Undesirable Cardiovascular Effects of Hot Drinks

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Abstract
Various estimates suggest that 80-90% of adults in the U.S. and elsewhere consume caffeinated hot coffee. For most nations, no one knows at what ages this habit begins but some suggest as early as childhood (e.g. 4-6 years of age, personal communications). In this physiological investigation college-age young single adults served as volunteer subjects. On separate occasions each consumed approximately 12-16 ounces of hot, caffeinated coffee and equal volumes of hot tap water containing no drugs or other known, harmful contaminants. Data were collected continuously, both while consuming the hot drinks and for 60 minutes after. Data included a standard limb lead electrocardiogram (ECG), estimates of systemic arterial systolic and diastolic blood pressures, cardiac sounds registered from the brachial artery, and estimates of blood flow in a finger (pulse plethysmography). A physiological, cardiovascular effects were seen immediately upon consuming the beverages and for at least 60 minutes after (i.e. changes in the ECG, heart rate, and peripheral blood flow). These effects could be divided in two, those due to temperature and others caused by caffeine. We conclude that hot, caffeinated coffee has previously-unreported cardiovascular effects that might be harmful. We also conclude that more physiological and pharmacological investigations are needed, especially in light of the confusing and voluminous literature for behavioral, epidemiological, meta-analytical, nutritional, and social effects of coffee.

Keywords
Wandering baselines; Tachycardia; Vasoconstriction; Physiological

Introduction
Caffeinated hot coffee is the world’s leading drug of choice [1-4]. It is estimated that in the U.S. and Europe at least ninety per cent of the adult populations consume such beverages several times each day [4,5]. It is also known that consumers prefer their hot coffee to be in the range of 50-60°C (i.e. as hot as 140°F; 6-8). The high end of this range of temperatures of liquid beverages is dangerously hot. If such a drink is poured on the exposed skin it causes full-thickness, third degree burns within 5 seconds [6-8]. These are the kinds of burns that produce permanent damage and scarring for life [9,10]. The prudence of consuming hot coffee and other hot drinks at such temperatures is questionable, especially when children and adolescents are involved.

All hot coffees and teas contain a lengthy list of known and unknown (thus uninvestigated) solutes [11,12]. They, and so-called ‘decaffeinated varieties’ also contain methylxanthines. Methylxanthines are purine derivatives whose ‘class representative’ is caffeine. But, there are other methylxanthines in coffee as well. All such compounds have multiple biochemical, pharmacological, physiological, and toxicological effects on human cells, tissues, organs and organ systems [13]. They can also interact with other drugs in a potentially-lethal manner [14].

Most methylxanthines are adenosine receptor antagonists [15-17]. To understand why this is important one needs to know the physiology and pharmacology of adenosine [18-20]. Adenosine is a ubiquitous physiological regulator (e.g. in the coronary and cerebral circulatory systems) [15-20]. Methylxanthines are also phosphodiesterase inhibitors [21-23]. Phosphodiesterases are a family of enzymes importantly involved in second messenger signaling, e.g. the cAMP system [24-26]. There are other effects of methylxanthines but they are too numerous to be highlighted here.

Because of the abundance of confusing and contradictory literature (e.g. behavioral, epidemiological, meta-analytical, nutritional and social), coupled with the paucity of physiological and pharmacological reports, we decided to do a simple physiological investigation of the potential cardiovascular effects of hot drinks. We hope our report will stimulate other biomedical and life scientists to conduct similar experiments.

Methods
College-age young single adults enrolled in Physiology courses at Rutgers University were the experimental subjects. They ranged in ages from 18-22 years, were male
and female, and came from a wide-variety of cultural and ethnic backgrounds. Most were enrolled in Experimental Physiology (a Byrne Family Freshman Seminartaught in spring semesters), Systems Physiology Lecture and Systems Physiology Laboratory (separate courses offered to juniors and seniors in both academic semesters), or Advanced Physiology (taught mainly to majors in the Department of Cell Biology and Neuroscience in all semesters).

On days of experimentation subjects arrived between 9 a.m. and 2 p.m. with their favorite hot coffees in hand (e.g. Starbucks, Duncan Donuts). Volumes ranged between 12-16 ounces (e.g. ~350-450 mL) and contained ~250-350 mg caffeine (requested by subjects and confirmed by vendors). While the drinks were warmed to about 52-54°C (laboratory heating plates) subjects were instrumented for continuous monitoring of cardiovascular physiological variables.

Instrumentation included a blood pressure cuff placed on the upper left arm. The cuff was attached to a pressure transducer (M17069, AD Instruments, Colorado Springs, CO) and to a mercury manometer so systemic arterial pressures could be monitored. After palpation a cardiomicrophone was placed over the left brachial artery (antecubital fossa) for continuous monitoring of arterial sounds (model MLT201, AD Instruments). Sounds could subsequently be correlated with pulsatile arterial blood pressure when the cuff was inflated/deflated. Cardiomicrophones were secured in place using Tegaderm Film (1624W, 3M Healthcare, St. Paul, MN). On the same arm a pulse plethysmograph transducer (modelTN1012/ST, ADInstruments) was secured to the distal segment of the index or middle fingers, whichever presented the greatest estimated surface area. It measures changes in finger volume during each cardiac cycle. We converted these volumetric measurements to estimates of finger blood flow by multiplying by heart rate (e.g. 72 cpm * 50 ul per pulse = 3.6 mL/min). The finger plethysmograph was secured with plastic surgical tape and was used to estimate changes in finger volume (an index of volumetric blood flow which varies throughout the cardiac cycle).

A standard limb lead Electrocardiogram (ECG) was obtained by attaching electrodes to the left and right wrists and the left ankle (LLI). This was used only to estimate heart rate (HR, cycles per minute, cpm). No other analysis of the ECG was made in this exercise (e.g. no estimates of intervals, segments or amplitudes of waves).

Finally a thermistor (Thermalert, model TH-8, Physitemp, Clifton, NJ) was attached to the instrumented finger (plethysmograph transducer) one segment proximal to the transducer. This was secured in place with surgical tape and could be used to monitor skin temperature near the plethysmograph. A second thermistor was positioned to monitor room temperature near the instrumented subject. All data were continuously collected using a data acquisition system (Power Lab, model 8/35, 8-channel A-D converter, running Lab Chart software, v8, MLSS10/8, AD Instruments) connected to a desktop computer (HP Compaq 8200 Elite).

Following instrumentation subjects were seated comfortably on an examination table with a tiltable backrest. The angle of the backrest was adjusted to the subject’s preferences. Subjects were then asked to sit quietly (no talking, no movements except respiration) for fifteen minutes while monitored cardiovascular variables achieved physiological steady state conditions. Once subjects were in the cardiovascular steady state, the pressure cuff was inflated (forearm and hand blood flow occluded) and cardiomicrophone sounds and pulsatile blood flow to the finger were transiently diminished/eliminated. Thirty seconds later the cuff was deflated and flow (sounds) was restored to the previously-ischemic forearm and hand. Data collected immediately before the period of inflation/deflation were considered baseline.

Caffeinated hot coffee

After collection of baseline data a research assistant retrieved the hot coffee from the heating plate, placed a large-bore drinking straw into the container, and brought the drink to the instrumented subject. To avoid arm/body movements and disturbances of the sensitive EEG electrodes, the research assistant held the drink while the subject drank through the large-bore straw (after carefully determining that the temperature was not injurious). When the drink was finished a timer was set so that blood pressure data could be collected at 15-minute intervals. Otherwise, all other data (ECG, heart rate, blood flow, skin temperature, room temperature) were monitored continuously both during drinking (2-3 minutes) and after.

When the experiment with hot coffee was completed, each subject returned a few days (weeks) later and repeated the exercise, this time consuming hot water in place of hot coffee (same volumes and temperatures). All other aspects of the dual exercises were the same (e.g. instrumentation, timing of data collection, position on examination table, etc.)

Statistical analysis

The experiment, including statistical design, was developed a priori. Analysis of Variance (ANova, completely random design, equal sample sizes) was used to identify initial variability between baseline and post-coffee data (e.g. 15, 30, 60 minutes), and between hot coffee and hot water. Tukey’s w-procedure and Least Significance Differences were used to compare means. All data are reported as means plus or minus one standard error of the mean. A probability of p<0.05 was used to identify statistically significant differences in means.

Results

General experimental outcomes-Figure 1 shows a horizontally-compressed view of an entire experiment for hot coffee (for easy perusal and quick reference, see Figure 1 legend for details). Note particularly the differences in finger plethysmography (volume, blood flow). Compared to baseline, finger plethysmography routinely increased while consuming hot drinks (more for coffee, but decreased thereafter (less for hot water).

Room and skin temperatures-Room temperature varied little during the experiments (21-23°C, hot coffee and hot water). Conversely, skin temperature rose with both drinks from 31 ± 1 to 36 ± 2°C (p<0.05) within 10-20 minutes after consumption of hot drinks. It returned to baseline values by 45-60 minutes.

Finger volume-As hot coffee was consumed then stored in the stomach (about 0-10 minutes) pulsatile finger volumes increased significantly from 30 ± 12 µL to 108 ± 12 µL per cardiac cycle (p<0.05) (Figure 2). This change peaked about 15-20 minutes after completing the drinks. Thirty to 60 minutes after drinking hot coffee finger volumes were 8 ± 3 and 6 ± 2 µL, respectively, or about one fifth baseline values (p<0.05).

With hot water finger volumes increased from 33 ± 15 µL to 87 ± 9 µL per cardiac cycle (p<0.05). The maximum finger volume was significantly less than seen with hot coffee. Finger volume also decreased steadily and significantly thereafter. For example, at 60 minute’s finger volume was 14 ± 2µL per cardiac cycle or about one half of its baseline value. The volumes at 30 and 60 minutes were significantly (p<0.05) greater than seen with hot coffee. Reactive hyperemia was also significantly reduced by hot coffee vs. hot water (Figure 3).

ECG isoelectric line and heart rate-For several minutes both hot coffee and hot water decreased stability of the ECG isoelectric line. During this period isoelectric lines wandered consistently in all subjects (Figure 4, row 6; see row 3 for pre-coffee, stable isoelectric line). Isoelectric lines wandered cyclically in both a positive and a negative direction (more in the positive direction, i.e. towards depolarization).

ECG waveform amplitudes and morphologies were also regularly distorted during this period of time. For example, one of the most striking observations were the high amplitude, tenting T-waves during baseline conditions (Figure 5). The subject whose data are featured in Figure 5 had been consuming caffeinated hot coffee since she was about age 5 years old.

Other observations included occasional ventricular premature beats (VPBs), ventricular salvos (VS), dual-peeked R and T waves, and...
Figure 1: Compressed view (horizontally) of an entire experiment. Panels 1-4 (top to bottom): cuff pressure, cardiomicrophone, plethysmograph, ECG. Note marked peripheral vasodilation (channel 3) shortly after consuming coffee, and sustained vasoconstriction between about 20-60 minutes after coffee (~450 ml, 330 mg caffeine, 52-54°C).

Figure 2: Time-dependent effects of hot coffee vs. hot water on changes in finger plethysmography (cyclic, volumetric blood flow during repetitive cardiac cycles). Note the significant (p<0.05) differences in maximum responses shortly after consuming the drinks, and at 30 and 60 minutes post-consumption of both. Compare with Figure 5. Asterisks indicate significant differences when compared with corresponding histograms in coffee group.

Figure 3: Peak reactive hyperemia following 30 sec periods of zero-flow ischemia in the presence of hot coffee and hot water. Note the significant (p<0.05) differences at 30 and 60 minutes post-consumption of these hot beverages. Asterisks indicate significant differences when compared with corresponding histograms in water group.
Figure 4: Baseline ECG (panel 3 top) vs. ECG obtained while a college-age young woman was drinking hot coffee (~450 mL, 52-55°C, 250 mg caffeine, panel 6 bottom). Note the wandering baseline (isoelectric line) shortly after she began drinking the hot coffee.

Figure 5: Standard limb lead ECG of college-age young woman who had been consuming coffee since about age five. Note the high amplitude T waves (bottom panel). Middle and top panels are finger volume (plethysmograph on index finger) and brachial arterial sounds (antecubital fossa), respectively.

Figure 6: This subject experienced ventricular premature beats (VPBs) and/or ventricular salvos (VS) shortly after consuming hot coffee (bottom record, center of row 6, note the several typical ECG cycles before and after the bout of arrhythmias; vertical axis compressed for emphasis). Top record (rows 1-3) was obtained in the same subject during pre-coffee baseline conditions.
Peripheral vasodilation and blockade of vascular resistance leading to a decrease in core body temperature (e.g. moisture evaporation at the skin (among other considerations) over-drinks, thermoregulatory heat loss the increased heat load, caused by consuming large volumes of hot beverages). As peripheral vasodilation occurred (increase in finger volume) we observed 10-20 minutes after consumption of either hot drink. As peripheral vasodilation occurred (increase in finger volume) we observed 10-20 minutes after consumption of hot coffee (but not hot water). They described muscle tremors in the arms, legs, and thorax (but not with hot water).

Discussion

Changes in temperature-We measured only room temperature and temperature of the skin in the instrumented arm/hand. We did not monitor temperature in any other body location. Clearly, however, there were at least two phases of changes in temperature with the consumption of hot drinks. First, as hot coffee (hot water) was consumed and stored (stomach) skin temperature increased. The increments in skin temperature are most reasonably explained on the basis of heat gain/storage transiently exceeding heat loss, with accompanying rise in core body temperature. Adding a large volume (350-450 mL) of hot liquid (52-54°C as it was consumed) to a stomach at 38°C will temporarily elevate stomach, abdominal and even general body temperature [27,28]. In response to elevated body temperature, mammalian thermoregulatory mechanisms designed to eliminate heat are activated [27,28]. This would explain the peripheral vasodilation (increase in finger volume) we observed 10-20 minutes after consumption of either hot drink. As peripheral vasodilation occurred in nonapical skin pads of the fingertips and elsewhere, relaxed microcirculatory vasculature (primarily precapillary arterioles but possibly precapillary sphincters, meta-arterioles and even postcapillary venules) would have accommodated an increased volume of flowing warm blood to enhance loss of excess heat [29,30].

Within 10-20 minutes after consuming hot coffee, subjects regularly complained of 'feeling warm'. By 20-30 minutes they were cooling down or even cold. Similar comments were not made by subjects consuming hot water. The decrease in finger blood flow at 30-60 minutes can be explained, with other considerations, on the basis of compensatory thermoregulation. It is likely that with the increased heat load, caused by consuming large volumes of hot drinks, thermoregulatory heat loss via peripheral vasodilation and moisture evaporation at the skin (among other considerations) over-compensated leading to a decrease in core body temperature (e.g. subjects complaining of cooling off, being cold during this period of time). This could have led to neurogenically-mediated peripheral vasoconstriction and heat conservation [29,30]. However, there are additional/alternative explanations.

Caffeine-mediated vasoconstriction-Following consumption of coffee, caffeine would have been absorbed into the systemic circulation. After consuming hot drinks it would take several minutes, perhaps 10-30, for the following sequence of events to unfold: a) transfer of coffee and caffeine from the stomach to the small intestine, b) absorption of coffee and caffeine into the systemic circulatory system and delivery to the peripheral microvasculature, c) distribution and binding of caffeine to adenosine receptors in the microvasculature and d) subsequent biochemical/physiological responses in the contracting vascular smooth muscle cells of resistance arterioles.

As mentioned above, caffeine and other methylxanthines are potent and efficacious adenosine receptor antagonists [15-17,21,23]. Adenosine is produced ubiquitously by the body [31-33]. It is a particularly important vasodilator of both coronary [17,33] and cerebral resistance arteries [34]. Naturally-occurring adenosine is also a vasodilator in skeletal muscle and subcutaneous fat [35-37]. Adenosine receptors are located primarily on the vascular smooth muscle cell membranes of arterioles and not in capillaries (the latter lack vascular smooth muscle cells and have no vasomotor activity). Thus, one reasonable, physiological explanation for the reduction in finger blood flow between 30-60 minutes post-coffee, is caffeine-mediated, peripheral vasoconstriction via blockade of vascular adenosine receptors. Of course it is most reasonable to invoke thermoregulatory mechanisms coupled with caffeine-mediated vasoconstriction to account for the reductions in finger volume. This is supported by the fact that hot water (no caffeine) also led to peripheral vasomotor constriction. However, the decrease in flow was significantly less than that see with hot coffee.

Caffeine’s other untoward effects-As also mentioned above, all methylxanthines tested are inhibitors of phosphodiesterases (PDE). Phosphodiesterases are enzymes that, among other actions, convert nucleotides such as cAMP to non-cyclic compounds [21-24,38]. Non-cyclic nucleotides like ATP, ADP and AMP are then exposed to nucleosideases and dephosphorylases for further modification. Cyclic nucleotides (e.g. cAMP, cGMP) are important second messengers in cell-signaling. Thus, whatever signaling pathways PDEs regulate, caffeine has the potential to disrupt them.

Wandering baselines and arrhythmias

The mediastinum is a region of the thorax where the heart, great blood vessels, esophagus and other tissues lie in close proximity. Here the posterior, apical wall of the left ventricle and anterior wall of the esophagus can come in contact. The apex of the left ventricle and cardia/fundus of the stomach also lie in close proximity and are separated only by the thin, membranous diaphragm [39].
The mediastinum is also a region through which both motor and sensory, autonomic and enteric nerves pass. Such nerves enter and traverse the mediastinum in walls of the esophagus and trachea [40]. Moreover, the delicate, sensitive specialized cardiac conduction system begins at the sinoatrial (SA) node in the posterior wall of the right atrial appendage, spreads to the right and left atria, converges on the atrioventricular (AV) node, then passes into the ventricles [41]. The human cardiac conduction system is innervated by both divisions of the autonomic nervous system which nerves are carried to the heart in walls of the great blood vessels, the esophagus and other tissues.

All regions and cells of the cardiac conduction system are heat sensitive and respond to changes in temperature [42,43]. For example, increasing temperature increases automaticity and pacemaker potentials in slow-response cells of the SA node. This can and does increase heart rate [42,43]. The opposite occurs with cold temperatures. It is conceivable, therefore, that as hot drinks pass through the esophagus and are transiently stored in the stomach, their temperatures influence transmembrane potentials in cells of: a) the cardiac conduction system, b) autonomic nerve tracts innervating the cardiac conduction system, and c) other motor/sensory nerves, including enteric neurons of the esophagus and stomach. Additional work is needed to refute or support the above reasoning.

**Caffeine and peripheral vasoconstriction**

Caffeinated hot coffee routinely caused peripheral vasoconstriction beginning as early as 15-20 minutes after its consumption. The decrements in finger volume were highly significant (p<0.05) when compared with corresponding baseline. More physiological investigation is needed to help clarify the effects of caffeine on the human cardiovascular system.

There are several limitations in our experimental design. For example, had this experiment not been conducted using small, formal university courses (low enrollments where students were required to participate for a grade), a double-blind, random-selection design example, had this experiment not been conducted using small, formal university courses (low enrollments where students were required to participate for a grade), a double-blind, random-selection design was selected from the observed cutaneous vasoconstriction. Moreover, drinking a large quantity of fluid in a relatively short period of time has been shown to increase sympathetic nerve activity. More physiological investigation is needed to help clarify the effects of caffeine on the human cardiovascular system.

**Conclusions and limitations**

Despite the importance of caffeine/adenosine-receptor interactions, we cannot rule out contributions of hemodynamic, neuroregulatory and/or thermoregulatory mechanisms to the vasoconstrictor response. After all vasoconstriction was seen, even though to a significantly lesser extent, when hot water replaced hot coffee. Ingestion of caffeine also activates the sympathetic nervous system, which could have contributed to the observed cutaneous vasoconstriction. Moreover, drinking a large quantity of fluid in a relatively short period of time has been shown to increase sympathetic nerve activity. More physiological investigation is needed to help clarify the effects of caffeine on the human cardiovascular system.

There are several limitations in our experimental design. For example, had this experiment not been conducted using small, formal university courses (low enrollments where students were required to participate for a grade), a double-blind, random-selection design would have been preferred. Moreover, group demographics should be collected in future experiments, including coffee-drinking habits (e.g. daily/weekly caffeine consumption, etc.).

**References**


