

Nicotine Effects on Thermoregulatory Responses of Men and Women During Acute Cold Exposure

Cheatham, C.C., N. Caine-Bish, M. Blegen, E.S. Potkanowicz and E.L. Glickman. *Aviation, Space, and Environmental Medicine*. 75: 589-595, 2004.



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HPER 6760

July 5, 2011



Introduction - Thermoregulation

- **Thermoregulation during cold exposure**
 - **Decrease heat loss**
 - **Peripheral vasoconstriction**
 - Decrease from 0.2-0.3 L/min to near zero (Johnson et al., 1986)
 - **Increase in sympathetic nervous system activity**
 - **Increase in metabolic heat production**
 - Increase between 1.3 to 4.2x RMR (0 to 10°air) (Horvath et al., 1956)
 - **Increase in muscle shivering**
 - **Nonshivering thermogenesis**

- **Body systems involved in thermoregulation**
 - **Nervous system**
 - **Cardiovascular system**
 - **Neuroendocrine system**
 - **Muscular system**



Introduction - Nicotine

- **Nicotine Administration**
 - Increase in sympathetic nervous system activity (Benowitz et al., 1986)
 - Stimulation of sympathoadrenal system (Benowitz et al., 1986)
 - Muscle Relaxation
- **Effects of nicotine administration**
 - Metabolic rate
 - Increase of 6 to 11% (Dill et al., 1934; Hiestand et al., 1940)
 - Hormonal changes
 - Circulatory and cardiovascular changes
 - Metabolic changes
- **Nicotine and cold thermoregulation**



Purpose

To examine the effects of nicotine on the thermoregulatory, cardiovascular, metabolic, and hormonal responses during acute cold exposure.



Significance of Study

With approximately 30% of military personnel being tobacco users, it is essential to understand if nicotine impacts the body's ability to maintain body temperature during cold exposure



Review of Literature

Add key findings from previous studies that have led to the questions being examined in the present study.



Methodology – Subjects Characteristics

- Subject Characteristics
 - 6 males and 6 females (18-35 years)
 - Healthy and free of medication use
 - Smoking History
 - At least 13 cigarettes per day for 1 year
 - Confirmed by 7 day smoking record
 - Females
 - Eumenorrheic
 - Only tested during FOL phase (Days 1-8)



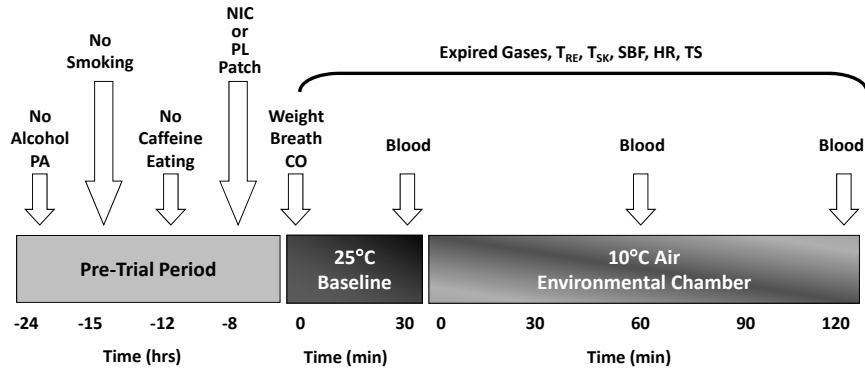
Methodology – Subjects Characteristics

Variable / Sex	Males	Females	P-Value
Age (yrs)	22.6 ± 1.0	20.9 ± 1.6	0.047
Height (cm)	178.1 ± 5.0	164.6 ± 6.9	0.003
Weight (kg)	81.3 ± 18.6	59.6 ± 7.2	0.024
Body Fat (%)	12.9 ± 5.1	18.9 ± 4.2	0.052
VO _{2max} (mL·kg ⁻¹ ·min ⁻¹)	44.1 ± 7.0	33.6 ± 3.2	0.008
Ave. Cigarettes per day	19 ± 4	18 ± 4	0.733
Smoking Duration (yrs)	4.0 ± 1.7	4.3 ± 2.4	0.797



Methodology - Design

- Experimental Trials
 - GXT and Anthropometric Assessment
 - Cold Air Trial (2 trials: NIC and PL)



CO, Carbon Monoxide; HR, Heart Rate; NIC, Nicotine; PA, Physical Activity; PL, Placebo; SBF, Skin Blood Flow; T_{REY} , Rectal Temperature; T_{SKY} , Skin Temperature; TS, Thermal Sensation



Methodology – Variables

- Thermoregulatory Variables
 - Heat Production – Metabolic Measurement Cart
 - Core Temperature – Rectal Thermister Probe
 - Mean Skin Temperature – 4 sites (Chest, Arm, Thigh, Calf)
 - Skin Blood Flow – Finger (Laser Doppler Flowmetry)
 - Tissue Insulation – Derived Value
 - Thermal Sensation – Gagge Scale
- Blood Variables
 - Plasma Nicotine Concentration (Gas Chromatography)



Methodology - Statistics

- Statistical Analysis
 - 3-Way ANOVA with Repeated Measures
 - Sex (Males vs. Females)
 - Treatment (Placebo vs. Nicotine) – RM
 - Time – RM
 - Post-Hoc Analysis
 - Tukey HSD, Simple Effects Analysis with Bonferroni)
 - Level of Significance ($P < 0.050$)



Results – Plasma Nicotine ($\text{ng}\cdot\text{mL}^{-1}$)

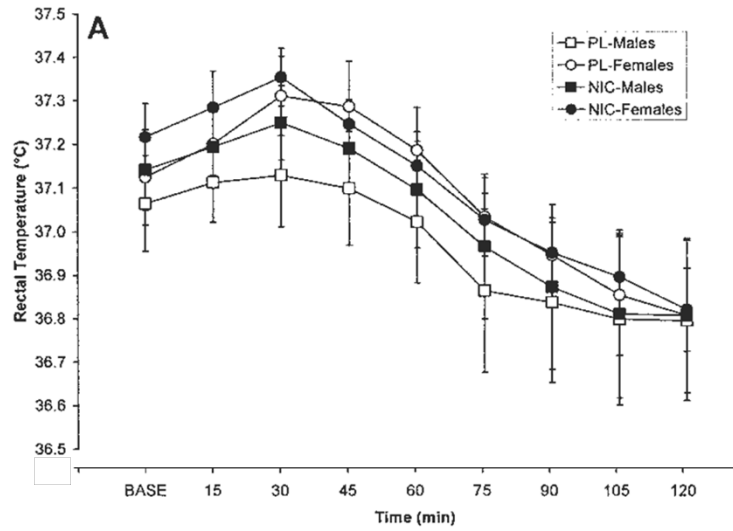
TABLE I. PLASMA NIC CONCENTRATION ($\text{NG}\cdot\text{ML}^{-1}$) AT BASE AND 120 MIN OF COLD EXPOSURE IN MEN ($N = 6$) AND WOMEN ($N = 6$) DURING PL AND NIC TREATMENTS (MEAN \pm SE).

Treat/Sex/Time (min)	BASE	120	Total
Placebo			
Men	1.5 \pm 0.6	1.5 \pm 0.5	1.5 \pm 0.4
Women	1.1 \pm 0.4	1.2 \pm 0.4	1.1 \pm 0.3
Total	1.3* \pm 0.3	1.3* \pm 0.3	1.3 \pm 0.2
Nicotine			
Men	20.7 \pm 3.2	13.0 \pm 2.8	16.9 \pm 2.3
Women	14.5 \pm 0.7	8.1 \pm 1.2	11.3 \pm 1.3
Total	17.9* [†] \pm 2.0	10.8* [†] \pm 1.7	14.3 \pm 1.5

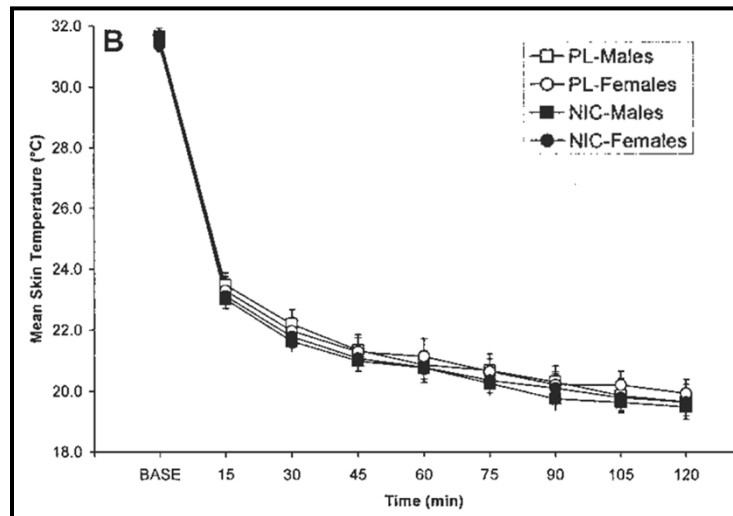
BASE, Baseline; * $p \leq 0.05$ PL vs. NIC at given time point; [†] $p \leq 0.05$ BASE vs. 120 min for NIC treatment.

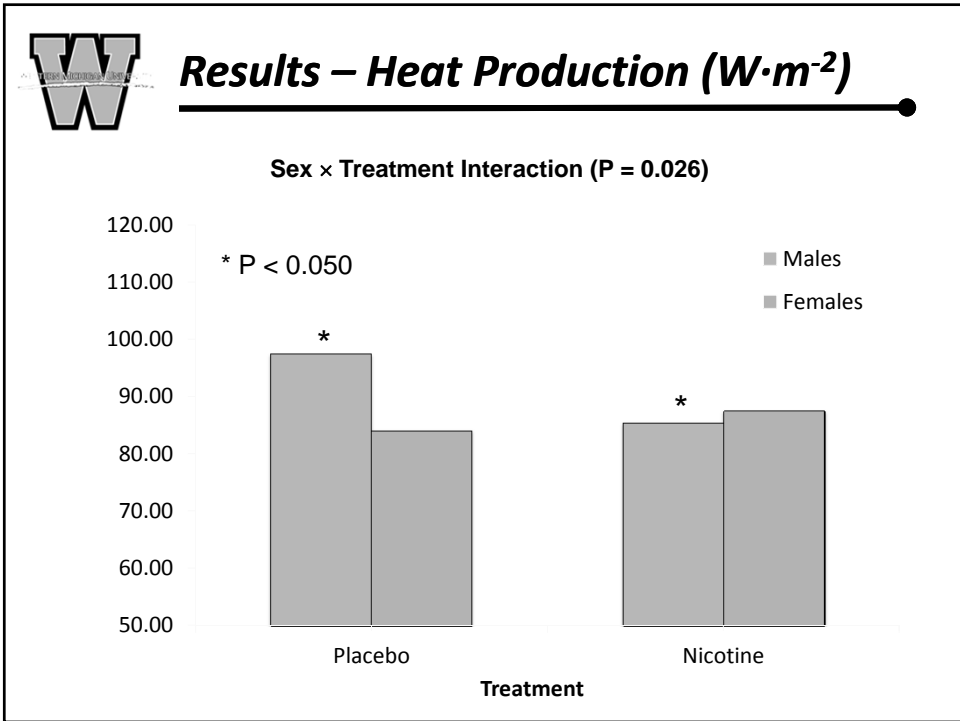
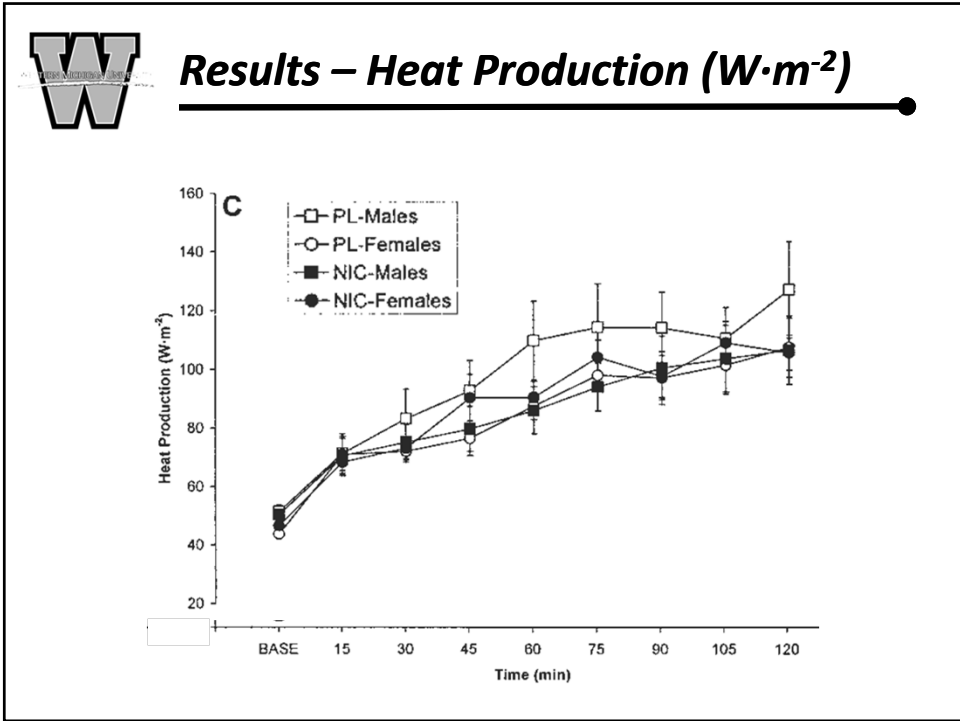


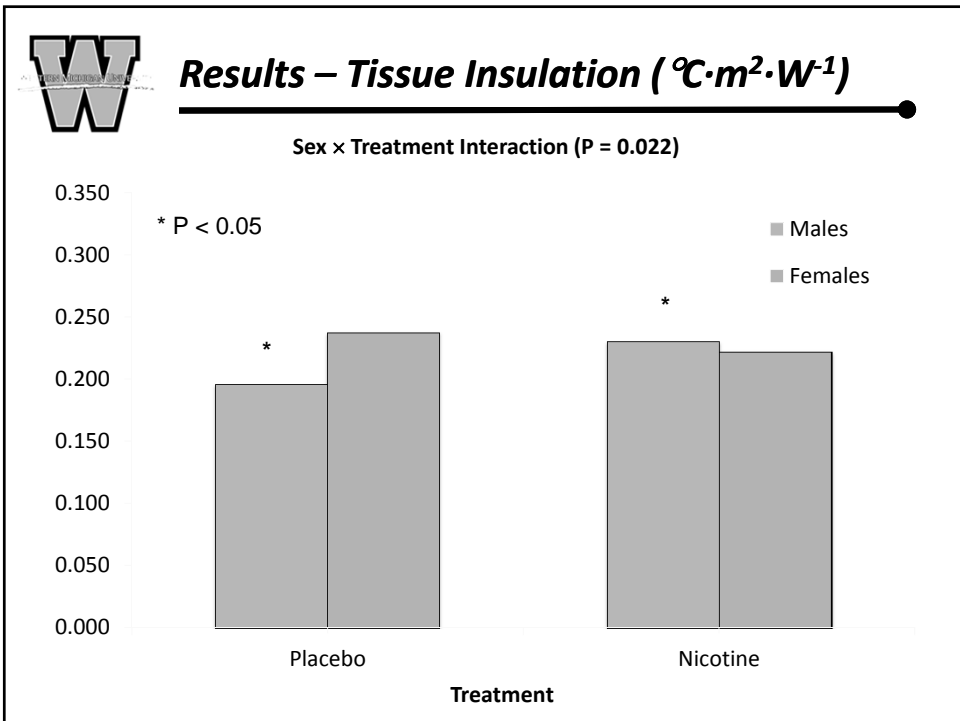
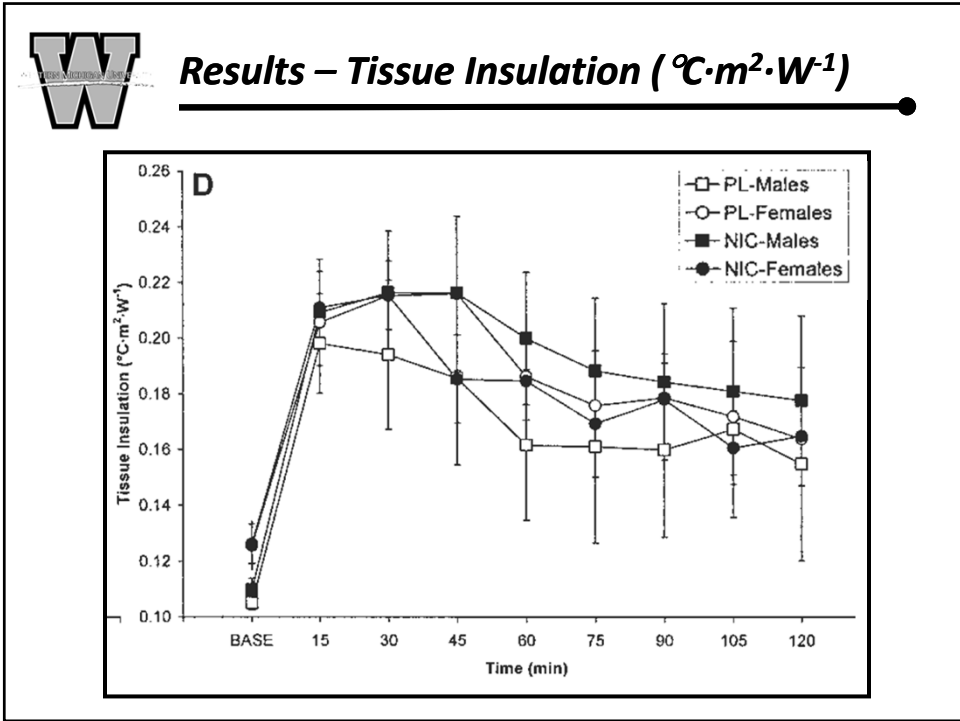
Results – Rectal Temperature (C)



Results – Mean Skin Temperature (°C)

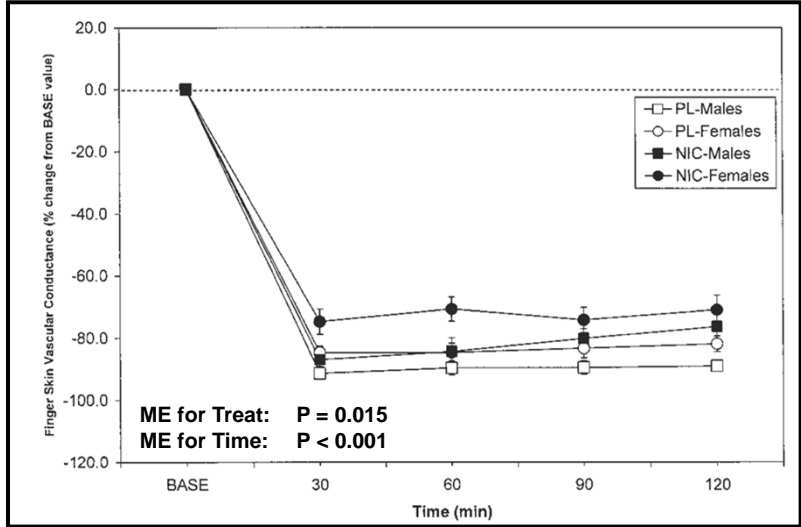




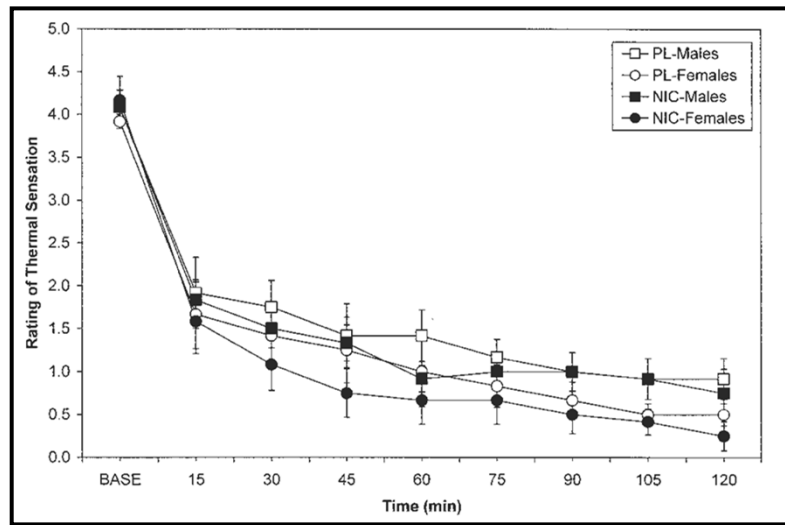




Results – Finger Skin Blood Flow (% BASE)



Results – Thermal Sensation





Results – Thermoregulatory Variables (Summary)

- Placebo vs. Nicotine
 - Rectal Temperature
 - No difference
 - Heat Production
 - In males, NIC < PL
 - Mean Skin Temperature
 - No difference
 - Tissue Insulation
 - In males, NIC > PL
 - Finger Skin Blood Flow
 - NIC > PL



Discussion

- **Heat Production (Males: NIC < PL)**
 - Norepinephrine (NIC < PL)
 - NIC and inhibition of muscle shivering
 - Insulation (NIC > PL)
- **Tissue Insulation (Males: NIC > PL)**
 - Nicotine and sympathetic nervous system activity
 - Decrease in muscle shivering and thus a decrease in muscle blood flow
 - Limitations in methodology
- **SBF_{FIN} (NIC > PL)**
 - Lower norepinephrine during NIC trial
 - Only in males
 - Inhibition or mediation of sympathetic nervous system activity by nicotine
 - Decreased reliance on peripheral vasoconstriction to reduce heat loss



Conclusions

- Nicotine administration alters selected thermoregulatory responses during acute cold exposure
- The effects of nicotine on the thermoregulatory variables seems to be sex specific with males exhibiting greater changes
- The ability to maintain core temperature does not seem to be affected by nicotine administration



Recommendations

- Alter thermoregulatory stress
 - Less severe
- More homogenous sample



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RESEARCH ARTICLE

Nicotine Effects on Thermoregulatory Responses of Men and Women During Acute Cold Exposure

CHRISTOPHER C. CHEATHAM, NATALIE CAINE-BISH, MARK BILGEN, EDWARD S. POTKANOWICZ, AND EILEEN L. GLECKMAN

Abstract: Due to the impact of nicotine (NIC) on the physiological processes involved in temperature regulation during cold exposure, it is conceivable that NIC may affect the body's thermoregulatory abilities during a cold stress. Thus, the purpose of this study was to examine the effects of NIC on thermoregulatory responses during acute cold exposure. **Methods:** There were six men and six women between the ages of 18 and 25 yr who participated in this study. All subjects were active, apparently healthy smokers. Each subject performed two cold air trials consisting of a 30-min baseline period (BASE) and a 120-min exposure to 10°C air. One cold air trial was performed following a NIC, dosing using a 21-mg transdermal patch while the other trial was performed after a placebo (PL) treatment. **Results:** During the cold air trials, there were no differences in rectal temperature (T_{re}) or mean skin temperature (T_{sk}) between the PL and NIC treatments in either sex ($p > 0.05$). However, in men, heart production (M) was 12% lower ($p < 0.05$) and tissue insulation was 17% higher ($p < 0.05$) during the NIC treatment compared with the PL treatment during the cold air trials. In women, no differences in M or tissue insulation were detected. In both men and women, finger skin vascular conductance (FSVC), expressed as a percentage of the BASE value, was higher during the NIC treatment compared with the PL treatment during the cold air trials ($p < 0.05$). Lastly, throughout the cold air trials, there was no difference in thermal sensation between the PL and NIC treatments ($p > 0.05$). **Discussion:** In conclusion, although NIC administration resulted in sex-specific alterations in M and tissue insulation during cold exposure, the response in T_{re} was unaffected. **Keywords:** transdermal patch, gender differences, sex differences, cold thermoregulatory responses, smoking.

WHEN EXPOSED TO the cold, the primary challenge faced by the body is the maintenance of internal body temperature. Body temperature, distinct

found that may affect temperature regulation during prolonged cold exposure is nicotine (NIC). At NIC dosages comparable to those observed during smoking, NIC has been shown to increase sympathetic nervous system activity and increase the circulating concentrations of norepinephrine and epinephrine (5). This increase in sympathetic nervous system activity causes an increase in cutaneous vasoconstriction and a decrease in skin temperature (4,13,14,40). In studies using a transdermal NIC patch, Muller et al. (29) reported no changes in skin blood flow or skin temperature after application of a transdermal NIC patch, while Betscher et al. (31) observed a 20% decrease in skin blood flow after application of the transdermal NIC patch compared with a control day. It has been shown that metabolic rate, and thus M, is increased by low and moderate NIC consumption, although the magnitude of change is somewhat variable. Some studies have reported increases in resting metabolic rate between 6 and 11% (9,20), while others have reported a more modest increase (8). The methodologies employed in the aforementioned investigations may account for the variability in the experimental findings, as smoking abstinence was not always confirmed. Therefore, it is possible that resting metabolic rate was already elevated due to smoking prior to baseline measurements (32). In a later study, after confirming smoking abstinence via expired carbon monoxide levels, Perkins (33) measured resting metabolic rate in 18 male smokers after administration of a low-dose and



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