

Anne E. Kazak
The Children's Hospital of Philadelphia
34th and Civic Center Blvd.
Room 1486 CHOP North
Philadelphia, PA 19104-4399

Validation of the Sensitization-Homeostasis Theory: A Letter to the Editor Regarding
Shadel et al. (2011)

Shadel et al. reported in *Health Psychology* on the impact of asking smokers who had been abstinent for two days to smoke two cigarettes (Shadel et al., 2011). Craving and relapse for these subjects were compared to those of control smokers that remained abstinent. The exposure to nicotine prompted an immediate decrease in craving. But this was followed the next day by a rebound in craving that surged above that experienced by controls. Rather than easing withdrawal, exposure to nicotine hastened relapse. This study represents a critical advance as it provides the final validation of the clinical aspects of the sensitization-homeostasis theory of nicotine addiction (DiFranza & Wellman, 2005).

This theory holds that nicotine owes its addictive property to the fact that it suppresses craving. Homeostatic neuroplastic adaptations to oppose the direct action of nicotine would cause a rebound in craving when the effect of nicotine wears off. The theory presented a clinical picture in which craving and other withdrawal symptoms appear during nondaily tobacco use. Initially, a single cigarette keeps withdrawal symptoms at bay for days at a time, but the duration of relief provided by one cigarette shortens progressively over time as tolerance develops. The progressive shortening of the latency to withdrawal would drive a progressive escalation in tobacco use, explaining the trajectory of smoking from one cigarette per week to chain smoking. Each of these predictions has been validated by clinical studies (DiFranza et al., 2011).

The theory also holds that recovery from addiction involves homeostatic neuroplastic adaptations that mimic the effect of nicotine by suppressing craving. Exposure to nicotine during recovery would have an immediate effect of suppressing craving, but would trigger the dismantling of these adaptations. This in turn would trigger a delayed resurgence of craving, potentially leading to relapse. This prediction remained the only clinical aspect of the sensitization-homeostasis theory yet to be confirmed by empirical data. By demonstrating that the self-administration of nicotine during abstinence had an immediate effect of suppressing craving, with a delayed effect of a resurgence of craving and relapse, the study by Shadel et al. completes the validation of the clinical aspects of the sensitization-homeostasis theory. Attention can now focus on identifying the neuroplastic adaptations that produce addiction, and those that cure it.

Joseph R. DiFranza
Robert J. Wellman
Department of Family Medicine and Community Health
University of Massachusetts Medical School
Worcester, Massachusetts

References

- DiFranza, J. R., Wellman, R. J., Mermelstein, R., Pbert, L., Klein, J. D., Sargent, J. D.,...Winickoff, J. P. (2011). The natural history and diagnosis of nicotine addiction. *Current Pediatric Reviews*, 7, 88-96.
- DiFranza, J. R., & Wellman, R. J. (2005). A sensitization-homeostasis model of nicotine craving, withdrawal, and tolerance: Integrating the clinical and basic science literature. *Nicotine & Tobacco Research*, 7, 9-26. doi: 10.1080/14622200412331328538
- Shadel, W. G., Martino, S. C., Setodji, C., Cervone, D., Witkiewitz, K., Beckjord, E.,...Shih, R. (2011). Lapse-induced surges in craving influence relapse in adult smokers: An experimental investigation. *Health Psychology*. Advance online publication. doi: 10.1037/a0023445