Cardiovascular and Cerebrovascular Effects in Response to Red Bull Consumption Combined With Mental Stress

Erik Konrad Grasser, PhD, MD, BSEE*, Abdul G. Dulloo, PhD, and Jean-Pierre Montani, MD

The sale of energy drinks is often accompanied by a comprehensive and intense marketing with claims of benefits during periods of mental stress. As it has been shown that Red Bull negatively impacts human hemodynamics at rest, we investigated the cardiovascular and cerebrovascular consequences when Red Bull is combined with mental stress. In a randomized cross-over study, 20 young healthy humans ingested either 355 ml of a can Red Bull or water and underwent 80 minutes after the respective drink a mental arithmetic test for 5 minutes. Continuous cardiovascular and cerebrovascular recordings were performed for 20 minutes before and up to 90 minutes after drink ingestion. Measurements included beat-to-beat blood pressure (BP), heart rate, stroke volume, and cerebral blood flow velocity. Red Bull increased systolic BP (+7 mm Hg), diastolic BP (+4 mm Hg), and heart rate (+7 beats/min), whereas water drinking had no significant effects. Cerebral blood flow velocity decreased more in response to Red Bull than to water (−9 vs −3 cm/s, p <0.005). Additional mental stress further increased both systolic BP and diastolic BP (+3 mm Hg, p <0.05) and heart rate (+13 beats/min, p <0.005) in response to Red Bull; similar increases were also observed after water ingestion. In combination, Red Bull and mental stress increased systolic BP by about 10 mm Hg, diastolic BP by 7 mm Hg, and heart rate by 20 beats/min and decreased cerebral blood flow velocity by −7 cm/s. In conclusion, the combination of Red Bull and mental stress impose a cumulative cardiovascular load and reduces cerebral blood flow even under a mental challenge. **© 2015 Elsevier Inc. All rights reserved.** **(Am J Cardiol 2015;115:183−189)**

Recently, we observed an overall negative hemodynamic profile in response to ingestion of 335 ml of Red Bull,[1] but, to date, there are no data available about whether ingesting an energy drink modifies hemodynamic variables associated with a short-term mental task using beat-to-beat cardiovascular and cerebrovascular measurements. Hence, the purpose of the present study was to determine the hemodynamic impact of a simple mental arithmetic task combined with previous ingestion of Red Bull. As a second aim, we investigated whether the perceived stress level and number of mistakes during mental stress were improved in response to previous consumption of Red Bull.

Methods

Twenty healthy young adults (10 women), aged 19 to 29 (22.1 ± 0.5) years, were recruited and paid for their participation. The mean height of the participants was 173.3 ± 2.0 cm, their body weight was 65.7 ± 2.4 kg, and their body mass index was 21.8 ± 0.6 kg m^{-2}. None of the subjects had any diseases or were taking any medication affecting cardiovascular or autonomic regulation. Based on a questionnaire (daily intake of coffee, energy drinks, and other caffeinated beverages), the estimated daily caffeine intake of study participants ranged from 1 to 4 drinks per day. All participants fasted for ≥12 hours and they were requested to avoid alcohol or caffeine for at least 24 hours before the test. The local ethics committee approved the study, and written informed consent was obtained from each subject.

All experiments took place in a quiet, temperature-controlled (22°C) laboratory and started between 08.00 A.M. and 09.00 A.M. Every subject attended 2 separate experimental sessions (each session separated at least by 2 days) according to a randomized cross-over design. On arrival at the laboratory, subjects were asked to empty their bladders if necessary and to sit in a comfortable armchair. Equipment for cardiovascular and cerebrovascular recordings was then attached. After a variable period for attainment of cardiovascular stability (usually 30 minutes), a baseline recording was made for 20 minutes. Then, the test subjects ingested, not blinded, either 355 ml of a degassed Red Bull drink containing caffeine (114 mg), taurine (1420 mg), and glucuronolactone (84.2 mg), sucrose, and glucose (39.1 g) or 355 ml of tap water at room temperature. Subjects were asked to ingest their drink in a convenient pace for over 4 minutes. After 80 minutes of postdrink cardiovascular recordings, a mental arithmetic task was performed for 5 minutes followed by 5 minutes recovery period.

Subjects subtracted continuously the number 6 or 7 (chosen at random) from a random 3 or 2 digit number for 5 minutes and were instructed to give the answer verbally. Each mental stress task comprised of 60 unique calculations, with 5 seconds interval between each calculation and was presented to the subjects on a monitor.[2] Immediately after

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Research relating to this study was funded partially by the SNF (SNF number: 122554) to JPM.

See page 189 for disclosure information.

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0002-9149/14/$ - see front matter © 2015 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.amjcard.2014.10.017

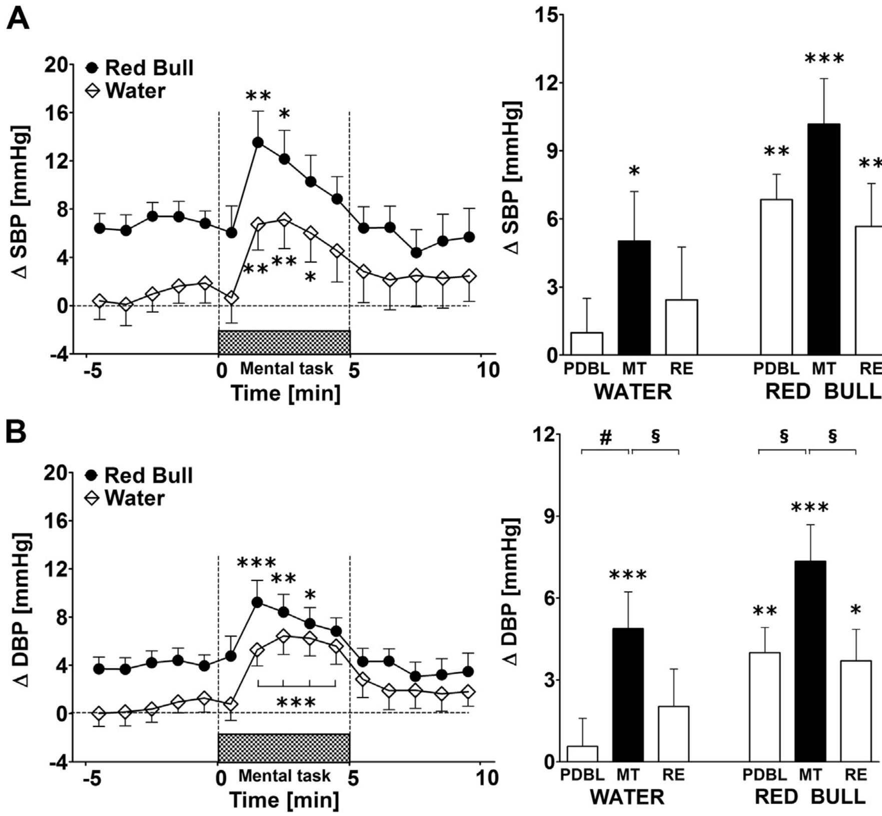

Figure 1. *Left panel*: Time course for changes in SBP *(A)* and DBP *(B)* starting 75 minutes (i.e., −5 minutes on the panel) after ingestion of Red Bull (*full circle*) or tap water (*open rhomb*). *Right panel*: Mean responses averaged over 5 minutes PDBL, 5 minutes MT, and 5 minutes RE relative to predrink baseline values and presented as a delta (i.e., average over the respective 5 minutes interval minus the average over the 20 minutes predrink baseline period) after tap water or Red Bull. *p <0.05, **p <0.01, and ***p <0.005 statistically significant differences over time from predrink baseline values (*left and right panels*). §p <0.05 and #p <0.01, statistically significant differences between PDBL, MT, and RE (*right panel*). All values are reported as means ± SE. DBP = diastolic blood pressure; MT = mental task; PDBL = postdrink baseline; RE = recovery period; SBP = systolic blood pressure.

the mental task, subjects were asked to rate their perceived stress using a standard 5-point Likert scale.[3]

Cardiovascular and electrocardiographic (cardiac intervals) recordings were performed using a Task Force Monitor (CNSystems, Medizintechnik, Graz, Austria) with data sampled at a rate of 1,000 Hz as described previously.[4] Cerebral blood flow velocity was measured using transcranial Doppler ultrasonography (Doppler-Box, DWL, Sipplingen, Germany). The left and the right middle cerebral artery was insonated at a depth of 40 to 55 mm using a 2 MHz probe, and the probe was fixed in place with an adjustable headset. Beat-to-beat values of systolic, diastolic, and mean velocity were recorded and merged real time with the Task Force Monitor to allow synchronous cardiovascular and cerebrovascular recordings.

Beat-to-beat values of cardiac interval, systolic blood pressure (BP), diastolic BP, cerebral blood flow velocity, and stroke volume were averaged over the 20 minutes predrink baseline period and minute by minute starting 5 minutes before (postdrink baseline), during (mental task for 5 minutes) and after the mental stress (recovery for 5 minutes). Heart rate was calculated by the appropriate RR interval. Cardiac output was computed as the product of stroke volume and heart rate. Mean BP was calculated from diastolic BP and systolic BP, respectively: mean BP = diastolic BP + 1/3 (systolic BP − diastolic BP). Total peripheral resistance was calculated as mean BP divided by cardiac output. Double product was calculated as heart rate × systolic BP and provides valuable information for the oxygen consumption of the myocardium.[5] Cerebrovascular resistance index was calculated as the mean BP at brain level (BP_{mean_brain}) divided by mean cerebral blood flow velocity. BP_{mean_brain} was calculated as the difference between mean BP at heart level and the hydrostatic pressure (BP_{hydro}) at the level of transcranial insonation (temporal bone window).[6]

Data are expressed as means ± SEM. Statistical analysis was performed by 2-way analysis of variance for repeated measures with time (6 time points: postdrink baseline, mental task 1 to 5 minutes) and treatment (water or Red Bull) as within-subject factors using statistical software (Statistix version 8.0; Analytical Software, St. Paul, Minnesota). The effects of each drink over time were analyzed by comparing values at each time point over the mental task and recovery period with the averaged postdrink baseline values recorded during the 5 minutes immediately before the mental task (Figures 1 to 4) using repeated measures analysis of variance with Dunnett's multiple comparison post hoc testing. Changes between postdrink baseline, mental task, and recovery were evaluated using repeated measures analysis of variance with Newman-Keuls post hoc testing (Figures 1 to 4). A Wilcoxon

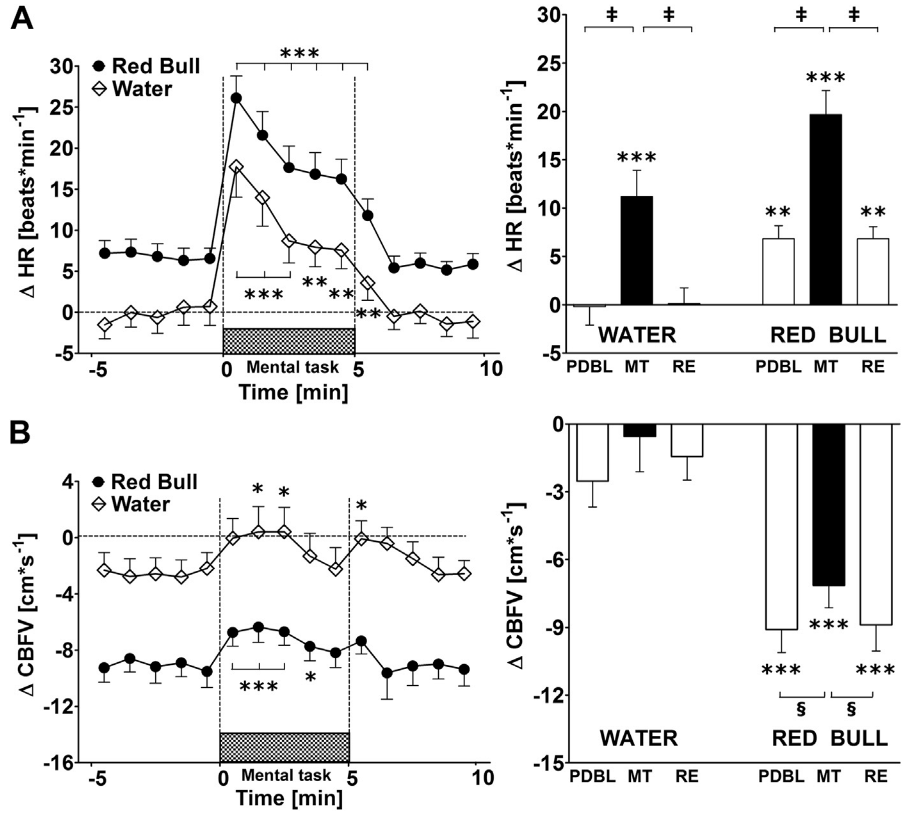

Figure 2. *Left panel*: Time course for changes in HR *(A)* and CBFV *(B)* starting 75 minutes (i.e., −5 minutes on the panel) after ingestion of Red Bull (*full circle*) or tap water (*open rhomb*). *Right panel*: Mean responses averaged over 5 minutes PDBL, 5 minutes MT, and 5 minutes RE relative to predrink baseline values and presented as a delta (i.e., average over the respective 5 minutes interval minus the average over the 20 minutes predrink baseline period) after tap water or Red Bull. *p <0.05, **p <0.01, and ***p <0.005 statistically significant differences over time from predrink baseline values (*left and right panels*). §p <0.05 and ‡p <0.005, statistically significant differences between PDBL, MT, and RE (*right panel*). All values are reported as means ± SE. CBFV = cerebral blood flow velocity; HR = heart rate; MT = mental task; PDBL = postdrink baseline; RE = recovery period.

matched pairs test was used to elicit differences in mistakes and stress perception in response to the drink (GraphPad Prism version 5, GraphPad Software, Inc, San Diego, California). All reported p values were 2-sided and the level of statistical significance was set as p <0.05.

Results

Predrink hemodynamic values were similar between the drinks, whereas Red Bull elevated significantly systolic and diastolic BP, heart rate, cardiac output, double product, cerebrovascular resistance, and decreased cerebral blood flow velocity over the postdrink period (Table 1 and Supplementary Tables 1 and 2).

No significant interaction (drink × time) effects were found for any variable tested. Addition of mental stress 80 minutes after ingesting Red Bull increased systolic BP and diastolic BP by about +3 mm Hg, heart rate by +12.8 beats/min, cerebral blood flow velocity by + 2.0 cm/s, cardiac output by + 1.0 L/min, and double product by + 1857 mm Hg beats/min (Figures 1 to 3). Mental stress applied after water ingestion invoked similar rises in systolic BP and diastolic BP (+4 mm Hg), heart rate (+11.4 beats/min), cerebral blood flow velocity (+2.0 cm/s), cardiac output (+1.0 L/min), and double product (+1665 mm Hg beats/min). Total peripheral resistance decreased similarly with Red Bull (−1.58 mm Hg min/L) and water (−1.73 mm Hg min/L) in response to mental stress (Figure 4). Ingestion of Red Bull and water did not influence stroke volume in response to mental stress (Figure 3).

Overall, the combination of Red Bull ingestion and mental stress application 80 minutes later caused total increases in systolic BP of +10.2 mm Hg, diastolic BP of +7.3 mm Hg, heart rate +19.7 beats/min, cardiac output of +1.6 L/min, double product of +3,137 mm Hg beats/min, and cerebrovascular resistance index of +0.32 mm Hg cm/s, whereas a decrease was found for cerebral blood flow velocity of −7.1 cm/s and total peripheral resistance of −2.3 mm Hg min/L (Figures 1 to 4).

Cardiac output (+0.01 vs +0.37 L/min) and stroke volume (+0.5 vs +5.7 ml) were significantly higher in the 5 minute recovery period compared with postdrink values before the mental task after ingestion of water, whereas ingestion of Red Bull increased stroke volume only (−0.4 vs +2.9 ml; Figure 3). Moreover, water ingestion significantly decreased total peripheral resistance (+0.14 vs −0.59 mm Hg min/L) in the recovery period compared with postdrink values before the mental task (Figure 4).

No significant differences between the drinks were found for a total count of mistakes and for stress perception during the mental task (Figure 5).

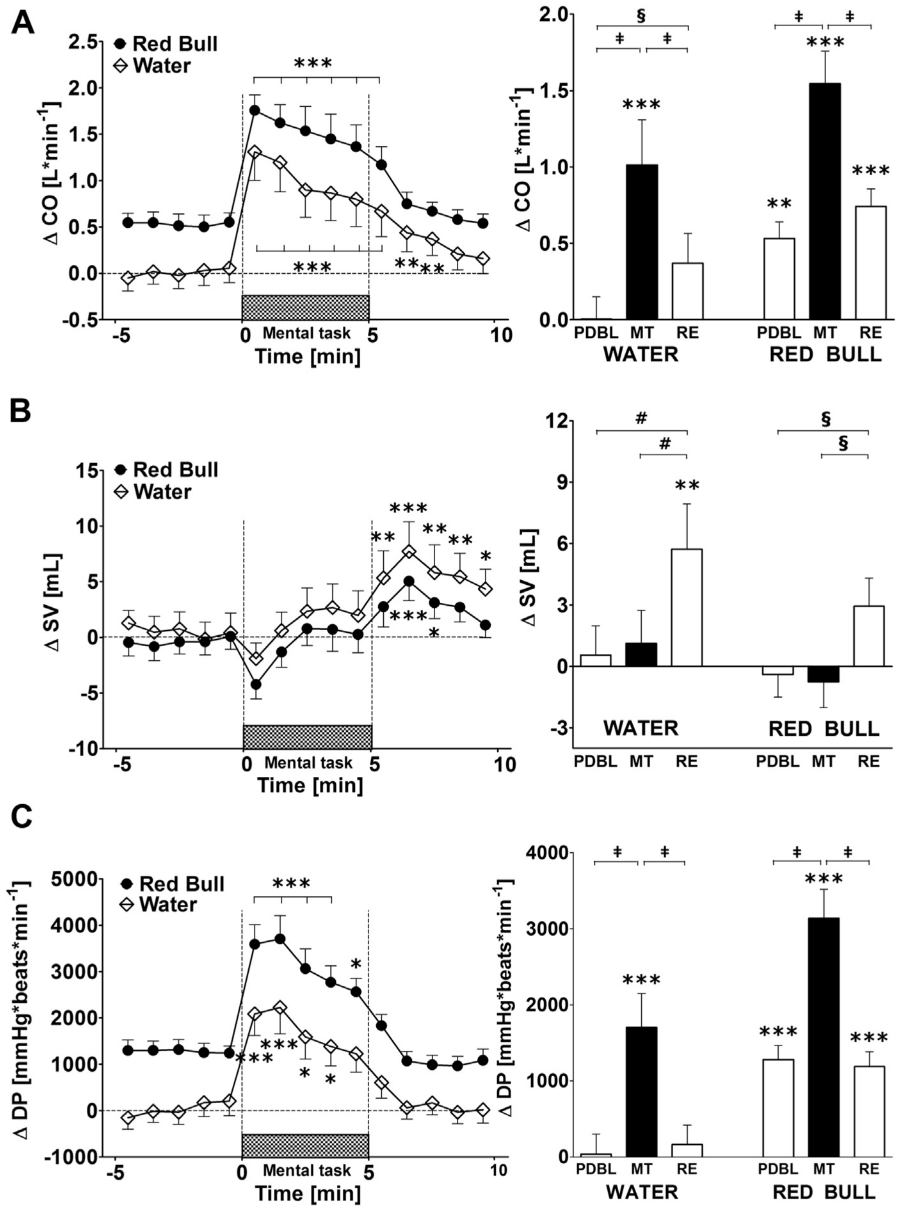

Figure 3. *Left panel*: Time course for changes in SV *(A)*, CO *(B)*, and DP *(C)* starting 75 minutes (i.e., −5 minutes on the panel) after ingestion of Red Bull (*full circle*) or tap water (*open rhomb*). *Right panel*: Mean responses averaged over 5 minutes PDBL, 5 minutes MT, and 5 minutes RE relative to predrink baseline values and presented as a delta (i.e., average over the respective 5 minutes interval minus the average over the 20 minutes predrink baseline period) after tap water or Red Bull. *p <0.05, **p <0.01, and ***p <0.005 statistically significant differences over time from predrink baseline values (*left and right panels*). §p <0.05, #p <0.01, and ‡p <0.005, statistically significant differences between PDBL, MT, and RE (*right panel*). All values are reported as means ± SE. CO = cardiac output; DP = double product; MT = mental task; PDBL = postdrink baseline; RE = recovery period; SV = stroke volume.

Discussion

This study examined the influence of a commonly available energy drink on cardiovascular and cerebrovascular parameters in response to a mental stress task in young and healthy humans using beat-to-beat measurement techniques. Our results presented here provide evidence that mental stress applied after the consumption of Red Bull led to a substantial augmentation of the heart's workload through elevations of BP, heart rate, and double product, which were accompanied by a sustained reduced cerebral blood flow velocity. These cardiovascular changes have been found additive rather than synergistic in response to mental stress, thereby suggesting that the hemodynamic consequences from a laboratory mental stress task are independent from ingesting either energy drink or tap water.

Recently, we observed in response to one 355 ml can of Red Bull detrimental effects on cerebral blood flow velocity in young and healthy humans.[1] These results cast doubt on a better overall performance, in particular under conditions of mental stress. As yet, we are not aware of a study in which the impact of an energy drink was investigated on cardiovascular and cerebrovascular parameters in response to a mental stress task. The onset of mental stress is associated with an increase in heart rate, cardiac output, arterial BP,

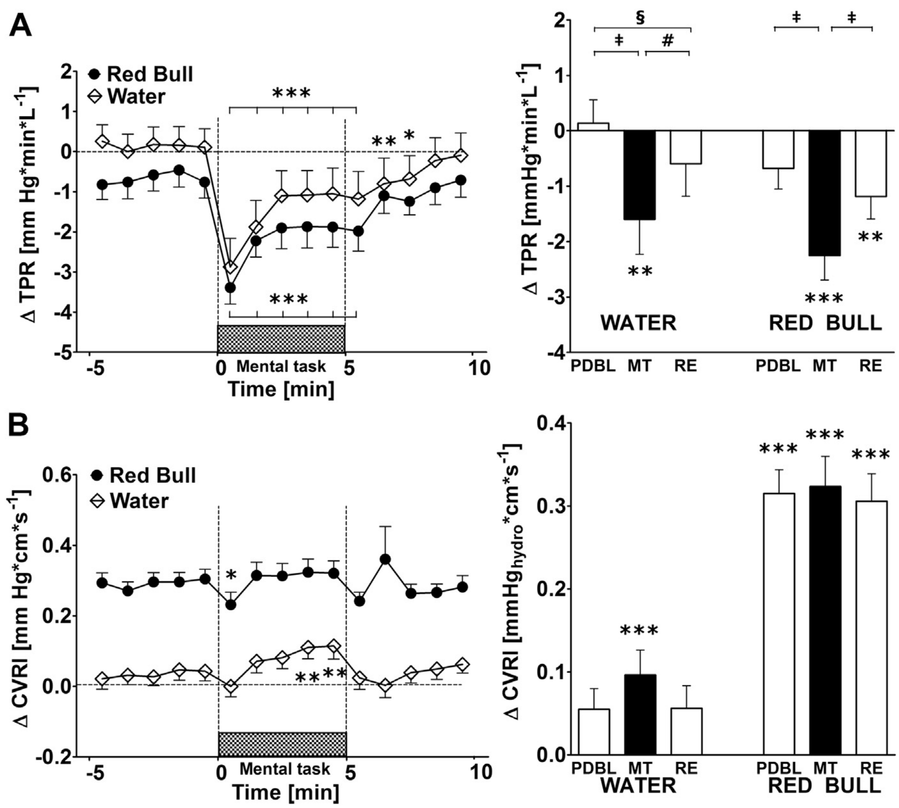

Figure 4. *Left panel*: Time course for changes in TPR *(A)* and CVRI *(B)* starting 75 minutes (i.e., −5 minutes on the panel) after ingestion of Red Bull (*full circle*) or tap water (*open rhomb*). *Right panel*: Mean responses averaged over 5 minutes PDBL, 5 minutes MT, and 5 minutes RE relative to predrink baseline values and presented as a delta (i.e., average over the respective 5 minutes interval minus the average over the 20 minutes predrink baseline period) after tap water or Red Bull. *p <0.05, **p <0.01, and ***p <0.005 statistically significant differences over time from predrink baseline values (*left and right panels*). §p <0.05, #p <0.01, and ‡p <0.005, statistically significant differences between PDBL, MT, and RE (*right panel*). All values are reported as means ± SE. CVRI = cerebrovascular resistance index; MT = mental task; PDBL = postdrink baseline; RE = recovery period; TPR = total peripheral resistance.

and vasodilatation in the skeletal muscles through activation of the autonomic nervous and endocrine systems.[7] In contrast, oral ingestion of a 250 mg caffeine containing beverage was found to raise BP variables substantially 1 hour after consumption.[8] Previous studies investigated cardiovascular responses to the combination of 250 mg of caffeine with a mental arithmetic task and reported additive effects on BP in healthy men.[9,10] In the present study, a mental arithmetic task additionally increased systolic BP and diastolic BP after the consumption of a 355 ml can Red Bull, which contains 115 to 123 mg caffeine,[11,12] and caused total increases of 10.2 mm Hg for systolic BP and 7.3 mm Hg for diastolic BP. Therefore, it seems reasonable to refer our observed changes in BP parameters, at least partly, to the caffeine content in the Red Bull drink and to the mental stress. What is of concern is that energy beverages are being marketed for improving performance of mental work and physical exercise. However, during exercise, caffeine consumption has been noted to be associated with reduced myocardial blood flow.[13] This could be because of the effect of acute endothelial dysfunction, which could also explain some of the hemodynamic changes noted in the present study of mental stress (which can often simulate physical stress) in the presence of an acute exposure to an energy beverage. In contrast, we previously investigated the impact of a Red Bull energy drink on microvascular endothelial function and were not able to find changes on acetylcholine or sodium-nitroprusside mediated endothelial function in response to ingestion of an energy drink.[1]

In response to the mental task, we observed a rapid and substantial increase in heart rate, cardiac output, and double product with no initial change in BP variables and a decrease in total peripheral resistance. After this initial response, BP variables rose immediately to its peak values and gradually returned afterward to postdrink baseline values. Throughout the mental task, heart rate and cardiac output values remained significantly over postdrink baseline levels whereas stroke volume remained unchanged. These observations suggest a specific cardiac reaction pattern in response to mental stress after consumption of energy drink and water because of constant elevated cardiac output values which originated from increases in heart rate but not stroke volume. In agreement with our findings, a recent study observed increased cardiac output and heart rate values in response to a monotonous driving task after the ingestion of a 250 ml can Red Bull which was mixed with 250 ml orange juice.[14]

In response to the mental arithmetic test, cerebral blood flow velocity rose immediately after the onset, plateaued for 3 minutes and gradually returned to postdrink baseline levels after cessation. This effect could be observed to a

Table 1
Individual cardiovascular pre- and post-drink parameters measured in 20 (first 10 are males and second 10 are females) young and healthy human subjects using a randomized cross-over study design

Treatment	Water	Water	*Red Bull*	*Red Bull*	Water	Water	*Red Bull*	*Red Bull*	Water	Water	*Red Bull*	*Red Bull*
Condition	Pre-drink	Post-drink	Pre-drink	Post-drink	Pre-drink	Post-drink	Pre-drink	Post-drink	Pre-drink	Post-drink	Pre-drink	Post-drink
Case	SBP [mmHg]	SBP [mmHg]	SBP [mmHg]	SBP [mmHg]	DBP [mmHg]	DBP [mmHg]	DBP [mmHg]	DBP [mmHg]	HR [bpm]	HR [bpm]	HR [bpm]	HR [bpm]
1 (20 years)	130	130	120	130	80	82	70	77	62	61	64	67
2 (23 years)	115	122	108	119	74	77	69	78	63	66	67	72
3 (29 years)	129	127	122	132	85	81	80	90	70	68	68	70
4 (20 years)	113	117	113	121	76	77	78	84	58	58	65	72
5 (24 years)	133	145	146	155	79	81	81	79	67	62	63	59
6 (22 years)	114	115	110	129	73	75	71	79	56	74	65	77
7 (22 years)	122	119	116	120	85	87	82	86	95	76	81	86
8 (19 years)	143	134	133	137	86	82	80	81	69	70	64	82
9 (23 years)	117	119	121	122	74	76	81	79	58	65	58	67
10 (24 years)	101	116	111	115	69	80	71	76	58	60	62	66
11 (23 years)	115	119	120	135	76	75	78	85	53	53	59	66
12 (20 years)	104	106	99	105	66	70	63	64	63	53	55	58
13 (22 years)	114	115	111	113	68	72	71	72	50	65	47	59
14 (23 years)	113	117	124	135	74	76	80	88	61	62	66	68
15 (20 years)	116	124	117	128	79	80	81	93	69	78	71	89
16 (20 years)	112	115	107	111	67	70	66	68	60	61	56	61
17 (21 years)	105	95	109	114	65	59	69	72	73	65	69	71
18 (22 years)	112	106	120	125	77	75	87	86	64	66	68	69
19 (21 years)	120	108	116	116	76	64	67	70	64	55	68	77
20 (23 years)	111	110	120	120	74	72	86	84	80	72	74	89
Average	117	118	117	124*	75	76	76	80*	65	64	65	71*
SEM	2	2	2	3	1	1	1	2	2	2	2	2

Pre-drink: Average over 20 minutes pre-drink baseline values; *Post-drink:* Average over the last 5 minutes before starting the mental task (i.e. average over the period from 75 to 80 minutes after the respective drink).
DBP = diastolic blood pressure; HR = heart rate; SBP = systolic blood pressure; SEM = standard error of means.
*p <0.005, comparing pre-drink *Red Bull* with post-drink *Red Bull* using a paired *t*-test. Data are presented as absolute values.

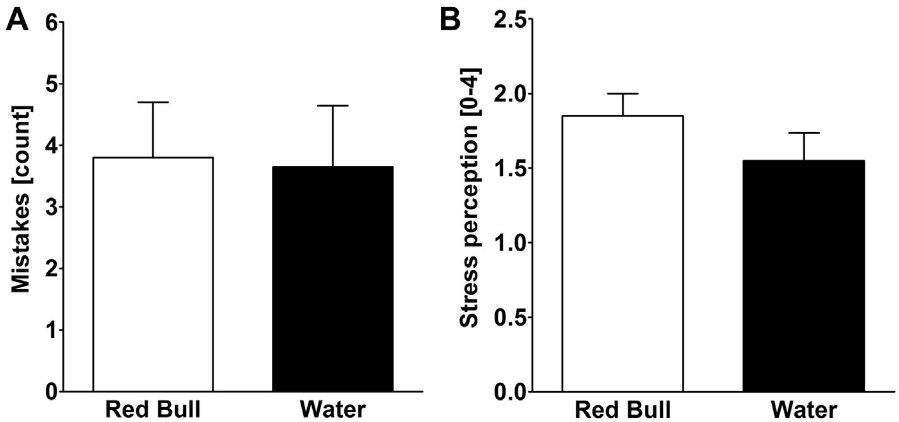

Figure 5. *(A)* Average over the test subject's mistake count for 60 arithmetic problems solved in 5 minutes (answers were given verbally). *(B)* Average over the subject's subjective stress perception derived immediately after the mental task using a 5-point Likert-scale. 0 = no stress; 1 = light stress; 2 = stressful; 3 = very stressful; 4 = very, very stressful.

similar extent for Red Bull and for water (+3.5% and +3.1%, respectively) and agrees with a study in which cerebral blood flow velocity was investigated in response to mental activities.[15] However, the combination of mental stress and Red Bull consumption caused a −11% lower cerebral blood flow velocity compared with predrink baseline levels, whereas the water drink had just a small effect (−0.8%). In line with this novel observation, our subjects' mistake quote and their perceived stress level were not better after ingestion of Red Bull in comparison to the water control.

Therefore, the benefit of using energy drinks with the intention to improve mental efforts or to cope better with mental stress seems questionable.

Disclosures

The authors have no conflicts of interest to disclose.

Supplementary Data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.amjcard.2014.10.017.

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