ANTICIPATION OF SMOKING ATTENUATES STRESS RESPONSE MEASURED WITH STARTLE POTENTIATION AND SELF REPORT IN NICOTINE DEPRIVED SMOKERS

Daniel E. Bradford[1], Rachel A. Korhumel[1], Anton Makhiboroda[1], Kristen M Grabinski[1], Greg J Raupp[1], John J. Curtin[1], & Megan E. Piper[1,2]

1. Psychology Department, 2. Center for Tobacco Research and Intervention, School of Medicine and Public Health

Background and Significance

Tobacco-related illnesses cause the death of more than 480,000 annually in the United States of America alone[1].

While half of smokers attempt to quit each year, most relapse even when using evidence-based cessation treatments[2].

Nuanced understanding of the cognitive-affective processes (e.g., stress) involved in relapse could inform new and better cessation treatment.

Response to stressors is an important yet understudied component of smoking relapse[3].

Stress induced relapse is multifaceted[4], but most research focuses on drug administration rather than other components such as anticipation of smoking.

The goals of this study were to precisely test the effects of anticipation of smoking and actual smoking on stress reactivity in deprived vs. continuing and non-smokers.

Sample and Procedure

Smokers were included if they smoked ≥10 cigarettes/day for at least 1 year, were not currently using smoking cessation treatment, and produced a carbon monoxide (CO) level ≥ 10 ppm.

Smokers were randomly assigned to abstain from nicotine for 24 hrs. prior to the experimental session or to smoke as usual. Abstinence was biochemically confirmed at the experimental session.

We measured stress reactivity via startle potentiation and self-reported anxiety to threat of shock using a modified version of the No-shock, Predictable Shock, Unpredictable shock (NPU) task[5].

Baseline: First, the Deprived, Continuing, and Non-Smoker s completed the shock task.

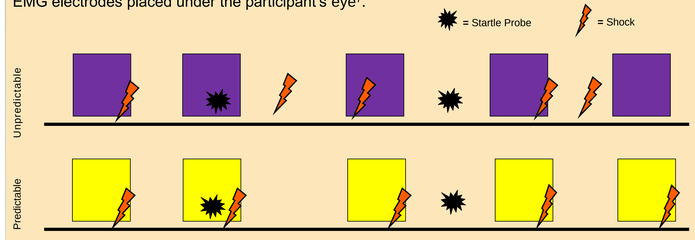
Anticipation: Next, all smokers took out a cigarette and held it; non-smoker controls held a bottle of water. Each participant was informed that they would be able to smoke (or drink water) after the next task run and the cigarette (or water) was placed directly below the computer screen where it remained during another completion of the shock task.

Consumption: Finally, participants were escorted outside to either smoke or drink water, ad lib, before completing the shock task a final time.

Shock Task and Stress Reactivity Measurement

Startle is a robust translational measure of stress reactivity resistant to responder bias[6].

We measured the eye-blink component of the startle response to 102 db acoustic startle probes via EMG electrodes placed under the participant's eye[7].



Participants viewed blocks of 3 colored square cues presented for 5 s each with a variable ITI.

Unpredictable shocks occurred at 2 or 4.8 s after cue onset or 3, 6, or 9 sec post-cue offset.

Predictable shocks always occurred 4.8 s post cue onset for every predictable block cue.

Startle potentiation was calculated as startle during all shock cues – no-shock cues (not shown).

We also assessed retrospective self-reported anxiety to the threat cues calculated as increase in anxiety to shock – no-shock cues.

Demographics and Manipulation Checks

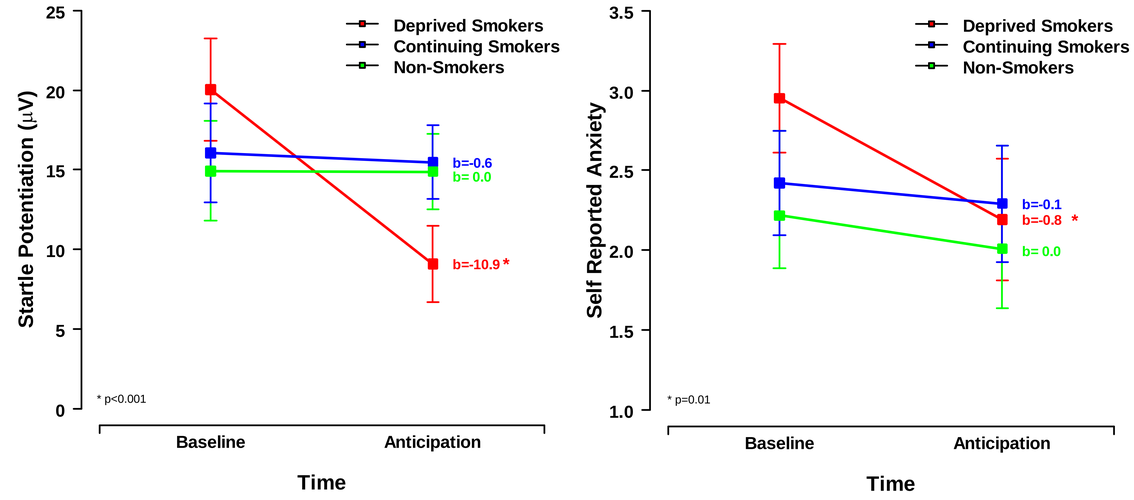
	Deprived Smokers	Continuing Smokers	Non-Smokers
Total N	34	37	37
Female (%)	47	51	51
White (%)	50	70	73
High school degree (%)	**44**	**57**	**84**
Age	43.2 (11.2)	42.1 (11.8)	38.9 (15.5)
Cigarettes per day	17.1 (5.3)	18.1 (6.6)	-
Years smoking daily	25.6 (10.6)	26.2 (11.1)	-
Screening FTND	5.50 (1.6)	5.43 (2.2)	-
General startle reactivity (uV)	54.6 (38.0)	52.6 (44.8)	66.3 (43.5)
Experimental session CO (ppm)	**3.6 (1.7)**	**18.4 (7.1)**	-
WSWS	**2.3 (0.5)**	**1.9 (.6)**	-
Cigarettes during consumption	0.9 (0.4)	0.9 (0.3)	-

All groups had comparable demographics except non-smokers were significantly more educated than smokers.

Prior to deprivation, the smoking groups were comparable on all smoking related variables.

The deprivation manipulation was successful – deprived smokers reported more withdrawal symptoms (p=0.010) and provided lower CO readings than continuing smokers (p<0.001).

Anticipation of Smoking Effects on Stress Reactivity



We analyzed startle potentiation and self-reported anxiety in separate general linear models each with a between subjects factor for smoking (deprived smokers, continuing smokers, non-smokers) and repeated measures for threat type (unpredictable, predictable) and task time (baseline, anticipation, consumption). General startle reactivity (assessed before baseline) was included as an interactive between subjects regressor to control for individual differences in magnitude of the startle response[8].

We decomposed the smoking factor with between-subject contrasts for Deprivation (continuing vs. deprived smokers) and Smoker Status (continuing vs. non-smokers).

We decomposed the task time factor with within-subject contrasts for Anticipation (baseline vs. anticipation of smoking/water) and Consumption (anticipation of smoking/water vs. post-cigarette/water consumption).

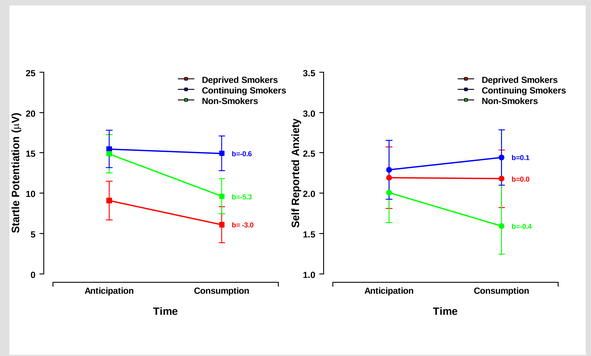
Anticipation of smoking had a greater dampening effect on overall startle potentiation for deprived smokers vs. continuing smokers (b=10.4, p=0.017).

Anticipation of smoking also had a greater dampening effect on overall self-reported anxiety for deprived smokers vs. continuing smokers (b=0.6, p=0.047).

The effect of anticipation of smoking/drinking water did not differ for continuing smokers vs. non-smokers in startle potentiation (p=0.903) or self-report (p=0.796).

None of the smoking group or task time effects differed by threat type (unpredictable, predictable; all p's > 0.05).

Consumption Effects on Stress Reactivity



There were no effects of consumption on startle potentiation or self-reported anxiety (p's>0.21).

Summary and Future Directions

We used a well-validated psychophysiological measure to assess the effects of anticipating and actually smoking on stress reactivity in smokers and non-smokers.

Anticipation of smoking was sufficient to reduce startle potentiation and self reported anxiety for deprived smokers compared to continuing smokers.

Smokers' stress reactivity was not affected by actual smoking beyond the earlier effects of anticipation thus our results somewhat conflict with smokers' report that actual smoking lowers their stress[9].

While some research shows selective effects of drug consumption or withdrawal on response to unpredictable threat, the broad effects of anticipation seen here may implicate distinct neurologically and/or psychological mechanisms from previous translational work which did not measure anticipation[10].

Although anticipation of smoking has not been extensively studied, our data suggests that this component of smoking may be an important target for clinical intervention.

Future research should assess the role of smokers' expectancies as well as the degree to which current smoking cessation treatments such as nicotine replacement and varenicline influence stress while anticipating and actually smoking.

References and Support

1. National Center for Chronic Disease Prevention and Health Promotion (US) Office on Smoking and Health. (2014). The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General. Atlanta (GA): Centers for Disease Control and Prevention (US).
2. Centers for Disease Control and Prevention (CDC). Quitting Smoking Among Adults --- United States, 2001--2010. MMWR. 2011;60:1513-1519
3. Kassel, J. D., Stroud, L. R., & Paronis, C. A. (2003).Smoking, stress, and negative affect: Correlation, causation, and context across stages of smoking. *Psychological Bulletin*,129(2), 270–304.
4. Piper, M. E., Schlam, T. R., Cook, J. W., Sheffer, M. A., Smith, S. S., Loh, W.-Y., … Baker, T. (2011). Tobacco withdrawal components and their relations with cessation success. *Psychopharmacology*, 216(4), 569–578.
5. Schmitz, A., & Grillon, C. (2012). Assessing fear and anxiety in humans using the threat of predictable and unpredictable aversive events (the NPU-threat test). *Nature Protocols*, 7(3), 527–532.
6. Grillon C, Baas J. A review of the modulation of the startle reflex by affective states and its application in psychiatry. *Clin Neurophysiol*. 2003;114:1557–1579
7. Blumenthal, T. D., Cuthbert, B. N., Filion, D. L., Hackley, S., Lipp, O. V., & van Boxtel, A. (2005). Committee report: Guidelines for human startle eyeblink electromyographic studies. *Psychophysiology*, 42(1), 1–15.
8. Bradford, D. E., Kaye, J. T., & Curtin, J. J. (2014). Not just noise: individual differences in general startle reactivity predict startle response to uncertain and certain threat. *Psychophysiology*, 51(5), 407–411.
9. Parrott, A. C. (1999). Does cigarette smoking cause stress? *American Psychologist*, 54, 817–820.
10. Koob, G. F., & Volkow, N. D. (2010). Neurocircuitry of addiction. *Neuropsychopharmacology Reviews*, 35, 217–238.

The research was funded by University of Wisconsin start-up funds and NIH grant 1KL2RR025012 for Megan E. Piper and NIH grant R01 DA033809 for John J. Curtin

This research was very recently accepted for publication in Journal of Abnormal Psychology's special section on mechanisms and consequences of stress sensitivity in psychopathology scheduled to be published in February of 2015.