Published in final edited form as:

Biol Psychiatry. 2010 April 15; 67(8): 699–701. doi:10.1016/j.biopsych.2010.02.014.

Reinforcing Effects of Smoking: More than a Feeling

Caryn Lerman^{1,*} and Janet Audrain-McGovern¹

¹ Transdisciplinary Tobacco Use Research Center, Department of Psychiatry and Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA 19104

Commentary

Relief of negative affect has long been considered a key factor in the motivation to self-administer nicotine and an important determinant of relapse following a quit attempt. Yet, the situational specificity of smoking effects on negative mood has been far from clear, that is until now. The well designed study by Perkins *et al.* in the current issue makes an important step toward addressing this question by elucidating, in a controlled laboratory setting, the conditions under which smoking (and nicotine) relieves negative affect (1). The study reveals robust effects of smoking on relief of negative affect due to nicotine abstinence; however, smoking effects on “induced” negative affect in a non-abstinent state are rather modest and inconsistent at best. Moreover, the effects that were observed were largely unrelated to nicotine intake, underscoring the importance of nonpharmacologic reinforcing effects of smoking.

Clinical Relevance of Smoking Effects on Negative Affect During Abstinence

Evidence that smoking reduces abstinence-induced negative affect is highly relevant to the treatment of nicotine dependence. As shown in Table 1, post-cessation increases in negative affect and decreases in positive affect predict smoking relapse in several independent clinical trials. Consistent with clinical data showing negative affect relief following a return to regular smoking in smokers with a history of depression (2), the findings of Perkins *et al.* (1) suggest that smoking relapse following brief abstinence may have negative reinforcing effects.

A conditioned association between smoking and relief of abstinence-induced negative affect may generate expectations regarding smoking’s ability to modulate affect irrespective of the situation. Smokers reporting more negative mood symptoms are more likely to report smoking motivated by a desire to reduce negative affect and, in fact, show a reduction in negative affect after smoking if they hold such beliefs (3). Thus, the expectations surrounding smoking’s role in affect management seem relevant for preventing relapse.

In addition to the relief of abstinence-induced negative affect, another function of smoking may be to lessen variability in affect throughout the day. For example, a rapid rise in

*Corresponding Author: Caryn Lerman, Ph.D., Transdisciplinary Tobacco Use Research Center, Department of Psychiatry and Abramson Cancer Center, University of Pennsylvania, 3535 Market Street, Philadelphia, PA 19104, (215) 746-7141 (telephone), (215) 746-7140 (fax), clerman@mail.med.upenn.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

negative affect over the hours following a quit attempt predicts greater risk of lapsing, but a gradual increase in negative affect over days does not (4). Recent research indicates that variability in positive and negative affect after smoking tends to diminish as adolescents become regular smokers (5), and that smoking appears to stabilize or decrease the variability in negative mood (6). Thus, variability in affect is a metric that warrants further attention in studies of smoking's negative reinforcing effects (7).

Beyond Self-Report Measures of Negative Affect

Before concluding that smoking, or nicotine, has little effect on negative affect due to sources other than abstinence, other measures of affective response should be considered. As Perkins *et al.* correctly point out, subjective measures of mood have their limitations. Physiological measures (e.g., cardiovascular, hormonal) have been utilized in prior studies to provide an objective assay of affective responses to stress. While there is some support for blunted cortisol responses to stress in smokers compared to non-smokers, the evidence for other physiological measures is mixed (8). Further, there is little evidence to suggest that smoking reverses stress-induced changes in objective physiological indices. Thus, the findings of Perkins *et al.* synergize with prior research using objective physiological measures, suggesting that effects of smoking and nicotine on stress-induced negative affect relief are modest at best.

Effects of smoking or nicotine on negative affective responses to emotional stimuli might be probed further, however, using neuroimaging approaches. For example, increases in amygdala activity correlate with self-reported smoking for calming effects (9). Perhaps most germane to the study by Perkins *et al.*, the negative affect reduction following smoking a nicotine versus a denicotinized cigarette is associated with increased smoking-induced dopamine release in a recent positron emission tomography study (10). This line of research could be extended using functional neuroimaging paradigms involving exposure to affective stimuli (e.g., emotional faces, affect-laden images). Available evidence supports the sensitivity of this approach for assessing limbic reactivity to mood manipulations as well as sensitivity to the effects of short-term anti-depressant treatment (11). The power of these approaches may lie in their greater sensitivity to detecting subtle affective responses that may nonetheless have important behavioral implications.

Does Smoking Reduce Negative Affect More for Some Smokers than Others?

A question for future research is whether there are individual differences in the effects of smoking on negative affect, induced either by abstinence or by other environmental stressors. Indeed, available evidence from human laboratory studies and clinical studies suggests that factors such as depression, personality, and genetics may be important in moderating these effects.

Depression

As smokers with a past history of depression often begin smoking cessation treatment with elevated levels of negative affect and lower levels of positive affect, these smokers may be especially sensitive to abstinence-induced changes in negative mood. Pre-treatment mood and affective disturbances in the early stages of smoking cessation treatment are predictive of an inability to quit as well as smoking relapse in these smokers (12). Because smoking is over-represented in individuals with depression, it is thought that smoking and/or nicotine play a role in the behavioral processes that facilitate affect regulation. With respect to depression, the question of whether smoking increases positive affect more for some smokers than others may be especially relevant. Indeed, the dispositional ability to

experience positive affect in response to things that are typically rewarding has been shown to moderate nicotine's ability to increase positive mood (13).

Personality

Personality traits usually connote consistency in response over time and across situations. Some smokers have more difficulty tolerating elevated levels of negative affect in any situation and may be more likely to smoke to relieve their symptoms. Impulsivity tends to be characterized in part by problems with emotional-regulation. Smokers high in impulsivity report greater negative affect relief after smoking a nicotine, but not a denicotinized cigarette (14). The desire for negative affect relief may drive seemingly impulsive decision-making in these individuals while attempting to abstain.

Genetics

Genetic contributions to the effects of nicotine on affect in rodent models of anxiety and depression are well documented. In human smokers, gene variants in the dopamine, serotonin, and opioid pathways have been associated with withdrawal-related negative affect or found to moderate effects of negative mood on smoking behavior (15). This evidence from self-report measures suggests that laboratory-based measures of negative affect in chronic smokers may also be subject to genetic heterogeneity. Indeed, genetic analyses within functional neuroimaging investigations of affective responses have generated some interesting results. Limbic reactivity to affective stimuli has been associated with common variants in the serotonin pathway, for example (16). Thus, there are likely to be specific genetic influences on neural reactivity to emotionally evocative stimuli, and neuroimaging may be a promising approach to understanding individual differences in smoking's negative reinforcing effects.

Summary

In light of the available evidence, it is reasonable to conclude, as suggested by Perkins *et al.*, that an important part of smoking's reinforcing properties are attributable to reductions in negative affect due to abstinence, and less so to effects on negative affect arising from other environmental sources. This important study helps to blaze the trail for future studies to disentangle effects of smoking versus nicotine on abstinence-induced negative affect, to elucidate the underlying mechanisms of such effects, and to parse out individual differences. An improved understanding of the when, how, and whom of smoking's negative reinforcing effects will guide the development of targeted therapeutic strategies to address this major public health problem.

Acknowledgments

This work was supported by a grant from the National Cancer Institute (P50CA143187).

References

1. Perkins KA, Karelitz JL, Conklin CA, Sayette MA, Giedgowd GE. Acute Negative Affect Relief from Smoking Depends on the Affect Situation and Measure but Not on Nicotine. *Biol Psychiatry*. 2010 (Epub ahead of print).
2. Kahler CW, Brown RA, Ramsey SE, Niaura R, Abrams DB, Goldstein MG, Mueller TI, Miller IW. Negative mood, depressive symptoms, and major depression after smoking cessation treatment in smokers with a history of major depressive disorder. *J Abnorm Psychol* 2002;111:670–675. [PubMed: 12428781]

3. Kassel JD, Evatt DP, Greenstein JE, Wardle MC, Yates MC, Veilleux JC. The acute effects of nicotine on positive and negative affect in adolescent smokers. *J Abnorm Psychol* 2007;116:543–553. [PubMed: 17696710]
4. Shiffman S, Waters AJ. Negative affect and smoking lapses: a prospective analysis. *J Consult Clin Psychol* 2004;72:192–201. [PubMed: 15065954]
5. Hedeker D, Mermelstein RJ, Berbaum ML, Campbell RT. Modeling mood variation associated with smoking: an application of a heterogeneous mixed-effects model for analysis of ecological momentary assessment (EMA) data. *Addiction* 2009;104:297–307. [PubMed: 19149827]
6. Weinstein SM, Mermelstein R, Shiffman S, Flay B. Mood variability and cigarette smoking escalation among adolescents. *Psychol Addict Behav* 2008;22:504–513. [PubMed: 19071975]
7. Baker TB, Piper ME, McCarthy DE, Majeskie MR, Fiore MC. Addiction motivation reformulated: an affective processing model of negative reinforcement. *Psychol Rev* 2004;111:33–51. [PubMed: 14756584]
8. Childs E, de Wit H. Hormonal, cardiovascular, and subjective responses to acute stress in smokers. *Psychopharmacology (Berl)* 2009;203:1–12. [PubMed: 18936915]
9. Rose JE, Behm FM, Salley AN, Bates JE, Coleman RE, Hawk TC, Turkington TG. Regional brain activity correlates of nicotine dependence. *Neuropsychopharmacology* 2007;32:2441–2452. [PubMed: 17356570]
10. Brody AL, Mandelkern MA, Olmstead RE, Allen-Martinez Z, Scheibal D, Abrams AL, Costello MR, Farahi J, Saxena S, Monterosso J, London ED. Ventral striatal dopamine release in response to smoking a regular vs a denicotinized cigarette. *Neuropsychopharmacology* 2009;34:282–289. [PubMed: 18563061]
11. Hammer CJ. Serotonin and emotional processing: does it help explain antidepressant drug action? *Neuropsychopharmacology* 2008;55:1023–1028.
12. Strong DR, Kahler CW, Leventhal AM, Abrantes AM, Lloyd-Richardson E, Niaura R, Brown RA. Impact of bupropion and cognitive-behavioral treatment for depression on positive affect, negative affect, and urges to smoke during cessation treatment. *Nicotine Tob Res* 2009;11:1142–1153. [PubMed: 19574407]
13. Cook JW, Spring B, McChargue D. Influence of nicotine on positive affect in anhedonic smokers. *Psychopharmacology (Berl)* 2007;192:87–95. [PubMed: 17277935]
14. Doran N, McChargue D, Spring B, VanderVeen J, Cook JW, Richmond M. Effect of nicotine on negative affect among more impulsive smokers. *Exp Clin Psychopharmacol* 2006;14:287–295. [PubMed: 16893271]
15. Lerman, C.; Perkins, KA.; Gould, T. Nicotine dependence endophenotypes in chronic smokers. National Cancer Institute. Phenotypes and Endophenotypes: Foundations for Genetic Studies of Nicotine Use and Dependence. In: Swan, G., editor. Tobacco Control Monograph No. 20. Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health, National Cancer Institute; 2009 Aug. NIH Publication No. 09-6366
16. Ray R, Loughhead J, Wang Z, Detre J, Yang E, Gur R, Lerman C. Neuroimaging, genetics and the treatment of nicotine addiction. *Behav Brain Res* 2008;193:159–169. [PubMed: 18599130]
17. Strasser AA, Kaufmann V, Jepson C, Perkins KA, Pickworth WB, Wileyto EP, Rukstalis M, Audrain-McGovern J, Lerman C. Effects of different nicotine replacement therapies on postcessation psychological responses. *Addict Behav* 2005;30:9–17. [PubMed: 15561445]
18. al'Absi M, Hatsukami D, Davis GL, Wittmers LE. Prospective examination of effects of smoking abstinence on cortisol and withdrawal symptoms as predictors of early smoking relapse. *Drug Alcohol Depend* 2004;73:267–278. [PubMed: 15036549]
19. Lerman C, Roth D, Kaufmann V, Audrain J, Hawk L, Liu A, Niaura R, Epstein L. Mediating mechanisms for the impact of bupropion in smoking cessation treatment. *Drug Alcohol Depend* 2002;67:219–223. [PubMed: 12095672]
20. Hall SM, Reus VI, Munoz RF, Sees KL, Humfleet G, Hartz DT, Frederick S, Triffleman E. Nortriptyline and cognitive-behavioral therapy in the treatment of cigarette smoking. *Arch Gen Psychiatry* 1998;55:683–690. [PubMed: 9707377]

Table 1**Predictive Validity of Affect Measures in Smoking Cessation Trials**

Affect Measure	Findings	Reference
Positive & Negative Affect Scale	Post-cessation increases in NA and decreases in PA predicted relapse	(12)
Positive & Negative Affect Scale	Post-cessation increases in NA predicted relapse; PA not significant	(17)
Mood Adjectives from Circumplex Model	Rapid post-cessation increases in NA predicted relapse	(4)
Positive Affect: 5-item positive adjectives scale Negative Affect: Profile of Mood States (POMS) and 4-item Distress Measure	Greater post-cessation declines in PA predicted relapse No association of POMS measure with relapse Increases in distress scale predicted relapse	(18)
Positive & Negative Affect Scale	Post-cessation increases in NA predicted relapse	(19)
Profile of Mood States	Large increases in NA on quit day predicted early relapse	(2)
Profile of Mood States State Trait Anxiety Inventory (STAI) - State subscale	Greater increase in NA predicted smoking at follow-up among those with-out a history of depression No association of STAI-State subscale with abstinence	(20)

Note: NA = Negative Affect; PA = Positive Affect.