

# The Acute Hemodynamic Effects of Caffeine During Different Body Positions in Normotensive Young Adults

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*The aim of this study was to investigate the acute cardiovascular hemodynamic effects of administration of a fixed dose of 130 mg of caffeine versus placebo in a sample of healthy young adults (N = 32, sex ratio 1/1), who were successively placed in four distinct positions (orthostatic before ingestion, orthostatic, supine and Trendelenburg vertical positions, after ingestion) on a gravitational inversion table. The experimental design was a single-center, parallel-group, double-blind, randomized, placebo-controlled clinical trial. Following the descriptive and inferential statistical processing of the data, a statistical significant pattern (p <0.05) of acute postural cardiovascular hemodynamic adaptation of the subjects was revealed, under the influence of caffeine versus placebo ingestion.*

*Keywords: caffeine, cardiovascular effects, postures, healthy adults*

Caffeine (1,3,7-trimethylxanthine) is a substance with a wide action range, with natural origin, from several species of plants (more than sixty), or synthetic origin [1]. In present, there is an increasing scientific interest in the role of caffeine in human health, considering that coffee is one of the most widely consumed drinks worldwide, as a usual component of daily diet [2]. Caffeine is a central nervous system stimulant, also affecting metabolic and cardiovascular functions, because induces an adrenergic stimulation, with the increase of catecholamine excretion [3]. The beneficial effects of regular coffee consumption are very complex and based essentially on the antioxidant effect against various free radicals. However, it seems that these effects should go beyond antioxidation, for example in reversing cognitive impairment [4]. Regarding the biochemical aspect, the effects of caffeine in the usual dose from dietary sources at the cellular level focus on adenosine antagonism in the receptors of the central nervous system [5]. Repeated caffeine intake, similar to other psychoactive substances, was incriminated in the development of the phenomena of tolerance, dependence and abuse, which are recognized through numerous epidemiological studies and clinically framed in relevant psychiatric diagnostic systems [5, 6].

Various studies have revealed the cardiovascular systemic effects of caffeine administration, both as a nutrient and as a pharmacological product. The most important cardiovascular effect, clinically demonstrated, is the temporary hemodynamic pressor one, with the strongest response in hypertensive subjects [7]. The transitory increase in blood pressure (BP) appears usually in the first hour after caffeine intake and lasts for 3 hours [8]. Basically, coffee consumption increases central BP and peripheral diastolic BP, but does not significantly affect the peripheral systolic BP [9]. It seems that data concerning acute BP changes, after caffeine consumption, are contradictory especially in healthy young subjects [9]. This is especially true for subjects with tolerance to chronic caffeine intake [1]. Also, it was established that caffeine has an ergogenic effect on endurance and near maximal heart rate responses, but does not influence maximal BP [10].

An important aspect refers to the existence of an additive influence of mental and behavioural stress on caffeine effects on BP [11]. Certainly, it was proven that for a 70-kg adult, the safe dose for one administration, taking into consideration the cardiovascular side effects, is 260 mg caffeine (about 2-3 cups of coffee) [12].

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Hemodynamic cardiovascular changes are directly influenced by body posture as a result of gravitational influences. BP is a physiological variable with a high level of regulation, based on central and peripheral mechanisms, with redundant and integrated character [13]. Knowing that during the occupational activities the human body can be placed in different positions, it becomes attractive to study in this context the effects of the administration of a usual dose of caffeine on the cardiovascular parameters. Moreover, in daily life, caffeine intake in people adopting occupational positions is frequent.

In the rich literature assigned to the study of the effects of caffeine on the human body, we could not identify research on the hemodynamic changes induced by caffeine in the context of adopting extreme positions. In contrast, numerous studies, often contradictory in terms of results, aimed at investigating the cardiovascular adaptation of the body placed in different positions, with the body tilted head-down [14].

### **Experimental part**

This study aimed to investigate the acute hemodynamic effects of caffeine intake versus placebo in a sample of 32 volunteers, healthy young adults, who were successively placed in distinct positions. The inclusion criteria in the experiment were: good health, common eating behaviour [15] normal BP values, with no significant pathological history in the last 6 months (cardiovascular disease, diabetes, various traumas or injuries, oncological conditions) [16-18], occasional consumption of coffee or caffeine-based products. Subjects who were afraid of posturing maneuvers or who did not like coffee were excluded. All participants gave informed consent for participation in the study, according to the ethical principles of research.

The experimental design was a single-center, parallel-group, double-blind, randomized, placebo-controlled clinical trial. The participants were randomly divided into two equal groups, with sex ratio 1/1. Thus, subjects from the experimental group (G1, N = 16, mean age  $22.75 \pm 3.38$ ) received a fixed dose of 130 mg of caffeine as 200 mL beverage (Arabica coffee) produced by a brewer espresso coffee maker. In contrast, each subject from the placebo group (G2, N = 16, mean age  $21.81 \pm 1.33$ ) received 200 mL of a placebo drink (decaffeinated coffee). We chose this dose specified by the manufacturer because usually, the caffeine content of espresso Arabica coffee is 71-120 mg/150 mL [19]. Also, in pharmacological practice, the caffeine content of drugs varies from 16 mg to 200 mg per tablet [5]. Both types of drinks were not sweetened and were ingested in about 10 minutes.

All tests took place between 8-12 a.m. Initially, we performed anthropometric measurements like weight (W), height (H) and we calculated the body mass index (BMI) according to standardized procedures. Then two sets of measurements were performed for each participant: before drink intake, in orthostatic position (P1) and after 30 minutes from beverage consumption, in three successive positions: orthostatism (P2), supine position (P3) and the head-down, vertical Trendelenburg position (P4). Before P1 and P2 subjects maintained a state of relaxation in supine position for 15 minutes. For P2, P3 and P4 subjects were maintained for 30 seconds in each posture, and then BP was measured. Subjects were required not to consume caffeine-based products or other psychoactive substances 48 hours before the experiment and to have a regular, non-excessive breakfast in the morning.

A gravitational inversion table (KIROMED Kft., Debrecen, Hungary) was used for posturing the subjects. Measurement of cardiovascular parameters – heart rate (HR), systolic BP (SBP), diastolic BP (DBP), mean BP (MBP), the difference between maximum and minimum BP (PP) – was performed using a device with integrated software ABPM50 Ambulatory Blood Pressure Monitor, Contec Medical Systems Co., Ltd., China, in the left brachial artery. The device provides pulse rate values, but considering the physiological cardiovascular status of the subjects, we used as a substitute the high correlated HR parameter [20]. As an additional variable, we calculated the SBP/DBP ratio for each situation.

Data processing was performed by descriptive statistical methods (determining the mean and standard deviation of the data series) and inferential methods (Shapiro-Wilk test for checking the normality of the data distribution, the unpaired two-samples t-test and the two-way ANOVA with repeated measures for continuous variables with normal distribution, followed by Bonferroni post hoc test).

### **Results and discussions**

Following the application of the Shapiro-Wilk test we found the existence of a normal distribution or approximately normally distribution for all data series. In Table 1 are presented the baseline anthropometric data of the two groups, after applying the unpaired two-samples t-test, and it can be observed the similarity of the groups.

**Table 1**  
SUBJECTS BASELINE CHARACTERISTICS, CALCULATED BY INDEPENDENT T-TEST

Group	G1 (N = 16)	G2 (N = 16)	p value	95% CI
Age (years)	22.75 ± 3.38	21.81 ± 1.33	0.31	-0.91 to 2.79
W (kg)	65.81 ± 14.03	62.00 ± 9.20	0.37	-4.75 to 12
H (cm)	170.13 ± 10.27	168.38 ± 9.82	0.62	-5.51 to 9.01
BMI (kg/m <sup>2</sup> )	22.55 ± 3.04	21.75 ± 1.22	0.80	-0.86 to 2.47

Legend: values are shown as mean ± standard deviation; p = significance level; 95% CI = 95% confidence interval of the mean differences; G1 = experimental group; G2 = placebo group; N = number of subjects; W = weight; H = height; BMI = body mass index.

To assess the effect of beverage ingestion for the selected postures on the recorded parameters (Table 2), a two way ANOVA with repeated measures was carried out, after checking the ANOVA assumptions. Thus, we considered the factors based on two levels for the Group (G1 and G2) and on four levels for the Postures (P1, P2, P3, and P4). A level  $p < 0.05$  was considered as statistically significant. For the data where the sphericity was not assumed, the Greenhouse-Geisser correction was used. Also, for effect size, we calculated the Partial Eta-squared.

**Table 2**  
STATISTICAL INDICATORS OF THE RECORDED DATA FOR THE G1 AND G2

Group	Position	HR beats/min	SBP mm Hg	DBP mm Hg	SBP/DBP	MBP mm Hg	PP mm Hg
G1 (N = 16)	P1	83.56 ± 14.71	125.19 ± 7.91	75.38 8.44±	1.68 ± 0.18	93.73 ± 7.52	47.19 ± 4.85
	P2	84.56 ± 15.31	127.38 ± 10.34	74.00 ± 13.19	1.77 ± 0.36	93.42 ± 10.27	47.69 ± 12.06
	P3	72.50 ± 12.80	129.75 ± 9.78	73.56 ± 11.22	1.80 ± 0.27	92.04 ± 10.03	51.19 ± 8.71
	P4	73.69 ± 9.56	129.38 ± 10.32	70.19 ± 10.93	1.88 ± 0.26	89.10 ± 9.36	53.31 ± 9.06
G2 (N = 16)	P1	85.44 ± 10.46	136.00 ± 11.44	85.13 ± 6.53	1.60 ± 0.11	102.67 ± 7.52	50.88 ± 8.79
	P2	87.56 ± 15.70	135.00 ± 11.46±	86.31 8.00±	1.57 ± 0.13	103.31 ± 7.47	48.69 ± 9.29
	P3	76.75 ± 9.81	128.31 ± 10.68±	75.06 ± 7.50	1.72 ± 0.14	90.50 ± 7.08	53.25 ± 8.43
	P4	77.19 ± 9.63	123.25 ± 10.53	70.50 5.76±	1.75 ± 0.13	86.81 ± 6.23	52.75 ± 8.44

Legend: values are shown as mean ± standard deviation; G1 = experimental group; G2 = placebo group; N = number of subjects; HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; MBP = mean blood pressure, PP = pressure difference between high and low blood pressure; P1 = vertical orthostatic position, before drink ingestion; P2 = vertical orthostatic position, after drink ingestion; P3 = supine horizontal position, after drink ingestion, P4 = vertical Trendelenburg position, after drink ingestion.

Regarding HR (Fig. 1), the results of Tests of Within-Subjects Effects for comparing significant difference between the means showed a non-significant main effect for Group and for the interaction Group x Postures ( $p > 0.05$ ), but a significant main effect for Postures,  $F(1.988, 29.824) = 28.004$ ,  $p < 0.001$ , Eta-squared = 0.651. After applying the Bonferroni post-hoc test for pairwise comparisons for the Groups and for the Postures, the results were statistically significant only for Postures, as differences between mean scores of P1/P3, P1/P4, P2/P3 and P2/P4 ( $p < 0.05$ ).

For SBP (Fig. 2), according to the same interpretation algorithm, we put into evidence a non-significant main effect for Group ( $p > 0.05$ ), but significant main effect for Postures,  $F(3, 45) = 4.57$ ,  $p = 0.007$ , Eta-squared = 0.234, and for interaction Group x Postures,  $F(3, 45) = 12.809$ ,  $p < 0.001$ , Eta-squared = 0.461. For the post-hoc analysis, the results were not statistically significant ( $p > 0.05$ ). In other words, although there are no differences between groups and positions in terms of mean values of SBP, caffeine administration in subjects from G1 increases mean SBP values from P1 to P2 and P3, with a slight decrease for P4, while in subjects from G2 appears an obvious progressive decrease of mean SBP.

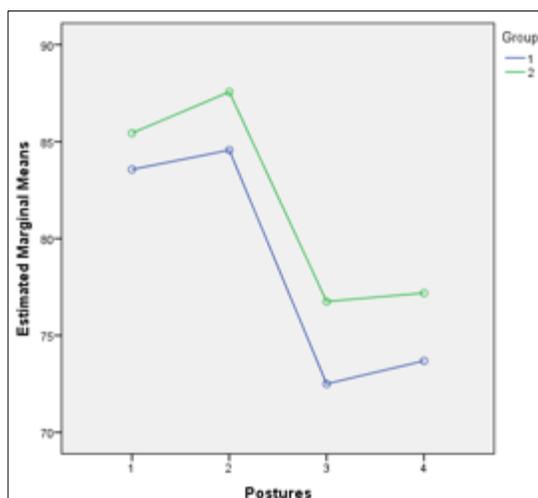


Fig. 1. Estimated marginal means of heart rate (HR)

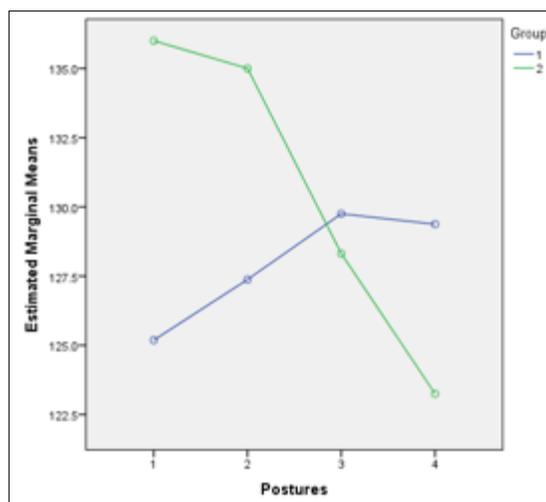


Fig. 2. Estimated marginal means of systolic blood pressure (SBP)

As for DBP (Fig. 3), we found a significant main effect for Group,  $F(1, 15) = 5.174, p = 0.038, \text{Eta-squared} = 0.256$ , for Postures,  $F(1.548, 23.216) = 18.436, p < 0.001, \text{Eta-squared} = 0.551$ , and for interaction Group x Postures  $F(3, 45) = 9.764, p < 0.001, \text{Eta-squared} = 0.394$ . For the post-hoc analysis, the results were statistically significant for pairwise comparisons of Group and Postures, for all variants of posture combinations, excepting the variant P1/P2 ( $p > 0.05$ ). In the case of subjects from G1, after caffeine intake, the mean DBP decreases slightly from one posture to another, while for subjects from G2, after a slight increase between P1 and P2, the parameter decreases more sharply between P2, P3, and P4.

For SBP/DBP (Fig. 4), we ascertained a non-significant main effect for Group and for the interaction Group x Postures ( $p > 0.05$ ), but a significant main effect for Postures,  $F(1.687, 25.307) = 9.362, p < 0.001, \text{Eta-squared} = 0.384$ . For the post-hoc analysis, the results were statistical significant for Postures for the pairwise comparisons of all variants of postures ( $p < 0.05$ ).

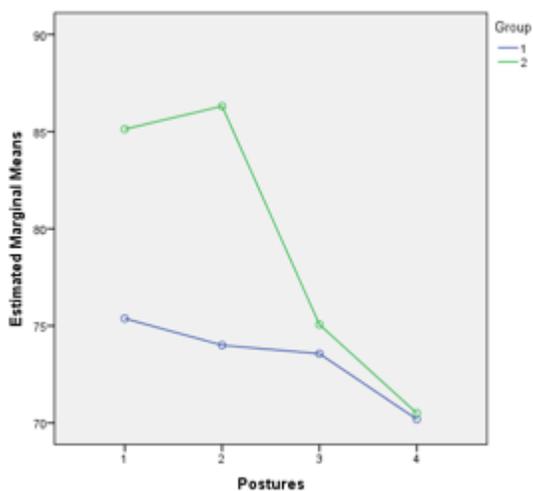


Fig. 3. Estimated marginal means of diastolic blood pressure (DBP)

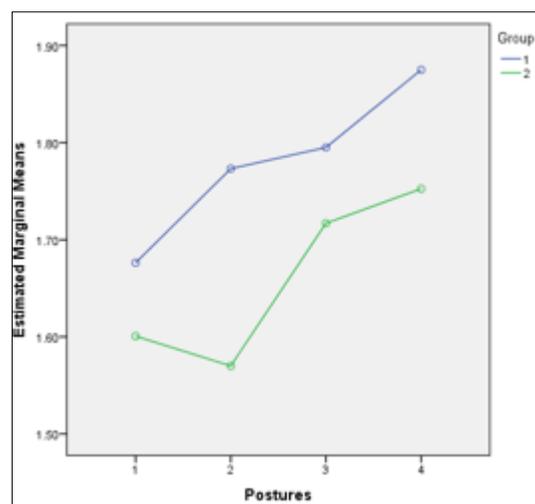


Fig. 4. Estimated marginal means of ratio between systolic and diastolic blood pressure (SBP/DBP)

For the next parameter, MPP (Fig. 5), we put into evidence a non-significant main effect for Group ( $p > 0.05$ ), but significant main effect for Postures,  $F(3, 45) = 30.945$ ,  $p < 0.001$ , Eta-squared = 0.674, and for interaction Group x Postures,  $F(1.718, 25.772) = 16.003$ ,  $p < 0.001$ , Eta-squared = 0.516. For the post-hoc analysis, the results were statistically significant for Postures, as differences between mean scores of P1/P3, P1/P4, P2/P3, P2/P4 and P3/P4 ( $p < 0.05$ ). We can observe the tendency of a slight decrease of MBP in subjects from G1 after caffeine administration, between P1, P2, P3, and P4, while in subjects of G2 the decrease of MBP appears and it is more marked between P2, P3, and P4.

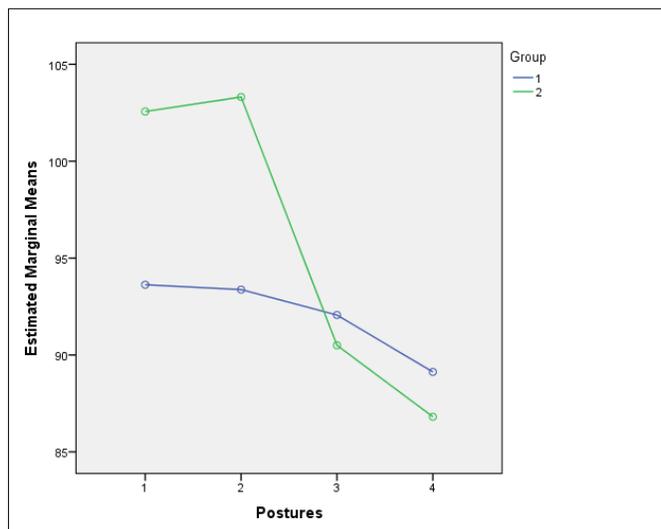


Fig. 5. Estimated marginal means of mean blood pressure (MBP)

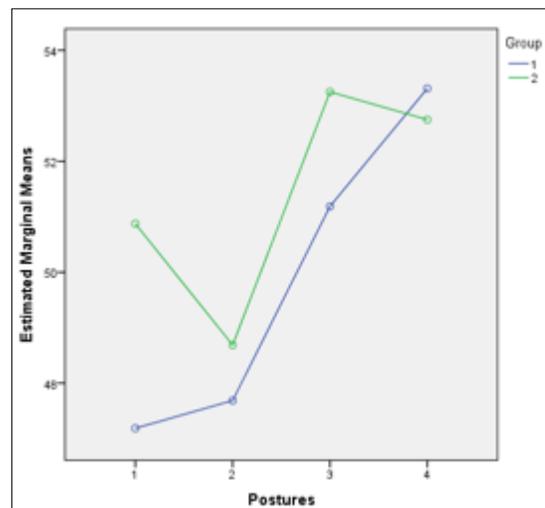


Fig. 6. Estimated marginal means of difference between maximum and minimum blood pressure (PP)

Finally, for PP (Fig. 6), we obtained a non-significant main effect for Group and for the interaction Group x Postures ( $p > 0.05$ ), and a significant main effect for Postures,  $F(2.399, 35.987) = 4.444$ ,  $p = 0.014$ , Eta-squared = 0.229. At post-hoc analysis, the results were not statistical significant ( $p > 0.05$ ).

Overall, our data highlighted the existence of statistically significant results ( $p < 0.05$ ) for both main effects of Postures and interaction Group x Postures in the case of SBP, DBP, and MBP. Only the simple main effect of Postures was found in the case of HR, SBP/DBP and PP, and only the simple main effect of Group in the case of DBP. Also, the post-hoc analysis identified statistically significant differences ( $p < 0.05$ ) between the means scores for Group factor only for DBP, and for Postures, for HR, DBP, MPP and SBP/DBP, for most combinations of pairwise comparisons.

In other words, caffeine administration clearly exerts hemodynamic effects at the level of SBP, DBP, and MBP, under changing body posture. At the same time, changing the body posture as a particular main effect, according to the proposed experimental design, has determined significant effects on the cardiovascular adaptation of the human body, influencing HR, SBP/DBP, and PP. In contrast, caffeine intake as the simple main effect only influenced DBP values. The obtained values of Partial Eta-squared, higher than 0.13, indicate a large effect size in all statistically significant situations.

A special attention should be given to the SBP/DBP indicator. In physiological conditions, between SBP and DBP there is a large linear correlation [21], and the ratio is used in practice to evaluate the balance between sympathetic and parasympathetic tone, at rest or during effort [22-24]. The reference value for the resting state in a healthy status, especially for night time can be approximated by Golden Ratio (GR), which is about 1.618 [22]. In our case, we observe mean values close to GR in the case of P1 and P2 in subjects from G2. In contrast, the transition to positions P3 and P4 progressively increases the value of the ratio, both in the case of G1 and G2 subjects.

In this study, the most important hemodynamic changes, under the combined action of caffeine and the gravitational effects induced by changing the body position, are adaptive. The interaction effect Group x Postures on BP suggests that the acute effects of caffeine ingestion depend on the type of the postures. The acute peripheral pressor effect of caffeine has been experimentally demonstrated mainly by increasing vascular resistance than the cardiac output [12, 25], but there are also authors that disprove this growth [9], or highlight it only in caffeine-naive subjects [26]. The vasoconstrictive effects of caffeine are mediated by the cerebrovascular adenosine receptor system, which can undergo a process of adaptation over time to chronic coffee consumption [27], fact that explains the development of the caffeine tolerance

phenomenon. In our case, the investigated subjects are persons without caffeine addiction, so the mentioned effect was excluded.

To take into account the postural, gravitationally induced effects on BP, it should be mentioned that the head-down Trendelenburg position leads to a temporary increase of venous return and preload, cardiac output and perfusion index [28]. Certainly, the stroke volume variation is subjected to the body posture [29, 30], but the pressure hemodynamic effects, especially in people with hypotension, heart failure or aortic stenosis are the subject of dispute between various authors [31-33]. In clinical practice, the Trendelenburg position is used mainly with small or medium angles of inclination, in which there is no significant influence in the dominant parasympathetic cardiac control [34]. The chosen experimental protocol included placing the subjects in the vertical Trendelenburg position, which exerts maximum gravitational effects on the cardiovascular system, and explains the occurrence of significant hemodynamic postural changes.

By combining the exposure of subjects to postural changes and caffeine ingestion in a metabolically active dose, we were able to obtain significant results in terms of variation of the investigated cardiovascular parameters. The practical applicability of the results refers to the dissemination of information related to the influence of caffeine consumption on cardiovascular parameters, especially in the case of changing body posture. In everyday life, there are frequent situations where, in the context of caffeine consumption, the human body suffers different gravitational influences in relation to the adopted positions. Knowing these elements, we can only use the positive physiological effects of coffee consumption and we can reduce the potentially harmful effects of caffeine at the cardiovascular level.

The results of the ANOVA confirm that each parameter has a significant specific dynamic, taking into consideration the Group factor, the Postures factor and/or the interaction Group x Postures factor. As a limitation of the study, it should be noted that we only considered the effects of caffeine as the bioactive chemical component of coffee. However, coffee contains many other potentially active substances, but the most important metabolic effects are related to caffeine. In fact, it has been proven that the metabolic and performance effects of caffeine are similar to those of coffee consumption [35].

## Conclusions

The findings of our study refer to the existence of some different significant main effects for the variables considered in the experimental design. Thus, it is noticeable the effect of interaction Group x Postures in the case of SBP, DBP, and MBP, which confirms that the administration of caffeine causes different hemodynamic adaptations during the change of body positions. The simple main effect of Postures was identified in the case of HR, SBP, DBP, MBP, SBP/DBP, and PP, a fact that demonstrates the direct effect of changing posture on cardiovascular parameters. Instead, the simple main effect of Group occurred only in the case of DBP, which argues that caffeine consumption, regardless of body posture, only influences DBP. Overall, a statistically significant pattern ( $p < 0.05$ ) of acute postural cardiovascular hemodynamic adaptation of the subjects was revealed, under the influence of caffeine versus placebo ingestion.

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