Cardiology in the Young

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Non-linear analysis of heart rate variability for evaluating the acute effects of caffeinated beverages in young adults

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Abstract

Caffeinated beverages are the most consumed substances in the world. High rate of uptake of these beverages leads to various cardiovascular disorders ranging from palpitations to coronary failure. The objective of the study is to ascertain how the complexity parameters of heart rate variability are affected by acute consumption of caffeinated beverages in young adults.

Electrocardiogram measurements were performed before consuming drinks. After consuming the drinks, measurements were done again at 30 minutes and 60 minutes. Heart rate variability signals were acquired from electrocardiogram signals. Also, the signals were reconstructed in the phase space and largest Lyapunov exponent, correlation dimension, approximate entropy, and detrended fluctuation analysis values were calculated.

Heart rate increased for energy drink and cola groups but not in coffee group. Non-linear parameter values of energy drink, coffee, and cola group are increased within 60 minutes after drink consumption. This change is statistically significant just for energy drink group.

Energy drink consumption increases the complexity of the cardiovascular system in young adults significantly. Coffee and cola consumption have no significant effect on the non-linear parameters of heart rate variability.

Introduction

Caffeine which is a methylxanthine compound is probably the most consumed stimulant in the world. It increases the autonomic nervous system activity and blocks adenosine receptors (A1 and A2) by releasing the plasma catecholamines.[1] This effect induces tachycardia and hypertension and also increases respiratory rate, bronchodilatation, lipolysis, and diuresis.[2] It is a dominant ingredient in many beverages, such as coffee, tea, energy drinks, and cola-type drinks. These are the most popular beverages that are consumed uncontrollably by young people for the increasing effect upon attention, arousal, and physical performance. In the last decades, there are increasing reports of especially energy drinks related with cardiovascular events, seizures, and death.[3] The effects of these beverages must be investigated in detail because of the high-rate consumption and occasional acute adverse health effects. There are numerous studies which investigated the acute effects of caffeinated beverages on haemodynamic parameters, such as blood pressure and heart rate variability.[1,4–6] For instance, Hajsadeghi et al[7] reported a significant heart rate decline and Peveler et al[8] showed a significant increase in systolic blood pressure after the consumption of energy drink. Consequently, a number of studies have shown the adverse effects of caffeinated beverages on cardiovascular system, but the dynamics and the mechanism are still ambiguous.

Linear and non-linear methods are being used for a better understanding of physiological signals and systems. Time-domain and frequency-domain analysis which are linear methods can only present first- and second-order statistics of the signals so they can give limited information about the system. However, non-linear methods reveal and characterise the dynamics and the complexity of the systems in detail. For instance, the physiological interaction between the heart period and autonomic nervous system is being determined by the analysis of heart rate variability using linear and non-linear methods.[9] However, analysing heart rate variability through time and frequency domains focus only on sympathovagal balance assessment which is inadequate to describe the complex time behaviour of heart rhythm.[10] Since the cardiovascular system is complex and do not show regular periodicity, it cannot be completely explained by linear methods. To overcome this adequacy, non-linear methods are being used extensively. For instance, Koichubekov et al,[11] Pivatelli et al,[12] and Neves et al[13] analysed heart rate variability by evaluating the non-linear indices, such as largest Lyapunov exponent, approximate entropy and correlation dimension in patients with hypertension, stable angina, and coronary disease, respectively. Also, Tsai et al reported that detrended fluctuation analysis shown better predictive ability for clinical outcomes when compared to traditional heart rate variability analysis methods.[14] In the literature,

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there are some studies which investigated heart rate variability time series with detrended fluctuation analysis and reported the accuracy of the method.[15,16] To our knowledge, there are no reports in the literature on non-linear analysis of heart rate variability used to investigate the acute effects of caffeinated beverages on cardiovascular system. For this reason, our study will be the first for this subject in the literature.

However, due to the fact that the effects on the human body are not fully known and the interest in these beverages has increased, the need for further study in this issue has arisen. In this study, it is aimed to ascertain how the complexity parameters of heart rate variability are affected by acute consumption of caffeinated beverages. In this respect, expressive information can be obtained about the system's dynamic structure in more detail.

Materials and methods

Participants

Fourty-eight participants (20 female, 28 male) aged 18–24 years (mean 19.20 ± 0.48) were selected from the students of Aydın Adnan Menderes University. They were identified by applicant acceptance questionnaire which includes information about age, weight, height, body mass index, and caffeine consumption habit. The participants with a body mass index greater than 30 kg/m^2, a systemic disease, current alcoholism, smokers, and who has previous adverse reactions to caffeinated beverages were excluded from the study. All subjects were caffeine-naïve and grouped as energy drink (n = 12), coffee (n = 12), cola (n = 12), and control (n = 12). This study conforms to the Declaration of Helsinki and was approved by the Institutional Medical Ethics Committee of Adnan Menderes University (Protocol number: 2017/1211). Informed consent was obtained from all individual participants included in the study.

Experimental protocol

All experiments were performed at the same time of the day for avoiding the different responses due to circadian rhythm. The room was isolated from external factors with the room temperature of about 20°C and relative humidity between 40 and 60%. All participants were instructed to abstain from alcohol and caffeine-containing foods for at least 72 hours prior to the test and to come with an overnight (12 hours) fasting.

Electrocardiogram signals were recorded before and after the consumption of the drinks in 30 minutes and 60 minutes. Coffee group consumed 473 ml of Nescafe classic, energy drink group consumed 473 ml of Red Bull energy drink, cola group consumed 473 ml of Coca Cola, and control group consumed the same amount of water within 5 minutes. These drinks contain 3784 mg, 1514 mg, and 404 mg caffeine, respectively.[17,18]

Data acquisition

Electrocardiogram recordings were obtained from the participants for 5 minutes in rest and sitting position. Disposable Ag–AgCl electrodes were placed following the Einthoven triangle configuration. Electrocardiogram measurement was performed with sampling frequency of 200 Hz using ECG100C unit and BIOPAC Acqknowledge acquisition software (Biopac System Inc., Santa Barbara, CA) connected to a personal computer. We analysed the 5-minute electrocardiogram signal to extract the heart rate variability signal. All analyses were performed according to the standards set by Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology.[19]

For acquiring the heart rate variability time series, Pan and Thompkins algorithm was used.[20] R peaks were detected automatically and R–R intervals are obtained. The time duration between two consecutive R peaks is termed as RR interval (t_{RR}).[21] The sample size of the heart rate variability time series is 1000. The heart rate is determined as:

$$Heart\ Rate = \frac{60}{t_{RR}}.$$

Non-linear analysis

Phase space reconstruction

For non-linear analysis, heart rate variability time series was reconstructed in the phase space using data's time-delayed copies. Embedding dimension and time-delay values were calculated using Cao's method[22] and mutual information method[23] for reconstruction process. Largest Lyapunov exponent, correlation dimension, and approximate entropy parameters were calculated from the attractor which was reconstructed in the phase space. For this purpose, we used MATLAB (The Mathworks Inc., USA). They represent the complexity and irregularity of the system which was investigated. These were explained in the study of Caliskan et al[24] in detail.

Detrended fluctuation analysis

Detrended fluctuation analysis is used to evaluate the fractal behaviour of non-stationary RR dynamics by eliminating extrinsic trends to remove spurious long-term correlations.[25] It allows us to have a differentiated view on the correlative structure of variability caused by physiological processes in time series.[26] It is a suitable method for the evaluation of heart rate variability which is a short and non-stationary time series data since it is a modification of the root mean square analysis.[27] In this analysis, first of all linear and polynomial fitted trends which are called the external trends are removed from the integrated time series. Detrended integrated time series was added up in individual scales for calculating the detrended fluctuations. Then, fluctuations are plotted logarithmically against timescales. This graph is consisted of two distinct curves separated by one point. The fractal correlation characters of the time series are obtained from the slopes (α1 and α2 exponent) of the log–log graph. If α is between 0 and 0.5, the large and small values of the time series are more likely to alternate. While α = 0.5 corresponds to white noise, α = 1.5 corresponds to Brownian noise, and if α is between 0.5 and 1.0 then there are positive correlations present in the time series.[28] For healthy subjects, α1 tends to 1 (unity) and is bigger than α2 value.[16]

In this study, heart rate variability time series was analysed by detrended fluctuation analysis. Both short-term (α1) and long-term (α2) exponents were calculated in order to have detailed information about the fractal characters of the system. Detrended fluctuation analysis parameters were calculated using Kubios HRV Standard (Kubios Heart Rate Variability analysis software version 3.1.0; Kupio, Finland).

Statistical analysis

Statistical analysis of the data was performed using SPSS Statistics for Windows, Version 22.0. (SPSS Inc., Chicago, IL, USA). For

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Table 1. The characteristics of the participants

		Energy drink	Coffee	Cola	Control
Age (year)		19.17 ± 0.32	19.25 ± 0.45	19.33 ± 0.40	19.58 ± 0.48
Height (m)		1.74 ± 0.03	1.71 ± 2.08	1.72 ± 2.47	1.73 ± 0.02
Weight (kg)		67.13 ± 4.31	70.40 ± 3.73	69.73 ± 4.28	71.44 ± 3.76
Body mass index (kg/m^2)		21.90 ± 0.87	23.91 ± 0.93	23.23 ± 1.21	23.91 ± 1.25
Heart rate (bmp)	Pre	83.16 ± 2.39	76.60 ± 3.06	81.30 ± 2.20	76.16 ± 2.23
	30 minutes	86.64 ± 2.71	76.78 ± 3.40	82.44 ± 2.53	76.29 ± 2.80
	60 minutes	87.96 ± 3.35	76.95 ± 4.33	83.09 ± 2.38	76.58 ± 3.12
	P	0.045	0.439	0.744	0.164

comparing the groups, first of all Shapiro–Wilk normality test was applied to determine the normality of the distribution. If the result of Shapiro–Wilk normality test was bigger than 0.05, the data were normally distributed and were analysed using one-way analysis of variance with Bonferroni post-test, but if the result was less than 0.05 the data were not normally distributed and were analysed using Kruskal–Wallis non-parametric test. Repeated one-way analysis of variance test was used for the comparison of different measurement time data of the same group. Descriptive statistics were presented as mean ± standard error of the mean. A p-value of less than 0.05 was considered to indicate statistical significance.

Results

Table 1 displays the characteristics of the groups. There was no significant difference in age, height, weight, and body mass index values between the groups. Furthermore, 60-minute heart rate values of the energy drink and cola groups were increased with regard to pre-drink heart rate values. Only, the increase in energy drink group was statistically significant ($p = 0.045$). There was no change for coffee group. Heart rate values of control group did not change significantly across time.

Non-linear analysis results of heart rate variability for experimental groups are shown in Table 2. Heart rate variability time series was reconstructed in the phase space in order to investigate the dynamics of the system in detail. Embedding dimension and time-delay values were determined as 3 and 2, respectively. Using the embedding dimension and time-delay values, heart rate variability time series was reconstructed in the phase space. Largest Lyapunov exponent and correlation dimension values of energy drink group at 60 minutes after consumptions were significantly increased when compared to pre-drink largest Lyapunov exponent values (Figs 1 and 2) ($p = 0.016$, $p = 0.003$, respectively). These non-linear parameters were increased slightly for coffee and cola groups but these changes were not statistically significant. Also, they did not change for control group across time. Similarly, approximate entropy, detrended fluctuation analysis $-\alpha 1$, and detrended fluctuation analysis $-\alpha 2$ values were increased within 60 minutes of consumption when compared to pre-drink values (Table 2). However, the differences were not statistically significant. There is no statistically significant alteration for the non-linear parameters at 30 minutes of consumption for all experimental groups. Furthermore, both for largest Lyapunov exponent and correlation dimension values, there is a statistically significant difference between energy drink and control group at 60 minutes of consumption ($p = 0.014$, $p = 0.011$). This is as the same for coffee group in correlation dimension parameter also ($p = 0.023$).

Discussion

The acute effects of caffeinated beverages on complexity parameters of heart rate variability were investigated in this study. The principle finding is that energy drink consumption increases the complexity of the cardiovascular system in young adults significantly. Coffee and cola consumption have no significant effects on the non-linear parameters of heart rate variability.

In the last decades, especially young people consume caffeinated beverages more frequently for efficient alertness, physical strength, and mood enhancement. Insufficient information about the adverse effects of these beverages makes its consumption uncontrolled among young people. There are many case reports about their life-threatening adverse effects such as cardiac arrest, myocardial infarction, and atrial fibrillation.[29–31] There exist great health concerns worldwide because of the widespread use of these beverages. For this reason, its effects on young human must be investigated in more detail.

Heart rate variability analysis is a mostly preferred method since it divulges information about the influence of the autonomic nervous system activity on the heart and it is a reliable, informative, and applicable tool in daily practice.[16] The most important step is the extraction of the features containing all the relevant information about the system dynamics.[32] Time-domain, frequency-domain, and non-linear methods are generally used for this procedure. While time-domain and frequency-domain methods enable the quantification of heart rate variability on different timescales, non-linear methods provide additional information regarding the dynamics and structure of beat-to-beat time series.[9] Linear analysis methods have some limitations since it has sensitiveness about the band definition (low frequency, from 0.04 to 0.15 Hz and high frequency, from 0.15 to 0.40 Hz).[13] Also, the physiological signals are not constant on time and do not show regular periodicity. Therefore, they cannot be explained accurately by linear analysis methods.[33] Non-linear analysis outperforms time- and frequency-domain methods by providing a continuous analysis of the signal and detailed information about the system dynamics. These methods were applied in various studies in which the effects of different diseases on heart rate variability were investigated.[12,21,34]

In our study, we have shown that energy drink and cola consumption have risen the heart rate values when compared to

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Table 2. Non-linear parameters of the groups before, after 30 minutes and 60 minutes of drink consumptions. P refers to the differences between the pre and 60th minute values of groups

		Energy drink	Coffee	Cola	Control
Largest Lyapunov exponent	Pre	0.661 ± 0.070	0.890 ± 0.190	0.600 ± 0.071	0.565 ± 0.076
	30 minutes	0.929 ± 0.061	1.041 ± 0.213	0.645 ± 0.125	0.562 ± 0.043
	60 minutes	1.673 ± 0.059	1.059 ± 0.459	0.721 ± 0.096	0.571 ± 0.057
	P	0.016	0.922	0.954	0.440
Correlation dimension	Pre	0.859 ± 0.026	0.923 ± 0.139	0.903 ± 0.023	0.902 ± 0.023
	30 minutes	0.914 ± 0.009	0.944 ± 0.022	0.914 ± 0.026	0.907 ± 0.015
	60 minutes	0.957 ± 0.031	0.965 ± 0.017	0.918 ± 0.019	0.901 ± 0.029
	P	0.003	0.391	0.438	0.676
Approximate entropy	Pre	0.259 ± 0.040	0.233 ± 0.018	0.144 ± 0.011	0.201 ± 0.070
	30 minutes	0.265 ± 0.034	0.248 ± 0.028	0.160 ± 0.059	0.203 ± 0.053
	60 mintes	0.301 ± 0.056	0.264 ± 0.031	0.169 ± 0.043	0.183 ± 0.040
	P	0.998	0.307	0.740	0.994
Detrended fluctuation analysis-α1	Pre	0.866 ± 0.034	0.773 ± 0.054	0.659 ± 0.073	0.707 ± 0.084
	30 minutes	0.914 ± 0.045	0.816 ± 0.066	0.759 ± 0.086	0.708 ± 0.067
	60 minutes	0.977 ± 0.081	0.865 ± 0.046	0.758 ± 0.099	0.712 ± 0.082
	P	0.976	0.382	0.461	0.104
Detrended fluctuation analysis-α2	Pre	0.346 ± 0.017	0.286 ± 0.034	0.283 ± 0.053	0.348 ± 0.064
	30 minutes	0.351 ± 0.028	0.281 ± 0.024	0.283 ± 0.056	0.359 ± 0.049
	60 minutes	0.356 ± 0.027	0.288 ± 0.025	0.283 ± 0.048	0.347 ± 0.031
	P	0.230	0.642	0.121	0.476

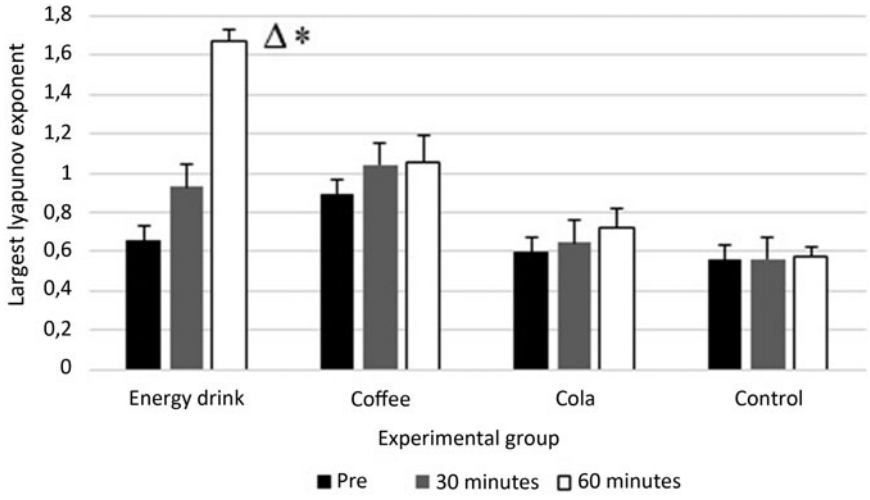

Figure 1. The variation of largest Lyapunov exponent values of the groups during the experiment. Δ statistically significant versus pre-drink value of energy drink group ($p = 0.016$) and * statistically significant versus 60-minute value of control ($p = 0.014$).

pre-drink values. The increment for energy drink group was consistent with the studies in which reported a significant increase in heart rate after energy drink consumption.[5,35] In addition, there are no studies that evaluate the acute effects of cola consumption on haemodynamic parameters in the literature. Therefore, there is no opportunity to compare the results we obtain. Furthermore, there was an interesting finding that in contradiction to other groups, there was no alteration in heart rate of coffee group. This is in line with the study of Hara et al[36] which reported no effect of coffee consumption in non-habitual coffee consumers. Also, Ammar et al[6] reported that there was no alteration in heart rate with acute dosing of caffeine in healthy volunteers. The difference between energy drink–cola groups and coffee group might be due to the other ingredients of these beverages. One of the major contents of energy drink is taurine which is well known to rise heart rate.[37] Also, glucose is one of the ingredients of both energy drink and cola and it has been shown that glucose ingestion or administration affects cardiac function and increases cardiac output.[38]

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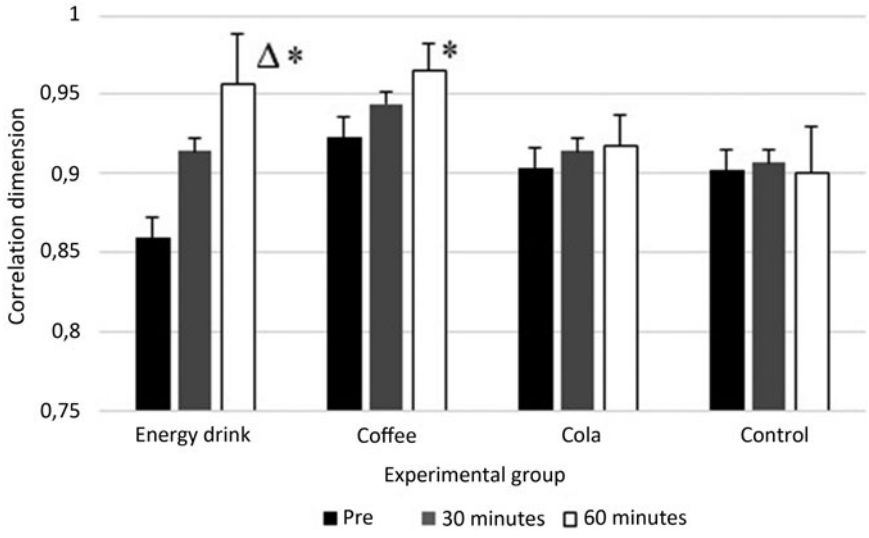

Figure 2. The variation of correlation dimension values of the groups during the experiment. Δ statistically significant versus pre-drink value of energy drink group ($p = 0.003$) and * statistically significant versus 60-minute value of control ($p = 0.011$, $p = 0.023$, respectively).

On the other hand, we calculated largest Lyapunov exponent and correlation dimension parameters and found a statistically significant increase between the pre-drink and post-drink values of energy drink group. Also, these parameters increased for coffee and cola groups but these increments were trivial. These parameters give information about the system's chaoticity and according to our results it can be deduced that caffeinated beverage consumption has a significant effect on the complexity of heart rate variability. In addition, there are no studies that evaluate the acute effects of caffeinated beverage consumption on heart rate variability by analysing these non-linear parameters in the literature. Therefore, there is no opportunity to compare the results we obtain.

Entropy is the measure of the degree to which the occurrence of a value depends on its predecessors in the input.[11] High values of the entropy indicate high irregularity and complexity in time series data.[9] In our study, we found an increment in approximate entropy values of the experimental groups when compared with pre-drink values for 30 and 60 minutes of caffeinated beverage consumption. This result is in agreement with Yeragani et al's study[39] in which approximate entropy values are increased when compared to control group and concluded that caffeine consumption increased heart rate variability at rest. Furthermore, we investigated the detrended fluctuation analysis parameters which quantify the absence or presence of fractal correlation properties in RR intervals.[16] In many studies, detrended fluctuation analysis parameters were investigated and the researchers suggested this analysis as an ideal way to have more accurate information about the complexity of heart rate variability.[16,25] However, there are very few studies related to the non-linear analysis of heart rate variability signals after caffeine consumption. Papaioannou et al[15] reported a significant increase in long-term scaling exponent α after caffeine ingestion, while the placebo induced no significant change. Our result is in agreement with this study. In the literature, it was reported that increased complexity and chaos were related to pathological phenomena.[40] Also, there exist various studies which observe a significant decrease in detrended fluctuation analysis of -α values of heart rate variability. It has shown that the complexity decreased in the presence of a systemic disease.[12,14] The main reason of the difference may be the existence of a disease in the participants and the breakdown of the balance in the systems.

We acknowledge several limitations in this study. Relatively small number of the participants is one of the most important limitations of the present study. Also, we have evaluated only one dose of caffeinated beverage consumption which can be accepted as a low dose. Higher doses of these beverages may affect the results. We recorded electrocardiogram signals for 5 minutes which can be accepted as a short recording duration. A 24-hour recording can be more effective. The exact mechanism of heart rate variability complexity is remained unknown and further studies must be planned.

Conclusion

In conclusion, energy drink consumption increases the complexity of the cardiovascular system in young adults. Coffee and cola consumption have no significant effect on the non-linear parameters of heart rate variability. For investigating the effects of caffeinated beverage consumption more accurately, further studies which investigate the higher doses of caffeinated beverages are being planned.

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Conflict of Interest. None.

Ethical Standards. The authors assert that all procedures contributing to this work comply with the Helsinki Declaration of 1975, as revised in 2008, and have been approved by the institutional committees (Institutional Medical Ethics Committee of Adnan Menderes University (Protocol number: 2017/1211)).

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