

Effect of Decaffeinated Versus Regular Coffee on Blood Pressure

A 12-Week, Double-Blind Trial

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The effect of decaffeinated versus regular coffee on blood pressure and heart rate was investigated. In a randomized double-blind, crossover trial, 45 healthy volunteers (23 women and 22 men, 25–45 years old) with a habitual intake of 4–6 cups coffee/day received 5 cups of regular coffee each day for a period of 6 weeks, and 5 cups of decaffeinated coffee for the next 6 weeks or vice versa. The background diet was kept constant. The total amount of caffeine ingested was 40 mg during the decaffeinated coffee period and 445 mg during the regular coffee period. Use of decaffeinated coffee led to a significant but small decrease in systolic (mean \pm SEM, -1.5 ± 0.4 mm Hg; $p=0.002$) and diastolic (-1.0 ± 0.4 mm Hg; $p=0.017$) ambulant blood pressure and to a small increase in ambulant heart rate ($+1.3 \pm 0.6$ beats/min; $p=0.031$). Individual differences in rate of caffeine metabolism did not explain differences in long-term response of blood pressure to caffeine. We conclude that in normotensive adults replacement of regular by decaffeinated coffee leads to a real but small fall in blood pressure. However, it remains to be established whether a mass switch from regular to decaffeinated coffee would significantly reduce the total incidence of hypertension-related disorders. (*Hypertension* 1989;14:563–569)

Coffee is the most widely used stimulant in Western society. In the Netherlands, 94% of adults drink at least 1 cup/day, and the per capita intake is 4.5 cups/day.¹ An increasing proportion of consumers is switching from regular to decaffeinated coffee. In the Netherlands, the market share of decaffeinated coffee grew from 2% in 1984 to 4% in 1987. In the United States, the proportion is already 20%.² The switch is motivated partly by the well-documented negative effects of caffeine on the quality of sleep and partly by other purported negative effects, including those on the cardiovascular system. However, surprisingly little is known about the actual long-term effect of switching to decaffeinated coffee and how this switch will affect risk factors for coronary heart disease.

Epidemiological surveys on the relation between coffee consumption and blood pressure have yielded

contradictory findings.^{3–5} Controlled trials showed that in subjects who have abstained from caffeine for a number of days blood pressure rises acutely after a caffeine load. The extent of this acute pressor effect of caffeine depends on the amount and frequency of previous caffeine intake and on the rate of caffeine metabolism; subjects with a high coffee intake appear to be less sensitive to the pressure-elevating effect of caffeine.⁶ This was confirmed by one experiment that showed no effect of caffeine consumption on blood pressure after 4 weeks⁷; however, the diet was not controlled, and the power of this trial was small.

In the present study, we compared the effect of regular and decaffeinated filter coffee on blood pressure in a randomized, controlled trial with healthy volunteers.

Subjects and Methods

Design

Our null hypothesis was that consumption of decaffeinated instead of regular coffee for 5–6 weeks would not affect blood pressure. The alternative hypothesis was that decaffeinated coffee would lower blood pressure. We decided that the trial should have a statistical power of 85% to detect an effect on blood pressure of 2 mm Hg at the $p < 0.05$ confidence level (two-tailed test). Calculations

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showed that we would need 46 subjects to meet these objectives. In addition, we hypothesized that any effect of caffeine on blood pressure would be inversely correlated with the fasting serum caffeine concentration after overnight abstinence from coffee. This level reflects the individual caffeine clearance rate; subjects with low fasting levels may have a higher rate of caffeine metabolism and may therefore be more susceptible to the pressor effect of caffeine.⁸

The study comprised a randomized double-blind, crossover trial with a 6-week study period on regular filter coffee followed by a 6-week period on decaffeinated filter coffee or vice versa. Subjects were randomized over the two treatment orders (caf→decaf vs. decaf→caf, where caf is regular filter coffee and decaf is decaffeinated filter coffee) as follows. After admission into the study, subjects were grouped by sex. Both groups were then divided into a subgroup of "high" (median and above median) and one of "low" (less than median) blood pressure. Within each cell, subjects were grouped into pairs of similar age, and one member of each pair was randomly allocated to each treatment sequence.

Coffee cartons, each containing 10 packages (see below), were labeled by two persons not involved in the trial. The label carried the subject's name and number and the week of consumption. The project leader (M.vD.), the research dietitians, and all other persons involved in the study, as well as the subjects, were blind to the kind of coffee consumed. In addition, subjects were blind to the study design; they did not know if and how often they were switched between types of coffee.

During the trial, the subjects consumed 2 cups of either regular or decaffeinated coffee before noon, 1 in the afternoon, and 2 in the evening. Consumption of tea and other caffeine-containing products and drugs were prohibited with the exception of chocolate, which was allowed in amounts containing up to 25 mg caffeine/day. Once a week the subjects visited a research dietitian, who checked food intake by a dietary recall, weighed the subject, gave out coffee cartons for the next week, and collected empty packages from the previous week. Subjects recorded in diaries any signs of illness, medications used, amount of chocolate eaten, and any deviation in coffee consumption. Twice-weekly contacts with the investigators, a weekly newsletter, and coverage of the progress of the trial by the local media helped to keep up subjects' morale and motivation.

Subjects

The subjects were volunteers from the general population living in or near Nijmegen, a mixed industrial/college town of 150,000 inhabitants in the eastern part of the Netherlands. They were recruited via publicity in local newspapers and through posters in university buildings. After they had been thoroughly informed about the purpose and protocol of the study, 150 subjects declared themselves eager to participate and filled out a questionnaire.

TABLE 1. Baseline Characteristics of the 45 Participants

Characteristics	Mean±SD	Range
Age (yr)	38±7	25-45
Body mass index (kg/m ²)	23.2±4.0	18.8-31.3
Blood pressure (mm Hg)		
Systolic	124±13	102-138
Diastolic	76±13	62-90

Baseline characteristics were taken 30 days before the start of the experiment. Blood pressures were from a casual reading during pre-experimental physical examination.

Of these 150, 60 subjects (31 men and 29 women) met our criteria for initial eligibility, which were: age between 17 and 45 years, apparently healthy, abstinence from smoking for the past year, no use of medication, not on a prescribed diet, no use of oral contraceptives, not pregnant, not working night-shifts, and a habitual coffee consumption of 4-6 cups/day. These 60 then underwent a physical and laboratory examination and kept a 3-day dietary record. Fifteen proved ineligible; the reasons were serum cholesterol more than 6.7 mmol/l (260 mg/dl) ($n=9$), various medical reasons ($n=3$), living too far from the clinic ($n=2$), or job change ($n=1$). The remaining 45 subjects (23 women and 22 men) were admitted to the study. Ten were employed by the university, five by other educational institutions, two by the municipality, and 12 by other employers. Another five were students, 10 were housewives, and one was unemployed. Table 1 provides their baseline characteristics.

The protocol for the study, which had been approved by the local ethical committee, was explained to the volunteers, and all subjects gave their written informed consent. Subjects were asked to maintain their usual pattern of activity and to keep up a stable body weight.

Coffee

The coffee used was similar to the most popular types of regular and decaffeinated coffee sold in the Netherlands, but it was processed and packaged especially for the trial. The coffee was supplied in blank, single-cup disposable packages that contained (mean±SD) 5.4±0.1 g coffee for the regular and 5.1±0.2 g for the decaffeinated coffee; the difference was caused by the extraction of caffeine with dichloromethane. Each package fitted into the bottom of a plastic holder that could be placed on top of a cup or beaker. Hot water (110-150 ml) was poured into the holder, and it then dripped through the coffee package and its filter paper bottom into the cup. The regular and decaffeinated coffee were similar in taste. We prepared 60 cups of coffee from random packs and analyzed them in duplicate for caffeine. The mean amount±SD was 83.5±12.6 mg/cup for the regular and 3.1±0.3 mg/cup for the decaffeinated coffee. The subjects recorded in their diary each day what kind of coffee they thought they were receiving.

Blood Pressure Measurements

For the blood pressure measurements, an automatic blood pressure device was used (oscillometric method, Takeda Medical UA-751, Adquiment Medical BV, Rotterdam, The Netherlands). Mean difference \pm SD between a standard sphygmomanometer and this automatic blood pressure device, when used in parallel in routine measurements in our outpatient clinic, was 4.2 ± 5.1 mm Hg for systolic and 2.5 ± 4.3 mm Hg for diastolic blood pressure, without apparent drift in time (206 measurements over a 3-month period). Subjects measured their ambulant blood pressure and heart rate at 7:30 and 10:00 AM and at 1:00, 5:30, and 10:30 PM 1 day per week. Each of the 5 weekdays and 1 weekend day was used once in each period, in random order. Each subject used the same blood pressure device at all times. After a 5-minute rest, four measurements were recorded per session in a sitting position. Blood pressure, heart rate, date, and time were printed automatically, and the printed output was collected and checked by the dietitian at each weekly visit. The first measurement of each session was dropped and the other three were averaged. The mean ambulant blood pressure was calculated for each measurement day as the mean of the five session means. Mean arterial pressure was calculated as $(\text{systolic} + 2 \times \text{diastolic blood pressure})/3$.

At the end of each treatment period, blood pressure was also measured at our hypertension clinic with a noninvasive automatic device, the Arteriosonde 1225 (Roche, Medical Electronic Division, Orangeburg, New Jersey). The measurements took place 40 minutes after subjects had consumed their first morning cup of coffee. For this 20-minute session, the subjects remained in a sitting position in a quiet room in the physiological laboratory, and a reading was taken every 2 minutes. All readings except the first one were averaged to give the hospital blood pressure.

Blood Sampling and Analysis

Fasting blood samples were obtained on days 16, 35, and 42 of each treatment period. An additional sample was collected on day 22 at midday to check for caffeine. Serum was obtained by low-speed centrifugation within 1.5 hour and then stored at -80° C. Serum caffeine was measured by reversed-phase, high-performance liquid chromatography.⁹

Statistical Analysis

The fasting serum caffeine levels, the blood pressures and heart rates during consumption of regular or decaffeinated coffee, as well as the differences in these variables between the two treatment periods were all normally distributed as indicated by the Shapiro Wilk statistic.¹⁰

An exact test based on a *t* distribution and on pooled estimates of variance¹¹ indicated that both carry-over and period effects were absent. The *t*

values of the estimates ranged from -1.18 ($p=0.24$) for a period effect for ambulant heart rate, to $+0.56$ ($p=0.58$) for a period effect for diastolic ambulant blood pressure. Treatment effects were calculated for each subject as the change from the means of weeks 5 and 6 of the decaffeinated to those of the regular coffee period; treatment effects were examined by a two-sided *t* test.¹¹

Results

Compliance and Blinding

All 45 subjects completed the experiment successfully. Both the diaries and frequent personal interviews indicated excellent adherence to the protocol. Empty packings were returned by the subjects for 99.7% of all 18,900 coffee packages distributed. The mean \pm SD of the caffeine concentration in serum collected on the 22nd day of each period between noon and 2:00 PM was 3.2 ± 1.5 mg/l (range 0.3–7.0) when subjects consumed regular and 0.2 ± 0.3 mg/l (range 0.0–1.2) when subjects consumed decaffeinated coffee. One subject had one value over 1.0 on decaffeinated coffee, and one other subject had one value below 1.0 on regular coffee. Both subjects showed levels in the expected range at the seven other blood sampling occasions; we therefore ascribed the two outliers to chance. Subjects apparently remained unable to tell which type of coffee they received. According to the diaries, when subjects were receiving regular coffee, they correctly identified the type of coffee on 54% of the days, they were wrong on 19% of the days, and they could not tell on 27% of the days. When subjects received decaffeinated coffee these percentages were 27, 46, and 27, respectively. Evidently very few subjects were able to recognize the switch from regular coffee to decaffeinated coffee or vice versa. Caffeine intake was 435 mg/day on regular coffee and 25 mg/day on decaffeinated coffee. According to the dietary recalls, other differences in nutrient intake between treatment periods were negligible, with mean \pm SD differences of 1 ± 4 energy % for intake of total fat, $1 \pm 2\%$ for polyunsaturated fatty acids, 20 ± 200 mg/day for calcium, 30 ± 600 mg/day for sodium, and 50 ± 400 mg/day for potassium. The mean change in body weight from weeks 5 and 6 to weeks 11 and 12 was 0.14 kg (range -2.8 to 1.9 kg). The value of -2.8 was because of one man in whom a fever developed due to bronchitis during week 11 and 12. For all other participants the change in body weight was less than 2 kg.

Blood Pressure and Heart Rate

Independent of treatment sequence, use of decaffeinated coffee led to a slightly but significantly lower mean systolic (-1.5 mm Hg; $p=0.002$), diastolic (-1.0 mm Hg; $p=0.017$), and mean arterial (-1.14 mm Hg; $p=0.004$) ambulant blood pressure and to a somewhat higher ambulant heart rate ($+1.3$ beats/min; $p=0.031$). Means and 95% confidence

TABLE 2. Effects of Consumption of 5 Cups Decaffeinated or Regular Coffee/Day for Periods of 6 Weeks Each on Group Average Ambulant Blood Pressure and Heart Rate in 45 Healthy Volunteers

Variables	Ambulant blood pressure (mm Hg)			Ambulant heart rate (beats/min)
	Systolic	Diastolic	Mean arterial	
Regular coffee	110.9	69.6	83.4	65.1
Decaffeinated coffee	109.4	68.6	82.2	66.4
Difference (N=45)	-1.5	-1.0	-1.2	+1.3
Caf→decaf (n=23)*	-1.4	-1.2	-1.3	+2.0
Decaf→caf (n=22)†	-1.5	-0.8	-1.0	+0.6
95% CL's for Δ (N=45)	-2.3,-0.7	-1.8,-0.2	-2.0,-0.6	+0.1,+2.5
p value (two-sided)	0.002	0.017	0.004	0.031

Caf, regular coffee; decaf, decaffeinated coffee; CL, confidence limits.

*Subjects who received regular coffee during the first 6 weeks and decaffeinated coffee during the next 6 weeks.

†Subjects who received decaffeinated coffee during the first 6 weeks and regular coffee during the next 6 weeks.

intervals are presented in Table 2. Thirty of the 45 subjects had a lower systolic (Figure 1) and diastolic blood pressure when they were consuming decaffeinated than when they were taking regular coffee.

The results were fairly insensitive to the time frames chosen for comparison: Treatment effects on systolic blood pressure and heart rate were significant ($p < 0.050$) when either the means of the sixth weeks of the two treatment periods, or the means of weeks 5 plus 6, 4 to 6, 3 to 6, 2 to 6, or 1 to 6 were compared. For diastolic pressure, p values were less than 0.031 for comparisons of the means of weeks 6, 5 plus 6, and 4 to 6 and less than 0.089 for weeks 3 to 6, 2 to 6, and 1 to 6. The measurements of blood pressure and heart rate over the course of the day, averaged for the two measurement days in the last 2 weeks of each treatment period (Figure 2), show that the effect of decaffeinated coffee on blood pressure and heart rate was present throughout the day. Analysis after exclu-

sion of the subject who became ill in week 11 and 12 yielded the same results. The results were similar for men and women.

The blood pressure measurements by Arteriosonde in the hospital, made 40 minutes after consumption of the first morning cup of coffee, showed almost the same mean effect of decaffeinated coffee on systolic (-1.7 mm Hg; $p = 0.14$), diastolic (-0.7

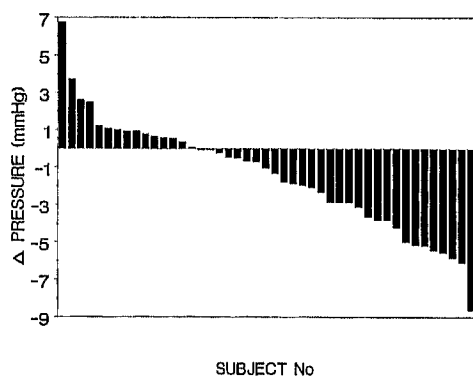


FIGURE 1. Bar graph showing effects of drinking decaffeinated instead of regular filter coffee on systolic blood pressure in 45 normotensive volunteers. Subjects consumed 5 cups decaffeinated coffee/day for a period of 6 weeks (n=22) followed by 5 cups regular coffee/day for another 6 weeks, or vice versa (n=23). Bars represent the 45 individual differences in mean systolic blood pressure, calculated as mean of measurements in week 5 and 6 of decaffeinated minus mean of measurements in week 5 and 6 of regular coffee period.

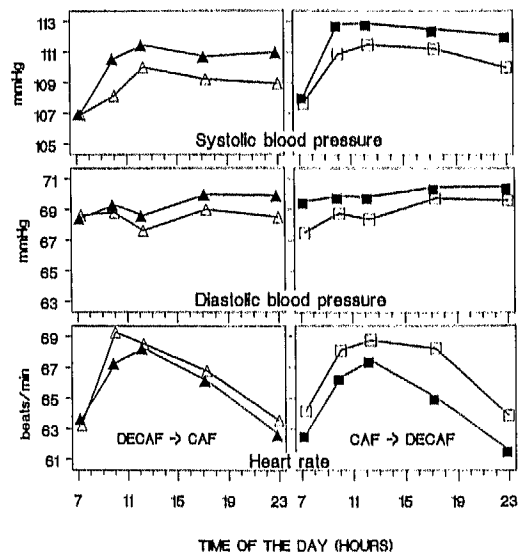


FIGURE 2. Line graphs showing effect of consumption of decaffeinated (decaf) or regular (caf) filter coffee on blood pressure and heart rate over the course of the day. Decaf→caf refers to 22 subjects who consumed 5 cups decaffeinated coffee/day for a period of 6 weeks, followed by 5 cups regular coffee/day for another 6 weeks (left panels). Caf→decaf refers to the other 23 subjects, who first received 5 cups regular coffee and then 5 cups decaffeinated coffee (right panels). Graphs represent means of measurements in weeks 5 and 6 of each period. Each symbol represents mean of 22 (Δ) or 23 (□) subjects and is based on six measurements per subject for each point in time, three on a random day in the fifth and another three on a random day in the sixth week. Closed symbols represent regular and open symbols decaffeinated coffee use.

TABLE 3. Effects of Consumption of 5 Cups Decaffeinated or Regular Coffee/Day for Periods of 6 Weeks Each on Group Average Hospital Blood Pressure and Heart Rate in 45 Healthy Volunteers

Variables	Hospital blood pressure (mm Hg)			Hospital heart rate (beats/min)
	Systolic	Diastolic	Mean arterial	
Regular coffee	104.6	71.3	82.4	69.3
Decaffeinated coffee	102.9	70.6	81.4	70.5
Difference ($N=45$)	-1.7	-0.7	-1.0	+1.2
Caf→decaf ($n=23$)*	-0.7	0.0	-0.3	+1.7
Decaf→caf ($n=22$)†	-2.7	-1.4	-1.8	+0.7
95% CL's for Δ ($N=45$)	-3.9,+0.5	-2.3,+0.9	-2.6,+0.6	-1.5,+3.9
p value (two-sided)	0.137	0.356	0.203	0.395

Hospital blood pressure was measured in the hospital by Arteriosonde. Caf, regular coffee; decaf, decaffeinated coffee; CL, confidence limits.

*Subjects who received regular coffee during the first 6 weeks and decaffeinated coffee during the next 6 weeks.

†Subjects who received decaffeinated coffee during the first 6 weeks and regular coffee during the next 6 weeks.

mm Hg; $p=0.36$), and mean arterial (-1.02 mm Hg; $p=0.20$) blood pressure and on heart rate (+1.2 beats/min; $p=0.39$) as those made by the subjects at home with the automatic device (Table 3). However, the number of measurements per subject was much smaller (eight compared with 30 per period) and the standard error proportionally larger, which probably explains the nonsignificant p values.

Serum Caffeine

The three values for fasting serum caffeine obtained on days 16, 35, and 42 of the regular coffee period were averaged per subject. Levels ranged from 0.41 to 3.75 mg/l, with a mean \pm SD of 1.43 ± 0.93 mg/l. The effect of treatment on systolic, diastolic, and mean arterial pressure was not correlated with the concentration of caffeine in serum after overnight abstention from coffee; Pearson correlation coefficients were -0.095 ($p=0.57$) for the ambulant and -0.11 ($p=0.47$) for the hospital mean arterial blood pressure. Such correlations can be degraded by high within-subject variability. However, the between-person variance of the individual averages of the three caffeine measurements was more than five times as large as the within-person variance. Therefore, attenuation of correlation coefficients by within-person variation¹² could not explain the low associations.

Discussion

Blood Pressures

Our results indicate that chronic consumption of 5 cups decaffeinated coffee/day in comparison with regular coffee causes a significant but small fall in mean ambulant blood pressure and a rise in heart rate in normotensive men and women. Compliance was very high: 99.7% of all coffee packages distributed were returned by the subjects, and the mean serum caffeine concentration during the day was 16-fold higher when subjects were consuming regular than when they were consuming decaffeinated coffee. During the decaffeinated coffee period, subjects still ingested 15–40 mg caffeine/day, an amount

that has occasionally been shown to have effects on the central nervous system in humans. However, the fact that we detected a difference between the two treatments probably indicates that the ingestion of such small amounts of caffeine during the decaffeinated coffee periods did not significantly limit the study. The fact that subjects were unable to correctly identify the type of coffee that they were consuming shows that blinding was effective. In addition, the absence of changes in body weight, in nutrient intakes, and in amount of physical exercise as indicated by the diaries, demonstrated that the differences in blood pressure and heart rate were due to the type of coffee consumed rather than to confounding factors.

This finding agrees with some but not all epidemiological studies. Lang et al^{13,14} reported a positive association between coffee consumption and systolic and diastolic blood pressure in several thousand subjects in France and Algeria. The observed differences between coffee users and abstainers were in the order of 2–3 mm Hg. In a cross-sectional survey of 5,147 Australians, Shirlow et al³ found that caffeine consumption within the last 3 hours was associated with significantly increased mean systolic and diastolic blood pressure (4 and 2 mm Hg, respectively) in both sexes. Other epidemiological studies, however, found no relation^{15,16} or a weak inverse association between caffeine consumption and blood pressure.^{4,17}

From experimental studies, there is clear evidence for a blood pressure-elevating effect of caffeine after acute ingestion in caffeine users who had abstained from caffeine for at least 1 week.^{18–20} Furthermore, caffeine ingestion by caffeine users who abstained from caffeine for only 12–24 hours produced a significant increase in blood pressure and decrease in heart rate at 1–4 hours after ingestion of caffeine.^{6,21,22} However, as far as we know, ours is the first controlled study showing a long-term effect of caffeine on blood pressure. Ammon et al⁷ studied the effect of consumption of 8 cups regular versus decaffeinated coffee on blood pres-

sure during periods of 4 weeks each. A switch to caffeine produced a small increase in blood pressure during the first few days, with levels falling and returning to baseline thereafter. We did not observe a transient rise in blood pressure, possibly because we measured blood pressure weekly, whereas Ammon et al⁷ took blood pressure measurements every day. Robertson and colleagues^{18,19} also observed complete tolerance to caffeine after 7 days of caffeine ingestion. Previous studies may have failed to detect a small long-term effect because of a lack of statistical power; from the graphs in various publications, we estimated mean differences in mean arterial pressure between placebo and caffeine of -2.7 , -2.19 and -1.18 mm Hg, similar to our value of -1.1 . Another reason for the discrepancy with the present study may be duration; the adaptation of blood pressure to a different type of coffee could take more than 4 weeks.

Whitsett et al²¹ found no differences between the acute response of blood pressure and heart rate to caffeine as such and to caffeine in the form of coffee, in either caffeine users or nonusers. This suggests that the effect of regular versus decaffeinated coffee on blood pressure is caused by the difference in caffeine content rather than to some other ingredient and that other caffeine sources such as cola and tea may cause the same effect when consumed in substantial amounts.

Extrapolation

Our subjects were normotensive, young, non-smoking adults. Robertson and colleagues^{18,19} and Smits et al²³ found that the pressor response to caffeine in subjects with borderline hypertension resembles, and in hypertensive subjects surpasses, that in normotensive subjects. This suggests that our results may also apply to subjects with (borderline) hypertension. Because the acute response of blood pressure to caffeine has been found to be greater in older than in younger caffeine users,⁶ and because smoking may enhance the effect of caffeine on blood pressure,²⁴ our findings could also be applicable to older persons and to smokers; this should be a subject of further investigation.

Mechanisms

The pharmacological basis of the blood pressure-increasing effect of caffeine has not been fully elucidated, but caffeine may exert its circulatory effects by competition with endogenous adenosine for purinergic cardiovascular receptors.²⁵

Fasting serum caffeine levels reflect the clearance rate of caffeine. The greatest acute blood pressure response to caffeine occurred in those subjects with the lowest baseline caffeine levels¹⁹ and in caffeine nonusers⁶; a negative correlation was found between the coffee-induced blood pressure increase and the fasting plasma caffeine level in 30 normotensive healthy subjects.⁸ However, in the present study no

such correlation could be found. The reason for this discrepancy is not clear.

Heart Rate

A depression in heart rate after caffeine ingestion has been reported previously,^{6,8,18,21,22} although some studies showed no effect.^{7,19} It may represent a baroreceptor-mediated effort to limit the caffeine-induced increase in blood pressure.^{20,21} Thus, our findings on heart rate further support the notion that a switch to decaffeinated coffee does induce significant hemodynamic alterations.

A high resting heart rate has been associated with increased cardiovascular morbidity and mortality.^{26,27} A rapid pulse could, however, be a proxy for poor physical fitness, which in its turn has been shown to be associated with increased cardiovascular and coronary mortality rates.²⁸ Therefore, the lower heart rate observed in our subjects while they were consuming regular coffee should not be constructed to indicate a reduced risk of cardiovascular mortality.

Public Health Implications

Although a difference of 1.5 mm Hg in the effect of regular versus decaffeinated coffee on systolic blood pressure is small, the population-attributable risk, that is, the excess risk associated with a factor in the population as a whole, is not negligible, as coffee is a very common drink. According to Rose,²⁹ "we may estimate that all the life-saving benefits achieved by current antihypertensive treatment might be equaled by a downward shift of the whole blood pressure distribution in the population by a mere 2–3 mm Hg". However, it remains to be established whether a mass switch of the general population from regular to decaffeinated coffee would significantly reduce the total incidence of hypertension-related disorders.

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