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Editorial

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Towards an Understanding of the Acute Impacts of Exercise on Iron Absorption in Athletes

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The micronutrient, iron, is critical in an athlete's diet due to its role in processes such as RBC production (and therefore oxygen delivery), cellular energy metabolism, cognitive function, and immune regulation (1). However, depleted iron stores, iron deficiency, and in severe cases, anemia, are commonly reported in athlete populations, with the prevalence rate generally greater in females (~35%) compared with males (~10%) (1).

Determining the root cause of the high incidence of iron deficiency in athletes is complex, mainly due to the plethora of exercise-related mechanisms, and their interaction, that can contribute to the problem. These mechanisms include factors such as insufficient or restricted energy intake (2), menstruation (3), hemolysis (4), sweating (5), gastrointestinal trauma (6), and inflammatory-driven increases in the iron regulatory hormone, hepcidin (7).

This latter mechanism (hepcidin elevation), has become an interesting area of focus over the past 2 decades, presenting as a potential key rationale behind the frequent reports of iron deficiency in athletes. Hepcidin acts in a homeostatic manner to regulate iron absorption from the gut via its interaction with the ferroportin iron export channels (8). Importantly, when the body senses that iron concentrations are high, or there is the potential of infection/illness, hepcidin production by the liver is increased and iron absorption is reduced. Conversely, when iron concentrations appear low, hepcidin activity is reduced, resulting in a greater capacity for dietary iron uptake in the gut (8).

Importantly, one mechanism influencing the liver's production of hepcidin includes the inflammatory cytokine, IL-6 (9), which is also known to transiently increase in response to exercise (10). Interestingly, early athlete-related research in this area showed that exercise-induced increases in IL-6 result in a transient increase to circulating hepcidin concentrations during the 3–6 h period postexercise (11), which appear to subside after ~12 h of recovery (12). Of note, the magnitude of hepcidin response to exercise appears to be impacted by factors such as the duration of effort (13, 14), the underlying serum iron and ferritin stores of the athlete (14), the magnitude of inflammatory response (14), and the degree of energy deficit incurred from the activity (15).

As a result of this transient increase in hepcidin concentrations, the literature frequently speculates that the subsequent absorption of iron during the postexercise period might be reduced, which when occurring frequently in athletes across multiple training sessions, could help to explain why iron stores are commonly compromised in this population. However, research exploring the impact of exercise on actual iron absorption, per se, has to date been limited (15, 16), and not specifically focused on the impact of the transient period of peak hepcidin elevation in the 3–6 h postexercise window.

Accordingly, in this issue of *The Journal of Nutrition*, Barney and colleagues (17) have explored the impact of a prolonged running bout (98.8 ± 14.7 min, 21.2 ± 3.8 km, 4.7 ± 0.3 min/km) on IL-6, hepcidin concentrations, and dietary iron absorption in trained runners, compared with a control trial of no exercise. Here, athletes consumed a stable iron isotope with a standardized meal 2 h postrun, which was timed to match the potential for iron absorption with peak hepcidin concentrations at ~3 h postexercise. The data from this study showed that the running trial (in comparison to rest) resulted in a significant increase to circulating concentrations of IL-6 ($P < 0.05$), and a corresponding increase to plasma hepcidin concentrations by 52% ($P < 0.05$). Importantly, in response to this increased hepcidin activity, fractional iron absorption was significantly reduced by 36% after exercise ($P < 0.05$), confirming the prior speculation that transient exercise-induced increases in hepcidin activity occur in conjunction with negated iron absorption in the 3 h period postexercise. Of interest, this study also points out potential sex differences to the impact of exercise on hepcidin activity, whereby female athletes did not incur the same concentration of hepcidin increase to that of their male counterparts. Explanations such as differences in energy expenditure, inflammatory response, and baseline hematological profiles were proposed as potential rationale for this difference, although, it is likely that further sex-specific research is required to truly unpack the outcomes seen here.

The findings of the work by Barney et al. (17) further advance our understanding of iron deficiency in athletes, since objective confirmation now exists that exercise creates a transient period of reduced iron absorption, which seems to occur in the same time window (~3 h postexercise) where increased postexercise hepcidin elevations are well documented. Knowing this timeline of events will aid practitioners in making recommendations relevant to when athletes should consume meals of higher

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iron content, which appears to be in the immediate period postexercise (i.e. within 30 min of exercise cessation [16]), or once the transient period of hepcidin elevation has subsided (i.e. ~12 h postexercise [12]). This latter option might mean planning iron intake at the opposite end of the day to training; however, the impact of multiple daily training sessions on iron absorption, where the available time to recover from the initial exercise bout is diminished, remains to be explored. Furthermore, the nuanced differences in sex-related responses highlighted by Barney and colleagues (17) requires greater investigation, and notably, we should be placing an emphasis on female-specific research that considers integrated responses with all of the above-mentioned mechanisms associated with iron deficiency (i.e. energy intake, menstruation, etc.), especially given the higher incidence of this nutrient disorder reported in females.

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