Experimental Gerontology 110 (2018) 202–208

Contents lists available at ScienceDirect

Experimental Gerontology

journal homepage: www.elsevier.com/locate/expgero

Tart cherry concentrate does not enhance muscle protein synthesis response to exercise and protein in healthy older men

Sarah R. Jackman[a], Matthew S. Brook[b], Richard M. Pulsford[a], Emma J. Cockcroft[a], Matthew I. Campbell[a], Debbie Rankin[b], Philip Atherton[b], Kenneth Smith[b], Joanna L. Bowtell[a,*]

[a] Sport and Health Sciences, College of Life and Environmental Sciences, University of Exeter, Exeter, United Kingdom
[b] Medical Research Council-Arthritis Research United Kingdom Centre of Excellence for Musculoskeletal Ageing Research, University of Nottingham, Nottingham, United Kingdom

ARTICLE INFO

Section Editor: Borg Holly M Brown

Keywords:
Polyphenols
Inflammation
Deuterated water
Myofibrillar
Montmorency

ABSTRACT

Background: Oxidative stress and inflammation may contribute to anabolic resistance in response to protein and exercise in older adults. We investigated whether consumption of montmorency cherry concentrate (MCC) increased anabolic sensitivity to protein ingestion and resistance exercise in healthy older men.

Methods: Sixteen healthy older men were randomized to receive MCC (60 mL·d^{-1}) or placebo (PLA) for two weeks, after baseline measures in week 1. During week 3, participants consumed 10 g whey protein·d^{-1} and completed three bouts of unilateral leg resistance exercise (4 × 8–10 repetitions at 80% 1RM). Participants consumed a bolus (150 mL) and weekly (50 mL) doses of deuterated water. Body water ^{2}H enrichment was measured in saliva and vastus lateralis biopsies were taken from the non-exercised leg after weeks 1, 2 and 3, and the exercised leg after week 3, to measure tracer incorporation at rest, in response to protein and protein + exercise.

Results: Myofibrillar protein synthesis increased in response to exercise + protein compared to rest ($p < 0.05$) in both groups, but there was no added effect of supplement (MCC: 1.79 ± 0.75 EX vs 1.15 ± 0.40 rest; PLA: 2.22 ± 0.54 vs 1.21 ± 0.18; all %·d^{-1}). Muscle total NFκB protein was decreased with exercise and protein in MCC (NFκB: −20.7 ± 17.5%) but increased in PLA (NFκB: 17.8 ± 31.3%, $p = 0.073$).

Conclusion: Short-term MCC ingestion does not affect the anabolic response to protein and exercise in healthy, relatively active, older men, despite MCC ingestion attenuating expression of proteins involved in the muscle inflammatory response to exercise, which may influence the chronic training response.

1. Introduction

Progressive age-related loss of muscle mass (sarcopenia) commences in the 4/5th decade and accelerates from the 6th decade onwards with per annum losses in the order of 0.5–1.5% (Hughes et al., 2001), and ~1.5% per annum strength losses (Skelton et al., 1994). These declines lead to a loss of independence and impaired quality of life in otherwise healthy older individuals (Skelton et al., 1994), so interventions that limit age-related loss of muscle mass and function are urgently required.

The response of muscle protein synthesis (MPS) and breakdown (MPB) to nutritional intake and activity levels maintain muscle mass in healthy adults. Decreases in muscle mass occur as a consequence of MPB chronically exceeding MPS. Basal rates of MPS (Cuthbertson et al., 2005) and MPB (Volpi et al., 2001) do not seem to be affected by age per se in healthy men. Small elevations in MPB after resistance exercise (RE) related to the activation of the ubiquitin proteasome and autophagal lysosomal systems are not augmented in older people (Fry et al., 2013). However it is clear that older subjects display resistance to anabolic signals such as provision of essential amino acids (Cuthbertson et al., 2005) and RE (Kumar et al., 2009), resulting in attenuated MPS responses compared to their younger counterparts, which is pivotal to the progression of sarcopenia. The mechanisms underlying this blunted response to feeding and exercise are still unclear, but are likely associated with age-related declines in habitual activity (Breen et al., 2013; Schrack et al., 2014), and low level but chronic oxidative stress and inflammation.

Oxidative stress related carbonylation of muscle proteins has been associated with the age-related muscle mass loss in rodents (Chabi et al., 2008). Markers of oxidative damage are also elevated in muscle tissue biopsied from elderly men, with mitochondrial protein carbonyl adducts more abundant in muscle of old versus young men and

* Corresponding author at: University of Exeter, Sports and Health Sciences, St Luke's Campus, Heavitree Road, Exeter EX1 2LU, United Kingdom.
E-mail address: j.bowtell@exeter.ac.uk (J.L. Bowtell).

https://doi.org/10.1016/j.exger.2018.06.007
Received 20 November 2017; Received in revised form 30 May 2018; Accepted 7 June 2018
Available online 08 June 2018
0531-5565/

associated with reduced muscle strength (Valls et al., 2015). The inflammatory pathway is also implicated in age-related anabolic resistance. TNFα seems to impair MPS via decreased phosphorylation of proteins in the mTOR signaling pathway (Lang et al., 2002), that is critical for regulation of mRNA translation and the MPS increases required for muscle hypertrophy (Dickinson et al., 2011). In elderly muscle we found a 4-fold elevation in NF-κB concentration, which was associated with a reduction in concentration and phosphorylation of key components of the muscle protein synthesis response (mTOR, $p70^{s6}k$ and eIF4BP-1) to AA provision (Cuthbertson et al., 2005).

Control of this underlying inflammation would appear to be an appropriate target for therapeutic intervention. However, acute anabolic effects of RE seem to be, at least in part, mediated through a brief induction of NF-κB signaling and downstream inflammatory pathway gene expression (IL-6, IL-8, MCP-1) (Vella et al., 2012). Interestingly non-steroidal anti-inflammatory agents (NSAIDs) that inhibit cyclooxygenase activity (COX 1 and 2) exert opposite effects in young and elderly muscle: blocking the normal anabolic response to acute resistance exercise in young men (Trappe et al., 2002a), reducing the hypertrophy associated with an 8 week resistance training programme (Lilja et al., 2018), in parallel with abolition of the usual increase in the anabolic agent prostaglandin $F_{2\alpha}$, a COX product (Trappe et al., 2002b). In contrast daily consumption of acetaminophen or ibuprofen during a 12 week resistance training programme augmented (~25–50%) muscle hypertrophy and strength gains in elderly individuals (Trappe et al., 2011). Although muscle protein turnover data are not available, Trappe et al. (2013) demonstrated that NSAID consumption in parallel with a resistance training programme upregulated PGF2α receptors, and reduced intramuscular PGE2 production in the elderly. We propose therefore that this discrepancy in NSAID effects in the young and old, whereby anabolic sensitivity to exercise is restored in the old but not the young, by counteracting the low level chronic systemic inflammation present in the elderly. Certainly NSAIDs were not able to attenuate atrophy induced 2 weeks of immobilisation or enhance hypertrophy during 2 weeks of retraining in healthy older adults with low plasma C reactive protein concentration (Dideriksen et al., 2016).

The known side effects associated with chronic NSAIDs supplementation, including gastrointestinal injury (Laine, 2003), would prevent the chronic application of this prophylactic approach to ameliorate sarcopenia. However, there is increasing interest in the application of nutritional supplements with known anti-inflammatory effects such as omega-3 fatty acids, which restored anabolic sensitivity to amino acids and hyperinsulinaemia in older individuals (Smith et al., 2011). Tart cherries are rich in polyphenols, the anthocyanins and proanthocyanidins in particular (Ou et al., 2012; Mulabagal et al., 2009). In vitro cherries are potent anti-oxidants (Ou et al., 2012, Mulabagal et al., 2009) and inhibit COX1 (Ou et al., 2012, Mulabagal et al., 2009) and COX2 (Mulabagal et al., 2009) activity. In mice, tart cherry juice consumption increased hepatic superoxide dismutase and glutathione peroxidase activity and inhibited COX2 activity (Saric et al., 2009), possibly mediated by activation of the nuclear erythroid 2-related factor 2 (Nrf2) pathway resulting in increased synthesis of endogenous antioxidants (Birringer, 2011). A number of studies including our own have demonstrated that montmorency cherry juice improves functional recovery from a single bout of intensive resistance (Bowtell et al., 2011) or endurance exercise (Howatson et al., 2010), with associated reductions in circulating biomarkers of oxidative damage (protein carbonyls) and inflammation (C reactive protein). We hypothesised that this cherry-induced reduction in oxidative stress and inflammation will restore anabolic sensitivity in older adults. Our aim was to determine whether two weeks of daily montmorency cherry concentrate (MCC) supplementation enhanced the anabolic response to protein supplementation and resistance exercise in healthy older men, measured as free-living myofibrillar protein synthesis using the deuterated water technique (Wilkinson et al., 2014).

2. Methods

2.1. Participants

The study was approved by the local university ethics committee, and was conducted in compliance with the World Medical Association's Declaration of Helsinki (2008). We screened and recruited sixteen healthy older men aged 60–75 y, all of whom gave their written informed consent to participate. Exclusion criteria included allergy to local anaesthetic or iodine, reporting > 150 min moderate/vigorous activity per week (in addition to tasks of daily living), consumption of anti-inflammatory medication or nutritional supplements, neuromuscular problems or acute knee/ankle injuries and pain.

2.2. Experimental design

Participants completed a three week experimental period in this double blind randomized control trial, which included four laboratory visits. During the first week participants were instructed to maintain habitual activity and diet. During week 2 and 3 participants consumed 30 mL of either Montmorency cherry concentrate (MCC) or cherry flavoured isoenergetic placebo (PLA) twice per day (morning and

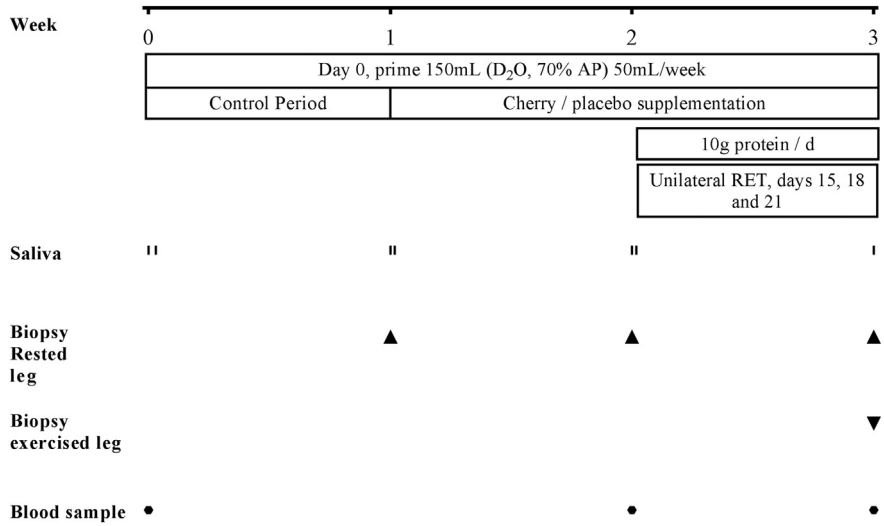

Fig. 1. Experimental protocol. RET = resistance exercise training, each session consisted of four sets of 8–10 repetitions at 80% one repetition maximum.