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EFFECTS OF CAFFEINE SUPPLEMENTATION ON CARDIAC AUTONOMIC MODULATION AND QT DISPERSION IN HEALTHY YOUNG MEN

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ABSTRACT

Background: There is no consensus on the effects of caffeine supplementation on the autonomic behavior of the heart. Aim: To evaluate the effect of caffeine supplementation on autonomic heart rate modulation and QT dispersion in healthy young men. Materials and Methods: a prospective randomized study. Twelve healthy young men (24.3±2.0 years) on non-consecutive days and at random were supplemented with two caffeine doses: (i) low (225mg/cps); (ii) moderate (450mg/cps); and, (iii) placebo. Volunteers were submitted to instantaneous heart rate evaluations at baseline and 60 minutes after supplementation. Then, the electrocardiogram was collected for 5 minutes at rest sitting. Heart rate variability (RMSSD index and low and high frequency) was analyzed at baseline and every 10 minutes after 60 minutes post supplementation. Additionally, QT dispersion was evaluated at the end of 60 minutes post supplementation. Results: there was a small and moderate effect size of the RMSSD and HF indexes between 40 and 50 minutes after caffeine supplementation. Regarding QT dispersion, small and moderate effect size observed for supplements of 225 and 450mg, respectively. Conclusion: Low and moderate caffeine doses promoted better cardiac autonomic modulation with vagal predominance at the end of one hour after supplementation. Additionally, QT dispersion showed small and moderate effect size at doses of 225mg/cps and 450mg/cps.

Key word: Caffeine. Autonomic nervous system. Electrocardiography.

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RESUMO

Efeitos da suplementação de cafeína sobre a modulação autônima cardíaca e dispersão QT de homens jovens saudáveis

Introdução: Não há consenso sobre os efeitos da suplementação de cafeína no comportamento autonômico cardíaco. Objetivo: Avaliar o efeito da suplementação de cafeína na modulação autonômica da frequência cardíaca e na dispersão do QT em homens jovens saudáveis. Materiais e Métodos: estudo prospectivo randomizado. Doze homens jovens saudáveis (24,3±2,0 anos) em dias não consecutivos e aleatoriamente foram suplementados com duas doses de cafeína: (i) baixa (225mg/cps); (ii) moderado (450mg/cps); e, (iii) placebo. Os voluntários foram submetidos a avaliações instantâneas da frequência cardíaca no início e 60 minutos após a suplementação. Em seguida, foi coletado o eletrocardiograma durante 5 minutos em repouso sentado. A variabilidade da frequência cardíaca (índice RMSSD e frequências baixa e alta) foi analisada no início do estudo e a cada 10 minutos após 60 minutos após a suplementação. Além disso, a dispersão do QT foi avaliada ao final de 60 minutos após a suplementação. Resultados: houve tamanho de efeito pequeno e moderado dos índices RMSSD e HF entre 40 e 50 minutos após a suplementação de cafeína. Em relação à dispersão do QT, tamanho de efeito pequeno e moderado observado para suplementos de 225 e 450mg, respectivamente. Conclusão: Doses baixas e moderadas de cafeína promoveram melhor modulação autonômica cardíaca com predomínio vagal ao final de uma hora após a suplementação. Além disso, a dispersão do QT apresentou tamanho de efeito pequeno e moderado nas doses de 225mg/cps e 450mg/cps.

Palavras-chave: Cafeína. Sistema nervoso autonômico. Eletrocardiografia.

INTRODUCTION

Caffeine supplementation has been used to reduce sleep, increase wakefulness and a sense of alertness, improve physical and cognitive performance, sense of well-being, decrease in pain, and fatigue state (Tavares and collaborators, 2012; Salinero and collaborators, 2019).

However, the increase in gastric secretion, reflux, anxiety, insomnia and abstinence in relation to continuous use appear as adverse effects (Salinero and collaborators, 2019).

Regarding to the cardiovascular system, the current evidence available in the literature is conflicting. Some researchers have revealed that caffeine raises systemic blood pressure (SBP), heart rate (HR) and modulates heart rate variability (HRV) in a predominantly sympathetic manner (Bunsawat and collaborators, 2015; Cavalcante and collaborators, 2000).

During physical exercise, the authors have shown that improved performance could also be explained by a decrease in chronotropic reserve (Higgins and collaborators, 2012; Silvestre and collaborators, 2018).

On the other hand, there are studies showing that caffeine can induce an increase in parasympathetic modulation (Rolim and collaborators, 2018).

In this scenario, the important question is to understand the real effects of caffeine supplementation - considering mainly the dose - to its potential arrhythmogenic effect (Hibino and collaborators, 1997; Casiglia and collaborators, 2018; Voskoboinik and collaborators, 2018).

With technological advances, there are currently several tools to perform HR data analysis. Among them, there is the 12-lead electrocardiogram (ECG), which assesses the electrical impulse of the myocardium through electrodes connected to the patient (Guimarães and collaborators, 2003).

Demonstrated in graphic signals, it is possible to analyze, through the potential of cardiac cellular action, the heart rhythm. Such factors related also to the performance in the autonomic modulation of HRV, being of great importance to assess the sympathetic and parasympathetic autonomic nervous system (ANS) (Catai and collaborators, 2019).

Additionally, the analysis and evaluation of ECG data through the derivations of the QRS complex, is necessary to verify the electrocardiographic tracing and, more specifically, the QT interval, which represents the duration of the electrical systole (cardiac contraction). This complex represents the total duration of depolarization and ventricular repolarization, from the beginning of the QRS to the end of the T wave (Arai and collaborators, 2012).

According to the above, with the incipient and controversial knowledge in relation to caffeine supplementation in cardiovascular responses and with the possibility of implementing low-cost and easy-to-apply tools to assess cardiac autonomic modulation and QT dispersion, the present study aimed to evaluate the effect of caffeine supplementation on the autonomic HR modulation and QT dispersion in healthy young men.

MATERIALS AND METHODS

Study design and participants

This is a prospective randomized study, with repeated measures, double blind with analysis of intra - and inter-rater data and use of placebo (magnesium silicate, therapeutic talc). According to the Physical Active Readiness Questionnaire (Par-Q), the participants were healthy men, body mass between 70 and 80 kg, physically active (VO_2 peak > 25mL /kg / min), who did not consume more than 40 mg of caffeine daily (referring to two small cups of coffee).

The study excluded individuals who presented nausea or nausea during supplementation. In addition, any change in the electrocardiographic tracing suggestive of arrhythmias during cardiopulmonary exercise test was an exclusion criterion (Floriano e Reis, 2019).

Volunteers were informed on the possible risks involved in the experiment, before signing the Free and Informed Consent Form, accepted the conditions of the study and authorized the disclosure of the data.

The Research Ethics Committee of Hospital Universitário Clementino Fraga Filho/Universidade Federal do Rio de Janeiro under no. CAAE 36888314.7.0000.5257. All volunteers signed an informed consent form to participate in the research.

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Protocol

The evaluation protocols were performed at the Grupo de Pesquisa em Avaliação e Reabilitação Cardiorrespiratória (GECARE) with controlled temperature (22-24ºC), and humidity (60-70%).

The participants were instructed to prepared for the tests on the day before and on the day of the tests - avoiding consumption of caffeinated drinks and physical exercise, seeking to have an adequate night of sleep, light food at least two hours before the tests and wearing comfortable clothes that favor sweating.

The collections took place in the following order: (i) Cardiopulmonary exercise test to assess health conditions and assess physical fitness (Floriano and collaborators, 2019); and, (ii) Evaluation of HRV and QT dispersion during randomized supplementation of two doses of caffeine (low 225 mg/cps, moderate 450 mg/cps) and placebo on three visits on different days (magnesium silicate, pharmaceutical talc) (Goldstein and collaborators, 2010).

Caffeine supplementation

Supplementation performed with two dosages of caffeine (low 225 mg/cps, moderate 450 mg/cps) and placebo (magnesium silicate, pharmaceutical talc) at an interval of 48 hours between three visits. It is worth mentioning that the supplementation was blind for the evaluators and for the evaluated ones, and was carried out respecting the following order: 1) the volunteers arrived at the laboratory and stayed 5 minutes in rest in a comfortable chair; 2) Then, randomly by lot in opaque envelopes, the participants were supplemented with doses of caffeine or placebo by means of a capsule (orally) with 200 ml of filtered water; 3) after supplementation, the volunteers remained seated and monitored by means of a heart rate monitor for 60 minutes; 4) Finally, at the end of the 60 minutes, the volunteers underwent an ECG(Task Force of the European Society of Cardiology, 1996).

Analysis of heart rate variability

The HR and its variability were obtained through the cardiofrequencimeter (Polar V800, Finland) with the strap and the receiver positioned at the height of the xiphoid process. The collection was carried out in the first 5 minutes before supplementation and during the 60 minutes after supplementation. IRR records were extracted from Polar V800 and exported to Kubios HRV® software, where ectopic artifacts and beats were first excluded. Then, the 5-minute pre-supplementation stretches and the 5-minute stretches between 20-30 (T20), 30-40 (T30), 40-50 (T40) and 50-60 (T50) minutes after supplementation were selected and analyzed: 1) in the time domain by the mean of the standard deviations of the normal IRR (SDNN) and by the square root of the mean of the successive squared differences between the adjacent IRR (RMSSD); 2) in the frequency domain (through spectral analysis by the fast Fourier transform) by the relative values of the BF and AF bands (normalized units) (Caetano and collaborators, 2015; Hopkins and collaborators, 2000).

Analysis of QT dispersion

For the collection and analysis of the QT dispersion, after 60 minutes of supplementation, the volunteers were monitored by electrocardiography system (Wincardio USB, Brasília, Brazil) in the long DII derivation kept in the sitting position. The QT dispersion obtained by measuring the means of the QT intervals - which comprises the distance in ms of the Q wave from the QRS to the end of the T wave of the electrocardiographic tracing - of the three subsequent central beats of the 25 ms stretch. Such analyses have been measured by two trained and blinded evaluators (without knowledge of supplementation). Additionally, the QT dispersion was corrected for the HR using the formula $QTc = QT / \sqrt{IRR}$ (Arai and collaborators, 2012).

Assessment of adverse events

During caffeine supplementation (60 minutes total), the following adverse events were traced by observation and recording on an evaluation form: nausea, dizziness, anxiety, tachycardia and electrocardiographic changes (supraventricular and/or ventricular arrhythmias).

Statistical Analysis

The data were submitted to the normality test (Shapiro-Wilks test) and homogeneity test (Levene test). Next, the

Friedman test with repeated measures with Tuckey's post-hoc was used to compare the analysis indices in the time domain (SDNN and RMSSD) and frequency (BF and AF in normalized units) in the pre and post supplementation times. Additionally, the same test was also applied for the QT dispersion. Finally, to assess reliability in determining QT dispersion, correlation and concordance tests were applied in intra- and inter-evaluator analyzes. The correlations were classified as 0-0.1 trivial; Small 0.1-0.3; 0.3-0.5 moderate; Strong 0.5-0.7; 0.7-0.9 very strong; and 0.9-1 perfect (Hopkins and collaborators, 2000). Additionally, for all conditions, the effect size calculated using the Cohen criterion, which expressed in the following magnitudes: small [<0.41], moderate [0.41-0.70] and large [>0.70]. (Coe and collaborators, 2002). Analyzes were performed using the Sigma Plot for Windows version 11.0 software, copyright © 2008 Systat Software, Inc. The measurements were expressed as median (25% - 75) and the demographic and anthropometric data presented as mean ± standard deviation. The level of significance was set at $p < 0.05$.

RESULTS

Fourteen volunteers were screened, 2 of whom were excluded due to signal capture problems. Twelve healthy, eutrophic young men with a level of physical activity classified as active (VO_2 peak 36.3 ± 7.9 mL/kg/min) were evaluated.

Table 1 - Characterization of the studied volunteers.

Variable	n = 12
Age (years)	24.3 ± 2.0
Anthropometric characteristics	
Body mass (kg)	74.3 ± 8.6
Height (m)	1.7 ± 0.1
BMI (kg/m^2)	25.0 ± 2.21
Cardiopulmonary test (TCP)	
VO_2 (L/min)	2.7 ± 0.6
VO_2 ($mL/kg/min^{-1}$)	36.3 ± 7.9
Caffeine supplementation	
Low dosage (mg / kg)	3.1 ± 0.4
Moderate dosage (mg / kg)	6.1 ± 0.7

(Mean ± standard deviation) BMI: body mass index; VO_2: oxygen consumption.

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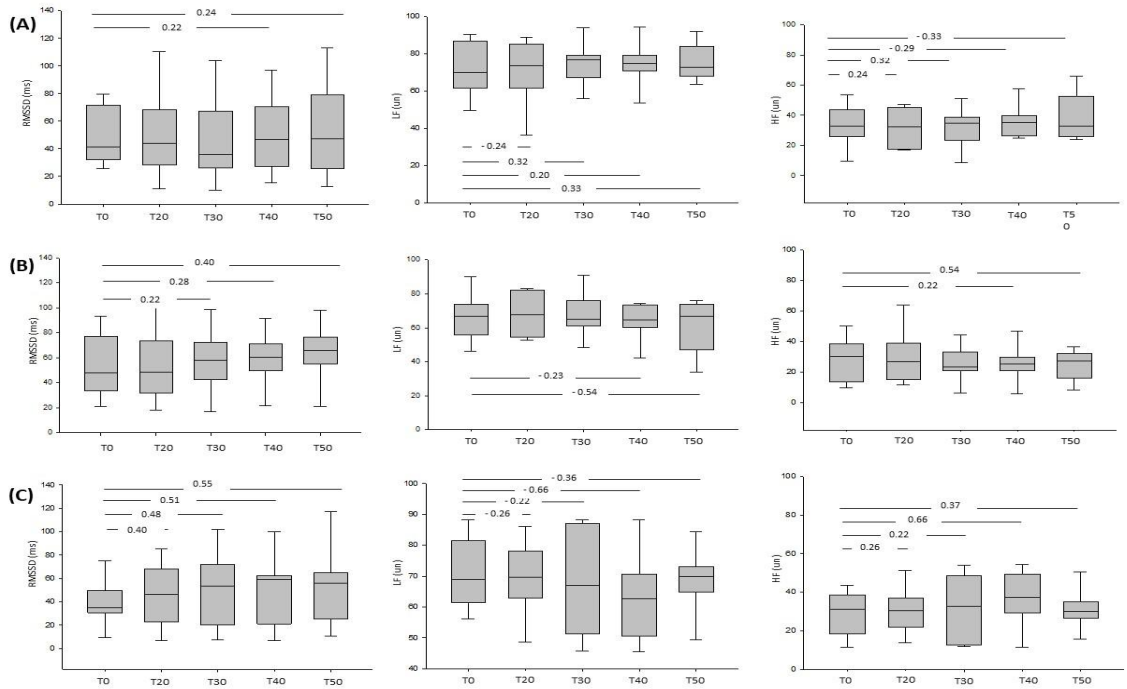

Figure 1 - Heart rate variability data at baseline (T0) and at times 20 (T20), 30 (T30), 40 (T40), 50 (T50) minutes after supplementation: (A) placebo; (B) 225 mg / cps of caffeine; (C) 450 mg / cps of caffeine. Size of the Cohen effect that was expressed in the following magnitudes: small [<0.41], moderate [0.41-0.70] and large [> 0.70].

The average dosage of low supplemented caffeine was 3 mg/kg and the moderate dose was 6 mg / kg (Table 1).

Regarding the tracking of adverse events, 3 volunteers presented isolated ventricular extra systoles, 1 showed signs of anxiety and 1 showed nausea after 60 minutes of supplementation.

For HRV observed data that, under supplementation conditions, there was no significant difference. However, during the supplementation of the dose of 225 mg/cps or 450 mg/cps of caffeine, a small and moderate effect size was observed in the RMSSD, BF and AF indices compared to baseline. However, the placebo condition had a small effect size for the same indexes at the time studied (Figure 1).

Regarding QT dispersion during supplementation, there was no significant difference between caffeine and placebo doses. On the other hand, a small and moderate effect size was observed in comparisons between 225 mg/cps and 450 mg/cps, respectively (figure 2).

Regarding QTc and HR, there were no significant differences and no response related to the size of the effect.

Finally, in order to assess the reliability of QT determination, the coefficient of intra and inter-rater determination showed strong and very strong indices for intra and inter-rater analyzes (Figure 3).

Additionally, Bland Altman showed agreement of A) 75%, B) 64%, C) 78% and D) 87% intra and inter-evaluators, respectively, shown in figure 4.

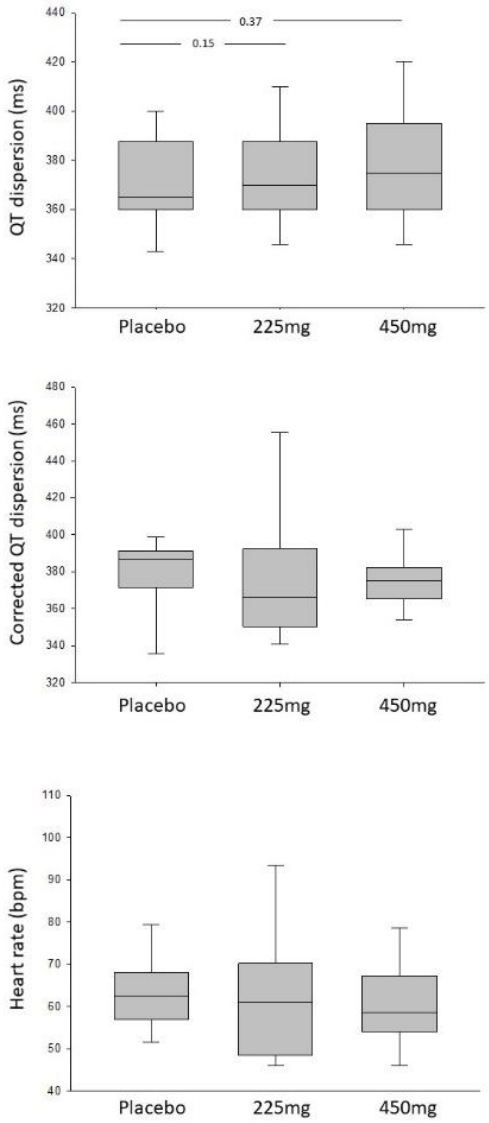

Figure 2 - QT dispersion, corrected QT dispersion and heart rate over placebo doses, 225 mg / cps and 450 mg / cps.

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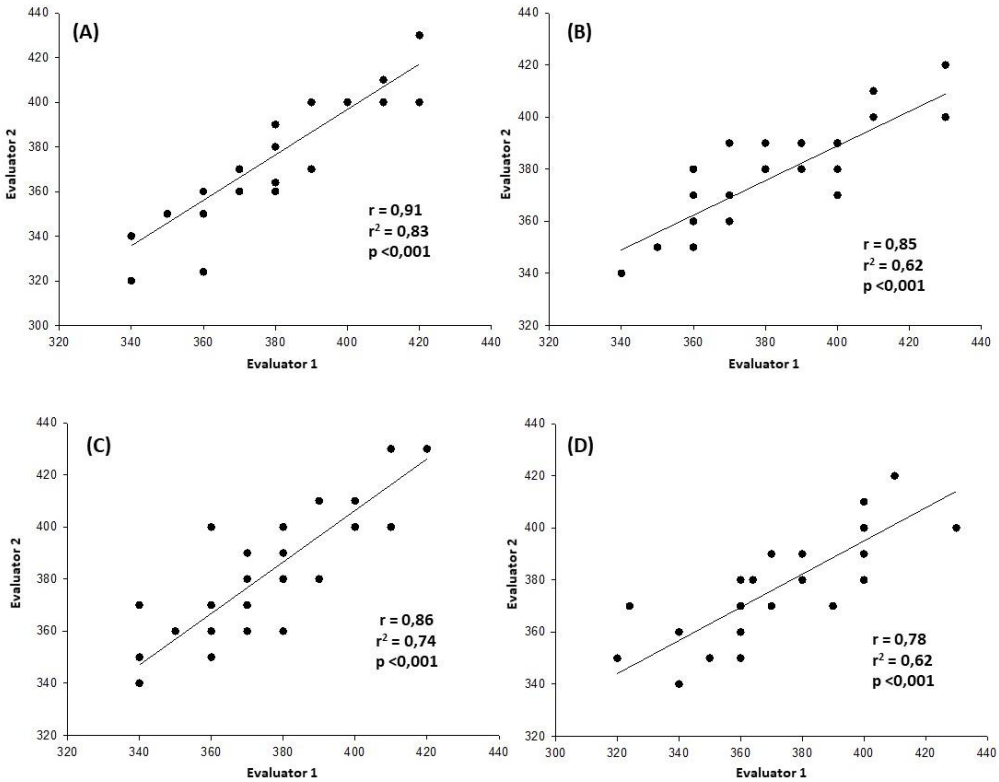

Figure 3 - Coefficients of correlation and intra-determination (A and B) and inter-evaluators (C and D).

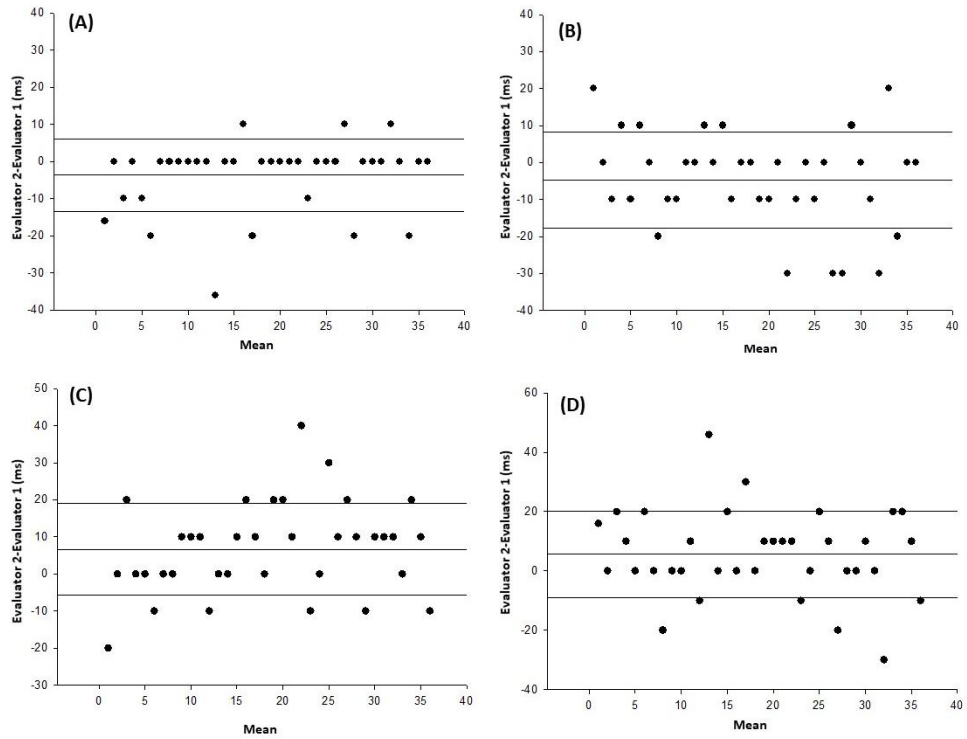

Figure 4 - Bland-Altman agreement between (A and B) and inter-evaluators (C and D).

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DISCUSSION

In the present study found, during caffeine supplementation in the 60 min period, at low (225mg/cps) and moderate (450mg/cps) doses, compared to the placebo dose, there was no significant difference in HRV.

However, a small and moderate effect size was observed in comparisons between 225 mg/cps and 450 mg/cps at the end of 40 and 50 minutes (T40 and T50) post supplementation, demonstrating that for time domain indices, there was an increase in parasympathetic modulation. Regarding the findings regarding the QT interval and HR, there were no significant differences and little response of the effect size.

Several studies have pointed out that caffeine is responsible for increasing sympathetic activity. Miranda and collaborators, (2013) evaluated 51 participants who were divided into two groups, where 27 participants in the group with the lowest caffeine consumption (< 35 mg) and 24 participants in the group with the highest caffeine consumption (>35 mg).

After supplementation, all were submitted to a 24-hour Holter due to a palpitation complaint. The presence of different arrhythmias was found with the use of Holter and less autonomic modulation by means of HRV indices, mainly from SDNN.

It was observed that in the group with the highest caffeine consumption, there was an increase in the sympathetic predominance, predominantly during the sleep period. However, the analysis restricted to this period also showed no association with more than 10 ectopic ventricular or supraventricular tachycardia.

Finally, the study concluded that light to moderate consumption of caffeine (approximately 100 mg/day) was not associated with the onset of severe arrhythmias. However, it did lead to a slight increase in sympathetic stimulation, especially during sleep. Corti and collaborators, (2002) described that caffeine acutely induces muscle sympathetic nerve activity and CF in participants who consumed coffee in an unusual way. The activity was investigated by microneurography on the fibular nerve in 15 healthy volunteers, blinded for intervention.

On the other hand, Rolim and collaborators, (2018) showed an increase in parasympathetic modulation in the use of caffeine. The authors carried out a double-blind study, evaluating 21 healthy young male subjects (22.3 ± 2.9 years, 25.2 ± 2.7 kg / m^2), unusual users of caffeine (<100 mg/day).

The subjects consumed an average of 3mg / kg of caffeine or placebo, the aim of the study being to investigate the effects of caffeine consumption on the parasympathetic cardiac modulation at rest - in the supine position and standing position - and during a submaximal exercise (85% of Peak HR), immediate and late active recovery. It was then observed that low doses of caffeine and placebo were not able to modulate global and parasympathetic cardiac activity at rest. Nevertheless, supplemented individuals with caffeine showed faster recovery after exercise, with parasympathetic hyperactivity. In this sense, our study, developed only at rest, observed an increase in parasympathetic modulation at the end of the T40 and T50 period after supplementation.

Crooks and collaborators, (2019) screened twelve healthy young people who completed an 18-day study conducted in a randomized, double-blind, placebo-controlled laboratory.

The subjects were exposed to three 48-hour sessions of total sleep deprivation, each separated by three days of recovery. In random and balanced order, subjects received placebo, 200 mg or 300 mg of caffeine at 12-hour intervals during each sleep deprivation session.

Every two hours during the scheduled wake, a 15-minute battery of neurobehavioral tasks were administered, during which HR and HR of the HRV power spectrum were measured.

Caffeine administration decreased HR and increased the PA component, indicating high parasympathetic modulation. It was also observed that the dose of 300 mg of caffeine did not significantly affect autonomic activity to a largely extent than the dose of 200 mg. There was no significant effect of 48h of acute total deprivation of sleep in CF, while there was a small increase over awake hours in PA.

There was no significant interaction of acute total sleep deprivation with caffeine. Circadian rhythmicity in CF and AF exceeded the magnitude of the effects of caffeine and acute total sleep deprivation. Thus, caffeine and total sleep deprivation produced only modest changes in cardiac autonomic modulation, unlikely to have immediate clinical implications in young, healthy adults.

Another point that deserves attention for performance analysis was that verified by Duncan and collaborators, (2009) in a study on the perception of caffeine as a placebo. In this study, the volunteers underwent weightlifting exercises under different conditions of use: caffeine dose, placebo dose named caffeine and placebo dose.

Although the study was double-blind, that is, the participants were not aware of which substance they were using, when they thought they had ingested caffeine (placebo), they believed they had less effort in lifting more weight. This was partly because they believed that the study design consisted of two doses of caffeine and one of placebo.

Likewise, in view of our study, the perception promoted by the placebo may have influenced the autonomic modulation during the time of the analyzed signal with results of greater HRV even under the conditions of placebo supplementation.

Regarding the dose of caffeine offered in the present study, it was observed in the literature review by Goldstein and collaborators (2010), which concluded that caffeine is effective in improving performance, when consumed in low to moderate doses (~ 3- 6 mg / kg); in addition, there is no more benefit when consumed in higher doses (≥ 9 mg / kg). However, in high doses, caffeine could have a deleterious effect on life-threatening health.

In the case study described for Willson and collaborators (2018) a young 16- year- old man, body mass of 91 kg, height of 1.73 m, and body mass index (BMI) of 30.4, overdosed after ingesting three drinks contained caffeine, in a short period of time, approximately 40 minutes, being sent to the hospital, where he died. This case has drawn attention, because the amount of caffeine was not considered lethal, and the adolescent was apparently healthy and did not have heart problems or allergic conditions reported by family members.

The cause of death was determined as an induction of caffeine causing probable arrhythmia. In this sense, possibly caffeine when consumed in a short period of time resulted in an increase in plasma caffeine concentrations in the blood.

Howsoever, White and collaborators (2016) that analyzed the pharmacokinetics and compared the fast or slow administration of cold or hot coffee versus cold energy drink in healthy young adults, was observed that caffeine absorption and exposure of coffee and energy drink were similar, regardless of temperature or rate of consumption of the drink.

According to Goldstein and collaborators (2010), caffeine proves more potent when consumed in an anhydrous state (capsule/tablet, powder), compared to coffee. Most research has used a protocol where caffeine taken 60 minutes before performance ensures optimal absorption; however, it has also been shown that caffeine can improve performance when consumed 15 to 30 minutes before exercise. What in this case, that was related to our study, although developed at rest.

Regarding findings in relation to the QT interval, Buscemi and collaborators (2011) who observed the acute effects of coffee in the QT interval in healthy individuals, found that, despite the fact that caffeine sharply increases SBP and DBP, as well as HR, does not acutely induce any significant changes in the duration of the QTc interval in healthy adult individuals.

In this sense, Brothers and collaborators (2017) that evaluated and compared the effect of acute supplementation of 2 and 3 mg/kg of caffeine in 15 participants, revealed that there were no negative responses on the dispersion of the QT intervals reflecting preserved ventricular repolarization. On the other hand, Fletcher (2017) supplemented 320mg of caffeine for 18 healthy young people, showed an increase in SBP and QT intervals.

These findings led to the authors assertive position in warning about careful caffeine consumption. Additionally, Basrai and collaborators (2019) that acutely supplemented caffeine alone or combined with taurine in 38 healthy adults, observed that caffeine alone was able to increase the HR response, but did not alter the behavior of the QT interval.

However, when caffeine was supplemented with taurine, the volunteers showed an increase in the QT interval and 11% of the participants experienced adverse events - such as palpitation, nausea, and headache. In the present study, despite the observation of a change in HRV behavior induced by caffeine, there was no significant change or an increase in the effect of caffeine supplementation on the QT interval. However, it should have noticed that, as in the study by Basrai and collaborators (2019) 4% of our volunteers had adverse effects.

Another relevant aspect taking into consideration in the present study, was the way of assessing QT dispersion. While most evaluators used a single interval of the ECG

trace for diagnosis defined that, the determination of the QT interval would be by averaging three consecutive beats of the ECG trace.

Additionally, to assess the reliability of the technique in our laboratory, both intra- and inter-rater analyzes were performed at the three different moments (RMSSD, AF and BF) in a blind manner, thus demonstrating greater precision in the evaluation criteria of the method for analyzing the QT. The purpose was to ensure good practices for more reliable results. However, an aspect of great relevance must be considered about the response of caffeine in the body.

Guest and collaborators (2018) observed that 95% of the metabolism of caffeine depends on the CYP1A2 gene variations. The effects of genetic polymorphism were observed through the collection and analysis of DNA, demonstrating that the single nucleotide polymorphism (-163A> C (rs762551) alters the inductive and activity of the enzyme CYP1A2 and has been used to categorize individuals as fast metabolizers and slow.

Individuals with the AC or CC genotype were considered as slow metabolizers and those with the AA genotype were considered fast metabolizers.

Additionally, Thomas collaborators (2016) examined the influence of the CYP1A2 polymorphism on post-exercise HRV. In response to caffeine intake with a repeated, double blind, placebo-controlled study, with 25 participants, 13 men and 7 women, who were identified by analysis of homozygous A/A genotype (A/A; 4 women and 7 men) or carrier C allele (C allele; 6 men and 3 women), being subsequently randomized into a caffeine or placebo group. Participants were instructed to abstain from drinks with caffeine or alcohol for 48 hours before the experimental trial.

HRV data were collected, and caffeine or placebo ingested as chewing gum. DNA analyzes were collected and CYP1A2 polymorphism was analyzed. Caffeine intake increased peak potency (682±140 vs. 667±137 W; p=0.008) and the mean power during the Wingate test (527±111 vs. 518±111 W; p<0.001) without differences between homozygous A/A and C with allele (p> 0.05). Reaction times were also similar in the two conditions (276±31 vs. 269±71 milliseconds; p=0,661) without differences between homozygous AA bearing the allele C.

However, it was observed an increase of adverse effects after the ingestion of caffeine, while non-homozygous AA had traces of collateral effect. The genetic variations of the CYP1A2 polymorphism did not affect the ergogenic effects derived from ingesting a moderate dose of caffeine. In this sense, it is feasible to consider that the controversies observed in different well-conducted studies may be related to individual responses genetically determined.

Finally, some limitations of the present study must be observed: i) the doses of caffeine could have been supplemented according to the body mass of each individual. However, there is a risk of impairment of blindness on the part of the researchers; ii) after supplementation, individuals could have undergone a blood or urine test to prove the caffeine effect dose, which could also compromise blinding.

Therefore, we decided to evaluate the HR response afterwards by its HRV; and finally, iii) individuals could have been subjected to genetic typing for caffeine and classified as responders and non-responders.

CONCLUSION

Caffeine supplementation increased cardiac autonomic modulation with vagal predominance.

Additionally, caffeine had a slight effect on changing the QT dispersion in the applied doses to the volunteer studied. Finally, adverse events were observed in 4% of volunteers.

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REFERENCES

1-Arai, K.; Kato, M.; Yamada, Y.; Ogawa, S.; Ohtsuki, T.; Nakamura, T.; Murayama, M. Relationships between QT interval and heart rate variability at rest and the covariates in healthy young adults. Autonomic Neuroscience. Vol. 173. Num. 1-2. 2012. p. 53-57. Disponível em: http://dx.doi.org/10.1016/j.autneu.2012.11.006.

2-Basrai, M.; Raeisian, M.; Zamanifar, S.; Zare, M.; Sadeghi, N.; Sadeghi, M.; Azimi, T. Energy drinks induce acute cardiovascular and metabolic changes pointing to potential risks for young adults: A randomized controlled trial. The Journal of Nutrition. Vol. 149. Num. 3. 2019. p. 441-450. https://doi.org/ 10.1093/jn/nxy303.

3-Brothers, R.M.; Parr, R.A.; Schneider, A.; Hart, L. R.; Sessler, D. I. Heart rate, blood pressure and repolarization effects of an energy drink as compared to coffee. Clinical Physiology and Functional Imaging. Vol. 37. Num. 6. 2017. p. 675-681. https://doi.org/10.1111/cpf.12357.

4-Bunsawat, K.; White, W. D.; Kappus, M. R.; Baynard, T. Caffeine delays autonomic recovery following acute exercise. European Journal of Preventive Cardiology. Vol. 22. Num. 11. 2015. p. 1473-1479. https://doi.org/ 10.1177 /2047487314554867.

5-Buscemi, S.; Rossi, M.; Crippa, A.; Luca, M. Acute effects of coffee on QT interval in healthy subjects. Nutrition Journal. Vol. 10. Num. 1. 2011. p. 15.

6-Caetano, J.; Alves, J.D. Heart rate and cardiovascular protection. European Journal of Internal Medicine. Vol. 26. Num. 4. 2015. p. 217-222. https://doi.org/10.1016/j.ejim.2015 .02.009.

7-Casiglia, E.; Sacco, M.; Gottardi, F.; Cavalla, P.; Bagatti, D. Caffeine intake reduces incident atrial fibrillation at a population level. European Journal of Preventive Cardiology. Vol. 25. Num. 10. 2018. p. 1055-1062. 2018. https://doi.org/10.1177/204748731 8772945.

8-Catai, A.M.; Souza, F.C.; Dantas, E.H.M.; Machado, R.C.; Mendes, R.R. Heart rate variability: are you using it properly? Standardisation checklist of procedures. Brazilian Journal of Physical Therapy. Vol. 24. Num. 2. 2019. p. 91-102. https://doi.org/10.10 16/j.bjpt.2019.02.006.

9-Cavalcante, J.W.S.; Santos, L.C.; Pereira, R.I. Influência da cafeína no comportamento da pressão arterial e da agregação plaquetária. Arquivos Brasileiros de Cardiologia. Vol. 75. Num. 2. 2000. p. 97-101. http://dx.doi.org/10.6063/motricidade.12942.

10-Coe, R. In: Annual Conference of the British Educational Research Association, 12-14 set. 2002, Exeter, Devon, Inglaterra. University of Exeter. 2002.

11-Corti, R.; Pizza, F.; Santoni, S.; Zangrando, A. Coffee acutely increases sympathetic nerve activity and blood pressure independently of caffeine content: role of habitual versus nonhabitual drinking. Circulation. Vol. 106. Num. 23. 2002. p. 2935-2940. https://doi.org/10.1161/01.cir.00000462 28.97025.3a.

12-Crooks, E.; Cole, R.; Brown, S.; Richards, D. Cardiac autonomic activity during sleep deprivation with and without caffeine administration. Physiology & Behavior. Vol. 210. 2019. p. 112643. https://doi.org/10. 1016/j.physbeh.2019.112643.

13-Duncan, M.J.; Lyons, M.; Hankey, J. Placebo effects of caffeine on short-term resistance exercise to failure. International Journal of Sports Physiology and Performance. Vol. 4. Num. 2. 2009. p. 244-253.

14-Fletcher, E.A.; White, L.D.; Lopez, R.L.; Jones, M.L. Randomized controlled trial of high-volume energy drink versus caffeine consumption on ECG and hemodynamic parameters. Journal of the American Heart Association. Vol. 6. Num. 5. 2017. p. e004448. https://doi.org/10.1161/jaha.116.004448.

15-Floriano, R.S.; Orsini, M.; Reis, M.S. Importância do teste cardiopulmonar para a fisioterapia cardiovascular. Fisioterapia Brasil. Vol. 20. Num. 4. 2019. p. 578-591. https://doi.org/10.33233/fb.v20i4.2411.

16-Goldstein, E.R.; Guevara, L.L.; Norman, M.L.; Brooks, K.P. International society of sports nutrition position stand: caffeine and performance. Journal of the International Society of Sports Nutrition. Vol. 7. 2010. p. 5. https://doi.org/10.1186/1550-2783-7-5.

17-Guest, N.; Barrow, M.; Thomas, S. Caffeine, CYP1A2 genotype, and endurance performance in athletes. Medicine & Science in Sports & Exercise. Vol. 50. Num. 8. 2018. p. 1570-1578. https://doi.org/10.1249/mss.00000 00000001596.

18-Guimarães, J.I.; Azevedo, R.H.; Cavalcanti, G.S.; Camargo, F.A. Diretriz de interpretação de eletrocardiograma de repouso. Arquivos Brasileiros de Cardiologia. Vol. 106. 2003. p. 1-23. http://dx.doi.org/ 10.5935/abc.20160054.

19-Hibino, G.; Takahashi, Y.; Noguchi, M.; Kobayashi, H.; Kurihara, M. Caffeine enhances modulation of parasympathetic nerve activity in humans: quantification using power spectral analysis. The Journal of Nutrition. Vol. 127. Num. 7. 1997. p. 1422-1427. https://doi .org/10.1093/jn/127.7.1422.

20-Higgins, J.P.; Babu, K.M. Caffeine reduces myocardial blood flow during exercise. The American Journal of Medicine,. Vol. 126. Num. 8. p. 730. 2012. http://dx.doi.org/10.1016 /j.amjmed.2012.12.023.

21-Hopkins, W.G. Measures of reliability in sports medicine and science. Sports Medicine. Vol. 30. Num. 1. 2000. p. 1-15. https://doi.org/10.2165/00007256-200030010-00001.

22-Miranda, D.E.G.A.; Barbosa, E.C.; Teixeira, P.H.; Souza, L.F.; Garcia, F.A. Avaliação dos efeitos da cafeína sobre a modulação autonômica e o ritmo cardíaco em pacientes com queixa de palpitações. Revista Latino-Americana de Marcapasso e Arritmia. Vol. 26. Num. 2. 2013. p. 63-70.

23-Rolim, P.S.; Aguiar, J.R.; Tavares, L.G. Caffeine increases parasympathetic reactivation without altering resting and exercise cardiac parasympathetic modulation: A balanced placebo design. European Journal of Sport Science. Vol. 19. Num. 4. 2018. p. 490-498. https://doi.org/10.1080/17461391.2018. 1532532.

24-Salinero, J. J.; Lara, B.; Del Coso, J. Effects of acute ingestion of caffeine on team sports performance: A systematic review and meta-analysis. Research in Sports Medicine. Vol. 27. Num. 2. 2019. p. 238-256. https://doi.org/10.1080/15438627.2018.155214 6.

25-Silvestre, J.C.; Gianoni, R.; Pereira, P.E. Cafeína e desempenho físico: metabolismo e mecanismos de ação. Revista Brasileira de Fisiologia do Exercício. Vol. 17. Num. 2. 2018. p. 130-137. http://dx.doi.org/10 .33233/rbfe.v17i2.

26-Task force of the european society of cardiology and the north american society of pacing and electrophysiology. Standards of measurement, physiological interpretation, and clinical use. European Heart Journal. Vol. 93. Num. 5. 1996. p. 1043-1065. https://doi.org/10. 1161 /01.CIR.93.5.1043.

27-Tavares, C.; Sakata, R.K. Caffeine in the treatment of pain. Brazilian Journal of Anesthesiology. Vol. 62. Num. 3. 2012. p. 387-401. https://doi.org/10.1016/s0034-7094(12)7 0139-3.

28-Thomas, R.M.; Mcallister, A.S.; Moore, P.L.; Smith, G.P. Influence of a CYP1A2 polymorphism on post-exercise heart rate variability in response to caffeine intake: a double-blind placebo-controlled trial. Irish Journal of Medical Science. Vol. 186. Num. 2. 2016. p. 285-291. https://doi.org/10.1007/s 11845-016-1478-7.

29-Voskoboinik, A.; Kalman, J.M.; Kistler, P M. Caffeine and arrhythmias: time to grind the data. JACC: Clinical Electrophysiology. Vol. 4. Num. 4. 2018. p. 425-432. https://doi.org/10.1016/j.jacep.2018. 01.012.

30-White, J.R.; Miller, K.G.; Shaw, R. A.; Lee, W.M.; Malone, R. Pharmacokinetic analysis and comparison of caffeine administered rapidly or slowly in coffee chilled or hot versus chilled energy drink in healthy young adults. Clinical Toxicology. Vol. 54. Num. 4. 2016. p. 308-312. http://dx.doi.org/10.3109/15563650.2016.1146 740.

31-Willson, C. The clinical toxicology of caffeine: A review and case study. Toxicology Reports. Vol. 5. 2018. p. 1140-1152. https://doi.org/10.1016/j.toxrep.2018.11.002.

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