Energy Drinks Prolong Early Repolarization ($J\text{-}T_{peak}$) Phase in a Healthy Population

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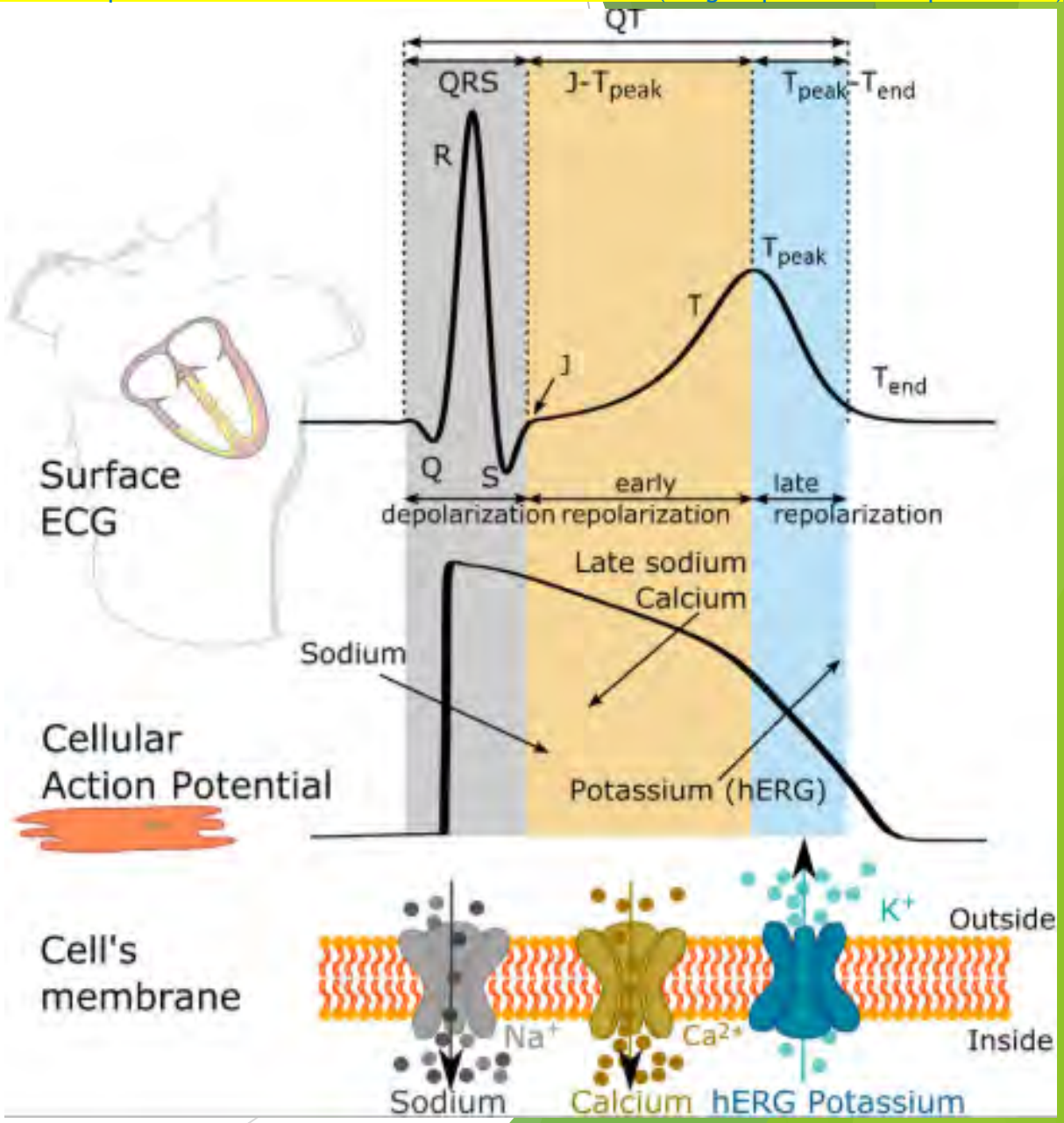
Background

- Energy drinks continue to be the fastest growing beverage market with sales expected to reach $60 billion dollars in the next several years.
- However, consumption of energy drinks linked to adverse clinical effects such as stroke, seizure, hypertension, myocardial infarction, arrhythmia and cardiac arrest.
- QTc prolongation is documented even in healthy individuals.
- Energy drink-associated visits to emergency departments in the US nearly doubled between 2007 and 2011 from 10,068 to 20,783.

Background (continued)

- No standardized safety protocol currently exists in the United States for products labeled as dietary supplements.
- Recent data shows J-T_{peak} (JTp) is a more specific marker for proarrhythmic potential than is QTc.
- Drugs such as dofetilide, quinidine, and high-dose caffeine that selectively block the human ether-a-go-go related gene (hERG) potassium ion channel prolong QTc by prolonging both early repolarization (JTp) and late repolarization (measured by T_{peak}-T_{end} [Tpe] interval), and are associated with an increased risk of torsade.
- In contrast, other drugs such as ranolazine and verapamil that also block inward late sodium and L-type calcium channels prolong QTc by prolonging Tpe but not JTp, and have demonstrated reduced risk of torsade.

Cardiac action potential intervals and ionic currents of interest. (Image reproduced with permission.)

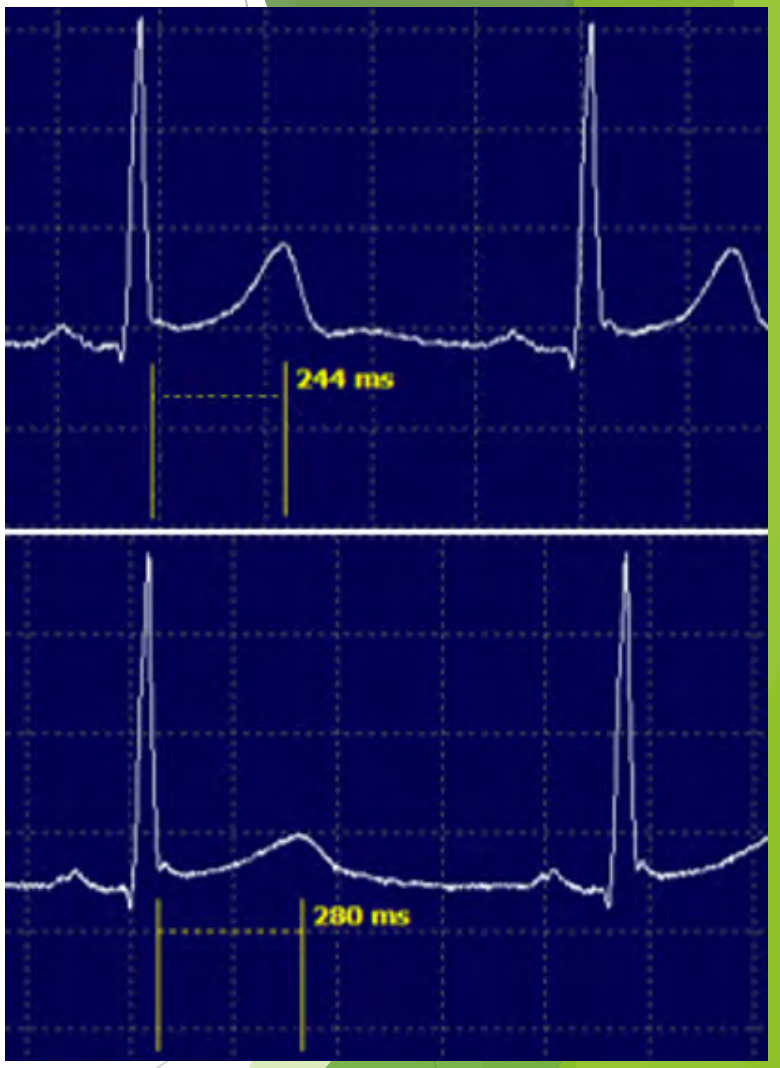


Background (continued)

- In 2018, the C-Energy-X Study (Kozik T, Carey M, Bhattacharyya M et al) studied the effects of Monster® (second leading US energy drink) on a cohort of 22 healthy subjects between the ages of 18 to 40 years.
- Baseline blood pressures and 12-lead Holter monitoring were performed following a period of rest and again after three minutes of walking on a treadmill. Subjects then drank two 16-oz Monster® drinks and similar measurements occurred before and after three-minute periods of exercise.
- Results showed increased mean blood pressure, mean heart rate, and frequent T-wave flattening and inversion, and QTc prolongation of between 23ms at rest and 50ms during exercise following energy drink consumption.

Objective and Methods

- **The aim of our follow-up study was to provide a secondary analysis of data from the C-Energy-X trial to quantify the effect of energy drink consumption specifically on the early repolarization corrected for heart rate (JTpc) interval and thus a more specific risk estimation for torsade.**
- EKG tracings from 22 healthy subjects (mean age: 28 ± 7yrs; 12 males, 10 females) who participated in the C-Energy-X Study were uploaded to the H-Scribe software (Mortara Instruments, Milwaukee, Wisconsin).
- Two evaluators independently measured JTp and RR intervals from all subjects in the resting and exercise phases both at baseline and post-energy drink consumption.
- Values were corrected for heart rate using the linear correction formula JTpc=JTp+0.150(1-RR), where RR is the R-to-R interval.
- Mean JTpc values from each phase were analyzed using a paired sample two-tailed *t*-test.



EKG tracing of a patient prior to and following energy drink consumption (above and below, respectively) in which J-T_{peak} prolongation and T-wave flattening were observed.

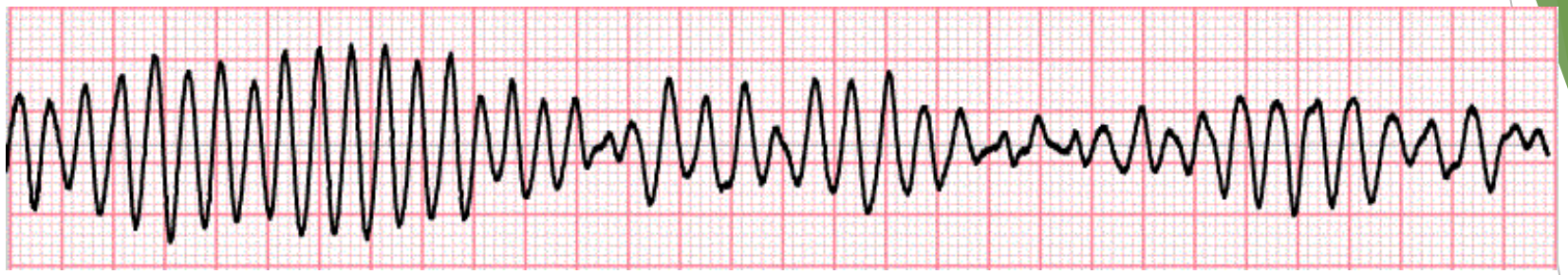
Results

- In the resting phase following energy drink consumption (PCr), there was a statistically significant increase in JTpc intervals for 17 out of 22 (77%) subjects by an overall mean of 10.5ms (baseline=234 ± 21.3ms; PCr=245 ± 22.0ms; *p*=0.015).
- In the exercise phase following energy drink consumption (PCe), there was a trended increase, albeit not statistically significant, in JTpc intervals for 14 out of 22 (64%) subjects by an overall mean of 0.8ms (baseline=225 ± 15.7ms; PCe=226 ± 17.9ms; *p*=0.845).
- Mean discordance in JTpc measurements between evaluators was 0.055ms.

Phase	J-T_{peak} (ms)		Mean J-T_{peak} prolongation (ms)	*t*-value	*p*-value
	Baseline	Post-energy drink consumption			
Rest	234 ± 21.3	245 ± 22.0	10.5	-2.65	0.015
Exercise	225 ± 15.7	226 ± 17.9	0.8	-0.20	0.845

Results of study with sample size N=22. JTpc=J-T_{peak} interval corrected for heart rate.

Discussion



- In the resting phase, statistically significant JTpc prolongation occurred, a feature of selective hERG channel blockade, portending increased risk of torsade.
- It has been estimated each 10ms increase in QTc contributes approximately a 5-7% increase in risk of torsade.
- Assuming JTpc prolongation accounts for approximately 50% of QTc prolongation in the setting of energy drink consumption, the average participant in our study theoretically experienced up to a 10-14% increased risk of torsade.
- This risk would almost certainly be higher with greater quantities of consumed energy drink or in individuals who have preexisting channelopathies such as congenital long QT syndrome or are concurrently taking QT-prolonging medications.

Discussion (continued)

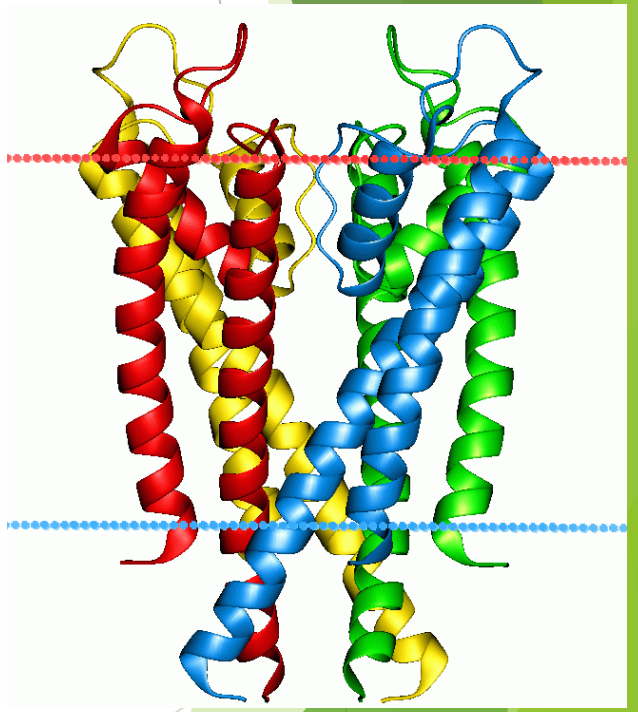
- In contrast, a significant JTp prolongation was not observed during the exercise phase.
- One possible explanation is that our study was insufficiently powered to detect a significant interval change in this condition.
- Another possibility relates to data demonstrating QTc and Tpe prolongation following aerobic exercise, a complex physiologic state shown to cause increased catecholamine activity, interleukin-6 release, and electrolyte fluctuations
- The JTp-prolonging effect of energy drink consumption may have been “masked” by the stronger Tpe-prolonging effect of aerobic exercise. Protective effect?
- However, the direct effect of exercise on early repolarization, especially in the setting of energy drink consumption, remains unclear and warrants further study.

Limitations

- C-Energy-X applied an open-label non-randomized design utilizing one brand of energy drink on a small, young and healthy sample overall with no placebo arm.
- JTp interval estimations were performed visually on H-Scribe by evaluators using on-screen calipers and were occasionally limited by artifact, especially during the exercise phase.

Conclusion

- In our sample of young healthy adult subjects, energy drink consumption was associated with prolongation of the early repolarization phase corrected for heart rate (JTpc) in the resting phase, suggesting a predominantly hERG channel blockade-mediated increase in risk of torsade de pointes.
- No statistically significant JTpc prolongation was detected following energy drink consumption when aerobic exercise was incorporated.



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THANK YOU!