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Effects of Heat Stress on Arterial Compliance in Smokers: A Pilot Study

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Effects of Passive Heat Stress on Thermoregulation in Smokers Versus Non-Smokers

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Abstract

Context: Maintaining thermal balance under heat-stress depends on appropriate increases in sweating and skin blood flow (cutaneous vasodilation). Given the multiple effects on nicotine on the body, it is unknown if sweating and cutaneous vasodilation are impaired, or possibly enhanced in smokers during heat stress. **Objective:** To examine the effects of passive heating on thermoregulatory responses (i.e., sweating and cutaneous vasodilation) in smokers versus non-smokers. **Design:** 1 passive heat trial per subject. **Patients or Other Participants:** 14 male smokers (26 ± 7 y; 180.0 ± 5.5 cm; 81.2 ± 20.7 kg; 3.2 ± 1.9 packs/week) and 12 male non-smokers (26 ± 8 y; 172.4 ± 33.2 cm; 81.2 ± 20.7 kg) volunteered to participate. **Intervention:** Subjects were passively heated using a water perfused, tube-lined suit until core temperature (TC) increased 1.5°C from baseline. At baseline and each 0.5°C TC increase, core and skin temperatures (Tsk) were assessed. On an exposed forearm, skin blood flow (SKBF) via laser doppler flowmetry, local sweat rate (LSR), sweat gland output (SGO), and sweat gland activation (SGA). Data were analyzed via LabChart 8.0 and ImageJ. Statistical procedures were performed with SPSS v.20.0. **Main Outcome Measures:** SKBF, LSR, SGO, SGA, Tsk, and TC were all assessed via a two-way ANOVA. Sweat sensitivity, SKBF sensitivity, TC at sweat and SKBF onset, total body sweat-rate and percent body mass loss were all assessed via independent t-tests. **Results:** There were no significant differences in any measures between smokers and non-smokers (all $p > 0.05$). TC and Tsk increased significantly ($p < 0.01$) from baseline to 1.5°C TC increase ($37.0 \pm 0.3^{\circ}\text{C}$ to $38.4 \pm 0.2^{\circ}\text{C}$ and $34.1 \pm 0.5^{\circ}\text{C}$ to $40.1 \pm 0.4^{\circ}\text{C}$, respectively). Independent of group, SKBF, LSR, and SGO increased significantly ($p < 0.01$) from baseline until TC increased 1.0°C (19.5 ± 13.6 to $65.3 \pm 19.4\%$ of max SKBF, 0.0 to 1.0 ± 0.5 $\text{mg}\cdot\text{cm}^{-1}\cdot\text{min}^{-1}$, and 0.0 to 9.2 ± 2.6 $\mu\text{g}\cdot\text{cm}^{-1}\cdot\text{min}^{-1}$, respectively). Other notable measures were TC at sweat onset ($37.0 \pm 0.3^{\circ}\text{C}$), total body sweat-rate (0.51 ± 0.21 $\text{L}\cdot\text{hr}^{-1}$), and percent body mass loss ($-0.5 \pm 0.1\%$). **Conclusion:** Passive heating similarly affected vasodilatory and sweating parameters in smokers and non-smokers. Therefore in these relatively young, male, light smokers, thermoregulation is neither hindered nor enhanced. **Funding:** This project was funded by the College of Education and Health Professions and Research & Sponsored Programs at the University of Arkansas and the Arkansas Biosciences Institute, the major research component of the Arkansas Tobacco Settlement Proceeds Act of 2000. Word Count: 419

Chapter 1: Introduction

As the climate continually becomes warmer around the world, heat stress is quickly becoming more of a concern across the population. Heat, whether generated actively through exercise or gained from external heat sources, causes the body's core and skin temperature to rise. This heat storage causes an imbalance in the thermal equilibrium of the body. In order to maintain thermal equilibrium in the body, heat that is produced/gained must equal the amount of heat that is dissipated from the body. Dissipation of heat from the human body occurs primarily in two ways: evaporation of sweat and convective heat loss through increased skin blood flow.

Sweating is a mechanism of thermoregulation which dissipates heat through evaporation of water from the skin. Sweating is controlled by the sympathetic nervous system, and acetylcholine is the main neurotransmitter associated with the sweating response. During the sweat response, acetylcholine is released from cholinergic sudomotor nerves and binds to muscarinic receptors on the sweat gland in response to changes in body temperature (Shibasaki & Crandall, 2011). Increased sweating may occur by increasing the output of sweat per gland and/or by increasing the number of glands activated. Sweating continues until the individual reaches their maximum sweat rate, after which no further increases in sweating will occur.

Skin blood flow is another mechanism of thermoregulation. Heat is dissipated convectively with skin blood flow. The mechanism controlling this response is cholinergic nerve activation by the release of transmitters that have not been fully explained yet, but peptides involved include calcitonin gene-related peptide (CGRP), vasoactive intestinal polypeptide (VIP), and nitric oxide (NO) (Kellogg et. al., 1995),

(Shibasaki & Crandall, 2010). When faced with heat stress, adrenergic vasoconstriction and active vasodilation control blood flow in non-acral areas to alter skin blood flow. This means that there is a small increase in cutaneous blood flow due to a release of vasoconstrictor tone and an increase in cutaneous blood flow from active vasodilation (Inoue et. al., 1998). Increased skin blood flow allows for the removal of heat from the body by transporting the heat from the muscles and organs closer to the environment where heat can be released. Similar to sweating, each individual also possesses a maximum skin blood flow, after which no further increases in skin blood flow will occur.

There are many factors which can alter the effectiveness of thermoregulation within the body, however it is unknown if smoking is one of them. One of the main chemicals in cigarettes is nicotine, which has been shown that it may stimulate or depress certain functions in the body (Kool et. al., 1993). One example of how it stimulates the body is that over the course of prolonged cigarette smoking, it has been shown that the sympathetic nervous system is activated 24 hours a day (Kilaru, Frangos, et al., 2001). Since the sympathetic nervous system is what controls sweating, it could be that the sweat response in smokers would be greater than that of non-smokers. Conversely, nicotine in cigarettes causes norepinephrine to be released, which in turn increases cutaneous vasoconstriction (Kool et. al., 1993), and is associated with a drop in skin blood flow (Mundel & Jones, 2006). This may cause an impairment in thermoregulation because less heat will be released to the environment. The net effect on thermoregulation is unknown for smokers, especially when challenged with heat stress. Therefore, the purpose of this study is to examine how passive heat stress affects thermoregulation in smokers versus nonsmokers.

Chapter 2: Literature Review

Introduction

During heat stress, the human body is constantly working to maintain a state of equilibrium. This equilibrium in the human body may only exist if the amount of heat that is actively generated by the body or externally placed on the body is equal to the amount of heat that the body is able to dissipate. As the body heats up, the core and skin temperature of the body rise steadily. This rise in core and skin temperature triggers the body to engage in compensatory responses in order to dissipate this heat from the body. Dissipation of this heat occurs in two primary ways: evaporative heat loss through the means of sweating and convective heat loss through an increase in skin blood flow.

Basic Thermoregulation

Heat Stress

Increases in heat storage in the body are detected through increases in core temperature and skin temperature. As heat storage increases, efferent signals travel to the brain to alert the hypothalamus of the disturbances to the thermoregulatory equilibrium. The body responds convectively by dilating cutaneous blood vessels and evaporatively by preparing glands to secrete sweat (Shibasaki & Crandall, 2011).

Sweating

Sweating is a mechanism of thermoregulation which dissipates heat through evaporation of water from the skin. Increased sweating may occur through an increase

in the output of sweat per gland and/or by increasing the number of glands activated.

The frequency of sweat expulsions per minute has been shown to increase linearly with a rise in body temperature.

Sweating is controlled by the sympathetic nervous system (Shibasaki & Crandall, 2011). Efferent signals about core and skin temperature are relayed to the hypothalamus. When core and skin temperature exceed that which allows for equilibrium in the body, the hypothalamus begins a signal to the sweat gland (Shibasaki & Crandall, 2011). During this process, acetylcholine is released from cholinergic sudomotor nerves and enter the sweat gland and stimulates the muscarinic receptors of the clear cells. An influx of calcium ions occurs in the cells which allows for an influx of sodium ions as well, which ultimately allows for an influx of chloride ions through electric coupling. Through the process of osmosis, water enters the cell until the gradient is removed when the intracellular concentration threshold is achieved, and sodium-potassium pumps are activated on the luminal membrane. Active transports of the sodium and chloride ions along with water is transported into the glandular lumen commences, which is the precursor of sweat. (Taylor & Machado-Moreira, 2013).

The amount that a person is able to sweat depends on the “sensitivity” of the sweat glands. The more sensitive a person’s sweat glands are to heat, the high the ability of that person to effectively maintain thermoregulatory equilibrium. Once the process of sweating begins in an individual, it does so by slowly recruiting more sweat glands in order to increase the amount of sweat secreted (Taylor & Machado-Moreira, 2013). Once the maximum number of glands has been recruited by the individual, the

amount of sweat secreted will then increase, allowing for a higher response to the thermoregulatory demands (Taylor & Machado-Moreira, 2013).

High rates of sweating cannot be maintained by the body for extended periods of time. Reasons for the mechanism of a decrease in sweat is unknown, especially as internal body temperatures remain high (Shibasaki et. al., 2006). Theories include conditions such as dehydration, yet decreases in sweat rate still occur in individuals that are well hydrated (Shibasaki et. al., 2006).

Skin Blood Flow

An increase in blood flow from the body core to the skin allows for the removal of heat from the body through the transportation of the heat from the muscles and organs closer to the skin through convection so that heat may be released. Adrenergic vasoconstriction and active vasodilation control blood flow in non-acral areas to alter skin blood flow. Adrenergic vasoconstriction is controlled by the secretion of norepinephrine from adrenergic nerves. During heat stress, the norepinephrine acts on postsynaptic receptors stopping the vasoconstriction (Kellogg et. al., 1995). This means that there is first a release of vasoconstrictor tone, and then an increase in cutaneous blood flow from active vasodilation (Inoue et. al., 1998).

The body's response to heat through an increase in skin blood flow is not uniform throughout the body. The greatest increase in skin blood flow is found on the thigh, followed by the forearm, and the lowest values on the back and chest. These differences are most likely due to the role of a co-transmitter that is assumed to be present, and also due to variations in sweat gland output (Smith et. al., 2013). The co-

transmitter that is assumed to be present has not been fully identified or explained yet (Shibasaki & Crandall, 2010), but it may be different throughout the body which may be an explanation for why there are differences. Although specific co-transmitters have not been identified, suggested neuropeptides which might play a role in this include calcitonin gene-related peptide (CGRP), vasoactive intestinal polypeptide (VIP), and nitric oxide (NO) (Shibasaki & Crandall, 2011).

During exercise, increased skin blood flow as a means of heat dissipation becomes more complicated than during passive heat stress. During passive heat stress, blood flow is not needed in the muscles or other inactive tissues, so skin blood flow can be maximally used as a way of dissipating heat. This isn't true when exercise is occurring. During exercise, a redistribution of blood flow away from inactive tissues (including the skin) toward the active muscles takes place. These contracting muscles during exercise also produce heat as energy is expended, and since skin blood flow is supposed to aid in the dissipation of this heat, a competition exists between blood flow moving toward the active muscles and blood flow remaining at the skin to aid in heat dissipation (Kenney & Johnson, 1992). However, studies have shown that blood flow toward the muscles is not attenuated, meaning that cutaneous blood flow only reaches a percentage of its maximum (Savard et. al., 1985), meaning it is less efficient than during passive heat stress.

Smokers

Sweating and Smoking

Over the course of prolonged cigarette smoking, it has been shown that nicotine causes the sympathetic nervous system to be activated 24 hours per day (Kilaru, Frangos, et al., 2001), possibly through a release of epinephrine caused by the nicotine (Kool et. al., 1993). Nicotine has the ability to stay in the body for long periods of time. Although half of the nicotine will be gone after two to three hours, the other half has the ability to stay within the body for twenty or more hours. This means that the nicotine may be slowly released from tissues during this time. Because nicotine causes the sympathetic nervous system to be activated, this is why it may stay at a heightened response 24 hours per day (Kilaru, Frangos, et. al., 2001).

Because the sympathetic nervous system would be activated already, it may be hypothesized that sweat onset would occur sooner in smokers. Also, it may be presumed that there would be a greater release of acetylcholine, which would in turn cause heightened responses of muscarinic receptors that control sweating. This means that a smoker would have a greater thermoregulatory response, or a higher sweat sensitivity, therefore enhancing evaporative heat loss to allow for cooling (Taylor & Machado-Moreira, 2013). It is well known that other factors effect sweating (e.g., heat acclimatization, gender, training), meaning that individual sweat responses are modifiable. However, there are no known studies specifically examining differences in sweating between smokers and non-smokers.

Skin Blood Flow and Smoking

Studies have shown that as more cigarettes are smoked during the day, skin blood flow continually decreases with each cigarette smoked (Gore & Chien, 1998).

Nicotine may cause a release of catecholamines, particularly norepinephrine (Kool et. al., 1993, Meekin et. al., 2000), which causes cutaneous vasoconstriction (Cryer et. al., 1976, Gourley & Benowitz, 1997, Sorensen et. al., 2009). With each cigarette, more nicotine is allowed into the body which allows for more norepinephrine to be released. This allows for a continual steady increase in cutaneous vasoconstriction, which results in decreased skin blood flow. Because of this, it is possible that a smoker may have an impaired ability to increase skin blood flow during heat stress. This would result in an impaired thermoregulatory response, therefore a smoker may not be able to dissipate as much heat from the body as a non-smoker. Further review of literature shows that some have found no differences between smokers and non-smokers (Meekin et. al., 2000), while others have observed differences (Meekin et. al., 2000). This may be partly due to how much the individual smokes, suggesting heavy smokers may have a tolerance for nicotine (Meekin et. al., 2000). Another alteration of function that nicotine causes is an impaired acetylcholine induced skin vasodilation which was found in young smokers. This is likely due to a diminished nitric oxide dependent vasodilation, which is similar to the effect of aging skin endothelial function (Fujii et. al., 2012) and would result impaired vasodilation.

Summary

Despite these mechanistic hypotheses of how smoking may influence thermoregulation, it is unknown whether or not smoking affects thermoregulation. As discussed above, nicotine effects may show increases in sweating, yet decreases in skin blood flow. It is important to fully understand the thermoregulatory responses of

smokers because independent of smoking status, heat stress is a health problem that our society is facing today.

Chapter 3: Materials and Methods

Subjects

Males age 18-49 were included in the study, including 14 male smokers (26 ± 7 y; 180.0 ± 5.5 cm; 81.2 ± 20.7 kg; 3.2 ± 1.9 packs/week) and 12 male non-smokers (26 ± 8 y; 172.4 ± 33.2 cm; 81.2 ± 20.7 kg). Before participating, subjects read and signed informed consent documents approved by the University of Arkansas Institutional Review Board. This study was part of a larger study examining cardiovascular changes during passive heating.

Pre-Trial Design

Each participant refrained from exercise and alcohol twenty-four hours, food four hours and caffeine eight hours prior to each trial. Also prior to the trial, participants were asked to drink 500 mL of water the night before the trial, and another 500 mL of water two to three hours before the trial. Smokers were asked to smoke one hour prior to their trial time.

Upon arrival at the laboratory, participants provided a small urine sample; from this sample, urine specific gravity was determined to ensure subjects started trials in a euhydrated state. Participants' nude body mass (bladder emptied) was taken. Subjects also ingested a temperature sensor pill, the CorTemp™ Core Body Temperature Sensor (HQ Inc.).

Procedures

One heat trial was performed per subject. In this trial, participants were placed in a tube lined, water-perfused suit that covered the entire body except for the hands, feet, head and neck. They were then asked to place a rain suit over the top of the tube lined suit. Once that was complete, the participant was asked to lie in a supine position for 30 minutes while water at 34 °C was run through the suit. After the 30 minutes was complete, baseline measurements of core temperature, mean skin temperature, and skin blood flow were taken of the participant. Once the baseline measurements were complete, the heating began by running 49°C water through the suit. Measurements were taken when core temperature increased (from baseline) by 0.5°C, 1.0°C, and 1.5°C. Measures included core temperature, sweat gland activation, local sweat rate, and skin blood flow (see below). Once the heating phases were complete, cold water was run through the suit to begin the cool-down phase. In order to obtain maximal skin blood flow, local heating to 42°C began for thirty minutes. After the cool-down phase, core temperature and skin blood flow were measured, and the test was complete.

Measurements

Skin temperature was assessed by thermocouples (2000 Thermocouple Meter) attached to the right side of the body at the lateral subdeltoid, pectoral, lateral calf, and quadriceps. Heart rate (Polar, Inc.) was assessed via a heart rate monitor (SunTech Tango; Raleigh, NC). Blood pressure was measured by an electrospymomanometer (SunTech Tango; Raleigh, NC) on the participant's left arm.

After wiping away all the dripping sweat from the area, sweat gland activation was measured by placing a 0.442 in^2 circular piece of iodine-impregnated paper on the right forearm for ~3 seconds and then removed for analyzing. This measure was

recorded 2-3 times per time point. The exact spot was marked and used for each measurement. Each of the circles were taped to a sheet of paper, and immediately scanned into a computer at the end of the trial. Images were saved as “tif” files for data analysis via ImageJ.

Local sweat rate was measured by placing a small capsule on the right forearm which was completely adhered to the skin. Dry nitrogen gas from a Radnor tank at a constant temperature flowed through the capsule at 300 ml/min. The nitrogen gas allowed for zero humidity within the capsule which in turn meant that any increases in humidity were due to the subject’s sweat. This information was used to calculate local sweat rate. This equation to calculate local sweat rate is listed below:

$$Local\ Sweat\ Rate\ \left(\frac{mg}{cm^2\ min}\right) = \frac{humidity \times 0.0003}{2.85}$$

Skin blood flow (moorLAB Laser Doppler Perfusion Monitor and a PF 5020 Temp Unit) was measured through the use of a probe connected to a monitor which was placed on the anterior side of the right forearm. This allowed for skin blood flow to be measured via the Doppler effect, where laser light was backscattered from red blood cells moving in the cutaneous microcirculation (Holloway & Watkins, 1977).

Data and Statistical Analysis

Data were analyzed via LabChart 8.0 and ImageJ. Skin Blood Flow, Mean Skin Temp, Local sweat rate, and Core temperature measurements were each taken at each

time point, and is an average of the measurements when the first and second blood pressures were taken.

Local heating for maximum skin blood flow was made by taking a 30 second time at the maximum skin blood flow. Percent of maximum skin blood flow was calculated via the following equation:

$$\% \text{ max} = \frac{\text{skin blood flow measurement}}{\text{local heating skin blood flow measurement}}$$

Skin blood flow onset was measured by pinpointing visually when the exact increase began, and core temperature at this time point was also recorded. Skin blood flow maximum during passive heat stress was measured by pinpointing visually when the steady increase plateaued, and core temperature at this time point was also recorded. Skin blood flow sensitivity was determined by calculating the change in skin blood flow divided by the change in core temperature between the visually pinpointed onset and the visually pinpointed plateau.

Local sweat rate onset was measured by pinpointing visually when the exact increase began, and the core temperature at this time point was also recorded. Local sweat rate maximum was measured by pinpointing visually when the steady increase plateaued via excel graphs of the data, and the core temperature at this point was also recorded. The excel graphs were constructed by copying and pasting from Lab Chart 8.0 to Microsoft Excel the data of local sweat rate and core temperature. A simple line graph was constructed independently by two individuals with core temperature as the independent variable and local sweat rate as the dependent variable. Lines of best fit were visually placed on the graph in order to pinpoint the plateau. For those values that

differed, plateau was visually assessed on Lab Chart 8.0, and a value was agreed upon by two individuals. Sweat sensitivity was determined by calculating the change in local sweat rate divided by the change in core temperature between the visually pinpointed onset and the visually pinpointed plateau.

Sweat gland activation was determined via the measurements calculated by ImageJ. Two to three circles were analyzed per time point. This was done by opening each separate image of the circles in ImageJ, using the 'find edges' option, setting the image to 8-bit grayscale by clicking '8-bit' and black and white by clicking 'make binary', and clicking 'analyze particles'. To set limits, upper and lower size limits were input via the prompted screen, which is the minimum and maximum size that is allowed for a dot to be counted. Below the limits, the boxes that were checked include: display results, clear results, exclude on edges, record starts. Also, 'outlines' was selected under the 'show' box (Gagnon et. al., 2012). Once this was complete, ImageJ generated the number of sweat glands per circle, and the average number of sweat glands activated was recorded. Sweat gland output was calculated by dividing local sweat rate of the adjacent site by sweat gland activation at each time point.

Data were assessed for outliers via Microsoft Excel. Outliers included any value that was outside two standard deviations of the mean value for each measurement. All outliers were assessed by a second individual to ensure the data were accurate before statistical procedures began.

Statistical procedures were performed with SPSS v.20.0. Skin blood flow, local sweat rate, sweat gland output, sweat gland activation, skin temperature, and core temperature were all assessed via a two-way ANOVA. This two-way ANOVA measured

the differences in the repeated measures from each time point between smokers and non-smokers. Sweat sensitivity, skin blood flow sensitivity, core temperature at sweat and skin blood flow onset, total body sweat-rate and percent body mass loss were all assessed via independent t-tests. The independent t-tests measured the difference between smokers and non-smokers at each of the points listed. Means, standard deviations, and levels of significance were all recorded. All values with a p-value of less than 0.05 were considered significant.

Chapter 4: Results

Measures of Body Temperature

No significant differences were found in any measures between smokers and non-smokers (all $p > 0.05$). In all subjects, core and skin temperature increased significantly ($p < 0.01$) from baseline to 1.5°C increase ($37.0 \pm 0.3^\circ\text{C}$ to $38.4 \pm 0.2^\circ\text{C}$ and $34.1 \pm 0.5^\circ\text{C}$ to $40.1 \pm 0.4^\circ\text{C}$, respectively). Table 1 contains core and mean skin temperature values of smokers and non-smokers for each time point of the trial.

Table 1. Measures of Thermometry

Measurement	Group	Baseline	0.5 °C	1.0 °C	1.5 °C
Core Temperature (°C)	Smokers	37.1 ± 0.2	37.4 ± 0.2	37.9 ± 0.2	38.4 ± 0.2
	Non-Smokers	37.0 ± 0.3	37.3 ± 0.3	37.8 ± 0.3	38.3 ± 0.2
Mean Skin Temperature (°C)	Smokers	34.3 ± 0.4	39.2 ± 0.4	39.9 ± 0.4	40.3 ± 0.4
	Non-Smokers	33.9 ± 0.5	38.6 ± 0.6	39.5 ± 0.4	40.0 ± 0.4

Measures of Sweat

No significant differences were found in any sweat measures between smokers and non-smokers (all $p > 0.05$). Independent of group, local sweat rate and sweat gland output increased significantly ($p < 0.01$) from baseline until core temperature increased 1.0°C (0.0 to $1.0 \pm 0.5 \text{ mg}\cdot\text{cm}^{-2}\cdot\text{min}^{-1}$, and 0.0 to $9.2 \pm 2.6 \text{ }\mu\text{g}\cdot\text{cm}^{-2}\cdot\text{min}^{-1}$, respectively). No further increases in local sweat rate and sweat gland output were observed from 1.0°C to 1.5°C. With a p-value of 0.588, sweat gland activation did not significantly

increase with heating from 0.5°C to 1.5°C (115.5 ± 27.8 to 112.0 ± 15.9 gland·cm⁻²), but did increase from baseline to 0.5°C (0.0 to 112.0 ± 15.9 glands·cm⁻²). Other notable measures of sweat were core temperature at sweat onset (smokers: 37.0 ± 0.2 °C; non-smokers: 37.0 ± 0.3 °C), sweat sensitivity (smokers: 0.9 ± 0.3 cm²/min/°C increase; non-smokers: 0.9 ± 0.3 cm²/min/°C increase), total body sweat-rate (smokers: 0.52 ± 0.24 L·hr⁻¹; non-smokers: 0.50 ± 0.18 L·hr⁻¹), and percent body mass loss (smokers: -1.5 ± 0.4 %; non-smokers: -1.5 ± 0.5 %). Table 2 contains local sweat rate, sweat gland output, and sweat gland activation values of smokers and non-smokers for each time point of the trial.

Table 2. Measures of Sweat

Measurement	Group	0.5 °C	1.0 °C	1.5 °C
Local Sweat Rate (mg·cm ⁻² ·min ⁻¹)	Smokers	1.1 ± 0.3	1.2 ± 0.2	1.0 ± 0.5
	Non-Smokers	0.9 ± 0.3	1.2 ± 0.2	1.2 ± 0.3
Sweat Gland Output (µg·cm ⁻² ·min ⁻¹)	Smokers	8.6 ± 3.4	9.6 ± 3.4	9.2 ± 2.6
	Non-Smokers	11.6 ± 9.1	14.4 ± 8.7	15.6 ± 11.6
Sweat Gland Activation (glands·cm ⁻²)	Smokers	122.5 ± 27.0	116.4 ± 25.6	117.9 ± 16.9
	Non-Smokers	110.8 ± 27.0	112.8 ± 16.2	108.1 ± 14.6

Measures of Skin Blood Flow

No significant differences were found in any measures between smokers and non-smokers (all $p > 0.05$). Independent of group, skin blood flow increased significantly ($p < 0.01$) from baseline until core temperature increased 1.0°C (19.5 ± 13.6 to 65.3 ± 19.4 % of maximum skin blood flow). No further increases in skin blood flow were observed from 1.0°C to 1.5°C. Other notable measures of skin blood flow were core

temperature at skin blood flow onset (smokers: $37.0 \pm 0.2^{\circ}\text{C}$; non-smokers: $37.0 \pm 0.3^{\circ}\text{C}$) and skin blood flow sensitivity (smokers: 32.2 ± 16.4 % of max/ $^{\circ}\text{C}$ increase; non-smokers: 39.1 ± 10.7 % of max/ $^{\circ}\text{C}$ increase). Table 3 contains skin blood flow values of smokers and non-smokers for each time point of the trial.

Table 3. Measures of Skin Blood Flow

Measurement	Group	Baseline	0.5 °C	1.0 °C	1.5 °C
Skin Blood Flow (% of max SKBF)	Smokers	21.3 ± 12.1	50.0 ± 19.5	64.7 ± 20.4	68.3 ± 18.9
	Non-Smokers	18.0 ± 15.1	48.7 ± 17.2	65.9 ± 19.1	71.0 ± 19.7

Chapter 5: Discussion

The purpose for conducting this study was to compare thermoregulation in smokers versus non-smokers during passive heat stress. The main findings from this study are that there is no difference in the body's thermoregulatory responses between smokers and non-smokers. This means that smoking does not impair or enhance the body's ability to thermoregulate during passive heat stress.

In regards to the overall effects of passive heating, responses were as expected. The hypothesis was that as core and skin temperature would steadily rise and that skin blood flow and sweating would also increase. Since core and temperature drive the responses of the body to sweat and cutaneously vasodilate (Shibasaki & Crandall, 2011), increases in local sweat rate, sweat gland output, sweat gland activation, and local sweat rate were all important outcome variables.

For sweating, it was hypothesized that the sweat response would be enhanced in smokers compared to non-smokers. Because the nicotine that is found in cigarettes may keep the sympathetic nervous system active for up to 24 hours (Kilaru, Frangos, et al., 2001), it would seem that the sweat response would be able to come on faster and that the sensitivity would be higher. However, according to Table 2, the results indicate that there are no differences between smokers and non-smokers in any aspect of the sweat response.

There are a variety of factors which may have caused this outcome in the study. The first factor to be considered is the chemicals in the cigarettes. Current literature is limited to a study of nicotine, but cigarettes contain several more chemicals than just

nicotine. Therefore, other unknown chemical changes may have been taking place in the body as well. Another factor relating to this topic is age and level of physical fitness. Both of these factors affect the way the body sweats, so differences in age and level of physical fitness may have played a role in the ability of the body to sweat more than the cigarettes effect on the sweat response. Attempts to combat this difference were made by matching age and level of physical fitness of participants. One thing that may not have been matched, however, is heat acclimatization. Heat acclimatization can cause similar changes in sweat responses (higher sweat capacity) (Fox et. al., 1964) to nicotine.

With skin blood flow, it was hypothesized that the response would be lower in smokers in comparison to non-smokers. As previously discussed, skin blood flow decreases steadily with each cigarette that is smoked (Gore & Chien, 1998). However, no differences were recorded between smokers and non-smokers in any aspect of skin blood flow. Others have shown no difference in skin blood responses between smokers and non-smokers (Meekin et. al., 2000). However, differences have been observed between light smokers and heavy smokers. This may be a result of heavy smokers having a tolerance to nicotine (Meekin et. al., 2000).

The main effects of nicotine on skin blood flow is that it allows for a continual release of norepinephrine, which in turn allows for a continual increase in cutaneous vasoconstriction, therefore decreasing skin blood flow (Kool et. al., 1993). However, passive heating may have offset the decreases generally seen from nicotine. High skin temperature during passive heating leads to massive vasodilation. Thus the effects of nicotine on vasoconstriction may have been overridden/overwhelmed. Since a

difference in smokers and non-smokers was not observed in this study, there may be a variety of factors to be considered. One factor to be considered again is other chemicals existing in the cigarettes. Another factor to be looked at is the design of the study. In one study looking at the differences in cutaneous blood flow during heating, it was found that age has a larger effect than smoking on cutaneous blood flow responses (Avery et. al., 2009). At the same time, this study did see differences in cutaneous blood flow between smokers and non-smokers, yet the design of the study was different. Heating was applied in the aforementioned study using only a laser on the forearm (Avery et. al., 2009), yet the current study used passive heat stress over the entire body, not just a laser on the forearm.

In conclusion, the overall finding of the study is that there are no differences in the body's thermoregulatory responses between smokers and non-smokers. Implications of the study indicate that cigarettes, particularly the nicotine in cigarettes, does not impair or enhance the body's ability to thermoregulate during passive heat stress.

Further research should be conducted on younger smokers where is age range is not so much a factor in the study. Further research should also be conducted in relation to other chemicals which exist in cigarettes, and also comparing light and heavy smokers.

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References

1. **Amano, T., Koga, S., Inoue, Y., Nishiyasu, T., Kondo, N.** (2013). Characteristics of sweating responses and peripheral sweat gland function during passive heating in sprinters. *Eur J Appl Physiol*, 113, 2067-2075.
2. **Avery, M., Voegell, D., Byrne, C., Simpson, D., Clough, G.** (2009). Age and cigarette smoking are independently associated with the cutaneous vascular response to local warming. *Informa UK Ltd*, 16: 725-734.
3. **Cryer P., Haymond M., Santiago J., et al.** (1976). Norepinephrine and epinephrine release and adrenergic mediation of smoking associated hemodynamic and metabolic events. *N Engl J Med*, 295, 573.
4. **Fox, R., Goldsmith, R., Hampton, I., Lewis, H.** (1964). The nature of the increase in sweating capacity produced by heat acclimatization. *J. Physiol*, 171, 368-376.
5. **Fujii, N., Reinke, M., Brunt, V., Minson, C.** (2012). Impaired acetylcholine-induced cutaneous vasodilation in young smokers: roles of nitric oxide and prostanoids. *Am J Physiol Heart Circ Physiol*, 304, H667-H673.
6. **Gagnon, D., Ganio, M., Lucas, R., Pearson, J., Crandall, C., Kenny, G.** (2012). Modified iodine-paper technique for the standardized determination of sweat gland activation. *J Appl Physiol*, 112(8), 1419-1425.
7. **Gore, A., & Chien, Y.** (1998). The Nicotine Transdermal System. *Clinics in Dermatology*, 16(5), 599-615.
8. **Gourlay S., & Benowitz N.** (1997). Arteriovenous differences in plasma concentration of nicotine and catecholamines and related cardiovascular effects

after smoking, nicotine nasal spray, and intravenous nicotine. *Clin Pharmacol Ther*, 62, 453.

9. **Holloway, G. and Watkins, D.** (1977). Laser Doppler measurement of cutaneous blood flow. *J. Invest Dermatol*, 69(3), 306-9.
10. **Inoue, Y., & Shibasaki, M.** (1996). Regional differences in age-related decrements of the cutaneous vascular and sweating responses to passive heating. *Eur J Appl Physiol*, 74, 78-84.
11. **Inoue, Y., Shibasaki, M., Hirata, K., Araki, T.** (1998). Relationship between skin blood flow and sweating rate, and age related regional differences. *Eur J Appl Physiol*, 79, 17-23.
12. **Kellog, D.W., Pergola, P.E., Piest, K.L., Kosiba, W.A., Crandall, C.G., Grossmann, M., Johnson, J.M.** (1995). Cutaneous active vasodilation in humans is mediated by cholinergic nerve cotransmission. *Circulation Research*, 77, 1222-1228
13. **Kenney, W.L., & Johnson, J.M.** (1992). Control of skin blood flow during exercise. *Official Journal of the American College of Sports Medicine*, 24(3), 303-312.
14. **Kenney, W.L., Morgan, A.L., Farquhar, W.B., Brooks, E.M., Pierzga, J.M., Derr, J.A.** (1997). Decreased active vasodilator sensitivity in aged skin. *Am J Physiol*, 272, H1609-1614.
15. **Kilaru, S., Frangos, S., Chem, A., Gortler, D., Dhadwal, A., Araim, O., et al.** (2001). Nicotine: A Review of Its Role in Atherosclerosis. *American College of Surgeons*, 193(5), 538-546.

16. **Kool, M., Hoeks, Al, Boudier, H., Reneman, R.** (1993). Short and long term effects of smoking on arterial wall properties in habitual smokers. *JACC*, 22(7), 1881-1886.
17. **Meekin, T., Wilson, R., Scott, D., Ide, M., Palmer, R.** (2000). Laser Doppler flowmeter measurement of relative gingival and forehead skin blood flow in light and heavy smokers during and after smoking. *J Clin Periodontal*, 27, 236-242.
18. **Mundel, T., Jones, D.** (2006). Effect of transdermal nicotine administration on exercise endurance in men. *Exp Physiol*, 91(4), 705-713.
19. **Savard GK, Nielsen B, Laszczynska J, Larsen BE, Saltin B.** (1985). Muscle blood flow is not reduced in humans during moderate exercise and heat stress. *J Appl Physiol*, 64(2), 649-57.
20. **Shibasaki, M., & Crandall, C.** (2010). Mechanisms And Controllers Of Eccrine Sweating In Humans. *Frontiers in Bioscience*, S2(1), 685-696.
21. **Shibasaki, M., Wilson, T., Crandall, C.** (2006). Neural control and mechanisms of eccrine sweating during heat stress and exercise. *J. Appl Physiol*, 100, 1692-1701.
22. **Smith, C., Kenney, W., Alexander, L.** (2013). Regional relation between skin blood flow and sweating to passive heating and local administration of acetylcholine in young, healthy humans. *Am J Physiol Regul Integr Comp Physiol*, 304, R566-R573.
23. **Sorensen, L., Jorgensen, S., Petersen, L., Hemmingsen, U., Bulow, J., Loft, S., Gottrup, F.** (2009). Acute effects of nicotine and smoking on blood flow,

tissue oxygen, and aerobic metabolism of the skin and subcutis. *Journal of Surgical Research*, 152, 224-230.

24. **Taylor., & Machado-Moreira.** (2013). Regional variations in transepidermal water loss, eccrine sweat gland density, sweat secretion rates and electrolyte composition in resting and exercising humans. *Extreme Physiology & Medicine*, 2(4), 1-29.