Commentaries on Viewpoint: The curious case of anabolic resistance: old wives’ tales or new fables?

ALTERNATIVE ASSESSMENT NEEDED?

TO THE EDITOR: We appreciate Burd et al. (1) providing an interesting perspective on whether anabolic resistance contributes to age-associated muscle wasting. In our opinion this perspective illustrates the need to consider alternative assessments of muscle protein turnover. The authors state that, “Such a gradual decline in muscle mass would likely be too small to detect using contemporary stable isotope methodology...” It must be asked then, why do these methods continue to be the norm? Perhaps a better approach is to initiate an intervention and assess outcomes over a longer period of time so that “other things” that happen during the day are accounted for, and it can be determined whether an intervention adds up to meaningful differences. In this regard there is much to be learned from exercise intervention studies where increasing energy expenditure by purposeful activity decreases other energy expenditure throughout the day, resulting in no net increase in expenditure (2). We (3) and others (4) have used the approach of measuring protein synthesis over weeks using deuterium oxide. We found that feeding protein after each bout of aerobic exercise does not increase cumulative mixed muscle protein synthesis over 6 wk in older individuals, which is counter to what would be predicted from acute studies (3). However, VO2 max, an important predictor of morbidity and mortality, did improve more in those who consumed protein after exercise, indicating mitochondrial adaptation. Ultimately the goal of an intervention is to improve functional outcomes. Given current methodological limitations, perhaps other approaches should be considered.

REFERENCES


Benjamin F. Miller,
Assistant Professor
Karyn L. Hamilton
Colorado State University

TO THE EDITOR: The article “The curious tale of anabolic resistance: old wives’ tales or new fables?” (1) is an overbearing exposé that anabolic resistance is a fallacy. Just looking slightly beyond the human and ageing literature firmly refutes doubts over its existence and importance in muscle wasting both observationally (e.g., cancer, immobilization, heart failure (4)) and mechanistically (5). Moreover, it is churlish to condemn mechanistic explanations where molecular “readouts” (e.g., mTOR signaling) in several ageing studies have been consistent with muscle protein synthesis (MPS; note: a relationship that remains ambiguous in other arenas). We agree discord in the ageing literature needs addressing. Although a number of the proposed reasons are already being well controlled (i.e., prior nutrition/training status) other considerations warrant closer attention. For instance, the brief (~1.5 h) stimulation of MPS after feeding is sufficiently transient that small differences may be masked over longer measurement periods (e.g., as in Fig. 1). Let’s also examine data from a chronic setting. Exercise training studies have illustrated that muscle hypertrophy is blunted in ageing (3), consistent with acute observations in MPS (2). Still, the authors raise a good point in terms of defining how anabolic resistance is involved in the absence of overt sarcopenia and where its detection may predict atrophy in excess to that observed (~1–2%/yr >65 yr, failing other adaptive changes in protein turnover). Thus it is not impossible that anabolic resistance may have additional consequences; contributing to declines in muscle function that precede muscle atrophy, perhaps? Although there remain many questions, and in the absence of other plausible mechanisms (i.e., sarcopenia without changes in protein turnover...?) the “fable” of anabolic resistance (which when contextualized to i.e., exercise/feeding, is not quite so puzzling) continues to do as all good fables do and convey an important message to the field.

REFERENCES