

Extraordinary changes in body composition and performance with supplemental HMB-FA+ATP

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The authors of this letter read with deep skepticism the recent report from Lowery et al. (9), employing a supplement that provided 3g of beta-hydroxy-beta-methyl butyrate as a free acid (HMB-FA; three doses of 1g each) plus 400mg of oral adenosine triphosphate (ATP) in young men who resistance-trained for 12wk. These authors (9) report gains in lean mass and performance that are greater than those reported in a similarly astonishing earlier study from Wilson et al. (16). Our skepticism of the results reported by Lowery et al. (9) exists on several levels. However, our collective disbelief of these data rests on the collective experience of the authors of this letter, who have conducted more than 60 resistance training studies, who have never observed gains in lean body mass that are of a similar incredibly uniform magnitude as those reported by Lowery et al. (9). As opposed to the often-observed heterogeneity in resistance training-induced hypertrophy, Lowery et al. (9) must have observed remarkably consistent between-group changes in muscle mass to find statistical significance between the supplemented and placebo groups. This is remarkable in that this was seen in a total of 17 subjects (n=9 placebo, n=8 HMB-FA+ATP). We are particularly skeptical that the 'divergence' between the HMB-FA+ATP versus placebo groups occurred in the face of what the authors refer to as an optimal training paradigm, with optimal nutrition, and the advice of an experienced dietitian. Would the authors be willing to share subjects' individual data? We ask since the mean gain in lean body mass in the supplemented group was ~8.5kg (9), meaning there were some subjects who gained more and uniformly so for the treatments (in only 17 subjects, however, they were divided between groups) to be so robustly different? This is also an astounding gain when one considers that the subjects were previously resistance-trained and so would have had less propensity to gain lean body mass (10). We could not find the absolute values for the beginning and final values for body composition and so readers would have to make assumptions (since the reported data were incomplete) as to how much body composition changed. Would the authors be willing to present these data?

We are aware of a previous letter from Hyde et al. (6) in which these authors asked for clarification from Lowery et al. (9) on their methods. Thus, our skepticism is clearly shared by others and, given the number and research experience of the authors on this letter, quite widespread. In their reply to this letter (6) Lowery et al. (9) went to great lengths to compare their rates of hypertrophy with those previously reported by other studies. Importantly, however, a number of studies discussed by Lowery et al. (9) as having comparable 'rates' of hypertrophy were markedly (5wk) shorter than their 12wk intervention (12). Thus, while 'rates of hypertrophy' (assessed with different methods and in different labs (3, 8, 12, 14), in different study populations, being overfed and not exercising (3), with different dietary backgrounds (3, 8, 12, 14), consuming different supplements (8, 12, 14), may have been similar (or greater) to those seen by Lowery et al. (9) the total accrued (over 12wk) fat- and bone-free (i.e., 'lean') mass cannot be assumed to be linear, nor equivalent to that seen in their study. Further, what is revealing is the astonishing performance differences reported by Lowery et al. (9), which implies not only greater total lean mass gains but extraordinary functionality to the accrued lean mass or by some other unexplained mechanism. That is, why did HMB-FA+ATP impart an astonishing 'functional overreaching' response with the optimal training paradigm, with great dietary support, and in highly trained and motivated subjects and not in the placebo group?

It is important to understand the limitations of dual-energy x-ray absorptiometry (DXA), which derives by difference at- and bone-free mass, which is a variable that is not equivalent to muscle (5, 11). The limitations of DXA and ultrasound, the two muscle-based outcome measures have been clearly outlined in a recent review (5). For DXA: ***“Cannot specifically discern skeletal muscle mass”*** [bold and italics]

added] and quality as can CT [computerized tomography] and MRI [magnetic resonance imaging]" (5). For ultrasound: "Technical skill required. Excess transducer pressure and orientation can influence muscle size measurements. Identification of reproducible measurement sites critical. Care needed to make muscle is in relaxed state. Conditions such as proximity to exercise bout, hydration, are important to control" (5). Lowery et al. (9) report nothing with respect to the ultrasound machine used, the hydration status of their subjects, or proximity to an exercise. It would be useful for readers if Lowery et al. (9) could let the readers know the training level of the researcher(s) who conducted the ultrasound tests, noted whether more than one researcher carried out testing, whether these testers were blinded to the group assignment while completing/analyzing the thickness measures, and clarify the temporal aspects of testing to determine if there may be any associated confounding issues.

In the response to Hyde et al (6) the authors' purport to have selected "...a responsive population who possess a quantity of lean mass indicative of previous responses to resistance training...." Notwithstanding the scientific inaccuracy of this statement, the authors must have gone through a screening process of sorts to recruit 17 subjects with lean mass "...an order of magnitude [we note that an order of magnitude is defined as 10-times greater so this cannot be the case] higher than average lean mass typically seen in recreationally trained subjects..." Could the authors please state what the exact criteria for inclusion as a subject in this study were? Can the authors please detail the screening process describing how many subjects were recruited and screened to reach this number of subjects meeting these criteria? Please also clarify if the subjects were randomised to treatment and placebo groups or pair matched.

The only supplement for which we have data showing a mechanistic underpinning for the activity of HMB is for the calcium salt form (13) and we are unaware of any similar proof-of-principle mechanistic data for the free acid form of HMB. In the only human study to show any plausible effect of HMB on human muscle protein turnover (13), we note that leucine had the same anabolic effects. We also note that dietary protein can exert a positive effect on gains in muscle mass with resistance training (1). Thus, it is surprising that, given the expert dietary advice and total protein intake of the subjects studied by Lowery et al. (9) that the differences in lean mass between the HMB-FA+ATP and placebo groups are as impressive as they are and are ascribed to an, as yet mechanistically unproven, form of HMB and/or ATP. As an ingredient of the supplement used by Lowery et al (9), ATP would appear to be, given its extraordinarily low bioavailability (2) to be useless. However, we note that Wilson et al. (15), using the same study protocol as employed by Lowery et al. (9), reported that ATP (400mg/d) resulted in a positive effect on muscle mass, strength, and power gains. This is improbable given that oral ATP even up to doses of 5000mg/d [more than an order of magnitude greater than the dose used by Lowery et al.(9)] for 4wk leads only to increases in circulating uric acid with no detectable changes in ATP in the blood(2). Thus, as opposed to an ostensible increase in post-exercise blood flow induced by the ATP (7) in HMB-FA+ATP supplement, the magnitude of which we view as physiologically inconsequential, we find it biologically implausible that 400mg/d of oral ATP would exert any effect on processes leading to enhanced performance let alone hypertrophy.

Many of the authors of this letter have seen either or both Mr. Lowery and/or Dr. Wilson speak at various conferences on the topic of HMB. In addition, even a casual perusal of available social media sites reveals that Dr. Wilson has spoken on the topic of HMB. Thus, we ask, in accordance with all reasonable guidelines regarding full disclosure of potential conflicts of interest now in place at many journals (including the Journal of Strength and Conditioning Research - <http://journals.lww.com/nsca->

[jscr/Pages/InstructionsforAuthors.aspx - accessed Oct 1, 2016](#)) that Dr. Wilson and Mr. Lowery disclose whether they have ever received travel expenses, stipends, or honoraria, or shares associated with their work companies involved with ATP and/or HMB and/or whether they or their spouses have any public or private interests with Metabolic Technologies, Inc. and/or companies selling or dealing in oral ATP supplements or their affiliates? This is not an accusation and we fully accept that neither Dr. Wilson nor Mr. Lowery may have ever received such support, but believe this is an honest and reasonable question to ask on both scientific and ethical grounds (4) and it is standard practice to make such disclosures.

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