

**ACUTE EFFECTS OF ENERGY DRINK ON HEART RATE VARIABILITY
RECOVERY AFTER EXERCISE: A SYSTEMATIC REVIEW AND META-
ANALYSIS**

**EFFETS AIGUS DE LA BOISSON ÉNERGÉTIQUE SUR LA RÉCUPÉRATION DE
LA VARIABILITÉ DE LA FRÉQUENCE CARDIAQUE APRÈS L'EXERCICE :
UNE REVUE SYSTÉMATIQUE ET UNE MÉTA-ANALYSE**

ENERGY DRINK ON HEART RATE VARIABILITY RECOVERY

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SUMMARY AND KEYWORDS:

Introduction: The influence of energy drink (ED) on the analysis of autonomic parameters through post-exercise heart rate variability (HRV) remains undefined. We propose to assess the results of the principal studies that estimated the acute effects of ED intake on HRV recovery after effort.

Summary of facts and results: Searches were completed in the following databases: PubMed, MEDLINE via Ovid, Embase, Web of Science, CINAHL, Cochrane Library, Bireme, MedRxiv, and Scopus. The research commenced between July 2020 and March 2021. The terms necessary to identify the studies were “Energy Drink” AND “Exercise” AND “Recovery” AND “Heart Rate Variability”. Only clinical, crossover, and placebo-controlled trials were suitable for the final sample. Four studies were considered eligible, studies could not demonstrate significant values akin to the intervention with ED. The total sample size for performing the meta-analysis was 59 participants. The 99% confidence interval (CI) of our meta-analysis ranged from -2.13 to 0.36 with a combined effect size of -0.89 for SDNN (ms), -1.34 to 0.10 with a combined effect size from -0.62 for RMSSD (ms).

Conclusion: Our review supports that ED intake did not change the post-exercise HRV recovery in healthy adults.

Key-words: Autonomic Nervous System; Caffeine; Heart; Heart Rate; Exercise; Systematic review

RESUME

Introduction: L'influence de la prise de boisson énergisante (BE) sur la variabilité de la fréquence cardiaque post-exercice (VFC) reste mal définie. Nous proposons d'évaluer les résultats des principales études qui ont estimé les effets en aigu de la prise de BE sur la récupération de la VRC après effort.

Synthèse des faits et résultats: Les recherches ont été effectuées dans les bases de données suivantes: PubMed, MEDLINE via Ovid, Embase, Web of Science, CINAHL, Cochrane Library, Bireme, MedRxiv et Scopus. La recherche a commencé entre juillet 2020 et mars 2021. Les termes nécessaires pour identifier les études étaient “Boisson énergisante” ET “Exercice” ET “Récupération” ET “Variabilité de la fréquence cardiaque”. Seuls les essais cliniques, croisés et contrôlés par placebo étaient inclus dans l'échantillon final. Quatre études ont été considérées comme éligibles. Ces études n'ont pas pu démontrer d'effet significatif de la BE sur la VFC. La taille totale de

l'échantillon pour effectuer la méta-analyse était de 59 participants. L'intervalle de confiance (IC) à 99% de notre méta-analyse variait de -2,13 à 0,36 avec une taille d'effet combinée de -0,89 pour SDNN (ms), -1,34 à 0,10 avec une taille d'effet combinée de -0,62 pour RMSSD (ms). Conclusion: Notre revue porte à penser que la prise de BE n'a pas changé la récupération de la VFC après exercice chez des adultes en bonne santé cardio-vasculaire. Seuls les essais cliniques, croisés et contrôlés par placebo étaient pris en compte. Quatre études ont été considérées comme éligibles, les études n'ont pas pu démontrer de valeurs significatives apparentées à l'intervention avec BE. La taille totale de l'échantillon pour effectuer la méta-analyse était de 59 participants. L'intervalle de confiance (IC) à 99% de notre méta-analyse variait de -2,13 à 0,36 avec une taille d'effet combinée de -0,89 pour SDNN (ms), -1,34 à 0,10 avec une taille d'effet combinée de -0,62 pour RMSSD (ms).

Conclusion: Notre revue montre que la prise d'ED n'a pas modifié la récupération de la VFC après exercice chez des adultes en bonne santé.

Mots-clés : Système Nerveux Autonome ; Caféine; Cœur; Rythme cardiaque; Exercer; Revue systématique..

1. INTRODUCTION

Part of the physiological deviations produced by Energy Drink [ED] may involve changes in the autonomic control of heart rate (HR). ED has an intimate association with the cardiovascular system [1-4]. HR variability (HRV) is a non-invasive, simple and safe technique that estimates autonomic nervous system (ANS) function. The ANS is vital for maintaining homeostasis and, the estimation of HRV recovery after exercise has been widely applied as a technique to assess ANS adaptation (vagal resumption) under numerous conditions. Thus can be evaluated under interventions so as to comprehend if the use of specific components may delay post-exercise recovery, elevating the risk of cardiovascular complications [5].

Despite the frequent use of ED in physical exertion activities, in recent years, limited clinical trials have aimed to evaluate the effects of ED on HRV recovery after exercise. So, the limited number of participants in the samples and the quality of these tests raise the need for more in-depth analysis. In relation to the points discussed above, the subsequent question is highlighted: Does ED intake influence HRV recovery after effort? We performed a systematic review and meta-analysis of clinical trials to study the effect of ED on HRV post-exercise recovery in healthy individuals.

2. MATERIALS AND METHODS

The systematic review was conducted between July 2020 and March 2021, and was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [6]. The review are registered in PROSPERO (CRD42021237703).

The research question was performed via the strategy PICOS. After testing, the sensitivity of the search, we decided that the search was more sensitive with the terms:

"Energy Drink" AND "Exercise" AND "Recovery" AND "Heart Rate Variability" used in the electronic databases (PubMed, MEDLINE via Ovid, Embase, Web of Science, CINAHL and Cochrane Library and Bireme, and gray literature via MedRxiv and Scopus).

After identification in database, the articles were exported to the Rayyan QCRI program[®] to exclude duplicate articles and we performed a simple screening in the database using only the filter: study in humans and the reading of the title and summary. Criteria inclusion was defined: the use of ED intake and as a minimum one session of physical exercise was required. We involved studies that enforced a placebo as a control: 1) drinks with a corresponding flavor; 2) flavored water and 3) water. The main outcome was HRV indexes. We included non-randomized or randomized, crossover, single or double blind, placebo-controlled clinical trials.

2.1 Data Analysis

The papers that completed the entire analytical process and were appropriate for this review had their data extracted in a table with a description of the features of the study population, intervention and outcomes (Table 1).

The effects of CAF interventions on each index were calculated using the mean and standard deviation (MSD). The MSD were estimated as the difference between the intervention and control group before and after exercise. The data used for the construction of the meta-analysis was the period recorded before the exercise and the first period recorded after the exercise. After extraction, the data were organized in Microsoft Excel, and then manipulated in the Review Manager Program (RevMan 5.4.1) to develop the meta-analysis[7].

Heterogeneity was attained using the I^2 test, in which a number greater than 50% was considered to indicate substantial heterogeneity between the tests[8]. For the values

of “CI” and “Test for size of the general effect”, values of $p < 0.01$ (or, $< 1\%$) were judged significant. Furthermore, we enforced a random effects model, in preference to a fixed effect model, considering that this is a more conservative method that permits that the heterogeneity of the study may fluctuate beyond chance, providing further generalizable results [8].

Attributable to the low number of articles, no meta-regression was performed. All data was produced by the Review Manager Program (RevMan 5.4.1) For meta-analysis; linear methods were considered in the time (SDNN - standard deviation of all normal IBI recorded in a time interval, expressed in ms - and; RMSSD - square root of the square mean of the differences between adjacent normal IBI, in a time interval, expressed in ms)[7].

2.2 Analysis of the risk of bias

The risk of bias analysis was commenced under the guidelines of the Cochrane organization, via the Review Manager program (RevMan 5.4.1)[7]. The analysis of risk of bias was accomplished by two independent authors (AAP and CJRB), and a third (VEV) was consulted if there was any discrepancy in the judgments. In Table 1 we offer a summary of results of the analysis of risk of bias.

3. RESULTS

A total of 308 studies were acknowledged by searching all five databases. After eliminating duplicates ($n=67$), 241 publications were screened via filters in the databases and reading the title and/or abstract. From these, 34 outstanding articles were selected to read the full text. Lastly, four studies were involved in the systematic review[29-32]. The studies contained within this review were published between 2014 and 2020. The total sample size for performing the meta-analysis was 59 participants..

The study conducted by Clark et al.[4] was excluded from the quantitative analysis (meta-analysis) because of the use of HRV indices and study design different from the other studies.

The search process and the selection steps are demonstrated in the Flow Diagram of the PRISMA protocol (Figure 1). The studies characteristics are shown in Table 1.

Figure 3. Forest plot graphs for comparison of time domain indices amongst individuals who ingested ED and individuals who ingested placebo by means of SDNN (above) and (below).

Figure 2 presents the forest plot graphs for comparing time domain indices between individuals who ingested ED and individuals who ingested placebo using SDNN and RMSSD. We enforced a model of random effects and standard mean difference (Std. Mean Difference) to quantify the effect size (black diamonds); the proportion of the center of the diamonds represents the CI of 99%. A negative effect indicates impact on the group that ingested ED compared to controls. No significant change was observed for SDNN (ms) and RMSSD (ms), for the effect size we revealed a value of $p=0.07$ and a heterogeneity of 77% in the SDNN index (ms) and, $p=0.03$ for the effect size and 38% for heterogeneity for the RMSSD index (ms).

4. DISCUSSION

Our study was performed to evaluate the acute effect of ED intake on HRV recovery after exercise via a systematic review and meta-analysis. Despite the combined effect size values preferring the group that ingested ED, the values were very close to zero, considered as the nullity line of the statistic. Our meta-analysis provides evidence, from a statistical point of view, that ED intake did not significantly influence the HRV

1 post-exercise recovery compared to the placebo based on the time (SDNN and RMSSD)
2 and frequency (HF, LF and LF/HF) domain indices.
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4 The quality of the result of a systematic review is meticulously linked to the
5 quality of accessible studies on the proposed subject. Our study has a series of
6 restrictions, resulting from the original studies, so caution is essential when interpreting
7 the data. The scientific literature on ED is rare, and we evaluated its' influences in a
8 specific situation, which presented us with a small sample. Some of the scientific papers
9 included are unclear as to the process of randomization and allocation, increasing the
10 potential effects of confounding factors. The sample heterogeneity is one more factor
11 that necessitates careful consideration in this study. Our meta-analysis included males
12 and females with a mean age between 20 and 24 years old, yet, it was unclear if all
13 groups were involved in physical exercises.
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28 We attempted to bring these studies closer together and produce a reliable result
29 from clinical applicability. Yet, the facts that they have different exercise protocols,
30 different moments of ED ingestion and different VO2max indices need to be taken into
31 account.
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41 **5. CONCLUSIONS**

42 In conclusion, this review of placebo-controlled clinical trials with meta-analysis
43 supports that ED intake did not affect HRV post-exercise recovery in healthy
44 individuals between 20 and 24 years old. Even so, only four studies are insufficient to
45 offer the safety of ED before physical effort. We conclude that further clinical trials are
46 required to better appreciate the effects of ED on cardiovascular post-exercise recovery
47 metrics.
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None.

CONFLICT OF INTEREST

The authors declare have no conflict of interest.

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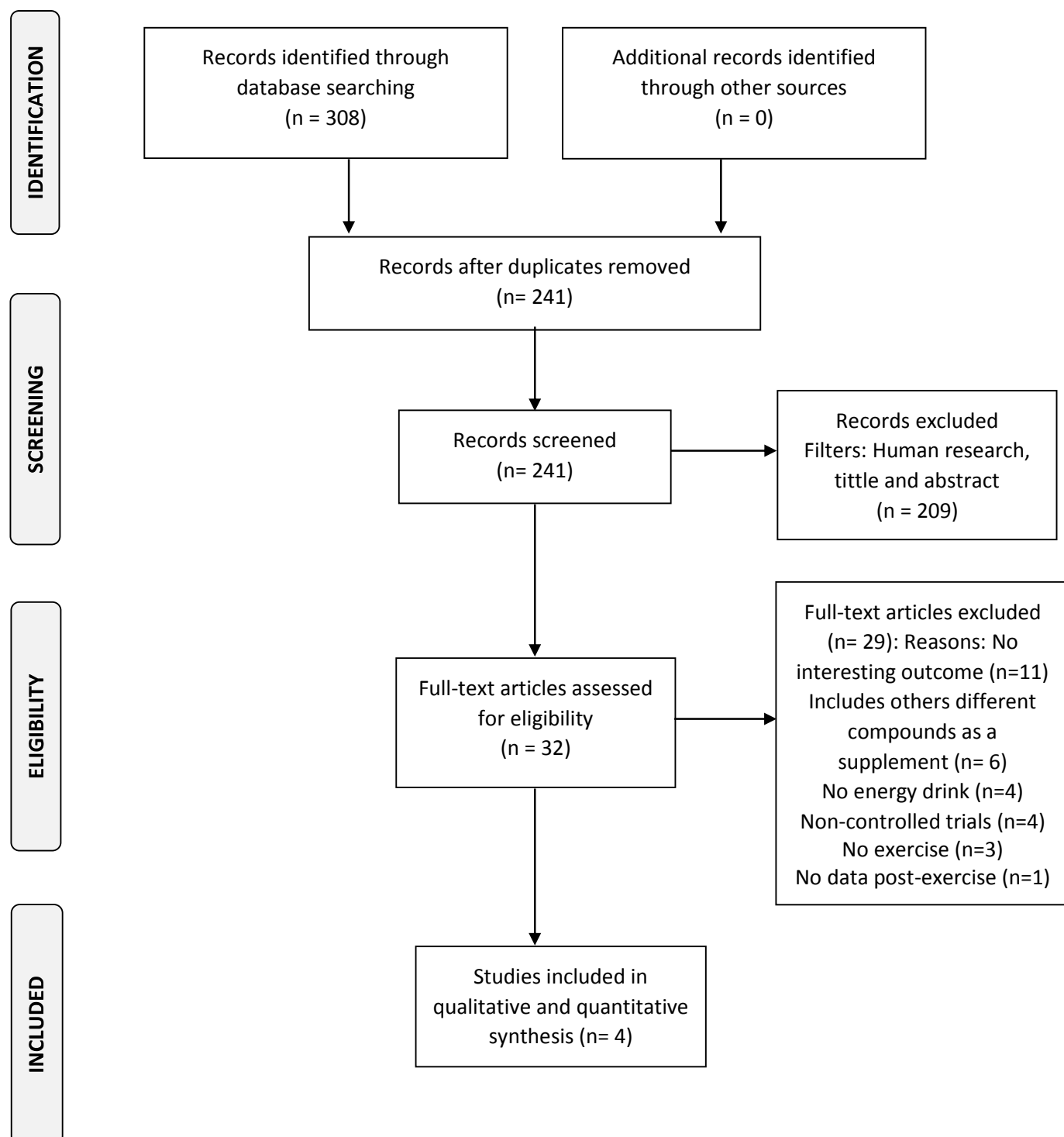
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PRISMA 2009 Flow Diagram



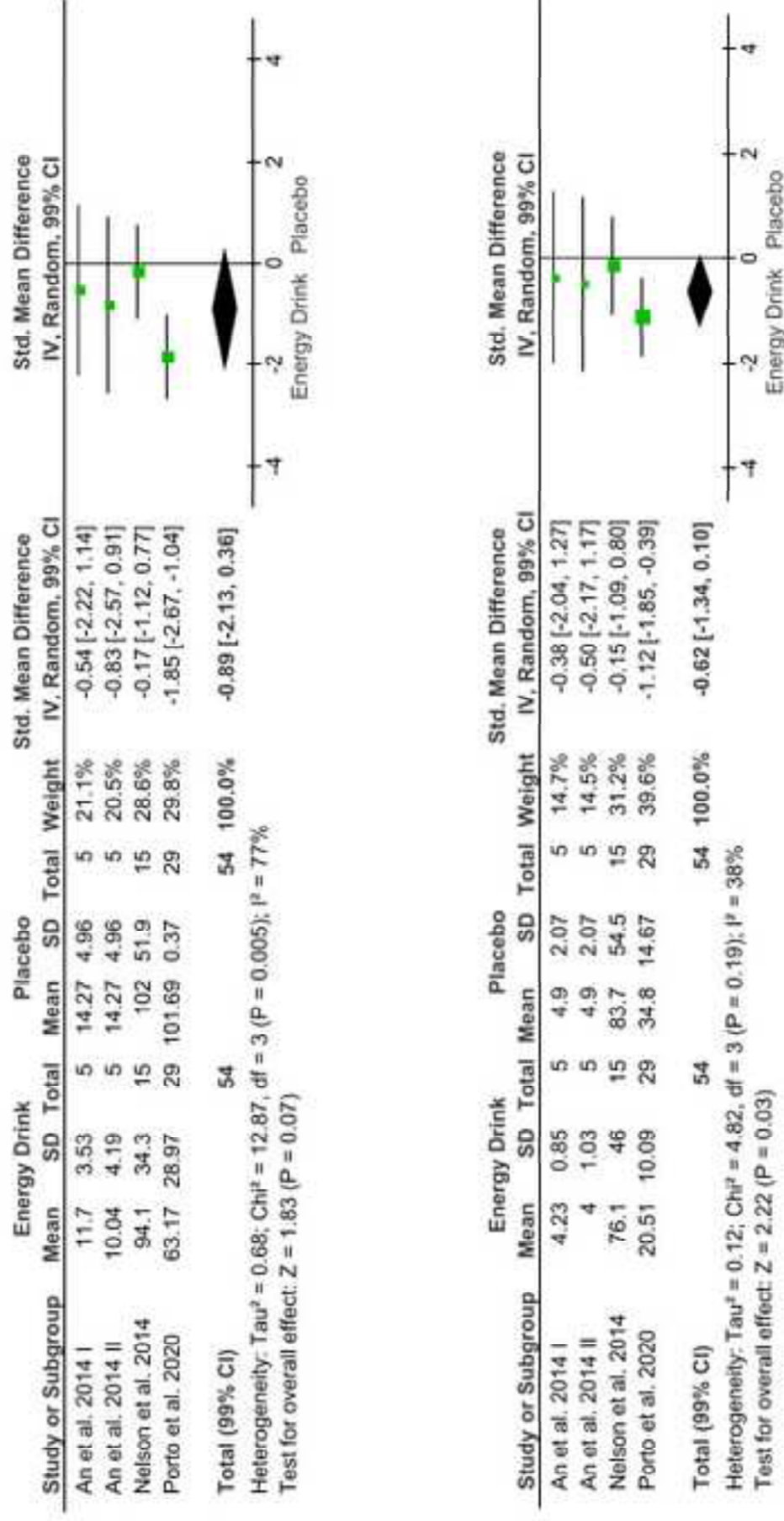


Table 1. Description of the selected articles by author and year, time ingestion BE, BE dose, placebo, analysis time, HRV index and main conclusions.

Author/years	Ingestion CAF (before exercise)	ED Dose	Placebo	Analysis Time	HRV Index	Main conclusions	Risk of Bias
An et al. (2014)	60 minutes	ECG I 91,50 ± 6,52mg/kg CAF ECG II	Water	After Exercise	SDNN, RMSSD, TP, VLF, LF (ms2), HF(ms2), LF/HF ratio. LF and HF (n.u)	In conclusion, intake of ED produced no significant changes in HRV after exercise	Random sequence generation (High) Allocation concealment (High) Blinding of participants (High) Blinding of outcome assessment (High) Incomplete outcome data (Low) Selective reporting (Low) Other bias (Low)
Nelson et al. (2014)	60 minutes	0,65Carbohydrate, 2 CAF, 25 Taurine, 5 Pana-ginseng, 1,5 Vitamin C, 0,04 Ribiflavin, 0,50 Niacin, 0,05 Vitamin B6, 0,15 Vitamin B12 mg/kg	taste-matched placebo	10 minutes	RMSSD, Normal RR, SDNN, LF, HF, LF/HF ratio and SampEn.	In conclusion, The ED did not have an impact on parasympathetic and sympathetic balance at rest via HRV analysis	Random sequence generation (Unclear) Allocation concealment (Unclear) Blinding of participants (Unclear) Blinding of outcome assessment (Unclear) Incomplete outcome data (Low) Selective reporting (Low) Other bias (High)
Porto et al. (2020)	15 minutes	45 Calories, 11,2 g Carbohydrate, 80 mg Sodium, 32 mg Caffeine, Taurine 400 mg, Niacin 4,6	Water	0-5,5-10, 15-20, 25-30, 35-40, 45-50, 55-60	SDNN, RMSSD, LF and HF(ms). LF and HF (n.u).	ED absorption before aerobic exercise did not significantly influence the recovery of heart rhythm	Random sequence generation (Low) Allocation concealment (Low) Blinding of participants (Low) Blinding of outcome assessment (Low) Incomplete outcome data (Low)

		mg, Pantothenic Acid 2 mg, Vitamin B6 0.5 mg, Vitamin B12 0.4 mg, Glucuronolactone 240 mg, inositol 20 mg)		minutes post-exercise	LF/HF ratio, SD1 and SD2	autonomic control undertaking moderate- intensity aerobic exercise.	Selective reporting (Low) Other bias (High)
Clark et al. (2020)	120 minutes	10 kcal, 296 mL drink containing a total of 140 mg of CAF, guarana, ginger, and green tea extract containing epigallocatechin gallate	Matched in taste and in color placebo	15 minutes post-exercise	RMSSD, RR, HF, LF and LF/HF	No significant changes in ANS function were shown after exercise	Random sequence generation (Unclear) Allocation concealment (Unclear) Blinding of participants (Unclear) Blinding of outcome assessment (Unclear) Incomplete outcome data (Low) Selective reporting (Low) Other bias (High)

RMSSD = square root of the square mean of the differences between adjacent normal RR intervals; SDNN = standard deviation of all normal RR intervals; TP= total power; LF = low frequency component; HF = high frequency component; LF / HF = ratio between low and high frequency components; SD1: dispersion of points perpendicular to the identity line, instantaneous record of beat-to-beat variability; SD2: scatter of points along the identity line; long-term record of HRV; TP = Total power; ApEN = Approximate entropy; SampEn = Sample Entropy; ED= Energy drink; CAF= Caffeine