Similar muscle protein synthesis rates in young men and women: men aren’t from Mars and women aren’t from Venus

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MEN HAVE MORE MUSCLE than women, and several attempts have been made to determine the physiological mechanisms responsible for this phenomenon by measuring the rates of muscle protein synthesis (MPS) and breakdown (MPB) without much luck so far. Except for one group of investigators who reported higher basal rates of MPS in women than in men (8), no one else has found differences between young men and young women in basal rates of muscle protein turnover (2, 3, 9, 14, 17) or rates of MPS during combined hyperinsulinemia and hyperaminoacidemia (17) or immediately after a bout of exercise (2). Aside from the inherent challenges in proving no difference, the studies so far do not provide definitive answers because they did not explore the maximal stimulatory effect of nutrients or take into account the prolonged period of muscle protein anabolism after a bout of exercise (10).

West et al. (22) in their study that appears in this issue of the Journal of Applied Physiology attempted to settle this issue by measuring the rate of MPS in young men and young women during overnight fasted conditions and after ingestion of a maximal anabolic dose of whey protein at rest and after exercise, covering almost the entire, if not the entire time period during which MPS is stimulated by increased contractile activity. In support of the general consensus so far, they too report no difference in the rates of MPS between young men and women in the fasted state or the fed state at rest or after exercise. It therefore seems safe to say that West et al. firmly put the final nail in the coffin of the notion that rates of MPS throughout the day are different between healthy young men and women. Although counterintuitive at first glance, this conclusion should probably not surprise us too much. Muscle mass remains steady from young adulthood to middle age in both men and women, and the relative muscle growth induced by resistance exercise training is not different between subjects/conditions. In support of the general consensus so far, they too report no difference in the rates of MPS between young men and women in the fasted state or the fed state at rest or after exercise. If therefore seems safe to say that West et al. firmly put the final nail in the coffin of the notion that rates of MPS throughout the day are different between healthy young men and women. Although counterintuitive at first glance, this conclusion should probably not surprise us too much. Muscle mass remains steady from young adulthood to middle age in both men and women, and the relative muscle growth induced by resistance exercise training is not different between the sexes (16, 21). Consequently, even if one were to find differences in the rates of MPS and MPB between young and middle-aged adult men and women, these differences would only represent differences in the turnover of muscle (i.e., the renewal rate of existing protein) but would not shed any light on why men have more muscle than women. Does this mean the final research in this area has come to a halt? Certainly not, because there appear to be sex differences in the rates of muscle loss during aging, inactivity, or in catabolic disease states (4, 12, 20, 23). Accordingly, we recently presented some evidence for substantial differences in the rate of MPS in old men and women and their anabolic response to feeding and exercise training (18, 19). A better understanding of the mechanisms responsible for differences in muscle catabolism between men and women deserves the focus of future research because it is essential for designing effective strategies to help curtail the adverse and often debilitating health consequences associated with reduced muscle mass and function.

The study by West et al. also provides further insight into the cellular mechanisms that are thought to control the rate of muscle protein turnover. By measuring the activation (phosphorylation) of the Akt-mTOR-p70s6k signaling pathway and the mRNA of the ubiquitin ligases MuRF-1 and atrogin-1 throughout the course of a day during fasted and fed conditions at rest and after exercise, they eliminate the concerns associated with single-snapshot data. Still, West et al. were unable to explain the oscillation of MPS over the course of the day by the changes in anabolic signaling activity; their data therefore adds to the often reported dissociation between the nutrient- and exercise-induced stimulation of MPS and the phosphorylation of anabolic signaling proteins (1, 5–7, 11, 13). Furthermore, although they did not measure rates of MPB, it is quite obvious that the changes in ubiquitin ligase gene expression in the study by West et al. (e.g., decrease in atrogen-1 expression after exercise) do not correspond to the expected changes in muscle protein breakdown [which increases in response to resistance exercise (10, 15)]. These discoveries should not make us dismiss such measurements; however, they should make us think about their utility. The critical involvement of mTOR and its downstream targets in muscle growth is undeniable. However, it now seems clear that relatively small changes in what are considered key anabolic signaling elements are not involved in the fine-tuning of muscle protein turnover rates and cannot and should not be used to predict potential differences in actual muscle protein turnover rates between subjects/conditions.

In summary, the answer to the question whether there are differences in muscle protein metabolism between healthy young men and women seems to be no. However, the actual drivers behind the differential response of muscle in men and women to aging, disuse, and catabolic disease remain to be elucidated.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

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