

# Effects of energy drink consumption on corrected QT interval and heart rate variability in young obese Saudi male university students

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**BACKGROUND AND OBJECTIVES:** Consumption of energy drinks has adverse effects on the heart that might be potentiated in obese individuals. Since the incidence of obesity and use of energy drinks is high among Saudi youth, we used non-invasive tests to study hemodynamic changes produced by altered autonomic cardiac activity following consumption of energy drinks in obese male students.

**DESIGN AND SETTING:** This cross-sectional study was carried out at Department of Physiology, College of Medicine, University of Dammam, Saudi Arabia, over a one-year period from December 2013 to December 2014.

**SUBJECTS AND METHODS:** In Saudi male university students we measured continuous ECG recordings and a one-minute deep breathing maneuver to measure the expiratory-to-inspiratory ratio, the mean heart rate range (MHRR), the mean percentage variability (M%VHR) and the corrected QT interval (QTc) at 0, 30 and 60 minutes after consumption of energy drink.

**RESULTS:** We enrolled 31 students (18 overweight/obese and 13 normal weights). QTc was significantly increased at 60 min as compared with the resting state in overweight/obese subjects ( $P=.006$ ). Heart rate variability was significantly less in obese as compared with normal weight subjects at 60 minutes as indicated by E:I ratio, ( $P=.037$ ), MHRR ( $P=.012$ ), M%VHR ( $P=.040$ ) after energy drink consumption. Significant increases in diastolic ( $P=.020$ ) and mean arterial blood pressure ( $P=.024$ ) were observed at 30 minutes in the obese group.

**CONCLUSION:** Hemodynamic changes after intake of energy drinks in obese subjects indicate that obesity and energy drinks could synergistically induce harmful effects. This finding warrants efforts to caution the obese on intake of energy drinks and timely intervention to motivate changes in life style.

Energy drinks are beverages consumed for an extra boost in vitality, promoting wakefulness, maintaining alertness and providing cognitive and mood enhancement.<sup>1,2</sup> With a reported 34.5 million consumers worldwide, marketing efforts are particularly aimed at college/university students.<sup>3</sup> A study at State University in the Central Atlantic region of the United States reported that over half of the college students drink at least one energy drink per month.<sup>4</sup> Another study conducted in 10 universities of North Carolina reported that more than one quarter of university students consume energy drinks.<sup>5</sup> Marketing of energy drinks is very successful in Saudi Arabia as well. According to Alsunni et al, of the total study par-

ticipants, 45.6% consumed energy drinks on a regular basis in company with friends.<sup>6</sup>

Heart rate variability (HRV) is a valuable noninvasive test to evaluate autonomic nervous system function.<sup>7</sup> Decreased parasympathetic nervous system activity or increased sympathetic activity will reduce HRV.<sup>8</sup> The QT interval is a measure of the time between the start of the Q wave and the end of the T wave in the heart's electrical cycle.<sup>9</sup> A lengthened QT interval is a biomarker for ventricular tachyarrhythmia like torsades de pointes and a risk factor for sudden death.<sup>10</sup> The corrected QT interval (QTc) is corrected for heart rate; this allows comparison of QT values over time at different heart rates and is widely used for detection of

patients at increased risk of arrhythmias.<sup>11</sup> Since 2005, the FDA and European regulators have made it obligatory to evaluate all new molecular entities for any effects on QTc.<sup>12</sup>

The major psychoactive constituent of energy drinks is caffeine. Energy drinks contain three to five times the amount of caffeine contained in cola. Effects of caffeine include nervousness and increased heart rate. High dose caffeine consumption might lead to atrial fibrillation, palpitations, headaches and seizure.<sup>13,14</sup> In Kuwait, the Ministry of Commerce banned energy drinks for individuals under 16 years of age after one of their young national players suffered a heart attack supposedly linked to consumption of an energy drink.<sup>15</sup> Since March 2014, the Saudi government has banned the sale of energy drinks at all government, health and education facilities.<sup>16</sup>

Acute ingestion of caffeine has been found to directly reduce parasympathetic nervous system activity, thereby reducing HRV.<sup>17</sup> Similarly, an increase in the mean QTc interval has been observed after energy drink consumption in healthy young adults.<sup>18</sup> However, other researchers were unable to find any significant difference in QTc after ingestion of caffeinated drink as compared with non-caffeinated drinks.<sup>19</sup>

Obesity is a leading preventable cause of death worldwide, with an increasing prevalence in adults and children. According to a WHO report, in 2014 more than 1.9 billion adults were overweight and/or obese throughout the world. This report mentioned that the prevalence of overweight and obesity in young males and females was 23% and 30%, respectively, in Saudi Arabia.<sup>20</sup> The incidence of overweight and obesity has been estimated as 64.5% in the eastern region of Saudi Arabia, the highest in the country.<sup>21</sup> Obese persons suffer from an increased mortality risk supposedly due to cardiovascular disorders related to an altered parasympathetic or sympathetic activation.<sup>22</sup> Some studies have shown the dependence of QTc behavior on body mass index (BMI) (more so in obese individuals compared with normal and overweight subjects).<sup>23,24</sup> Other investigators have failed to show any correlation between BMI and HRV as well as BMI and QTc interval.<sup>25,26</sup>

The possibility that obese people are more prone to the deleterious effects of energy drinks because of the cumulative or synergistic effects of obesity and energy drinks on autonomic activity needs more study. In the present study, we assessed the effects of energy drink consumption on autonomic balance in young Saudi male overweight and obese university students by measuring HRV and QTc, and compared these effects with those in normal weight subjects. Detecting autonomic

imbalance by such noninvasive techniques is simple and convenient.

## SUBJECTS AND METHODS

The study was carried out at Department of Physiology, College of Medicine, University of Dammam (UOD), Saudi Arabia. The recruitment and data acquisition extended from December 2013 to December 2014. Ethical permission for the project was obtained from the ethical committee deanship of Scientific Research at UOD.

The present study was a cross-sectional study using convenience sampling (nonprobability sampling) to recruit healthy Saudi male students. A sample size of 30 was arbitrarily decided to provide a normal distribution. Volunteers were recruited by advertising in the university. Thirty-one volunteers met inclusion and exclusion criteria. The inclusion criterion was an age of 18-22 years. Individuals were excluded if they were regular energy drink consumers, had any cardiac or respiratory disease, used any medication or herbal supplements, had any known sensitivity to taurine or caffeine, were trained athletes or exercising regularly. After obtaining height and weight measurements, they were categorized into normal weight (NW-BMI=18.5 to 24.9kg/m<sup>2</sup>) or over-weight /obese (OW/OB- BMI ≥25 kg/m<sup>2</sup>). Written informed consent was taken from all the volunteers.

Subjects were instructed to abstain from caffeine for at least 3 days prior to the session before coming to the lab. The subjects were also instructed not to eat or drink anything except water after 12:00 midnight before the day of the session.

Upon arrival at the laboratory, the subjects were briefed about the protocol. Waist circumference (WC) and hip circumference were measured with a non-stretchable plastic tape to get WC, waist-to-hip ratio (WHR) and waist-to-stature ratio (WSR). Subjects were wired for recording of electrocardiogram (ECG) and respiratory monitoring with the Power Lab 8/30 system (AD Instruments, Australia. <http://www.adinstruments.com/products/powerlab>) while seated in a comfortable position. A single-lead recording was done with the ECG electrodes placed on the right and left shoulders (equivalent to limb lead I) with an earth electrode at the back. The wires were connected through the ECG box to a bioamplifier (ML132-AdInstruments) connected to the PowerLab. Baseline data (0 minute) was recorded while subjects were breathing spontaneously for 7 minutes. The subjects were asked to perform deep breathing at a rate of 6 cycles per minute for one minute (inspiration for 5 seconds followed by

**Table 1.** Baseline characteristics of study participants.

	NW (n=13) Mean (SD)	OW/OB (n=18) Mean (SD)	P
Age (yrs)	20.6 (0.6)	20.5 (0.7)	.523
BMI (kg/m <sup>2</sup> )	22.4 (2.1)	34.5 (5.4)	<.001
WC (cm)	79.1 (7.0)	106.1 (11.9)	<.001
WHR (cm)	0.82 (0.04)	0.88 (0.08)	.02
WSR (cm)	46.2 (4.2)	62.1(5.9)	<.001

NW: normal weight, OW/OB: overweight/obese, BMI: body mass index, WC: waist circumference, WHR: waist to hip ratio, WSR, waist to stature ratio. MABP: mean arterial blood pressure.

were automatically picked for each respiratory cycle, and mean heart rate was calculated. The QT interval was automatically calculated by the dedicated ECG module of LabChart Pro using the threshold method for detection of beginning of QRS complex and the end of T wave. The average of at least 4 successive ECG complexes was taken. QTc was calculated by Bazett's formula ( $QTc = QT / \sqrt{OR}$ ) to adjust for heart rate. The normal QTc value in males is (<430 msec) and in females (<450 msec).<sup>29,30</sup>

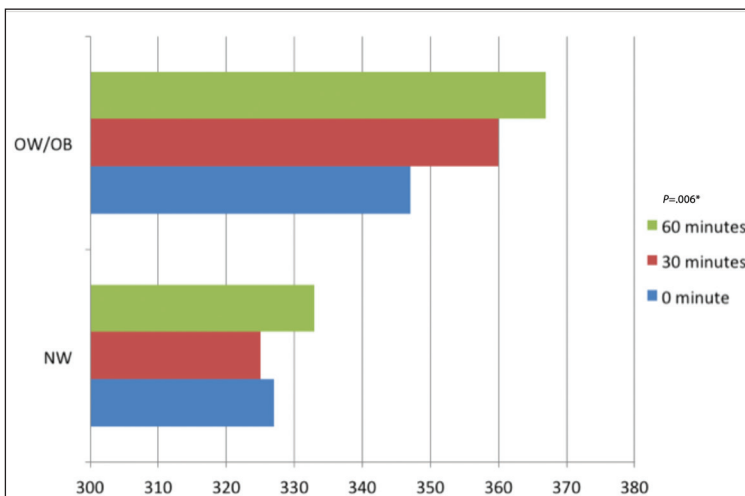
Data was entered into a preformatted excel worksheet. Means and standard deviations were calculated. A paired *t* test was used to compare the values of QTc and HRV within groups during different phases after consumption of energy drink. An unpaired *t*- test was used to compare the values of QTc and HRV between normal (NW) and overweight/ obese groups (OW/OB) at different points in time. For all tests, the level of significance was set at *P*<.05.

**RESULTS**

Twenty-one third year medicine, 7 second-year medicine and 3 allied-health science students were recruited. The baseline characteristics are given in **Table 1**. The mean age of the two groups was similar, whereas the mean BMI, WC, WHR and WSR were significantly higher in OW/OB as compared with the NW group.

**Figure 1** illustrates the QTc interval after consumption of energy drinks in NW and OW/OB groups. There was a significant increase in QTc (*P*=.006; CI: lower=-27.81, upper:-5.51) at 60 minutes (356.8±54) as compared with the resting state (340.2±57) in the OB group (but no significant changes were observed in the NW group (333.5±59 at 60 min; (327.0±61) at rest; *P*=.243; CI: lower: -18.17, upper: +5.06). The QTc interval at all timepoints (0, 30 and 60 minutes) was slightly higher in the OW/OB group, but the differences were not significant. Though the increase in the QTc in obese subjects at 60 minutes after ingestion of an energy drink was statistically significant compared with baseline, the prolongation was within normal limits for males.<sup>26,27</sup>

Assessment of HRV revealed that all three parameters were significantly less in OW/OB at 0 min (E:I ratio: 1.42; MHRR: 25.56; M%VHR: 34.51) and at 60 minutes post-drink consumption (E:I ratio: 1.38; MHRR: 24.28; M%VHR: 30.26) compared with the NW group at respective times i.e., 0 minute (E:I ratio: 1.55; MHRR: 33.77; M%VHR: 42.33) and 60 minutes post consumption (E:I ratio: 1.59; MHRR: 32.77; M%VHR: 41.41). Additionally the MHRR was also significantly less at even 30 minutes in the



**Figure 1.** Comparison of mean QTc interval of normal weight and overweight/obese subjects at rest, 0 minutes, 30 minutes and 60 minutes after consumption of energy drink.

expiration over 5 seconds). This one-minute recording was used to derive the measures of the HRV through ECG in each individual. The subjects were then provided with 5 mL/kg body weight of energy drink. A can of 250 ml of energy drink contained approximately 80 mg of caffeine that equals approximately 0.32 mg/mL or 1.6 mg/kg. Recording while deep breathing for one minute was repeated at 30 and 60 minutes after energy drink consumption.

Lab Chart Pro software (ADInstruments, Australia) was used for data analysis using the ECG analysis module. The widely used parameters for assessing the HRV include the expiratory to inspiratory ratio (E:I ratio), the mean heart rate range (MHRR), and the mean percentage variability (M%VHR).<sup>27,28</sup> The relevant HRV parameters were calculated by analyzing the one-minute deep breathing recordings in which the maximum and the minimum R-R intervals

OW/OB (27.17) group compared with NW (33.77) (Table 2).

The OW/OB group showed a statistically insignificant increase in HRV parameters at the 30 minute interval, but the HRV parameters showed a significant reduction at 60 minute (E:I ratio: 1.38; MHRR: 24.28; M%VHR: 30.26) compared with the values at 30 minutes post intake (E:I ratio: 1.47; MHRR: 27.17; M%VHR: 36.38) (Table 2).

## DISCUSSION

Consumption of energy drinks in obese individuals who have a greater tendency toward autonomic imbalance could lead to dangerous effects on cardiac functions.<sup>23</sup> Our study is probably the first to reveal the synergistic interaction between the high BMI and energy drinks that causes adverse effects on QTc and HRV.

The present study revealed a significant increase in the QTc interval after consumption of energy drink primarily after 60 minutes in OW/OB group. The same trend was seen in the different parameters of HRV, which were significantly reduced by energy drink consumption at 60 minutes in OW/OB group, but no significant changes were detected in NW groups. Steinke et al found a nonsignificant increase in QTc after energy drink consumption. Variability in QTc in their study might have related to the fact that they were recording chronic effects of energy drink consumption over a period of seven days, and the amount of energy drink used was constant in all subjects and not adjusted by body weight.<sup>19</sup>

The HRV in deep breathing is considered to be an indicator of parasympathetic function solely, whereas the effects on QTc could be attributed to the altered balance between the activity of sympathetic and parasympathetic system.<sup>10</sup> Cavka et al have recently shown that energy drinks raise the plasma levels of adrenaline and noradrenaline significantly above the preconsumption level within a period of 60 minutes.<sup>2</sup> The dual effects on QTc and HRV seen in the present study probably reflect a tendency towards autonomic imbalance in obese subjects that are comparable to those documented by other researchers.<sup>23,25,31,32</sup> A combination of reduced HRV along with prolongation of QTc has also been demonstrated in patients with untreated essential hypertension who do not exhibit cardiac hypertensive disease.<sup>10</sup> The precise pathophysiological mechanism of this variation is still not clear, but reduced vagal tone and increased sympathetic activity has been suggested to underlie such behavior.<sup>33</sup> There are reports of association of various anthropometric indices (WC, WHR and WSR) with cardiovascular abnormalities as these

**Table 2.** Heart rate variability (HRV) parameters. Expiratory to inspiratory ratio (E:I ratio), mean heart rate range (MHRR) and mean percentage variability in heart rate (M%VHR) of normal weight and overweight/obese (OW/OB) subjects at rest, 30 minutes and 60 minutes after consumption of energy drink (values are expressed as mean and standard deviation).

Variables	NW (n=13)	OW/OB (n=18)	Unpaired t test P value	95% CI of the difference
<b>E:I ratio</b>				
0 min	1.55 (0.15)	1.42 (0.17)	.042 <sup>a</sup>	0.004-0.245
30 min	1.57 (0.18)	1.47 (0.21)	.172	0.005-0.244
60 min	1.59 (0.30)	1.38 (0.17)	.021 <sup>a</sup>	0.033-0.378
<b>MHRR</b>				
0 min	33.77 (6.58)	25.56 (7.18)	.003 <sup>a</sup>	3.05-13.38
30 min	33.77 (7.15)	27.17 (7.63)	.023 <sup>a</sup>	0.98-12.23
60 min	32.77 (8.54)	24.28 (8.04)	.008 <sup>a</sup>	2.35-14.63
<b>M%VHR</b>				
0 min	42.33 (9.17)	34.51 (11.45)	.022 <sup>a</sup>	1.39-16.21
30 min	42.97 (11.59)	36.38 (12.56)	.114	1.73-15.24
60 min	41.41 (14.36)	30.26 (12.05) <sup>ab</sup>	.030 <sup>a</sup>	1.08-19.63

The test of significance applied was paired sample t test when comparing within the groups, and unpaired t test when comparing between the groups.

<sup>a</sup>P value significant; <sup>b</sup>P<.05 when compared with the baseline of the same group; <sup>c</sup>P<.05 when compared with the 30 min of the same group; CI: 95% confidence interval of the difference

indices are visibly higher in obese subjects as observed in our participants.<sup>34</sup> Low-grade inflammation is reported in obesity where abdominal fat releases various cytokines and pro-inflammatory substances that have been shown to damage the cardiovascular system and might be responsible for obesity-induced hemodynamic variations.<sup>35</sup> Caffeine levels in plasma have been shown to peak at around 60 minutes after consumption of caffeine drinks or energy drinks.<sup>36</sup> This might reflect maximum alteration in recorded parameters around that time in our participants.

Some investigators did not observe any significant relation of BMI with changes of QTc or HRV and suggested that normal QTc could be attributed to the absence of any complication or associated disease in the obese individuals studied.<sup>26,27</sup>

Energy drinks contain caffeine and other energy promoting ingredients such as glucose, taurine, vitamins, minerals and some herbal extracts. Caffeine has proven cardioactive and psychomotor effects, and the combi-

nation of caffeine with other energy boosting substances could further augment these effects.<sup>37</sup> Typically, one can of energy drink contains approximately 25-40 g of glucose which might lead to hyperglycemia. Hyperglycemia is considered to be cardiotoxic and is an important risk factor for acute myocardial infarction and other cardiovascular diseases.<sup>38</sup> Taurine, another ingredient of energy drinks, is an amino acid which has been found to have cardio-protective effects and is being used in the treatment of congestive heart failure, hypertension and other diseases.<sup>39</sup>

Autonomic disturbances appear to be reversible with weight reduction. In obese subjects, weight loss has been shown to result in a significant increase in parasympathetic control and some decrease in sympathetic control of heart.<sup>40</sup> Since autonomic imbalance is an early sign of obesity induced morbidity, avoidance of caffeinated drinks particularly energy drinks could be beneficial for the health of OW/OB individuals.<sup>41</sup>

Our findings in this study are limited by small sample size, inclusion of male gender only and a young age group. Thus, the results cannot be generalized to a wider population. Another limitation is that the data is not sufficient to identify single component/ingredients or mechanisms involved producing observed autonomic effects. We cannot propose on the basis of the present study that these acute effects could be sustained or might be exaggerated

in chronic energy drink consumers. The present study could be considered a foundation for comprehensive research related with obesity and energy drinks.

## CONCLUSION

The use of energy drinks is quite common among Saudi students, but awareness of components and potential health hazards is limited. The present study indicates that there is a reduced parasympathetic drive and/or increased sympathetic outflow in OW/OB as compared with NW subjects that is potentiated by consumption of energy drinks in the OW/OB. Though the QTc prolongation observed in the OW/OB at 60 minutes compared with the rest is statistically significant, the values did not cross the accepted normal limits of QTc in males. This alteration in autonomic balance observed at such an early stage by means of QTc and HRV warrants efforts to caution overweight/obese individuals about intake of energy drinks and timely intervention to motivate changes in lifestyle.

## Conflicts of interest

None.

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