Technical Note

Endothelial Response of Running a Marathon: A Tale of Three Runners

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ABSTRACT

International Journal of Exercise Science 6(3) : 236-241, 2013. The aerobic challenge of marathon running may disrupt the balance of reactive oxygen species (ROS) and endothelial function (EF). Training history may be protective against future risk of cardiovascular disease induced by disruption of ROS balance. In the context of a case study, we measured EF in three subjects using flow mediated dilation (FMD) 3 days before a marathon, within 90 minutes of finishing, and for 2 subsequent days. Subjects were selected based on their training type and history so that a heterogenous sample of athletes was represented. All subjects demonstrated a decline in EF immediately following the marathon (13.7% ± 1.7% to 8.4% ± 2.9%). Recovery of EF was related to aerobic capacity and training history. Marathon training should observe the principle of specificity to maintain ROS balance during physical activity.

KEY WORDS: Running, HIIT, endurance, ultrasound, exercise physiology, cardiovascular

INTRODUCTION

There is ample evidence that physical activity and aerobic exercise are associated with substantial cardiovascular health benefit. However, a recent case study published in The American Journal of Cardiology implicates marathon training and competition as being causal in a myocardial infarction by disrupting the balance between the production and buffering of reactive oxygen species (ROS). Presumably, the increase of ROS production related to the chronic aerobic exercise was causal in endothelial dysfunction, exercise induced hypertension, and coronary calcification (7). The authors concluded that some individuals are susceptible to oxidative stress associated with exercise, which may subsequently be causal in cardiovascular disease.

Previous work has found a relationship between endothelial dysfunction and development of coronary artery calcification in asymptomatic patients (17), presumably resulting from repeated uncoupling of endothelial nitric oxide generation in the presence of excess ROS. While it has been established that endurance exercise can result in ROS generation and disappearance of ROS scavengers (13), it is less clear what

influence training type, frequency, and race history could have on endothelial function. Recently, high intensity interval training (HIIT) has been proposed as a training strategy to improve aerobic fitness in athletes (3) and coronary artery disease patients (10), as it may offer improvements of maximal oxygen uptake and lactate threshold in well-trained runners (5). However, it is less clear if aerobic gains realized from HIIT or other training strategies offer protection from endothelial dysfunction during extended duration aerobic exercise, such as a marathon. Proponents advertise HIIT and other extreme training programs as safe and effective for this type of marathon event, despite the principle of specificity, which states that physical training programs should be specific to the mode of competition (14).

The purpose of this case study was to investigate if specificity of training offers adaptations that would be adequate in maintaining ROS balance as manifested by endothelial function during prolonged aerobic exercise. We hypothesized that training history and the principle of training specificity provide adaptations that mitigate endothelial dysfunction during an extended duration aerobic event.

METHODS

Participants

We chose three athletes who volunteered from the general population of marathon participants with markedly different training histories as subjects for this case study. One subject had a history of marathon running (Subject A), one was relatively new to running but was following a standard marathon training schedule (Subject B), and one ran very minimally but participated regularly in HIIT (Subject C). Further demographics of the three subjects and their training history are described in Table 1.

Protocol

All three subjects completed the same full marathon (26.2 miles/ 42.2 km) in October of 2011. All of the subjects provided written informed consent and all study methods and protocols were approved in advance by the Institutional Review Board at The Ohio State University. Prior to the marathon, a Bruce-protocol graded exercise test was performed. Maximal oxygen consumption was determined by collecting expired gases and measuring them with a metabolic analyzer (Parvomedics, Sandy, Utah, USA). Body composition was assessed via whole-body air-displacement plethysmography (Bod Pod, Cosmed, Rome Italy).

To quantify endothelial function, we measured flow mediated dilation (FMD) of the brachial artery. The right arm was extended and supported at an angle of ~80° from the torso and the brachial artery was imaged longitudinally using B-mode ultrasound (Vivid 7, General Electric Healthcare, United Kingdom) with a 14 MHz linear array probe. Baseline images were recorded at 30 Hz for 1 minute, and a pneumatic cuff placed ~3 cm distal to the olecranon process was inflated to >250 mmHg for a period of 5 minutes, using standardized recommendations for assessment of brachial artery reactivity (4). Peak diameter of the brachial artery following cuff release was determined using custom designed wall tracking software to eliminate observer bias, which yields significantly lower intraobserver

Table 1. Characteristics and training history.

Demographics	Subject A	Subject B	Subject C
Age	29	31	37
Sex	Male	Male	Male
Mass (kg)	68.9	92.5	93.0
Height (cm)	180	188	178
Ave. hours run/week	5.00	4.12	.15
Ave. miles run/ week (in prior 10 weeks)	40.50	30.71	2.30
Most miles in a single week	109.20	42.48	12.00
Ave. hours strength training/ week	0	0	6.5
Number of previous marathons	13	0	0
WHR	.75	.84	.85
Body fat (%)	9.8	15.8	20.5
VO_2max, ml/kg/min	65.0	55.4	41.7
VO_2max, ranking	Superior	Superior	Fair

Abbreviations: VO_2max, maximal oxygen uptake; WHR, waist to hip ratio.

Table 2. Brachial artery reactivity.

Measurement	Subject A	Subject B	Subject C
Baseline resting artery diameter (mm)	0.469	0.480	0.496
Baseline maximal artery diameter (mm)	0.553	0.554	0.556
Baseline FMD (%)	13.65	15.42	12.10
Post-race resting artery diameter (mm)	0.574	0.525	0.550
Post-race maximal artery diameter (mm)	0.634	0.575	0.578
Post-race FMD (%)	10.45	9.52	5.09
24h post-race resting artery diameter (mm)	0.573	0.530	0.505
24h post-race maximal artery diameter (mm)	0.664	0.604	0.550
24h post-race FMD (%)	15.88	13.96	8.91
48h post-race resting artery diameter (mm)	0.473	0.475	0.385
48h post-race maximal artery diameter (mm)	0.549	0.559	0.431
48h post-race FMD (%)	16.06	15.03	11.95

Abbreviations: FMD, flow mediated dilation.

variation when compared to manually analyzing baseline and peak artery diameters (16). FMD was calculated as the percentage increase in lumen diameter from baseline measurement. This was performed three days prior to the marathon, within 90 minutes of crossing the finish line, and at 24 and 48 hours following the race. The degree of vasodilation following the application of a shear stimulus has previously been shown to be a marker of nitric oxide in large human arteries (12). All measurements were obtained at the same time of day for each subject, as endothelial function has been shown to fluctuate as a function of the time of day in humans (15).

RESULTS

Compared with baseline measurements, all subjects demonstrated decreases in endothelium dependent dilation immediately following the marathon (Figure 1). The greatest impairment was found in subject C, and the fastest recovery

was noted in subject A, whose FMD value returned to baseline 24 hours following the event. Subjects B and C demonstrated a full restoration of baseline FMD values by 48 hours post-marathon (Table 2).

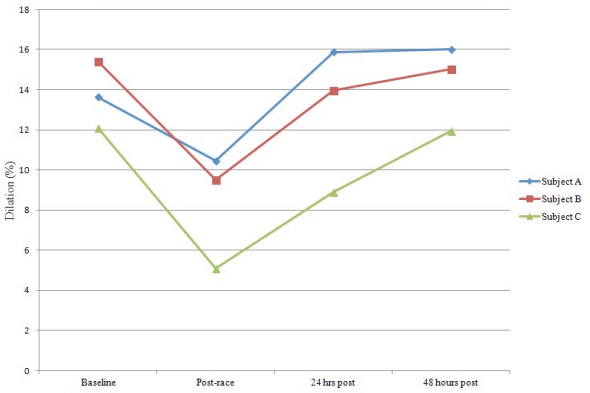

Figure 1. Changes in endothelium dependent dilation before, immediately after, and 24/48 hours after a marathon in three subjects.

DISCUSSION

A single bout of prolonged aerobic exercise resulted in impairment of EF in our subjects. Post-marathon, both subjects A and B maintained FMD values somewhat close to baseline levels. In contrast, FMD values in subject C dropped to a much greater degree following completion of the marathon. These findings support our hypothesis that specificity of training and training history may provide protective adaptations against endothelial dysfunction during long distance aerobic exercise.

The mechanism for impairment of EF following prolonged exercise may be an inactivation of nitric oxide synthase, thus leading to an impairment of vasomotor function. Previous work has found a positive role for aerobic exercise training in maintaining ROS balance (1), in support of our hypothesis that higher levels of aerobic fitness would be related to individuals with a more robust aerobic training background, even though both aerobic and resistance training have been reported to both improve FMD in healthy subjects (18). More specifically, production of nitric oxide has been mechanistically linked to production superoxide dismutase, a powerful antioxidant (6). Aerobic exercise training has been shown to up-regulate both nitric oxide and superoxide dismutase production (6). However, the sustained high intensity aerobic exercise, such as during a marathon, has been shown to increase oxidative stress to a level greater than moderate intensity aerobic exercise (8). Thus, prolonged intense aerobic exercise in individuals of lower aerobic fitness could theoretically lead to a greater disruption of ROS balance and subsequent impairment of endothelial mediated vascular function in the time period following a marathon.

In published literature, athletes may demonstrate an impairment of relative FMD when compared to control populations found within these studies (9), presumably as an effect of structural remodeling and an increased lumen diameter. While endothelial function has previously been noted as a barometer for cardiovascular risk (19), it is important to consider overall resting lumen diameter as related to training history. Sudden cardiac death, acute myocardial infarction, stroke, and unstable angina have all been independently associated with impaired endothelium dependent vasodilation of blood vessels, even when traditional risk factors and presence of coronary artery disease are controlled for (11). Interestingly, we noted an impairment of EF as measured in the brachial artery, despite the fact that the upper limbs are not the primary areas of metabolic activity during running. Our

findings suggest a global impairment of EF, which could precipitate atherothrombotic events in subjects with previously diagnosed atherosclerotic plaque (2). Furthermore, the mental stress associated with a race condition or in an individual who has not previously participated in a prolonged bout of high intensity aerobic exercise could also lead to a transient increase of risk for atherothrombotic events (20).

While only a case study, these results show that recovery of endothelial function in the days following a marathon is related to aerobic capacity and training history. It was also not clear what impact age, diet, weight, and body composition may have had on our findings as they were not standardized in these subjects. Future studies should consider larger groups of athletes with these variables in mind. However, training specificity could provide an optimum risk to benefit ratio between impairment of endothelial function associated with high intensity exercise and the many benefits that physical activity provides. Participants should consult with physicians or other allied health professionals and observe the principle of specificity of training prior to participation in a prolonged high intensity aerobic event, so as to maintain a positive risk to benefit ratio associated with physical activity.

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