Published in final edited form as:

Urology. 2014 May ; 83(5): 1093–1098. doi:10.1016/j.urology.2014.01.006.

Nicotine Acutely Inhibits Erectile Tumescence by Altering Heart Rate Variability

Christopher B. Harte^{a,b,*}

^aResearch Service, VA Boston Healthcare System, Boston, MA, USA

^bDepartment of Psychiatry, Boston University School of Medicine, Boston, MA, USA

Abstract

Objective—To examine potential mechanisms underlying nicotine’s effects on male sexual arousal by exploring the mediating role of heart rate variability (HRV).

Methods—The sample comprised 22 healthy, nicotine-naïve men ($M_{\text{age}} = 20.91$ years; $SD = 2.43$). Data were taken from a double-blind, randomized, placebo-controlled, crossover trial previously completed and published elsewhere. During each laboratory visit, time-domain parameters of HRV (standard deviation of normal-to-normal [NN] intervals [SDNN], square root of the mean squared difference of successive NN intervals [RMSSD], percent of NN intervals for which successive heartbeat intervals differed by at least 50 ms [pNN50]) were assessed, as well as objective (via penile plethysmography) and subjective indices of sexual arousal.

Results—Acute nicotine ingestion (compared to placebo) was associated with dysregulated sympathovagal balance, which in turn was related to relatively reduced erectile tumescence. HRV did not mediate relations between nicotine intake and self-reported indices of sexual arousal.

Conclusions—HRV mediated the association between nicotine ingestion and erectile capacity. Findings suggest that dysfunctional cardiac autonomic tone may be an underlying mechanism by which nicotine exerts its deleterious effects on erectile health.

Keywords

Nicotine; heart rate variability; cardiac autonomic function; sexual arousal; erectile physiology

Introduction

Epidemiological studies indicate that cigarette smokers are at increased risk for erectile dysfunction (ED) compared to nonsmokers^{1,2}. Moreover, laboratory investigations have shown that cigarette consumption among chronic smokers³, and ingestion of isolated

*Corresponding author: Christopher B. Harte, Research Service, VA Boston Healthcare System, 150 S. Huntington Ave. (116-B4), Boston, MA 02130, USA. Tel: (857) 364-4022. christopher.harte@va.gov.

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.

Conflicts of Interest: None declared.

nicotine (e.g., nicotine gum) among nonsmokers⁴ acutely reduces sexual arousal. This relationship also holds in the reverse direction; quitting smoking appears to promote improvements in erectile function^{5,6}.

Mechanisms by which tobacco/nicotine may affect erectile physiology remain relatively underexplored. Cigarette smoking may adversely impact penile hemodynamics via central⁷ or biochemical⁸ mechanisms, as well as peripherally⁹, via changes in heart rate variability (HRV). HRV is a way to noninvasively assess vagal cardiac tone, and reflects the level of variability from mean heart rate across time. Low levels of HRV (sympathetic nervous system [SNS] dominance, characterized by low inter-beat variability), leaves the heart vulnerable to arrhythmia and sudden death. Conversely, high levels of HRV (parasympathetic nervous system [PNS] dominance, evidenced by high variability of inter-beat intervals) represent healthy cardiac function.

A growing body of literature has begun to explore the inter-relations among cardiac autonomic function, tobacco use, and erectile health. It has been shown that acute nicotine intake impairs HRV¹⁰, whereas cessation of nicotine improves HRV^{11,12}. Further, HRV has been implicated in erectile function¹³. Specifically, individuals with ED have been shown to display dysregulated HRV, indicative of impaired cardiac autonomic regulation (i.e., sympathetic hyperactivity)^{14,15}. Moreover, smoking, HRV, and erectile health may all be interrelated; longitudinal¹⁶ and cross-sectional studies¹⁷ indicate that HRV mediates the relationship between smoking status and/or smoking intensity and erectile tumescence. These findings highlight the possible underlying role of cardiac autonomic function in the physiology of erection, and point toward a possible mechanism that explains the link between tobacco use and ED.

In an attempt to explore potential mechanisms underlying tobacco's effects on penile erection, this study examined the mediating role of cardiac autonomic function (assessed via HRV) among a sample of young, healthy, nonsmoking men from the United States without a history of cardiovascular disease (CVD) or myocardial infarct (MI). HRV was chosen as a potential mediator, given that this parameter is a marker of sympathovagal balance, which is a chief underlying mechanism of erectile response (i.e., parasympathetic dominance is pro-erectile, whereas sympathetic dominance is anti-erectile). It was hypothesized that acute nicotine administration (compared to placebo) would be associated with dysregulation of HRV, which in turn would be associated with reductions in erectile response.

Materials and Methods

Participants

Participants were 22 men recruited from an undergraduate psychology subject pool, as well as via community and online advertisements between 2006 and 2007. Participants in the current report were selected from an experiment previously completed and published elsewhere⁴. Inclusion criteria comprised being between 18 and 30 years of age, being currently sexually active, reporting a heterosexual sexual identity, reporting no more than 100 direct lifetime exposures to nicotine, and reporting healthy erectile function (scoring 26 on the Erectile Function (EF) domain of the International Index of Erectile Function

[IIEF]^{18,19}). Exclusion criteria were as follows: (i) current medication use or medical conditions known to affect sexual functioning; (ii) history of treatment for sexual dysfunction; (iii) presence of a sexually transmitted infection; (iv) an active psychiatric condition; (v) a known allergy to nicotine; (vi) current medication use that would adversely interact with nicotine (e.g., bupropion, varenicline); (vii) a current medical condition that could make nicotine administration unsafe (e.g., history of MI, stroke, cardiac dysrhythmias); (viii) conditions that would interfere with nicotine gum administration (e.g., jaw/chewing problems, bridgework, dentures); and (ix) history of CVD.

Procedure

A detailed description of experimental procedures can be found elsewhere⁴. In brief, during the first experimental session, self-report (e.g., socio-demographic information, medical, sexual, alcohol, and tobacco use history, and erectile function), cardiovascular (systolic and diastolic blood pressures [BP]), and anthropometric (height, weight) data were first collected. Participants were then randomized to receive either nicotine (6 mg) or placebo, both administered double blind in gum form^{*}. Participants were then instructed to measure their flaccid penile circumference (such that they would receive a tailored gauge size) and they were instructed on how to fit the plethysmograph. After a 30-minute waiting period, electrocardiographic (ECG; heart rate [HR], HRV) and sexual response data (resting penile circumference [RPC], erectile tumescence, continuous subjective sexual arousal [SSA]) were collected simultaneously while participants individually viewed audiovisual stimuli. Films consisted of an initial 3-minute non-sexual segment (documentary film presentation), immediately followed by an 8-minute erotic film presentation depicting heterosexual penile-vaginal intercourse. Only ECG data from the initial 3-minute baseline period were examined. The procedures of the second experimental session were identical to the first, and participants were administered the other treatment not received during the first session (either nicotine or placebo). After study completion, participants either received credit toward their psychology research requirement or were financially compensated (US \$30). All study protocols were approved by the University Institutional Review Board.

Measures

Self-report Survey—Participants completed a survey assessing socio-demographic characteristics, medical history (e.g., medical condition(s), current medications), smoking/nicotine history (number of direct lifetime exposures, passive tobacco smoke exposure [hours/week]), alcohol use history (number of alcoholic drinks consumed/week), and sexual function (per the IIEF¹⁸).

Electrocardiography—Autonomic cardiac function was assessed using a three-channel ECG and signals were recorded using a Model MP100WS data acquisition unit (BIOPAC Systems, Inc., Santa Barbara, CA, USA) and the software package AcqKnowledge III, Version 3.73 (BIOPAC Systems, Inc.). Normal-to-normal (NN) intervals were collected

^{*}One 4-mg nicotine gum piece increases plasma nicotine levels by approximately 8–10 ng/mL within 30 minutes, and has a half life of approximately 120 minutes⁴. Comparatively, a high-yield (0.7–1.2 mg) nicotine cigarette increases plasma nicotine levels by approximately 14 ng/mL within 10 minutes⁴. 6mg nicotine gum was administered to ensure that a participant's plasma nicotine level would be comparable to smoking one cigarette.

manually using the AcqKnowledge peak finder function, and artifacts were identified and removed. After cleaning ECG recordings, mean NN interval and mean HR were derived. Kubios HRV Analysis Software (Biosignal Analysis and Medical Imaging Group, University of Kuopio, Kuopio, Finland) was used to calculate timedomain HRV indices. These indices included the standard deviation of NN intervals (SDNN), the square root of the mean squared difference of successive NN intervals (RMSSD), and the percent of NN intervals for which successive heartbeat intervals differed by at least 50 ms (pNN50).

Erectile Responses—Genital responses were assessed via penile plethysmography using a mercury-in-rubber strain gauge (Hokanson, Inc., Bellevue, WA, USA) to capture dynamic changes in penile circumference. Signals were sampled at a rate of 80 samples/second, bandpass filtered (to 0.5 Hz), digitized (40 Hz), and recorded using a Model MP100WS data acquisition unit and the software package AcqKnowledge III, Version 3.73.

Subjective Sexual Arousal—Continuous SSA was measured during the film presentation using a hand-controlled device, previously shown to be a valid indicator of self-reported sexual arousal²⁰. This device consisted of a computer optical mouse mounted on a track divided into seven equally spaced intervals, where 0 indicated neutral, and 1–7 reflected increasingly higher levels of feeling sexually aroused. The signal was low-pass filtered (to 0.5 Hz) and digitized (40 Hz), and a software program written in MatLab (The MathWorks, Inc, Natick, MA, USA) transformed the signals into percentage of maximum arousal.

Data Reduction

Erectile responses and SSA scores were computed by averaging all data points within 5-second epochs, and then averaging all epochs within the neutral and erotic film segments. Within-session change scores were calculated for each participant's physiological and SSA recordings by subtracting the value of the mean arousal response throughout the neutral film presentation (sexually unaroused state) from the mean arousal response throughout the erotic film presentation (sexually aroused state). Data were formatted such that they were suitable for a test of statistical mediation. To this end, the experimental condition to which a participant was first assigned was dummy coded (placebo = 0, nicotine = 1). Across-session change scores for the mediator variables (HRV, reflected as SDNN, RMSSD, pNN50) and outcome variables (within-session change in penile tumescence, SSA) were formatted similarly by subtracting values obtained during the second session from respective values obtained during the first session. Across-session change was calculated for RPC by subtracting the mean RPC obtained throughout the neutral film presentation of the second session from the mean RPC obtained throughout the neutral film presentation of the first session.

Statistical Analysis

Potential covariates for inclusion in the mediation models were initially explored via Pearson product moment correlations. Given the number of correlations performed, a two-tailed alpha of $P < .01$ was considered statistically significant. Because differences in individual penis size cause differential circumferential changes during sexual arousal²¹,

flaccid penile circumference was added as a covariate for analyses involving erectile tumescence as a criterion variable. Tests of indirect effects were employed with an SPSS (SPSS Inc., Chicago, IL, USA) application developed by Preacher and Hayes²². This macro provides a test of the indirect effect (i.e., experimental condition [nicotine, placebo] on penile tumescence though resting HRV, with flaccid penile circumference as a covariate). Analyses were conducted separately for the three HRV variables (SDNN, RMSSD, pNN50). Furthermore, all analyses were repeated with RPC and SSA as criterion variables. The mediation application used a bootstrapping procedure ($n = 10,000$ bootstrap resamples), which generated a sampling distribution for ab . The simple indirect effects approach is a more powerful test of mediation²³, given that this technique is not dependent on the normality assumption underlying the Sobel²⁴ test and the causal steps approach to mediation proposed by Baron and Kenny²⁵. Of note, testing indirect effects is not dependent on the original path (association between the predictor variable [i.e., experimental condition] and the dependent variable [i.e., erectile tumescence]) being statistically significant²³. To assess indirect effects, 95% confidence intervals (CIs) were generated for the parameter estimates, and these were considered statistically significant if the confidence intervals did not include a value of zero.

Results

Participant Characteristics

The sample ranged in age from 18 to 25 years ($M = 20.91$ years; $SD = 2.43$) and the majority of the sample was White (63.6%) (Table 1). No participants were taking cardiac/cardiovascular medications; however, three participants reported taking other types of medications (antihistamine, $n = 1$; acne medication, $n = 2$)[†]. Participants reported a mean of 6.4 ($SD = 9.39$) direct exposures to nicotine during their lifetime (7 reported no exposure [31.8%] and 15 reported 1 – 100 exposures [68.2%]); 13.6% reported passive exposure to tobacco smoke for more than 30 minutes per day at least once per week. Participants with and without a history of direct nicotine exposure did not differ from one another on any cardiac (BP, HR, SDNN, RMSSD, pNN50) or sexual arousal (RPC, erectile tumescence, SSA) parameter.

Exploring Potential Covariates

Zero-order correlations among study variables are presented in Table 2. Experimental condition was positively associated with all HRV parameters (SDNN: $r = .75$, $p < .001$; RMSSD: $r = .70$, $p < .001$; pNN50: $r = .68$, $p < .001$), indicating that the administration of nicotine was associated with lower HRV. Body mass index was positively associated with resting diastolic BP ($r = .59$, $P = .004$) and inversely related to nicotine body concentration ($r = -.64$, $P = .001$); resting HR was positively related to SSA ($r = .58$, $P = .007$). Systolic BP was positively correlated with diastolic BP ($r = .68$, $P = .001$) and with RPC ($r = .65$, $P = .001$). Diastolic BP was also associated with RPC ($r = .65$, $P = .001$). Consistent with extent literature^{26,27}, the three measures of HRV were all significantly correlated with one another (SDNN and RMSSD: $r = .90$, $p < .001$; SDNN and pNN50: $r = .85$, $p < .001$;

[†]Results of the mediational analyses remained unchanged when excluding these individuals taking medications.

RMSSD and pNN50: $r = .96, p < .001$). Based upon these associations, HR was included as a covariate in the mediation analyses involving SSA as an outcome and systolic and diastolic BP were added as covariates in analyses with RPC as a criterion variable.

Mediation Analyses

After controlling for flaccid penile circumference, nicotine administration (compared to placebo) was associated with lower levels of RMSSD ($B = 48.49, SE = 10.72, P < .001$) and with reduced levels of erectile tumescence ($B = .56, SE = .24, P = .03$). Furthermore, the indirect effect of experimental condition on erectile tumescence through RMSSD was significant, as indicated by 95% CIs not containing a value of zero ($CI = .005, .930$). To strengthen the interpretation of the above mediation analyses, an additional analysis was conducted which reversed the mediator and criterion variable^{28,29}. Results were not consistent with mediation in this direction. That is, the indirect effect of experimental condition on changes in RMSSD through changes in erectile tumescence was nonsignificant ($CI = -.10, .29.81$). Contrary to the HRV parameter of RMSSD, the indirect effects of experimental condition on erectile tumescence through SDNN ($CI = -.29, .82$) and pNN50 ($CI = -.15, .58$) were nonsignificant.

Analyses were not consistent with mediation for RPC (pNN50: $CI = -.82, .20$; SDNN: $CI = -.94, .51$; RMSSD: $CI = -1.11, .19$), or for SSA (pNN50: $CI = -.03, .21$; SDNN: $CI = -.10, .17$; RMSSD: $CI = -.04, .20$). That is, HRV did not mediate relations between experimental condition and changes in RPC, nor did HRV mediate associations between condition and changes in sexual arousal measured subjectively.

Comment

The present study examined whether cardiac autonomic function mediated associations between acute nicotine intake (vs. placebo) and both objective and subjective measures of sexual response among healthy nonsmoking men. Results were consistent with a causal mediation chain, indicating that HRV (as reflected by RMSSD) mediated the relationship between acute nicotine administration and erectile tumescence. Alternatively stated, acute nicotine ingestion (compared to placebo administration) was associated with dysregulated HRV (low RMSSD, indicative of SNS dominance), which in turn was related to smaller magnitude of erectile tumescence.

Taken together, findings suggest that nicotine ingestion acutely disrupts autonomic modulation of cardiac function among nicotine-naïve healthy men. This is in line with results of prior studies showing acute cardiac dysregulatory effects of nicotine administration¹⁰ and improvements in autonomic modulation of the heart as a result of nicotine cessation^{11,12}. Further, findings underscore the possibility that cardiac autonomic tone is an underlying mechanism by which nicotine intake exerts its deleterious effects on erectile response. In fact, recent longitudinal¹⁶ and cross-sectional¹⁷ studies indicate that nicotine/tobacco consumption (and cessation) is associated with several parameters of HRV, which in turn are associated with erectile tumescence. More broadly, findings may point toward the underlying role of HRV in the physiology of erectile hemodynamics, as current findings were in concert with a growing body of literature demonstrating the relationship

between sympathovagal balance and erectile function^{13–15}. Although findings were consistent with a causal mediation chain, results by no means preclude the possibility that other centrally or peripherally mediating pathways are implicated in the association between nicotine ingestion and erectile function.

Although HRV mediated the relationship between nicotine intake and erectile tumescence, resting HRV did not mediate associations between nicotine and self-reported sexual arousal. The absence of this mediation effect may be due to the fact that nicotine administration does not appear to affect self-reported sexual arousal⁴, supporting the notion that nicotine attenuates genital arousal peripherally (in part, via HRV) rather than centrally (e.g., by impacting cognitive processes). Similar to findings of recently published reports^{13,17}, HRV did not mediate associations between nicotine consumption and RPC. One possible explanation is that HRV plays a role primarily with processes responsible for sexual arousal rather than in resting genital tone. However, this is purely speculative and further research is necessary to better characterize these processes.

The current investigation had several strengths such as: (i) the use of a randomized, double-blind, placebo-controlled crossover protocol; (ii) the use of objective (i.e., penile plethysmography) and subjective (i.e., SSA) sexual response outcome measures; (iii) exclusion of individuals with a history of MI, CVD, and cardiovascular medication use, all of which have been associated with cardiac autonomic imbalance³⁰; (iv) exclusion of smokers, which precluded potential long-term cardiovascular disruptions that may have deleterious effects on sexual arousal and/or HRV⁸; and (v) enrollment of only young men, which eliminated potential confounding of age-related effects on erectile health.

Despite these strengths, several study limitations warrant mention. First, the sample was relatively young in age and therefore it remains unclear whether present findings generalize to clinical samples of patients with ED who are characteristically older and have a higher prevalence of medical factors that may impact sexual function. Additionally, this study only sampled men with normal erectile function per the IIEF. Although this enhanced the internal validity of the study, it is unclear whether results can be extrapolated to men with erectile difficulties. Further, future studies are necessary to determine whether these results hold for long-term smokers who are administered nicotine. Second, given that nicotine was not titrated for each participant, some variability in plasma nicotine concentrations would have been present among the sample. Although our crude measure of nicotine levels (i.e., nicotine body concentration) was not associated with any of the mediator or outcome measures, individual differences in nicotine metabolism may exist, irrespective of nicotine dosing. Third, although penile plethysmography is a sensitive and reliable measure of erectile response, employing a method such as Doppler ultrasonography may have enabled a more proximal exploration into how nicotine and HRV affect specific erectile mechanisms such as blood flow. Moreover, despite the fact that our validated method of measuring self-reported sexual arousal was robust (given its continuous data collection method), this may have distracted participants from fully processing the audiovisual sexual stimuli. Finally, the inter-relationships among nicotine intake, cardiac function, and sexual arousal are complex. It is possible that the observed relationship between nicotine ingestion and erectile capacity through HRV is an epiphenomena of more primary etiological factors that are associated

with acute nicotine consumption and/or HRV (i.e., direct or indirect targeting of nitric oxide⁸). Thus, further research is necessary to determine whether this relationship is indeed mechanistic in nature.

Conclusions

This study examined whether HRV mediated associations between acute nicotine administration and both objective and subjective measures of sexual arousal. Results indicated that nicotine ingestion was associated with dysregulated sympathovagal balance, which in turn was related to relatively reduced erectile tumescence. Although in need of replication, findings suggest that dysfunctional cardiac autonomic tone may be an underlying mechanism by which nicotine/tobacco exerts its deleterious effects on erectile health.

Acknowledgments

Portions of this work were made possible by Grant Number 1 RO1 HD051676-01 A1 to Cindy Meston from the National Institute of Child Health and Human Development (NICHD). The contents are solely the responsibility of the author and do not necessarily represent the official views of the NICHD.

References

1. He J, Reynolds K, Chen J, et al. Cigarette smoking and erectile dysfunction among Chinese men without clinical vascular disease. *Am J Epidemiol.* 2007; 166:803–809. [PubMed: 17623743]
2. Tengs TO, Osgood ND. The link between smoking and impotence: Two decades of evidence. *Prev Med.* 2001; 32:447–452. [PubMed: 11394947]
3. Gilbert DG, Hagen RL, D'Agostino JA. The effects of cigarette smoking on human sexual potency. *Addict Behav.* 1986; 11:431–434. [PubMed: 3812052]
4. Harte CB, Meston CM. Acute effects of nicotine on physiological and subjective sexual arousal in nonsmoking men: A randomized, double-blind, placebo-controlled trial. *J Sex Med.* 2008; 5:110–121. [PubMed: 17971108]
5. Harte CB, Meston CM. Association between smoking cessation and sexual health in men. *BJU Int.* 2012; 109:888–896. [PubMed: 21883852]
6. Sighinolfi MC, Mofferdin A, De Stefani S, Micali S, Cicero AF, Bianchi G. Immediate improvement in penile hemodynamics after cessation of smoking: previous results. *Urology.* 2007; 69:163–165. [PubMed: 17270641]
7. Pomerleau OF. Nicotine and the central nervous system: Biobehavioral effects of cigarette smoking. *Am J Med.* 1992; 93:2S–7S. [PubMed: 1353943]
8. McVary KT, Carrier S, Wessells H. Subcommittee on Smoking and Erectile Dysfunction Socioeconomic Committee Sexual Medicine Society of North America. Smoking and erectile dysfunction: Evidence based analysis. *J Urol.* 2001; 166:1624–1632. [PubMed: 11586190]
9. Hering D, Kucharska W, Kara T, Somers VK, Narkiewicz K. Smoking is associated with chronic sympathetic activation in hypertension. *Blood Press.* 2010; 19:152–155. [PubMed: 20429695]
10. Sjoberg N, Saint DA. A single 4 mg dose of nicotine decreases heart rate variability in healthy nonsmokers: Implications for smoking cessation programs. *Nicotine Tob Res.* 2011; 13:369–372. [PubMed: 21350044]
11. Stein PK, Rottman JN, Kleiger RE. Effect of 21 mg transdermal nicotine patches and smoking cessation on heart rate variability. *Am J Cardiol.* 1996; 77:701–705. [PubMed: 8651120]
12. Harte CB, Meston CM. Effects of smoking cessation on heart rate variability among long-term male smokers. *Int J Behav Med.* 2013 [epub ahead of print].
13. Harte CB. The relationship between resting heart rate variability and erectile tumescence among men with normal erectile function. *J Sex Med.* 2013; 10:1961–1968. [PubMed: 23802770]

14. Chen CJ, Kuo TB, Tseng YJ, Yang CC. Combined cardiac sympathetic excitation and vagal impairment in patients with non-organic erectile dysfunction. *Clin Neurophysiol.* 2009; 120:348–352. [PubMed: 19101201]
15. Lee JY, Joo KJ, Kim JT, et al. Heart rate variability in men with erectile dysfunction. *Int Neurourol J.* 2011; 15:87–91. [PubMed: 21811698]
16. Harte CB, Meston CM. Association between cigarette smoking and erectile tumescence: the mediating role of heart rate variability. *Int J Impot Res.* 2013; 25:155–159. [PubMed: 23303335]
17. Harte CB. Concurrent relations among cigarette smoking status, resting heart rate variability, and erectile response. under review.
18. Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A. The international index of erectile function (IIEF): A multidimensional scale for assessment of erectile dysfunction. *Urology.* 1997; 49:822–830. [PubMed: 9187685]
19. Cappelleri JC, Rosen RC, Smith MD, Mishra A, Osterloh IH. Diagnostic evaluation of the erectile function domain of the International Index of Erectile Function. *Urology.* 1999; 54:346–351. [PubMed: 10443736]
20. Rellini AH, McCall KM, Randall PK, Meston CM. The relationship between women's subjective and physiological sexual arousal. *Psychophysiology.* 2005; 42:116–124. [PubMed: 15720587]
21. Howes RJ. Circumferential change scores in phallometric assessment: Normative data. *Sex Abuse.* 2003; 15:365–375. [PubMed: 14571540]
22. Preacher KJ, Hayes AF. Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. *Behav Res Methods.* 2008; 40:879–891. [PubMed: 18697684]
23. Hayes AF. Beyond Baron and Kenny: Statistical mediation analysis in the new millennium. *Communication Monographs.* 2009; 76(4):408–420.
24. Sobel ME. Asymptotic confidence intervals for indirect effects in structural equation models. *Sociol Method.* 1982; 13(1982):290–312.
25. Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *J Pers Soc Psychol.* 1986; 51:1173–1182. [PubMed: 3806354]
26. Kautzner, J.; Hnatkova, K. Correspondence of different methods for heart rate variability measurement. In: Malik, M.; Camm, AJ., editors. *Heart rate variability.* Armonk, NY: Futura; 1995. p. 119-126.
27. Lorenz TA, Harte CB, Hamilton LD, Meston CM. Evidence for a curvilinear relationship between sympathetic nervous system activation and women's physiological sexual arousal. *Psychophysiology.* 2012; 49:111–117. [PubMed: 22092348]
28. Shrout PE, Bolger N. Mediation in experimental and nonexperimental studies: New procedures and recommendations. *Psychol Methods.* 2002; 7:422–445. [PubMed: 12530702]
29. Preacher KJ, Hayes AF. SPSS and SAS procedures for estimating indirect effects in simple mediation models. *Behav Res Methods.* 2004; 36(4):717–731.
30. Salo TM, Kantola I, Voipio-Pulkki LM, Pelttari L, Viikari JSA. The effect of four different antihypertensive medications on cardiovascular regulation in hypertensive sleep apneic patients- Assessment by spectral analysis of heart rate and blood pressure variability. *Eur J Clin Pharmacol.* 1999; 55:191–198. [PubMed: 10379634]

Table 1

Characteristics of the Participant Sample

Characteristic	<i>M</i>	<i>SD</i>	<i>n</i>	%
Age (years)	20.91	2.43		
Education (years)	13.70	1.76		
Ethnicity				
White/Caucasian			14	63.6
Black/African-American			2	9.1
Latino			4	18.2
Asian			1	4.5
Other			1	4.5
Marital status				
Single			20	90.9
Married			2	9.1
Alcohol use (drinks/week)	9.25	11.26		
Weight (kg)	75.96	13.59		
Height (m)	1.82	.13		
BMI (kg/m ²)	22.99	3.20		
Nicotine direct ^a exposures (lifetime)	6.36	9.39		
Nicotine passive ^b exposures (hours/week)	.56	1.63		
First time direct exposure to nicotine			7	31.8
Nicotine body concentration (µg/kg)	81.09	12.54		
Sexual function ^c				
Erectile function	29.23	1.69		
Orgasmic function	9.18	1.82		
Sexual desire	8.23	1.41		
Intercourse satisfaction	12.14	2.10		
Overall satisfaction	7.50	2.20		
Cardiac function ^d				
Resting HR (bpm)	69.73	11.88		
Systolic BP (mm Hg)	126.56	11.11		
Diastolic BP (mm Hg)	73.68	8.86		

Note. *N* = 22. BMI = body mass index; BP = blood pressure; bpm = beats per minute; mm Hg = millimeters mercury; HR = heart rate; *M* = mean; *SD* = standard deviation.

^a A direct exposure was defined as ingesting nicotine pulmonarily (e.g., smoking a cigarette, cigar, or pipe), or buccally (chewing smokeless tobacco).

^b Passive nicotine exposure was defined as ingesting nicotine via indirect means (i.e., passive smoke exposure).

^c Assessed per the International Index of Erectile Function.

^d Assessed during the placebo condition

Table 2

Zero-order Correlations among Study Variables

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1 Experimental condition	–	.40	–.20	<u>–.42*</u>	–.03	.09	.02	–.13	–.22	.75**	.70**	.68**	.03	.47	.25
2 Age		–	–.13	<u>.02</u>	.04	.19	.10	.10	–.20	.39	.34	.31	.07	.09	.18
3 Alcohol use			–	<u>–.14</u>	.23	.11	.30	.46	–.31	.02	.04	.09	.28	–.39	–.11
4 Nicotine body concentration				–	<u>–.64*</u>	<u>–.11</u>	<u>–.27</u>	<u>–.40</u>	<u>.17</u>	<u>–.39</u>	<u>–.28</u>	<u>–.25</u>	<u>.21</u>	<u>–.50</u>	<u>–.19</u>
5 BMI					–	.28	.39	.59**	.02	.10	–.05	–.01	.51	.13	–.08
6 HR ^a						–	.29	.49	–.19	.08	.01	–.05	.05	.03	.58*
7 Systolic BP ^a							–	.68**	–.09	–.19	–.27	–.25	.65**	–.32	–.47
8 Diastolic BP ^a								–	–.16	.16	–.33	–.33	.65**	–.32	–.47
9 IIEF-EF									–	–.47	–.46	–.43	–.26	.13	–.10
10 SDNN ^b										–	.90**	.85**	–.02	.44	.25
11 RMSSD ^b											–	.96**	–.11	.49	.32
12 pNN50 ^b												–	–.05	.40	.34
13 Resting penile circumference ^c													–	–.31	–.08
14 Erectile tumescence ^d														–	.23
15 Subjective sexual arousal ^d															–

Note. $N = 22$. Experimental condition to which a participant was first assigned was dummy coded as placebo = 0, nicotine = 1; BMI = body mass index; BP = blood pressure; HR = heart rate; IIEF-EF = International Index of Erectile Function – Erectile Function score; pNN50 = percent of normal-to-normal intervals for which successive heartbeat intervals differed by at least 50 ms; RMSSD = square root of the mean squared difference of successive normal-to-normal intervals; SDNN = standard deviation of normal-to-normal intervals.

^a Assessed during placebo condition during resting state.

^b Across-session change scores in heart rate variability parameters calculated by subtracting values obtained during the second experimental session from respective values obtained during the first experimental session.

^c Across-session change calculated by subtracting the mean penile circumference value obtained throughout the neutral film presentation of the second experimental session from the mean penile circumference value obtained throughout the neutral film presentation of the first experimental session.

^d Calculated by subtracting within session change values (i.e., sexual response during neutral film presentation subtracted from sexual response during the erotic film presentation) obtained during the second experimental session from respective within-session change values obtained during the first experimental session.

* $P < .01$.

100 > *P*
**

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript