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Journal of Nutritional Biochemistry 24 (2013) 325–334

Journal of Nutritional Biochemistry

Metabolic response to green tea extract during rest and moderate-intensity exercise☆

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Received 28 October 2011; accepted 19 June 2012

Abstract

Background: Green tea catechins have been hypothesized to increase energy expenditure and fat oxidation by inhibiting catechol-*O*-methyltransferase (COMT) and thus promoting more sustained adrenergic stimulation. Metabolomics may help to clarify the mechanisms underlying their putative physiological effects.
Objective: The study investigated the effects of 7-day ingestion of green tea extract (GTE) on the plasma metabolite profile at rest and during exercise.
Methods: In a placebo-controlled, double-blind, randomized, parallel study, 27 healthy physically active males consumed either GTE (n=13, 1200 mg catechins, 240 mg caffeine/day) or placebo (n=14, PLA) drinks for 7 days. After consuming a final drink (day 8), they rested for 2 h and then completed 60 min of moderate-intensity cycling exercise (56%±4% VO_2max). Blood samples were collected before and during exercise. Plasma was analyzed using untargeted four-phase metabolite profiling and targeted profiling of catecholamines.
Results: Using the metabolomic approach, we observed that GTE did not enhance adrenergic stimulation (adrenaline and noradrenaline) during rest or exercise. At rest, GTE led to changes in metabolite concentrations related to fat metabolism (3-β-hydroxybutyrate), lipolysis (glycerol) and tricarboxylic acid cycle (TCA) cycle intermediates (citrate) when compared to PLA. GTE during exercise caused reductions in 3-β-hydroxybutyrate concentrations as well as increases in pyruvate, lactate and alanine concentrations when compared to PLA.
Conclusions: GTE supplementation resulted in marked metabolic differences during rest and exercise. Yet these metabolic differences were not related to the adrenergic system, which questions the *in vivo* relevance of the COMT inhibition mechanism of action for GTE.

Keywords: Green tea; Catechin; Metabolomics; Exercise; Catecholamine; Energy metabolism

1. Introduction

The concept of "challenging homeostasis" has been proposed as a novel approach to define biomarkers for nutritional related health [1]. It is thought that responses to a challenge of homeostasis will affect multiple pathways and provide information other than static homeostatic and disease-relevant end-point measures. These dynamic responses may be appropriate means to assess effects and mechanisms of nutritional interventions that may remain hidden under the large variation within a healthy population. Exercise is a physiological challenge to homeostasis of the human body. Metabolomics based on gas or liquid chromatography–mass spectrometry (GC/MS, LC/MS) is capable of measuring the multifactorial, integrative metabolic responses to an exercise challenge and/or a nutritional intervention or supplement [2–6].

Green tea has been reported to have a number of health-promoting effects, including antiobesity properties [7–10]. These health benefits are generally attributed to its polyphenol content, particularly to catechins that are often enriched in green tea extract (GTE). These are comprised epigallocatechin gallate (EGCG), epicatechin gallate and gallocatechin gallate, among others. EGCG is thought to be the most pharmacologically active of the catechins. GTE also contains caffeine. The antiobesity properties of GTE are attributed to both acute [11] and chronic [7,12] GTE supplementation augmenting energy expenditure (EE) and fat oxidation under resting conditions. However, this has not been consistently reported [13,14]. During moderate-intensity exercise, EE is elevated several times when compared to rest, and absolute rates of lipolysis and fat oxidation are 3–10-fold higher. The administration of GTE could at least in theory have an additive effect on fat metabolism above and beyond what is seen with exercise alone. Indeed, it has been observed that fat metabolism is up-regulated during exercise following both acute [15] and chronic [16] GTE supplementation. So far, differences in the metabolic effects of GTE between rest and exercise have not been investigated in a single study. It is also currently unknown whether the effects of GTE on fat metabolism or any other related metabolic effects are more prominent following acute or chronic GTE supplementation.

It has previously been observed that certain catechins in GTE target specific control points of the sympathetic nervous system [17].

☆ This research was funded by Unilever R&D.
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0955-2863/$ - see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.jnutbio.2012.06.017

EGCG has been suggested to directly inhibit catechol-*O*-methyltransferase (COMT), an enzyme that is responsible for degrading catecholamines [noradrenaline (NA) and adrenaline (A)] [18]. Inhibiting the degrading action of COMT would lead to elevated catecholamine concentrations, resulting in greater sympathetic nerve stimulation and thus higher rates of lipolysis. This is thought to elevate fat oxidation and EE at rest and during exercise [10]. The COMT pathway is likely to take effect following acute GTE supplementation. Alternatively, it has been suggested that chronic GTE supplementation may be the lead to an up- or down-regulation of various proteins and enzymes involved in fat metabolism [19,20]. However, there is no convincing evidence to support the acute or chronic mechanisms of GTE *in vivo*.

Based on the mixed study outcomes on fat metabolism following GTE supplementation and the lack of mechanistic evidence *in vivo*, the aim of the present study was to examine the effects of 7 days of GTE supplementation (1200 mg total catechins and 240 mg caffeine/day) on human metabolism at rest and during moderate-intensity exercise (56±%4% VO_2max). These effects were assessed in human plasma using GC–MS- and LC–MS/MS-based four-phase metabolite profiling [21]. This comprehensive metabolite profiling approach provided an unbiased and systemic investigation into the multifactorial metabolic response following GTE supplementation at rest and during exercise. We hypothesized that GTE ingestion for 7 days would induce metabolic changes consistent with increased lipolysis and that these changes could be maintained or enhanced during exercise after a single bolus intake of GTE. In addition, we tested the hypothesis that GTE stimulates the adrenergic system by measuring targeted profiles including various catecholamines.

2. Methods and materials

2.1. Study design

2.1.1. Participants

Twenty-seven healthy physically active male participants were recruited for the purposes of the study. Inclusion criteria were as follows: less than four cups of tea or coffee/day (thus less than ~400 mg caffeine/day), exercise 3–5 times/week, 30–90 min/session. Participants were randomly allocated into either a GTE group [n=13, age 22±5 years, weight 77.6±12.0 kg, body mass index (BMI) 24.3±3.0 kg/m^2] or a placebo (PLA) group (n=14, age 22±8 years, weight 78.8±10.2 kg, BMI 24.7±2.7 kg/m^2). All participants gave written informed consent to participate in the study. The study was approved by the University of Birmingham Ethics Committee.

2.1.2. Preliminary testing

One week prior to the first experimental trial, all participants visited the human performance lab for familiarization, assessment of health and an incremental exercise test using an electronically braked cycle ergometer (Lode Excalibur Sport, Groningen, the Netherlands) to volitional exhaustion (FatMax) [22]. Participants started by cycling at 95 W for 3 min, and work rate was increased by 35 W (W_{inc}) every 3 min (t_{inc}) until they reached exhaustion. The W_{max} was calculated by using the following equation [23]:

$$W_{max} = W_{out} + (t / t_{inc})W_{inc}$$

W_{out} is the power output of the last completed stage (in W), and t is the time (in minutes) spent in the final stage. W_{max} values were used to determine the workload of 50% W_{max} (~55% VO_2max) used in the experimental trials. Respiratory measures of oxygen consumption (VO_2) and carbon dioxide production (VCO_2) were assessed using an online gas analysis system (Oxycon Pro, Jaeger). Heart rate (HR) was measured continuously (Polar S625X; Polar Electro Oy, Kempele, Finland). VO_2 was considered to be maximal if two of the following three conditions were met: (a) a leveling off of (VO_2) with further increasing workloads; (b) an HR within 10 beats/min of the age-predicted maximum (220 bpm−age) and (c) a respiratory exchange ratio >1.

2.1.3. Experimental design

The study was designed as a placebo-controlled, double-blind, randomized, parallel study. Subjects in the assigned groups consumed either a GTE drink (1200 mg catechins, 240 mg caffeine) or a PLA drink for 7 days (Fig. 1).

On day 0 (D0), all participants arrived at the Human Performance Lab between 06:00 and 08:00 following a 10-h overnight fast and 24-h controlled diet on D0. Upon arrival, a flexible 20-gauge Teflon catheter (Venflon; Becton Dickinson, Plymouth, United Kingdom) was then inserted into an antecubital vein. A three-way stopcock (PVB Medizintechnik, Kirchseean, Germany) was attached to the catheter to allow repeated blood sampling during the trial. A resting blood sample (5 ml) was taken (t=0 min). Participants then rested for 2 h in a seated position. At the end of the rest period, a second resting blood sample (5 ml) was taken (t=120 min). Following this, participants began cycling at 50% W_{max} for 60 min. Throughout the exercise, blood samples (5 ml) were taken at t=140, 150, 160 and 180 min (Fig. 1). The catheter was kept patent by flushing it with 3–4 ml isotonic saline (0.9%; Baxter, Norfolk, United Kingdom) after each blood sample. The experimental trial was then repeated 8 days later. The only difference in the trials on D0 and D8 was the consumption of a single bolus of GTE (600 mg catechins, 120 mg caffeine) or PLA after the collection of the resting blood sample and prior to the resting period.

2.1.4. Diet and supplement

After the initial trial, participants were randomly assigned to ingest either GTE or PLA for 7 days (Fig. 1). The GTE and PLA supplements were provided in the form of a drink. Each drink was provided in a 330-ml can. The GTE (Taiyo International, Japan) and PLA compositions are displayed in Table 1. Participants were instructed to consume two drinks per day, one drink an hour prior to breakfast and another drink an hour prior to dinner. The supplementation period started on the day following the presupplementation trial. Subjects received daily reminders in the form of text messages in the morning and the evening to ensure compliance. Participants returned to the human performance lab on D8 having consumed the drinks for 7 days. In the 24-h period prior to D0, trial participants were asked to record a food diary, which was replicated prior to D8 trial.

2.1.5. Sample collection

All blood samples were stored on ice for no longer than 35 min. Subsequently, plasma was separated by centrifugation (1500*g*, 10 min, 4°C), aliquoted in 1-ml samples and stored at −80°C.

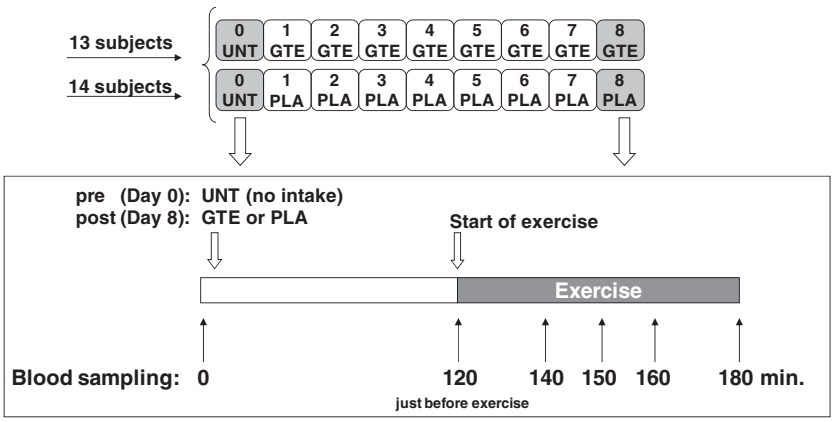

Fig. 1. Study design schematic.