**Acute Effects of Caffeine on Blood Pressure and Heart Rate in Habitual and Non-Habitual Coffee Consumers: A Randomized, Double-Blind, Placebo-Controlled Study**

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Caffeine, a major component of coffee, exhibits pharmacological actions on the cardiovascular system. In the present study, we examined the acute effects of caffeine on blood pressure (BP) and heart rate (HR) and the influence of habitual coffee intake on cardiovascular responses to caffeine. In this double-blind, placebo-controlled study, 136 young normotensive Japanese subjects were randomized. The subjects were first divided into 84 non-habitual and 52 habitual coffee consumers and further subdivided into placebo and caffeine groups; in the placebo group they had a cup of decaffeinated coffee, whereas in the caffeine group they had a cup of caffeinated coffee. In non-habitual coffee consumers, the systolic and diastolic BP at 30, 60, and 90 min after coffee intake were significantly higher in the caffeine group than in the placebo group. However, the pressor effect of caffeine disappeared in habitual coffee consumers. The changes in HR after coffee intake were similar between the placebo and the caffeine groups in both consumers of coffee. These results suggest that a single cup of caffeinated coffee is capable of increasing BP, and that the acute pressor effect of caffeine is diminished by habitual coffee consumption.

**Key words** —— coffee, caffeine, blood pressure, heart rate, habitual consumption, double-blind study

**Introduction**

Coffee is a widely consumed beverage worldwide. In addition to its stimulating action on the central nervous system, caffeine, a major component of coffee, has been demonstrated to exhibit some pharmacological actions on the cardiovascular system. For example, caffeine acts as a non-selective blocker of adenosine A<sub>1</sub> and A<sub>2</sub> receptors. Blockade of the A<sub>1</sub> receptors by caffeine accelerates the release of catecholamines from sympathetic nerve endings, and blockade of A<sub>2</sub> receptors inhibits the vasodilatory effect of adenosine. This suggests that caffeinated coffee and beverages containing caffeine may affect blood pressure (BP) and cardiac function. Indeed, several reports show that the acute intake of caffeine increases BP in humans, although with little effect on heart rate (HR). Other studies show that similar acute pressor effects are obtained with caffeinated coffee but not with decaffeinated coffee. The acute effects of caffeine were mostly evaluated in non-habitual or light habitual coffee consumers or in subjects after prolonged abstinence from caffeinated beverages, because repeated caffeine intake could develop tolerance to the pressor effect of caffeine. A few studies have been performed in the United States and Europe, to determine whether the acute pressor effect of caffeine is actually affected by the
amount and frequency of daily coffee drinking. Nevertheless, the results are controversial; Casiglia et al. and Corti et al. have reported that habitual coffee consumption reduces the acute pressor effect of caffeine, a finding not supported by Lane et al. In addition, such a study has never been conducted in Japan, a country where coffee is one of the most popular beverages. Therefore, in the present study, the acute effects of caffeine on BP and HR in habitual coffee consumers are compared with those in non-habitual coffee consumers, in young Japanese subjects, using a randomized, double-blind, placebo-controlled study.

Materials and Methods

1. Subjects

The study was conducted on 136 healthy normotensive Japanese 3rd-year students (20–22 years old) in the department of pharmaceutical sciences, International University of Health and Welfare. All the subjects who gave informed consent were required to fill a questionnaire documenting their weekly caffeinated coffee consumption. According to the information obtained from the questionnaire, the subjects were divided into two groups: 1) the non-habitual coffee consumers (who have two or less than two cups of caffeinated coffee per week), 2) the habitual coffee consumers (who have three or more than three cups of caffeinated coffee per week). The former group comprised 84 individuals and the latter 52. The average number of coffee cups for the non-habitual consumers was 0.5 ± 0.1 (mean ± SEM) cups per week, and it was 5.3 ± 0.2 (mean ± SEM) cups per week for the habitual consumers.

2. Study design and protocol

All subjects abstained from caffeinated beverages such as coffee, green tea, tea, and cola, for 12 hours before the study that began at 2:00 pm. Each of the non-habitual and the habitual coffee consumers were subdivided randomly into two groups: placebo and caffeine groups. The subjects in the placebo group had one cup of decaffeinated instant coffee (Gold blend red label®, Nestle, Kobe, Japan), and the subjects in the caffeine group had one cup of caffeinated instant coffee (Gold blend®, Nestle, Kobe, Japan). For the caffeinated drink, granules of caffeinated coffee (2.5 g) were dissolved in hot water (150 mL), while for the decaffeinated drink, granules of decaffeinated coffee (2.5 g) were dissolved in hot water (150 mL). All subjects were allowed to add sugar and/or milk in their drinks. Before and 30, 60, and 90 min after the decaffeinated or caffeinated coffee intake, systolic blood pressure (SBP), diastolic blood pressure (DBP), and HR were measured at the left upper arm, using a cuff-type automated oscillometric BP monitor (model HEM-706, Omron, Kyoto, Japan), and a mean of three readings was calculated.

3. Statistical analysis

Data of SBP, DBP, and HR were analyzed blindly by the operator using a personal computer. Statistical analysis was performed with an analysis of variance, followed by unpaired Student’s t-test for comparisons at each time point. A difference was considered statistically significant if \( P < 0.05 \). All values are expressed as means ± SEM.

Results

1. Acute effects of caffeine in the non-habitual coffee consumers

Before the coffee intake, there were no significant differences in the values of SBP, DBP, and
HR between the placebo and caffeine groups in the non-habitual coffee consumers (Table 1). The changes in these parameters after decaffeinated or caffeinated coffee intake are shown in Fig 1. In the placebo group, all SBP, DBP and HR values gradually decreased after decaffeinated coffee intake. In the caffeine group, however, BP did not decrease after caffeinated coffee intake, and both SBP and DBP were significantly higher when compared with those in the placebo group, suggesting that caffeine produces an acute pressor effect in the non-habitual coffee consumers. The pressor effect appeared at 30 min and reached a maximum at 90 min (at the end of the study), when SBP and DBP in the caffeine group were about 7 and 3 mmHg higher than those in the placebo group, respectively. Nevertheless, the change in HR after coffee intake was not different between placebo and caffeine groups. These results indicate that drinking caffeinated beverage increases both SBP and DBP without changing HR in the non-habitual caffeine consumers.

2. Acute effects of caffeine in the habitual coffee consumers

In the habitual coffee consumers, there were no significant differences in the SBP, DBP, and HR values between placebo and caffeine groups, before starting the experiment (Table 1). The changes in these parameters after decaffeinated and caffeinated coffee intake are shown in Fig 2. In both placebo and caffeine groups, SBP, DBP, and HR decreased after the coffee intake, the same way as in the placebo group in the non-habitual coffee consumers. The SBP and DBP in the caffeine group were not different from those in the placebo group during the whole course of the study after the coffee intake, suggesting that the acute pressor effect of caffeine is diminished in the habitual coffee consumers. The change in HR after coffee intake in the caffeine group was similar to that of the placebo group, suggesting that caffeine does not have any effect on HR regardless if the coffee consumer is habitual or non-habitual.

Discussion

The purpose of the present study is to examine whether there is a difference in the acute effects of caffeine intake on BP and HR between the habitual and the non-habitual caffeine consumers. The randomized, double-blind, placebo-controlled study was performed in young normotensive Japanese, and was conducted in habitual and in non-habitual caffeine consumers. The results clearly show that SBP and DBP after intake of caffeinated coffee are significantly higher than

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Values of SBP, DBP and HR before intake of decaffeinated coffee (placebo group) and caffeinated coffee (caffeine group) in non-habitual and habitual consumers of coffee</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-habitual consumers</td>
</tr>
<tr>
<td></td>
<td>placebo group</td>
</tr>
<tr>
<td>No. of subjects</td>
<td>40</td>
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<tr>
<td>No. of Male/Female</td>
<td>12/28</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>109.3 ± 1.8</td>
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<tr>
<td>DBP (mmHg)</td>
<td>65.8 ± 1.3</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>81.1 ± 1.8</td>
</tr>
</tbody>
</table>

Each value represents the mean ± SEM. Numbers of male and female subjects are also shown.
those after intake of decaffeinated coffee in the non-habitual coffee consumers. We have previously observed that similar pressor effects are obtained with caffeine-containing decaffeinated coffee (which is obtained by the addition of caffeine powder to decaffeinated instant coffee) but not with caffeine-free decaffeinated coffee (Ohide H, Miyagawa K, Nakatani Y, Takeuchi T, Yokoyama H, Amano T, Hara A. Applied practice for measurement of blood pressure in International University of Health and Welfare (4th Report): Influences of habitual drinking of coffee and teas on the acute pressor effect of caffeine. Abstract of the 132nd Annual Meeting of the Pharmaceutical Society of Japan 2012, 4, 340.), supporting that the pressor effects of coffee are primarily caused by caffeine. Therefore, the above findings in the present study suggest that caffeine intake acutely increases SBP and DBP in the non-habitual coffee consumers. In habitual coffee consumers, however, caffeine intake increased neither SBP nor DBP. These findings agree with the results obtained by other investigators, and disagree with a report in which habitual coffee consumption does not attenuate the pressor effect of caffeine.

Similar studies have shown that acute caffeine intake exerts a significant pressor action, with a
little or no effect on HR, in the non-habitual or light habitual consumers of caffeine or after prolonged abstinence from caffeinated beverages.\textsuperscript{1,3,6} These studies also show that BP usually rises within 30 min, and the maximum increase occurs 60–120 min after the oral intake of caffeine.\textsuperscript{1,3,4} The peak plasma concentrations of caffeine are obtained within 60–90 min after oral intake of caffeinated coffee or caffeine.\textsuperscript{4,11,12} These findings are consistent with the time-course changes in BP after acute intake of caffeinated coffee in the present study, in which BP increased within 30 min and reached its maximum at 90 min (at the end of the study) after the caffeinated coffee intake.

According to a review summarized by Nurminen \textit{et al.},\textsuperscript{11} 200–250 mg of caffeine increases SBP by 3–14 mmHg and DBP by 4–13 mmHg, and two cups of caffeinated coffee increases SBP by 3–5 mmHg and DBP by 4–11 mmHg. The results of the present study showed that even a smaller amount of caffeine (one cup of instant coffee contains about 70 mg of caffeine\textsuperscript{13}) causes a comparable pressor effect in the non-habitual coffee consumers; it increased SBP and DBP by a maximum of 7 and 3 mmHg, respectively. The pressor effects of caffeine are more pronounced in older subjects compared to young subjects,\textsuperscript{1,3} and in hypertensive subjects compared to normotensive subjects.\textsuperscript{1,6} However, our study shows that caffeine is effective in increasing BP even at small amounts and even in young normotensive subjects, when given to non-habitual coffee consumers.

In the present study, 67% of the habitual coffee consumers were male subjects, and 61% of the non-habitual coffee consumers were female. It is unlikely, however, that this sex disproportion in the subjects is responsible for the differences in BP responses to caffeine between non-habitual and habitual coffee consumers, because no sex difference were previously found for the pressor effects of caffeine.\textsuperscript{1,14} Alternatively, the disappearance of the pressor effect in habitual coffee consumers may be due to tolerance to caffeine, as demonstrated by previous reports,\textsuperscript{1,12} although the underlying mechanism of tolerance remains unclear. According to the studies that targeted the chronic (long-term) effects, repeated intake of caffeine has either no effect or a decreasing effect on BP.\textsuperscript{1,10} In addition, recent epidemiological studies have demonstrated that regular intake of coffee does not increase the risk of cardiovascular events, such as hypertension, coronary heart disease and stroke, because of the development of tolerance.\textsuperscript{15-18} Nevertheless, frequency and amount of habitual caffeine consumption needed to develop tolerance are not fully understand. Other sources of caffeine, such as green tea, tea, or cola, are also widely consumed in Japan, and it also remains to be determined whether habitual consumption of these beverages affects the pressor response after caffeinated coffee intake. Further studies are needed to understand the relationship between the acute pressor effect and habitual caffeine consumption.

We conclude that a single cup of caffeinated coffee is capable of increasing BP in young normotensive Japanese subjects, and that the acute pressor effect of caffeine is reduced by habitual coffee consumption. Therefore, it should be noted that intake of caffeinated beverages, including coffee, may disturb the measurement of BP if the measurement is made within a few hours after the drinking, especially in the non-habitual caffeine consumers.
References


