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Caffeinated energy drink intake modulates motor circuits at rest, before and after a movement

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ABSTRACT

Energy drinks are thought to improve certain aspects of athletic and cognitive performances. Moreover, less is understood about physiological mechanisms that might underlie these effects. The aim of this study was to examine the influence of sugar-free energy drink (SFED) ingestion on corticomotor excitability and plasticity. Fourteen college students consumed a commercially available SFED or a "dummy" drink. By using Transcranial magnetic Stimulation (TMS) we investigated resting motor threshold (RMT), motor evoked potential (MEP) amplitude and cortical silent period (CSP). Paired-pulse stimulation was used to assess short interval intracortical inhibition (SICI) and intracortical facilitation (ICF). Sensorimotor integration was investigated with the short- and long-afferent inhibition paradigms (SAI and LAI). Cortical plasticity was studied with the paired associative stimulation (PAS) paradigm. In addition, we examined the effect of SFED on simple reaction time (RT), pre-movement facilitation and post-exercise facilitation (PEF).

SFED consumption decreased ICF, shortened RT, increased pre-movement facilitation and PEF of the motor evoked potentials. These results demonstrate that SFED consumption induced a shorter RT that is paralleled by changes in cortical excitability at rest, prior and after a non-fatiguing muscle contraction. These acute changes in brain function might be of relevance in understanding the mechanisms underlying the enhancement of psychomotor performance.

1. Introduction

Energy drinks (ED) containing caffeine, taurine and glucuronolactone are very popular especially among college students and athletes [1–3]. For instance, college students drink EDs while studying and before exams because they believe in positive effects on memory, stress and fatigue [3]. Furthermore, in the area of athletic performance previous reports showed that consumption of caffeinated EDs increases total number of repetitions in bench press endurance exercise [4] increases maximum cycling velocity, enhancing alertness and cognition [5]. These data support the growing popularity of ED among athletes.

Although many studies focused on the behavioral effects of EDs in healthy human, to date no studies have investigated the impact of sugar-free ED (SFED) ingestion on cortical excitability and plasticity, which are the likely neurophysiological basis underlying the supposed cognitive and motor enhancing effects of EDs. Furthermore, despite the lack of a solid causal link between ED consumption and neuropsychiatric and cardiovascular adverse events previously published evidences warrant caution [6–12]. It is thus of pivotal importance to characterize changes in brain excitatory and inhibitory circuits after ED consumption.

The physiology of cortical circuitries can be investigated in humans by using transcranial magnetic stimulation (TMS) in both physiological and pathological conditions [13–15]. Stimulation of the primary motor cortex (M1) with TMS induces a muscular twitch and a motor evoked potential (MEP) in a contralateral target muscle. Using the acute intake of drugs of known mechanism of action, several TMS parameters have been characterized and now offer the possibility to investigate non-invasively changes in cortical circuitries in humans under different experimental conditions. For instance, resting motor threshold (RMT) is considered a marker of neuronal membrane excitability as it is modulated by voltage-gated sodium or calcium- channel blockers; changes in MEP amplitude obtained with different stimulation intensities are thought to reflect changes in the excitability of the corticospinal tract;

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cortical silent period (CSP) is obtained with a single-pulse TMS during a muscle contraction and it is an inhibitory cortical parameter (affected by GABA-ergic and dopaminergic drugs); short interval intracortical inhibition (SICI) and intracortical facilitation (ICF) are obtained by using a paired-pulse paradigm and are mediated by glutamatergic and gamma-aminobutyric acid (GABA)-ergic mechanisms within M1; short and long afferent inhibition (SAI and LAI) are parameters that reflect changes in M1 excitability induced by incoming sensory stimuli (sensorimotor integration) and are modulated by cholinergic and GABAergic drugs [16,17]. Thus, the study of these parameters after the acute intake of an ED could offer the possibility to investigate the effect of the drink on different cortical circuits. Furthermore, it is feasible to induce associative cortical plasticity in humans by using a paired associative stimulation (PAS) protocol [18] consisting of a peripheral nerve stimulation combined with a TMS of the M1 delivered an interval of 25 ms. PAS is capable of inducing synchronous activation of cortical synapses and long-term potentiation (LTP)-like effects [19–21] that can be detected with a long-lasting increase in MEP amplitude. This form of cortical plasticity has been characterized in previous pharmaco-TMS studies [22] and could offer the possibility of studying the effect of ED intake on cortical plasticity in humans.

Cortical excitability, determined by the amplitude of MEPs, can be assessed before or immediately after a muscle contraction. A large body of literature supports the hypothesis that acute exercise induces cortical adaptations within M1 [23]. For instance, cortical excitability assessed during a simple reaction time (RT) task provides information about premovement cortical excitability and movement preparation [24–26]. With a different paradigm it has been demonstrated that MEP amplitude increased after non-fatiguing exercise, a phenomenon called post-exercise facilitation (PEF) [27–29]. The post-exercise adaptations in MEP size are considered a marker of exercise-induced cortical plastic adaptations [29,30]. Hence, using the premovement facilitation and the PEF parading could offer the possibility to further characterize the ergogenic properties of EDs gaining insights regarding their effect on movement preparation and execution.

Caffeinated EDs are currently used to improve physical performance. In the present study we aim to investigate the effects of SFED intake on brain function in order to gain information regarding the mechanism that underlies the putative ergogenic effects of EDs. We hypothesized that drinking a commercially available SFED compared to a placebo drink would affect cortical physiology modifying TMS parameters of cortical excitability at rest and LTP-like plasticity. In addition, we hypothesized a positive modulation on movement preparation and exercise-induces cortical plastic adaptations.

2. Material and methods

2.1. Subjects

We studied fourteen volunteers (mean age 31.2 ± 9 SE years, 8 F). All participants were right-handed according to the Edinburgh Inventory 25–50 [31] and gave informed consent prior to participation. The healthy volunteers complied with the well-known inclusion criteria for TMS studies (no history of neurological and psychiatric disease, use of psychotropic drugs, pregnancy, cardiac pacemaker and medical implants). The study was approved by the local ethics committees (New York College of Podiatric Medicine) and conducted in accordance with the Declaration of Helsinki.

2.2. Experimental interventions

The study was designed as a randomized, double-blind, crossover, controlled trial in which volunteers were asked to consume a commercially available 8.4 oz can of SFED (sugar-free Red Bull) containing the following ingredients: Aspartame 0.01 $mg \cdot kg^{-1}$, Caffeine 2.0 $mg \cdot kg^{-1}$, Taurine 25 $mg \cdot kg^{-1}$, glucuronolactone 15 $mg \cdot kg^{-1}$, niacin 0.45 $mg \cdot kg^{-1}$, pantothenic acid 0.15 $mg \cdot kg^{-1}$, vitamin B6 0.05 $mg \cdot kg^{-1}$, riboflavin 0.04 $mg \cdot kg^{-1}$, vitamin B12 0.025 $mg \cdot kg^{-1}$. The "dummy" energy drink was prepared by a registered nurse and allocated in an empty can of sugar free Red Bull. The placebo drink was comprised of quinine flavored carbonated water with additional black currant, lime and apple flavors and had the same calories (~4 kcal/250 mL). Subjects were randomly assigned via restricted randomization to either real or dummy SFED.

Subjects participated to all experimental sessions: 1) cortical excitability, 2) paired-associative stimulation (PAS), 3) pre-movement facilitation, 4) post-exercise facilitation and were tested twice (SFED/placebo, eight visits in total). There was a 3 days washout period before subjects switched to the alternate arm of the study. For the PAS paradigm the washout period was 2 weeks. Subjects were assessed 45 min after drink interventions. All the different experimental session were performed in the morning (~10 AM).

2.3. Experimental procedure

All subjects were seated in an armchair. Surface EMG was recorded from the right abductor pollicis brevis (APB) muscle with disposable adhesive disk electrodes placed in a tendon-belly arrangement. The signal was amplified, filtered (bandpass 2 Hz to 5 kHz), digitized (Micro 1401, Cambridge Electronics Design, Cambridge, UK), and stored in a laboratory computer for off-line analysis. TMS was delivered through a focal figure-of-eight-shaped magnetic coil (diameter of external loop: 90 mm) connected to two Magstim 200 magnetic stimulators via a "Y" cable (The Magstim Company, Dyfed, UK). The coil was placed on the left motor cortex at the optimal position for eliciting MEPs from the right APB muscle ("hot spot"). The coil was held tangentially to the skull with the handle pointing backwards and laterally at an angle of 45° to the sagittal plane. This orientation of the induced electrical field is thought to produce a predominantly trans-synaptic activation of the cortico-spinal neurons [32]. During the experiments EMG activity was continuously monitored with auditory (speakers) and visual (EMG) feedback to ensure complete relaxation.

2.4. Cortical excitability

Several parameters of cortical excitability were investigated. RMT was determined as the minimum stimulator intensity to the nearest 1% to produce an MEP of 50 μV in five of 10 trials. To assess MEP recruitment, stimulus intensities of 100%, 110%, 120%, 130% and 150% of the RMT were delivered in a random order rate of 0.1 Hz. Mean peak-to-peak MEP amplitudes (20 at each stimulation intensity) were recorded. CSP was recorded while the subjects were performing about 50% of maximal voluntary contraction (EMG activity was monitored with an audio-video feedback). The CSP was evoked with single-pulse TMS at an intensity of 150% of RMT. The duration of fifteen CSPs was measured from the end of the MEP until the restart of a constant EMG activity. EMG traces were rectified but not averaged. SICI and ICF were studied with a paired-stimulation paradigm [33]. In this TMS paradigm a conditioning stimulus below motor threshold modulates the amplitude of the MEP produced by a test stimulus, inhibiting it at inter-stimulus intervals (ISI) < 5 ms (SICI) and facilitating it at ISI above 8 ms (ICF). The two magnetic stimuli were delivered through the same coil using a "Y" cable. SICI was induced with a conditioning stimulus set at 80% of RMT and delivered 2 ms before a test stimulus while for the induction of ICF the inter-stimulus intervals (ISI) was 10 ms. Ten unconditioned (test only) and 20 conditioned (10 at each ISI) stimulations were recorded. The average amplitude of the 10 conditioned MEP at both 2- and 10-ms ISIs was expressed as percentage of the average of the 10 unconditioned test MEP. The test stimuli alone were delivered in random order controlled by a laboratory computer (Signal software, Cambridge Electronics Design, Cambridge, UK). Afferent inhibition was elicited by stimulating the medial nerve at the wrist with a Digitimer D-