Postprandial nitrogen utilization and misinterpretation of data

Dear Sir:

A recent study by Lacroix et al (1) compared the postprandial nitrogen utilization of nitrogen from 3 different proteins, namely micellar casein (“slow protein”), milk soluble protein isolate (“fast protein”), and total milk protein (another “slow protein”). Their data suggest that slow protein induces better postprandial nitrogen utilization than does fast protein. According to Lacroix et al, “This result, together with the hypoaminoacidemia observed 4 h after the ingestion of [milk soluble protein isolate], strongly suggests that a too-rapid dietary [amino acid] delivery cannot support the anabolic requirement throughout the postprandial period.”

In my view, this is a misleading statement, because adult humans rarely, if ever, consume their dietary protein from one source only. Both fast and slow proteins have their advantages. For example, fast-acting protein hydrolysates may offer some advantages immediately after exercise (2). In addition, frequent ingestion of fast proteins may optimize muscle protein anabolism. Cribb et al (3) examined the effects of supplementation with hydrolyzed whey protein and casein on muscle strength and body composition during a 10-wk, supervised, resistance-training program. The results indicate that the whey hydrolysate group achieved a significantly greater gain in lean body mass than did the casein group (5.0 compared with 0.8 kg). The whey hydrolysate group also achieved significantly greater improvements in muscle strength than did the casein group in each assessment of strength. When the strength changes were expressed relative to body weight, the whey group still achieved significantly greater improvements in strength than did the casein group. The superiority of whey protein hydrolysate may have something to do with its strong insulinotropic effects and its rapid absorption and uptake (2). A surge of amino acids is rapidly transported to muscle tissue, where they may help trigger muscle protein synthesis at an accelerated rate. In contrast, slow-acting proteins may be better at minimizing muscle protein catabolism during prolonged periods between eating.

The author is a consultant to BioQuest Pharmaceuticals Inc.

Anssi H Manninen

Advanced Research Press, Inc
690 Route 25A
Setauket, NY 11733
E-mail: sportsnutrition@luukku.com

REFERENCES


Reply to AH Manninen

Dear Sir:

In our recent article entitled “Compared with casein or total milk protein, digestion of milk soluble proteins is too rapid to sustain the anabolic postprandial amino acid requirement” (1) we showed that casein ingested as a single protein meal in resting healthy human volunteers was better retained than was whey protein. This effect was mainly related to the fast absorption and subsequent enhanced postprandial oxidation of whey protein–derived amino acids. This result was obtained by directly measuring the postprandial metabolic fate of dietary protein based on tracer kinetic data. This was also in line with previous observations from our group and from others, which showed that the gastric emptying and amino acid absorption rates are major factors modulating postprandial amino acid metabolism (2–5). This issue is extensively discussed in the article.

In a letter to the editor, Manninen claimed that we misinterpreted our data. He wrote that our results suggest that slow proteins are better retained than are fast proteins and argued that these results are erroneous because the anabolic benefit of whey protein has been reported after intense exercise training. First, our conclusion was not a suggestion but a direct demonstration based on tracer kinetic data, and Manninen did not provide any data to suggest any misinterpretation of our data. Second, our study was conducted in healthy sedentary humans, and we did not extrapolate our findings to exercising subjects, especially bodybuilders. We mentioned in our discussion that whey protein had a positive effect on protein balance in the elderly (6, 7). The study mentioned by Manninen (8) was conducted under very specific conditions, ie, in bodybuilders supplemented with ∼1.4 g casein · kg\(^{-1}\) · d\(^{-1}\) of either casein or whey protein, corresponding to 112 g protein as supplement per day.

Manninen is right to postulate that humans rarely consume a unique source of protein. We fully agree and admit that the final interest of our study would be achieved by integrating general dietary habits, as was partly the case because the protein was given acutely. During the week preceding the test, volunteers consumed a habitual mixed diet, although it was standardized for protein as energy. We also draw attention to our final postulate that fast and slow proteins may exert a synergistic effect because the postprandial nitrogen utilization of total milk protein was not intermediary between casein and whey protein, but was the highest that we reported.

The authors had no conflict of interest to declare.

Letters to the Editor
Dear Sir:

The conclusion of the recent meta-analysis by Appleton et al (1) that depression is more likely in those whose intakes of long-chain polyunsaturated fatty acids (LCPUFAs), especially of n–3 fatty acids, are low suggests that depression could be a disorder of low-grade systemic inflammatory condition because LCPUFAs modulate proinflammatory events.

Recent studies showed that proinflammatory cytokines might cause depressive illness. This conclusion is based on the observations that 1) activation of the immune system and administration of endotoxin (lipopolysaccharide; LPS) or interleukin-1 (IL-1) to experimental animals induces sickness behavior that resembles depression (2); 2) activation of the immune system is observed in many depressed patients (3); 3) depression is more frequent in those with medical disorders associated with immune dysfunction (4); 4) treatment of patients with cytokines can produce symptoms of depression (4); 5) chronic treatment with antidepressants inhibits sickness behavior induced by LPS (5); 6) pro-inflammatory cytokines activate the hypothalamo-pituitary-adrenocortical axis (HPAA), which is activated in depressed patients (2); 7) cytokines activate cerebral noradrenergic systems, which is known to occur in depressed patients (4); and 8) several proinflammatory cytokines activate brain serotonergic systems, which have been implicated in major depressive illness and its treatment (6, 7). These results suggest that depression could be a low-grade systemic inflammatory condition.

The central nervous system regulates the production of the proinflammatory cytokines: tumor necrosis factor, IL-1, high mobility group-1, IL-6, and macrophage migration inhibitory factor through the efferent vagus nerve (8, 9). Acetylcholine, the principal vagal neurotransmitter, inhibits the production of proinflammatory cytokines through a mechanism dependent on the α7 nicotinic acetylcholine receptor subunit. Because vagal nerve stimulation (VNS) is of benefit in depression, I proposed that the beneficial effect of VNS in depression is due to its inhibitory action on the production of proinflammatory cytokines (10).

A significant decrease in n–3 fatty acids in plasma or in the membranes of red blood cells has been reported in subjects with depression (11–13). n–3 Fatty acids suppress the production of IL-1β, IL-2, IL-6, and TNF-α; therefore, n–3 fatty acids could play a major role in depression through their role in maintaining membrane fluidity, which influences neurotransmission, and in modulating the production of proinflammatory cytokines (14). In addition, antidepressants exhibit an immunoregulating effect by reducing the release of proinflammatory cytokines, by increasing the release of endogenous antagonists of proinflammatory cytokines such as IL-10 and, finally, by acting like inhibitors of cyclooxygenase (15). Double-blind placebo-controlled and other studies have shown that consumption of the n–3 fatty acids eicosapentaenoic acid and docosahexaenoic acid is associated with a longer period of remission in depressed patients (16–18). Thus, epidemiologic, experimental, and clinical data favor the idea that polyunsaturated fatty acids could play a role in the pathogenesis and treatment of depression. Well-planned larger trials with adequate power to detect clinically important benefits are required to determine the relevant dose of fatty acids to be used for the treatment of depression.

The author had no conflict of interest to declare.

Undurti N Das

UNL Life Sciences
13800 Fairhill Road, no. 321
Shaker Heights, OH 44120
E-mail: undurti@hotmail.com

REFERENCES