behavior as it occurs over time and under naturalistic conditions (Smyth & Heron, 2011). EMA methods have provided rich insight into aspects of tobacco dependence (Ferguson & Shiffman, 2011). For example, EMA studies of behavioral, affective, and situational variables in quitting smokers have revealed important information regarding the acute changes in emotional state that often precede lapses and relapses (e.g., Shiffman, Paty, Gnys, Kassel, & Hickcox, 1996). Although the unique methodological strengths of EMA make it a valuable research technique in its own right, particularly to characterize within-person processes, EMA can also be used as a potent complement to other empirical approaches (e.g., ambulatory blood pressure monitoring; Kamarck, Schwartz, Janicki, Shiffman, & Raynor, 2003). One methodological partnership with substantial, yet largely untapped potential for the study of tobacco dependence is the pairing of EMA with functional brain imaging. The goal of the paper is to outline the promise of this novel approach, with a focus on the combined use of EMA and functional magnetic resonance imaging (fMRI). We first describe a conceptual basis for combining these methods. Next, to provide a "proof of principle" example of this integration, we empirically anchor these considerations using preliminary data from an ongoing study. Finally, we conclude by briefly discussing ways in which technological advances are paving the way for using fMRI and EMA-based methods to develop innovative treatments for tobacco dependence.

INTEGRATING EMA AND FMRI: CONCEPTUAL FOUNDATIONS

A Brief Introduction to the Use of fMRI in Tobacco Research

Functional brain imaging refers to a group of methods that noninvasively measure direct or indirect signals associated with

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neural activity (for review, see Bandettini, 2009; Shibasaki, 2008). fMRI, which measures blood flow in the brain as a proxy for neural activity, is currently one of the most widely used functional brain imaging techniques. The flexibility of fMRI experimental paradigms provides a variety of ways for researchers to study the neural processes associated with behavior (Amaro & Barker, 2006; Chein & Schneider, 2003). For instance, researchers can investigate sustained changes in brain activation associated with a series of contiguously presented stimuli or transient changes associated with the display of individual events (Dale & Buckner, 1997; Huettel, 2012; Petersen & Dubis, 2012). In turn, this information can be analyzed in conjunction with variables assessed using other methods, including those that vary within (e.g., changes in affect) and between (e.g., different treatment conditions) individuals.

Like EMA, fMRI has made many contributions to tobacco research. In particular, fMRI has become a common approach for investigating reactivity to smoking cues, generating extensive data regarding patterns of brain activation that are associated with the presentation of cigarette-related stimuli (for review, see Engelmann et al., 2012). Further, fMRI studies have begun to examine various factors that affect responses to cigarette cues, such as genetic variability (Franklin et al., 2009; Franklin, Wang, Li, et al., 2011) and the use of behavioral (Janse Van Rensburg, Taylor, Benattayallah, & Hodgson, 2012; Janse Van Rensburg, Taylor, Hodgson, & Benattayallah, 2009), cognitive (Brody et al., 2007; Hartwell et al., 2011; Kober et al., 2010; Wilson, Sayette, & Fiez, 2013; Zhao et al., 2012), and pharmacological (Brody et al., 2004; Culbertson et al., 2011; Franklin, Wang, Suh, et al., 2011) interventions.

fMRI has also been used to characterize the effects of nicotine withdrawal on cognitive processing. For instance, several studies have demonstrated that brief abstinence from nicotine alters patterns of brain activation during the performance of effortful cognitive tasks (Froeliger, Modlin, Kozink, Wang, & McClernon, 2012; Kozink, Kollins, & McClernon, 2010; Kozink, Lutz, Rose, Froeliger, & McClernon, 2010; Sweet et al., 2010; Xu et al., 2005; Xu et al., 2006), and that these effects are moderated by age (Falcone et al., 2013), genotype (Loughead et al., 2009), and individual differences in performance (Nichols, Gates, Molenaar, & Wilson, 2013). More recently, fMRI has been used to characterize the mechanisms through which nicotine replacement therapy (Beaver et al., 2011; Cole et al., 2010) and other medications for the treatment of tobacco dependence (e.g., varenicline; Loughead et al., 2010) remediate withdrawal-related cognitive deficits.

In addition to those focusing on cue-reactivity and the neurocognitive changes associated with nicotine withdrawal, a number of studies have used fMRI to investigate reward processing and decision making in tobacco dependent individuals (for review, see Hommer, Bjork, & Gilman, 2011; Sweitzer, Donny, & Hariri, 2012). Such research has advanced the understanding of the motivational characteristics and biases that play an important role in the addiction to cigarettes, including the devaluation of nondrug rewards (Luo, Ainslie, Giragosian, & Monterosso, 2011), the relative preference for smoking over alternative sources of reinforcement (Bühler et al., 2010; MacKillop et al., 2012), and expectancy- (Wilson, Sayette, Delgado, & Fiez, 2008) and withdrawal-related (Addicott et al., 2012) shifts in reward processing. fMRI studies have also provided insight into the motivational substrates of individual differences in the frequency of smoking (Peters et al., 2011) and the severity of nicotine dependence (Sweitzer et al., 2012).

Combining EMA and fMRI to Study Tobacco Dependence

The fundamental objective of most fMRI research is to characterize mechanisms that guide behavior by studying the brain under controlled laboratory conditions. Until very recently, however, the links between the phenomena studied using fMRI and the real-world behavior to which such research aims to apply have rarely been assessed directly (Berkman & Lieberman, 2011; Hasson & Honey, 2012). As a result, the real-world relevance of laboratory-based fMRI research has often been unclear (see Mitchell, 2012, for more general discussion of this issue). In an effort to more firmly establish the ecological validity of functional brain imaging research, a growing number of studies from several domains of inquiry have adopted innovative methods for linking fMRI findings to behavior outside of the scanner and laboratory (Berkman, Falk, & Lieberman, 2011; Eisenberger, Gable, & Lieberman, 2007; Falk, Berkman, & Lieberman, 2012; Falk, Berkman, Mann, Harrison, & Lieberman, 2010; Falk, Berkman, Whalen, & Lieberman, 2011; Forbes et al., 2009; Mahmood et al., 2013; Nikolova & Hariri, 2012; Wang et al., 2013). One advantage of incorporating EMA methods into fMRI research is that they are particularly useful for establishing bridges between brain imaging data and behavior as it occurs in natural contexts, thereby enriching the potential generalizability of fMRI. For example, Forbes et al. used fMRI to measure reward-related brain activity and EMA to assess the occurrence of positive mood in real-world contexts in adolescents with and without major depressive disorder. By using both brain imaging and ecological assessments, the authors demonstrated that depressed (relative to nondepressed) adolescents exhibited atypical responses to rewards in a region of the brain called the striatum and that these neural effects were linked to lower ratings of positive affect in the natural environment. This connection to real-world behavior provided powerful evidence for the ecological validity and clinical relevance of the authors' fMRI results.

In the domain of tobacco dependence, a recent investigation by Berkman et al. (2011) provides an excellent example of the utility of incorporating EMA methods into fMRI research. In the study, fMRI was used to measure brain activity during a task tapping the ability to suppress unwanted actions in a sample of smokers shortly before they attempted to quit smoking. Subsequently, EMA methods were used to assess the relationship between self-reported craving and smoking during the first 21 days of the quit attempt. Greater activation during the suppression of actions in several brain regions (i.e., right inferior frontal gyrus, presupplementary motor area, and basal ganglia) at baseline was associated with a weaker correlation between craving and smoking during the quit attempt. The data obtained using EMA thus again provided strong support for the ecological validity and clinical relevance of the fMRI results.

The study by Berkman et al. (2011) also highlights some of the potential for fMRI to augment EMA research. Broadly, one common aim of EMA studies is to advance theory regarding the dynamics of behavior through a fine-grained examination of that behavior in relation to thoughts, emotions, and situational contexts. fMRI provides valuable information about

the neurobiological underpinnings of behavior that can be used as an important source of constraints for generating and testing hypotheses with EMA methods (for a general discussion of how functional brain imaging can be used to constrain hypothesis testing, see Henson, 2005; Ochsner & Kosslyn, 1999). The use of EMA allowed Berkman and colleagues to identify individual differences in the strength of the association between craving and subsequent smoking. The incorporation of fMRI, which shed light on the neural processes that appeared to mediate these individual differences, led to a much more detailed picture of the psychological mechanisms that are important for successfully quitting smoking than would have been gained through the use of EMA alone.

More generally, fMRI offers a useful method for addressing some of the limitations of EMA measures that rely upon self-report. A chief advantage of EMA is that it can reduce biases associated with the retrospective recall of information (Shiffman, Stone, & Hufford, 2008)—biases that may have a particularly important influence on the recollection of smoking behavior (Shiffman, 2009). To the extent that ecological assessments require self-report, however, they remain subject to other shortcomings. Individuals often have difficulty accurately accessing and/or verbalizing the motives, thoughts, and emotions that underlie their behavior (Nisbett & Wilson, 1977). In addition, individuals may be implicitly or explicitly motivated to respond inaccurately, especially when it comes to stigmatized or otherwise undesirable behaviors like tobacco use (an effect that may be heightened in clinical contexts, such as in those attempting to quit smoking). These limitations underscore the importance of examining objective measures of addiction-related processes (including smoking biomarkers, such as cotinine). fMRI offers an attractive option for such objective assessment, as fMRI data can be linked to a host of other useful sources of knowledge (e.g., nonhuman animal neuroscience research, human brain imaging research regarding the patterns of brain activation associated with various cognitive operations, etc.). Furthermore, because fMRI assesses nonverbal indices of cognitive and affective processing, it has the potential to provide information about the substrates of behavior that may be obscured by the various constraints associated with self-report.

In line with this idea, Falk et al. (2011) found that brain activity measured with fMRI predicted real-world changes in smoking behavior above and beyond information obtained using self-report. In the study, fMRI was used to quantify neural responses to health messages designed to promote smoking cessation in a sample of smokers who intended to quit. In addition, exhaled carbon monoxide (CO) samples were collected to quantify recent smoking behavior both during the experiment and 1 month following the fMRI session. Importantly, when added to a statistical model already containing relevant self-report variables (i.e., ratings of the ability to relate to the health messages and the extent to which the ads increased intention to quit smoking and abstinence self-efficacy), responses to the health messages in a brain region called the medial prefrontal cortex substantially improved the prediction of changes in behavior (i.e., reductions in exhaled CO from baseline to the 1-month follow-up). Remarkably, the model including both signal from the medial prefrontal cortex and self-report measures explained twice as much of the variance in behavior change relative to a model containing the self-report measures alone. Although these findings alone cannot establish causal links between brain activation and behavior because of the correlational nature of fMRI data (for discussion of how this issue can be addressed in part on the basis of converging evidence from alternative methods, such as lesion studies and the manipulation of neural activity using transcranial magnetic stimulation, see Fiez, 2001; Sack & Linden, 2003), they do provide a compelling example of how fMRI methods can serve as a valuable counterpart (and independent contributor) to traditional self-report assessments.

In sum, due to the unique and complementary strengths of each method, the integration of EMA and fMRI has the potential to advance the understanding of tobacco dependence in ways that are difficult or impossible to achieve through the use of either method in isolation. To demonstrate the promise that this integrative approach holds for uncovering important interactions between person- and situation-level variables associated with smoking, we briefly present preliminary findings from ongoing research in which we are examining how individual differences in reward functioning (assessed via fMRI) relate to within-person shifts in motivational state across varying situations in daily life (assessed via EMA) in the following section.

INTEGRATING EMA AND FMRI: AN EMPIRICAL EXAMPLE

We have recently initiated a program of research that combines fMRI and EMA to investigate clinically relevant variability in reward functioning among cigarette smokers. Specifically, building upon our previous findings (Wilson, Sayette, Delgado, & Fiez, 2005; Wilson et al., 2008; Wilson, Sayette, & Fiez, 2004, 2012), we are examining the hypotheses that certain situations (i.e., those in which cigarettes are perceived to be accessible) are associated with changes in reward functioning that increase the likelihood of relapse (situation-level variability) and that nondrug rewards generally have less of an impact on the behavior of some smokers than others (person-level variability). Furthermore, one of our primary goals is to use the complementary strengths of EMA and fMRI to explore the extent to which these levels interact. That is, we are testing the prediction that a subset of smokers (i.e., those with relatively less sensitivity to nondrug rewards) are particularly vulnerable to experiencing clinically meaningful reductions in reward sensitivity in high-risk situations. By probing reward-related brain function using fMRI along with various measures of reward valuation and decision making under naturalistic conditions using EMA—and by formally linking these sources of information to one another via multilevel statistical models—we aim to shed light on the motivational mechanisms that place *some* quitting smokers at a heightened risk for relapse *under particular conditions*. Moreover, we hope to use this information to develop and implement person specific (fMRI and EMA informed) intervention strategies.

In order to provide a practical illustration of the combined use of fMRI and EMA to investigate such person-by-situation interactions, we report here select preliminary results from the first 10 participants (5 males, 5 females) who completed our ongoing study. All participants were active, non-treatment-seeking smokers between the ages of 18 and 45 ($M = 26.2$ years old, $SD = 8.3$) who reported consuming at least 10 cigarettes/day ($M = 12.7$ cigarettes/day, $SD = 3.4$) for the past 12 months ($M = 3.4$ years smoking, $SD = 1.0$). Informed consent was

obtained from all participants. Participants completed an initial baseline screening session, followed by a laboratory-based experimental session during which fMRI data were collected. The fMRI experiment was conducted between 1 and 14 days after finishing the baseline session. In order to increase their motivation to smoke during the experiment, participants were instructed to abstain from all nicotine-containing products for 12 hr prior to the fMRI session. Before being placed in the scanner, participants were informed that the experiment would take 4 hr to complete and that they may be given a chance to smoke during a break in the study based upon their responses during the upcoming fMRI task.

Scanning was conducted at the Penn State Social, Life, and Engineering Sciences Imaging Center using a 3-Tesla Siemens Trio scanner (Siemens Corporation). As the selection of an fMRI paradigm that yields robust and reliable responses in brain areas supporting the processes of particular interest is critically important for the successful integration of fMRI and EMA, we chose an imaging paradigm that has been used to measure reward-related activity in several prior studies (Delgado, 2007; Delgado, Nystrom, Fissell, Noll, & Fiez, 2000). Each trial of the task began with a choice period lasting 2 s, during which participants guessed whether the numerical value of a card was higher or lower than the number 5 via button press. After the choice period, a number from 1–9 (excluding 5) was presented for 1 s, followed by feedback (also presented for 1 s) informing participants whether or not their guess was correct. Participants earned and lost points towards two potential outcomes for correct and incorrect guesses, respectively. One outcome was an additional $10 in compensation, which participants were informed would be given to them in cash at the conclusion of the experiment if they earned sufficient points. The other outcome was an opportunity to smoke. Specifically, participants were told that, if they earned enough points, they would be given the opportunity to smoke a cigarette during a brief break following the fMRI session. This opportunity to smoke during the study was designed to be salient and motivating, as participants were informed that, in the event that they did not earn sufficient points to consume a cigarette during the fMRI task, they would not have a chance to smoke until the completion of the 4-hr experiment session. The task included four trial conditions that were distinguished by the nature of the feedback that was delivered: (a) points earned towards the cash outcome, signaled by a green upward pointing arrow surrounded by a blue border (money-win trials); (b) loss of points towards the cash outcome, signaled by a red downward pointing arrow surrounded by a blue border (money-loss trials); (c) points earned towards the chance to smoke, signaled by a green upward pointing arrow surrounded by a yellow border (smoke-win trials); and (d) the loss of points towards the chance to smoke, signaled by a red downward pointing arrow surrounded by a yellow border (smoke-loss trials). Trials were separated by a jittered intertrial interval (12–14 s), during which a fixation cross was presented. Unbeknownst to participants, card values were selected only after the response was made for each trial to ensure an equal number of trials per condition. Participants completed a total of 108 interleaved trials (27 of each feedback condition) divided into six runs of 18 trials each. As elaborated below, we focus here on neural responses during money-win trials, as this condition offers the most direct extension of our previous work (Wilson et al., 2008) and provides a useful example of how fMRI and EMA data may be integrated.

Following the fMRI session, participants completed a 10-day EMA protocol that was scheduled to begin on the Saturday immediately following the experimental session. (The EMA protocol began an average of 3.6 days [*SD* = 0.97] after the fMRI session was completed.) During the first 2 days of the protocol, participants were instructed to smoke *ad libitum*. For the final eight days of the protocol, participants were instructed to attempt to refrain from smoking outside of the laboratory and were given the opportunity to earn monetary incentives contingent on verified smoking abstinence. On days 3 through 10, participants attended a brief laboratory session each evening, during which exhaled CO samples were obtained to assess abstinence status. Participants were instructed that they would be able to smoke one cigarette during the laboratory visit on specific days of the EMA protocol (i.e., days 5, 8, and 10). On such days, CO samples were obtained prior to smoking.

The EMA protocol was implemented on a Motorola Droid X2 smartphone (Android platform) using custom survey software and included three types of assessments: (a) interval contingent, (b) event contingent, and (c) signal contingent. Interval contingent recordings consisted of a single waking report completed at the beginning of each day. Participants complete an event contingent recording if they consume any portion of a cigarette (during days 3–10 only). The event contingent assessment measured basic information about the episode (time elapsed since smoking, location, quantity smoked), whether specific smoking triggers (e.g., others smoking) were present, whether coping was implemented in an attempt to avoid smoking, and craving and affect prior to and after the episode. Finally, participants were "beeped" to complete signal contingent recordings at seven semi-random times each day, with signals randomized to occur within 20 min of each of seven anchor times distributed throughout the day. (Participants completed an average of 82.4% [*SD* = 7.4%] of signal contingent surveys.)

During signal contingent assessments, which required approximately 2 min for completion, participants responded to items assessing a variety of constructs (e.g., nicotine dependence, affective valence and arousal). Of these, we focus here on items assessing perceived cigarette availability and reward-related processing in order to provide "proof of principle" as to how fMRI and EMA can be integrated to characterize person-by-situation interactions. We assessed perceived cigarette availability using a single item ("Right now, how easy would it be for you to obtain cigarettes and smoke?") modeled after prior EMA research (e.g., Shiffman et al., 1996), which was rated using a visual analog scale (VAS) anchored by "Impossible" and "Very easy" (scored on a 0–100 range). Given our primary interest in assessing responses to rewards, signal contingent surveys incorporated several measures of reward-related functioning that were selected to be conceptually related to the fMRI task described above. These included several items from a validated instrument derived from contemporary research and theory on the psychology of goals (Grouzet et al., 2005). Specifically, using a VAS (0–100) anchored by "Not at all" and "Extremely," participants rated the importance of eight goal domains (finances/money, image, self-acceptance, community feeling, physical health, spirituality, conformity, and hedonism; see Grouzet et al.). For the sake of illustration, we analyzed data from the item measuring the valuation of finances/money ("Right now, it is important for

me to have enough money to buy everything I want") in the preliminary analysis reported herein, as it provides a useful complement to the fMRI-based assessment of responsiveness to monetary rewards.

BrainVoyager QX software (version 2.4.2; Brain Innovation) and the NeuroElf toolbox (version 0.9c; www.neuroelf.net) for MatLab (version 8.0; The MathWorks) were used to preprocess and analyze the fMRI data. Following standard preprocessing steps (i.e., motion correction, slice scan time correction, spatial smoothing using a three-dimensional Gaussian filter, voxel-wise linear detrending, and high-pass filtering of frequencies), fMRI data were analyzed using a using a random-effects general linear model (GLM) with task-related regressors. Briefly, regressors for each type of outcome delivered during the card-guessing task (i.e., money-win, money-loss, smoke-win, smoke-loss) were convolved with 2-gamma hemodynamic response function and entered into a GLM to obtain parameter estimates (i.e., beta weights) for each participant. Subsequently, using an approach motivated by previous research (Fareri, Niznikiewicz, Lee, & Delgado, 2012), we conducted a group-level contrast of money-win versus money-loss outcomes in order to isolate a region of interest (ROI) in the left striatum (Tailarach coordinates: x = −11, y = 8, z = 4). Based upon Monte Carlo simulations conducted using NeuroElf, it was determined that a combined per-voxel threshold of $p < .005$ and cluster-extent threshold of 20 or more contiguous voxels would yield a corrected family-wise error rate of $p < .05$. These threshold parameters were applied to the group-based statistical map.

As expected, the left striatal ROI we identified exhibited a greater blood oxygen level-dependent (BOLD) response to monetary wins than monetary losses (see Figure 1). Mean parameter estimates reflecting the magnitude of the BOLD response to monetary wins were extracted from this striatal ROI and used as a person-level index of neural sensitivity to rewards. These mean parameter estimates were entered along with the select EMA data described above into a mixed-effects multilevel model. Specifically, a two-level model was fit to the data using SAS PROC Mixed (SAS Institute, 2003), with Level 1 reflecting variability in EMA ratings of perceived cigarette availability nested within persons and Level 2 reflecting between-person variability in the striatal response to monetary rewards; EMA ratings of the valuation of finances/money served as the dependent variable in the model. We were primarily interested in identifying a cross-level interaction, which would indicate that within-person associations at Level 1 (i.e., associations between momentary ratings of perceived cigarette availability and momentary ratings of the value of finances/money) varied as a function of the Level 2 variable (i.e., individual differences in the striatal BOLD response to monetary rewards).

We found a significant positive association between the striatal BOLD response to winning money during the fMRI task and average ratings of the value of finances/money during the 10-day EMA period, $t(8) = 3.29$, $p = .01$. Of particular relevance, we also found a significant cross-level interaction between the reward-related striatal BOLD response and the association between perceived cigarette availability and ratings of the value of finances/money, $t(552) = -2.60$, $p < .01$. As depicted in Figure 2, there was a negative association between cigarette accessibility and the value of finances/money for those with a low striatal BOLD response ($p < .02$) but no association for those with a high striatal BOLD response ($p = .93$).

As noted, these findings are presented for the purpose of illustration and are clearly preliminary, particularly given the small sample size. Nonetheless, they are consistent with the overarching hypothesis that reduced sensitivity of brain reward systems is one mechanism that may place a subset of smokers at elevated risk for experiencing decreases in the incentive value of nondrug rewards (e.g., money) when cigarettes are perceived to be accessible. For such smokers, this motivational shift may significantly increase the likelihood of relapse when cigarettes and nondrug rewards are concurrently available and the value of the former outweighs that of the latter. In addition, this effect would presumably have substantial implications for incentive-based approaches for treating tobacco dependence, such as those that employ contingency-management techniques (Stitzer & Petry, 2006). More broadly, these initial results demonstrate how fMRI and EMA can be combined to address hypotheses regarding how individual differences in neurocognitive functioning interact in clinically meaningful ways with within-person variability in the domain of tobacco dependence.

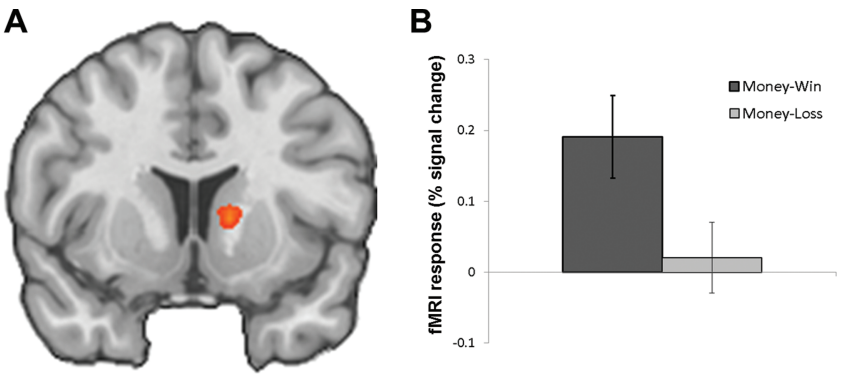

Figure 1. (A) Left striatal region exhibiting a significant greater response to money-win than money-loss trials during the fMRI card-guessing task at a corrected family-wise error rate of $p < .05$. (B) Mean percent signal change for the response to monetary wins (dark gray bar) and monetary losses (light gray bar) in the left striatum.

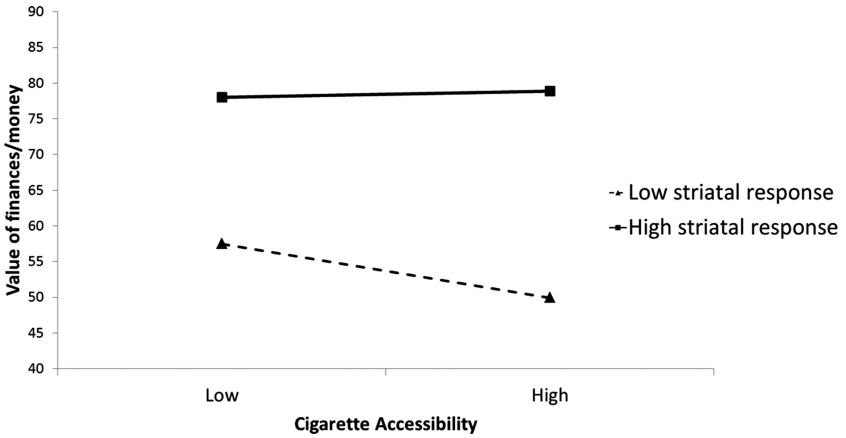

Figure 2. Modulatory effect of reward-related striatal activation on the relationship between perceived cigarette accessibility and the valuation of finances/money.

FUTURE DIRECTIONS: USING EMA AND FMRI IN NOVEL WAYS TO TREAT TOBACCO DEPENDENCE

In addition to the tremendous potential that that the integration of fMRI and EMA has for "basic" research, there are promising avenues for using these approaches in tandem to improve the treatment of tobacco dependence. Substantively, for example, our efforts to use these approaches to characterize reward functioning and motivation in smokers has implications for optimizing the use of incentives to motivate smoking cessation and treat tobacco dependence. That is, the information gained through the combined use of fMRI and EMA to assess reward sensitivity may prove useful for identifying individual and situational characteristics that render incentive-based interventions particularly effective or ineffective—knowledge that could be used to guide treatment selection and development.

Beyond such relatively straightforward applications, we believe that the combined use of fMRI to assess between-person indicators of vulnerability and EMA to identify the situations and contexts in which this susceptibility is maximally expressed has the potential to advance treatment in highly innovative ways. Recently, we and others have advocated an approach that uses EMA data collection to dynamically tailor intervention content and delivery (Smyth & Heron, 2011). We use the term Ecological Momentary Interventions (EMI; Heron & Smyth, 2010) to encompass treatments characterized by the delivery of interventions to people as they go about their daily lives. EMI can be tailored to provide treatment at particular moments of risk (e.g., a person participating in a smoking cessation intervention receives a text message on her mobile phone with tips for dealing with cravings if she reports high craving on EMA). Indeed, EMI have already shown promise in smoking cessation research (e.g., Brendryen & Kraft, 2008; Free et al., 2011; Obermayer, Riley, Asif, & Jean-Mary, 2004; Rodgers et al., 2005). For instance, Rodgers et al. demonstrated that the delivery of EMI in the form of phone-based text messaging significantly improved short-term smoking cessation rates relative to a non-EMI control condition. Interventions such as these that rely on automated systems (e.g., those administered via Web sites and using mobile technology) have the potential to reach large numbers of people without requiring a great deal of resources (e.g., clinician or researcher time, equipment, etc.) and are thus of great interest from the perspectives of efficiency, cost-effectiveness, and reach.

We have also argued that EMI can be tailored not only in time but also in content (e.g., Smyth & Heron, 2011). That is, you can not only get someone treatment at the right time (e.g., when craving is high) but provide the "right stuff"—namely, intervention content matched to what they need for that specific moment and situation. The integration of fMRI, such as that described in this paper, represent a rich person-level (or person-by-situation) source of information by which to tailor momentary interventions. For instance, fMRI could be used to identify strategies for increasing striatal responses to nondrug rewards (e.g., by manipulating reward magnitude/delay or tailoring incentives based upon individual preferences) in those responding weakly to standard treatment approaches. Using EMI, these individually tailored techniques could then be implemented in the specific situations associated with increased relapse risk, such as by delivering personalized motivational messages (e.g., those selected on the basis of fMRI research evaluating their effectiveness for engaging brain reward systems) when individuals indicate that cigarettes are accessible.

SUMMARY

EMA and fMRI have both yielded important findings regarding the nature and treatment of tobacco dependence. Although each approach is valuable when used independently, we believe that the integration of these powerful research methods holds even greater potential for the field of tobacco research. In our own work, this transmethodological approach is proving fruitful for characterizing motivational processes that likely play a key role in maintaining smoking. As presented, our preliminary results suggest that, for certain smokers, nondrug rewards (such as personal finances) hold significantly less value when cigarettes are perceived to available versus unavailable—an effect strongly linked to the functioning of brain reward systems. In addition to shedding light on the mechanisms underlying such person-by-situation dynamics, the combination of fMRI

and EMA/EMI may open new doors for developing innovative treatments for tobacco addiction.

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DECLARATION OF INTERESTS

None declared.

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