ERD

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From the Editor

We're not really into One Weird Tricks That Solve All Your Problems at Examine.com, except during our April Fool's Day e-mails. But I'm actually a fan of one. Well, two, if you count Adamantium Bone Broth™.

It's not the latest ergogenic or fat burner. Instead, it's a way to clarify exactly what a study's saying. And, sometimes more importantly, what it's not saying. Let's take as an example the paper studying fasted exercise from this volume of the ERD to show you what I mean.

Here, the population in this study was a group of healthy, young, trained women in energy balance with a BMI less than 25. The intervention was fasted, moderate-intensity aerobic exercise. The control condition was rest. And the outcome was an increase in 24-hour fat oxidation.

Spelling out the PICO for this study explicitly can tell you quite a bit. First, the results of this study may not apply to people who are not in this population, such as women with a higher BMI or untrained women. In fact, the motivation for performing this research in the first place was that previous studies looking at this issue were done only in men. Spelling out the population in detail also occasionally helps to resolve apparent conflicts in the literature. Sometimes two studies come up with two different results simply because the populations studied differed in some important way.

Conflicts between studies can also arise due to differences in intervention. This study specifically looked at moderate intensity aerobic exercise. Different intensities of aerobic exercise or resistance training may not yield similar results.

Then there's the curious choice of control group, which compared exercise to rest. So the results of this study alone do not address the effects of fasted versus fed exercise: instead, it compared fasted exercise to just laying around. If that's not a choice you care about, then the results of this study alone may not be useful to you - you'd have to bring in other research. The authors of this article did this in their discussion section for this exact reason.

Finally, there's the outcome, which specifically looks at fat oxidation over 24 hours. The main reason people may care about this is that they want to shed body fat. Increased fat oxidation could be one way to do this, but the question of body fat loss is not directly addressed here. Ignoring, misinterpreting, or oversimplifying the specific outcomes of a study is a common source of overhyping when research gets translated for public consumption.

Keeping PICO in mind while reading research can help you be more precise in interpreting what exactly a study's saying, what it's not, and whether it's relevant to your interests. It can also help you formulate questions you care about more clearly when thinking about nutrition and supplementation. I find it useful. Maybe you will, too.

If you don't, maybe it's because our population characteristics differ.

Gregory Lopez, *Editor-in-Chief*

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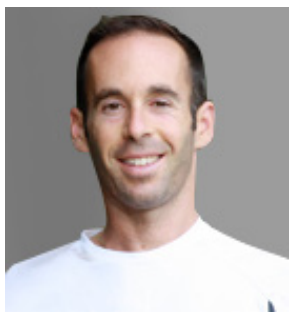

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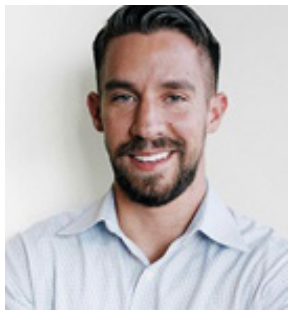

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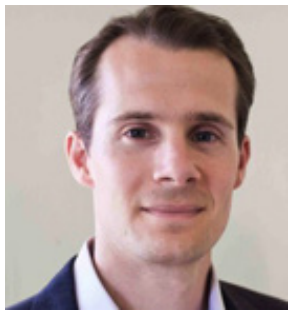

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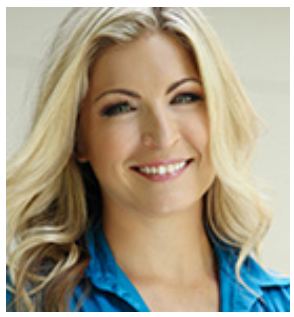

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One whey to go for exercise performance recovery

Whey Protein Supplementation Enhances Whole Body Protein Metabolism and Performance Recovery after Resistance Exercise: A Double-Blind Crossover Study.

Introduction

Anyone who has ever worked out has experienced some degree of muscle soreness afterward. One reason why this occurs is due to muscle fiber damage after exercise, which results in varying degrees of soreness and decreased performance that can last hours or days. The degree to which performance may decrease depends on the workout volume and intensity. An acute performance drop is a normal consequence of any training program. But for athletes, minimizing and quickly resolving these negative effects of training can help increase the amount of total training time. The more time an athlete can spend training, the better their chances are at improving in their respective sport.

One strategy for improved muscle recovery is to ensure you're getting enough dietary protein to meet your physical activity demands. The thinking is that increased protein leads to increased positive protein balance (i.e. greater protein synthesis than breakdown) in the body, in turn resulting in more rapid recovery of muscle performance. While it's important to get adequate amounts of protein in your diet, there's more to protein than just consuming enough to help achieve your fitness goals. There are many strategies that can help maximize protein's muscle-repairing effects. When paired with resistance training, protein has been shown to help increase muscle size and strength. Ingestion before or after training may theoretically provide further benefit (although this benefit may be mitigated by consuming sufficient protein during your day). Evenly distributing protein intake between meals can further augment its anabolic effects. Consuming protein before you go to bed may also cause a slight improvement in muscle protein synthesis (MPS) while you sleep. The type of protein is also important to amplifying the muscle protein synthetic response. For example, a rapidly digesting, leucine-rich, highly bioavailable whey protein has been seen to help boost MPS, making whey a preferable supplement for people aiming to maximize recovery and adaptations to resistance exercise.

The above strategies are often used by athletes in conjunction with one another. In fact, there is data to support the beneficial effects of protein supplementation on long-term improvements in muscular adaptations. But less research has been done looking at how post-exercise protein ingestion may aid recovery acutely (e.g., less than 24 hours). The study under review aimed to quantify the extent to which post-workout protein supplementation could improve muscle performance recovery after a bout of strenuous resistance exercise.

It is important for athletes to minimize the acute negative effects of training to help maximize total training hours. One way to accomplish this requires strategic intake of protein: consuming enough of it and at the right times. Many studies have looked at the long-term effects of protein consumption on muscle repair, but fewer have looked at its effects in an acute period. This study looks to quantify the effect of supplemental protein on muscle performance post-exercise.

Who and what was studied?

The primary research outcome of this study was to determine if consuming a whey protein supplement right after resistance training could enhance whole body net protein balance 10 hours after exercise. Two secondary aims were also investigated. The first was to assess differences in muscle damage repair between groups. The second was to determine if whole body net protein balance could be further enhanced and extended to the 24 hour mark by taking another protein serving 10 hours after the post-exercise one. The scientists conducting this trial hypothesized that protein supplementation would "enhance net protein balance at 10 and 24 hours of recovery, primarily by enhancing protein synthesis, and that this response would be associated with greater indices of exercise performance."

Twelve healthy young men (76 ± 8 kg, 24 ± 4 years old, 14% ± 5% body fat) who were resistance-training two to four times a week for at least six months were enrolled into the study. Participants were excluded from the study if they had consumed supplements in the last three weeks or were on medication that could affect protein metabolism.

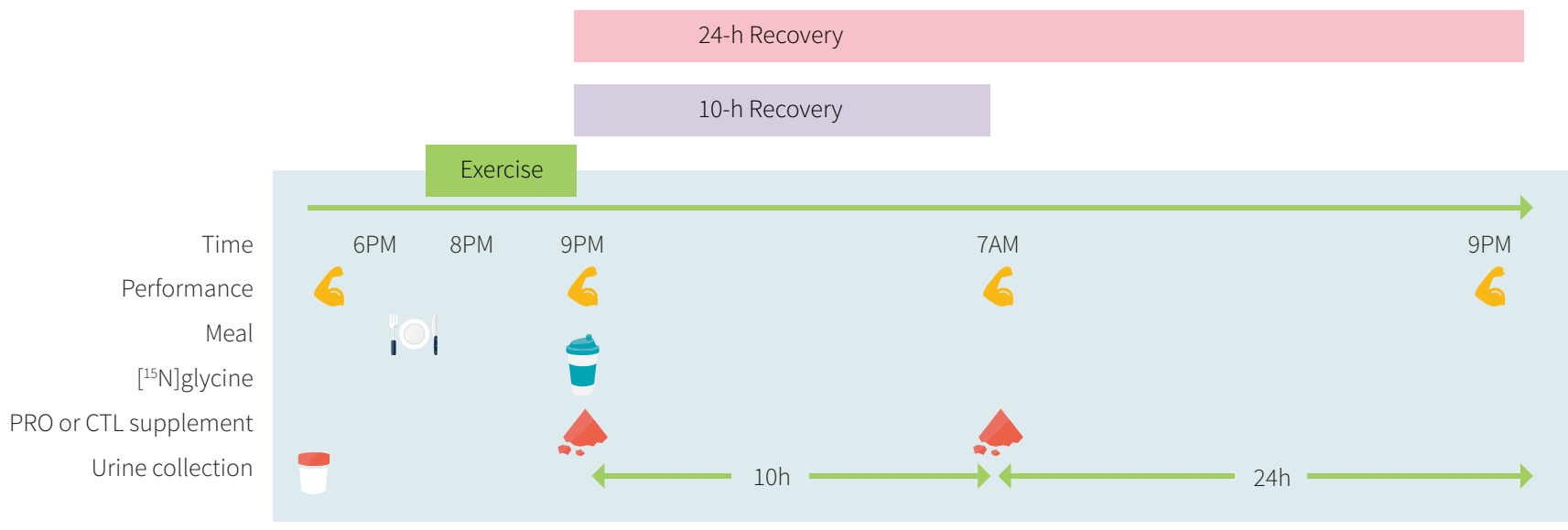
This double-blind, placebo-controlled, crossover study was comprised of three phases. Over the first two phases, participants undertook a whole-body resistance exercise program in the evening (about 8 p.m. to 9 p.m.). They then received either 25 grams of whey protein (whey protein blend with 2.4 grams of leucine) or a calorie-matched carbohydrate placebo immediately post-exercise and again 10 hours later. Subjects who had randomly been chosen to receive protein in the first part would receive the placebo in the second and vice versa. The trials were separated by a one week washout period.

A third and final phase was conducted that had no exercise or supplement component, to serve as the control for the first two. In all three, performance measures were taken at four time points as shown in Figure 1. These were used to assess the secondary outcome of how different supplements affected the repair of exercise-damaged muscles and included the following tests:

- Countermovement jump (similar to a jump squat) to assess neuromuscular fatigue
- Knee extension isometric maximal voluntary contraction to assess static strength/muscular endurance
- Knee extension repetitions to failure at 75% of 1 Rep Max (1RM) to assess dynamic strength/muscular endurance
- A 30 second Wingate test to assess anaerobic power output

Participants were on a controlled diet that was prepared and provided to them by a registered dietitian over the course of all three two-day trial periods to keep macronutrients and calories consistent with the athletes habitual intake. Diets were formulated to mimic participants' typical intakes as to not introduce further confounding variables. But this also means that participants were not matched for total protein intake which, ironically, could be a confounding factor. The average daily protein intake was 1.9 grams per kilogram of bodyweight per day (average total intake of 143 ± 16 grams/day), which is on the higher end of protein intake. The whole-body resistance exercise program involved a series of supersets (barbell bench press plus pulldowns and barbell overhead press and seated row) plus two isolation exercises (leg press and leg extension). The workout scheme was four sets of 10

Figure 1: Study Design



reps at 75% of their 1RM with two-minute rest intervals between sets.

To help measure protein balance, participants were given a dose of glycine, an amino acid, immediately post exercise. This particular type of glycine had been labeled with radioactive nitrogen to track its whereabouts in the body. The radioactive amino acid enables the measurement of whole body protein synthesis, protein breakdown, and net protein balance over short time periods. Researchers then measure the amount of radioactive nitrogen excreted in urine as ammonia and urea. By comparing the amount of the radiolabeled glycine that was ingested relative to radioactivity in the ammonia and urea (both byproducts of protein breakdown), the net protein balance was estimated. An oversimplified way of thinking about it is:

Glycine Ingested – Glycine Excreted = Whole Body Protein Balance

The whole process is more complex than the above equation would suggest, but it should give you a general idea of how this testing method works. If you want to learn more about this method, check out this open access review paper.

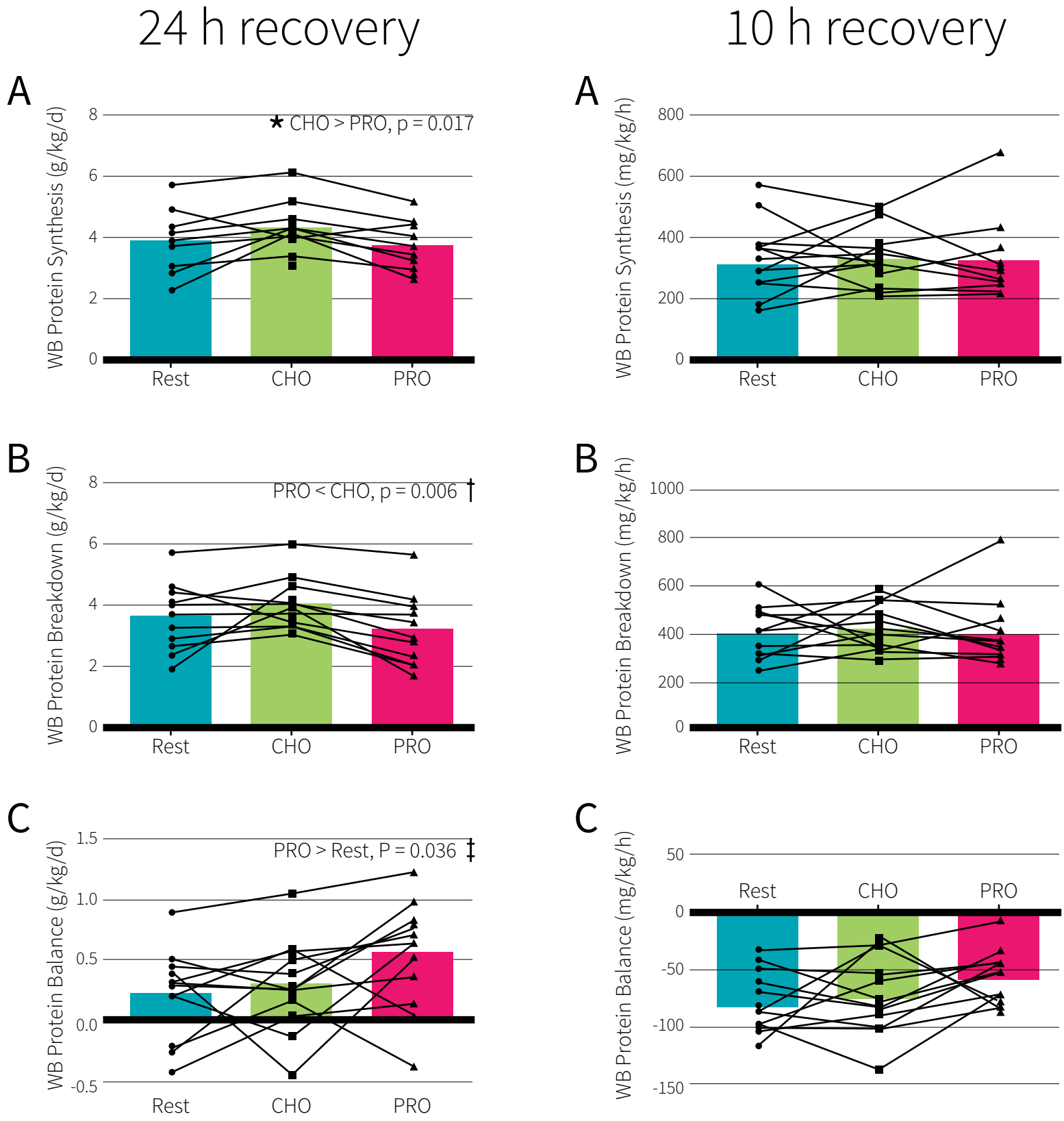
The aim of this study was to determine if a whey protein supplement could enhance whole body net protein balance 10 and 24 hours after exercise. A radioactively labeled glycine supplement was ingested by the participants to help measure changes in protein synthesis over these time periods. Exercise tests were also conducted to see if the protein supplement could increase exercise performance.

What were the findings?

The authors reported some of their results as standardized effect sizes (specifically, Cohen's d for stat nerds out there). Standardized effect sizes are a way to report the size of effects that may be measured differently. Thresholds for small, moderate and large effect sizes are 0.2, 0.5 and 0.8, respectively. At the 10-hour post-exercise mark (the primary endpoint), net protein balance was negative (i.e. protein breakdown was greater than synthesis) among all groups after their overnight recovery as seen in Figure 2. While not statistically significant, the calculated effect size of 0.61 indicates a medium effect of protein over the no exercise/supplement control trial. But the lack of statistical significance raises the question of whether this effect size is accurate. At the 24-hour post-exercise mark (a secondary end-

> "The average daily protein intake was 1.9 grams per kilogram of bodyweight per day (average total intake of 143 ± 16 grams/day), which is on the higher end of protein intake."

Figure 2: Results



point), net positive protein balance was enhanced in the protein group (effect size = 0.69), but not in the carbohydrate group. This effect was statistically significant.

In terms of exercise performance recovery (another secondary endpoint), performance significantly decreased across all tests at the immediate post-exercise testing session compared to baseline. Countermovement jump height decreased ~12%, maximal voluntary contraction decreased ~20%, knee extensions to failure dropped ~19%, and both peak and average anaerobic power in the Wingate test were reduced by ~7%.

When looking at the effect sizes of the exercise test at the 10- and 24-hour marks, researchers found a small-to-moderate beneficial effects in the protein group on countermovement jump height, maximal voluntary contractions, and anaerobic power during the Wingate test. At 24 hours, moderate benefit from protein supplementation was seen in maximal voluntary

contractions, knee extension repetitions to failure, and peak power for the Wingate.

Curiously, no correlations were apparent between net protein balance and maximal voluntary contractions, knee extension repetitions to failure, or Wingate power (peak or mean).

After a bout of resistance training, ingesting a pre-sleep protein supplement did not attenuate negative protein balance during sleep. When an additional dose of protein was ingested the next morning, a positive protein balance was observed 24-hours post-exercise. Protein supplementation also improved exercise performance recovery to a small or moderate amount 10 or 24 hours after the exercise bout. However, net protein balance did not correlate with recovery of exercise performance.

What does the study really tell us?

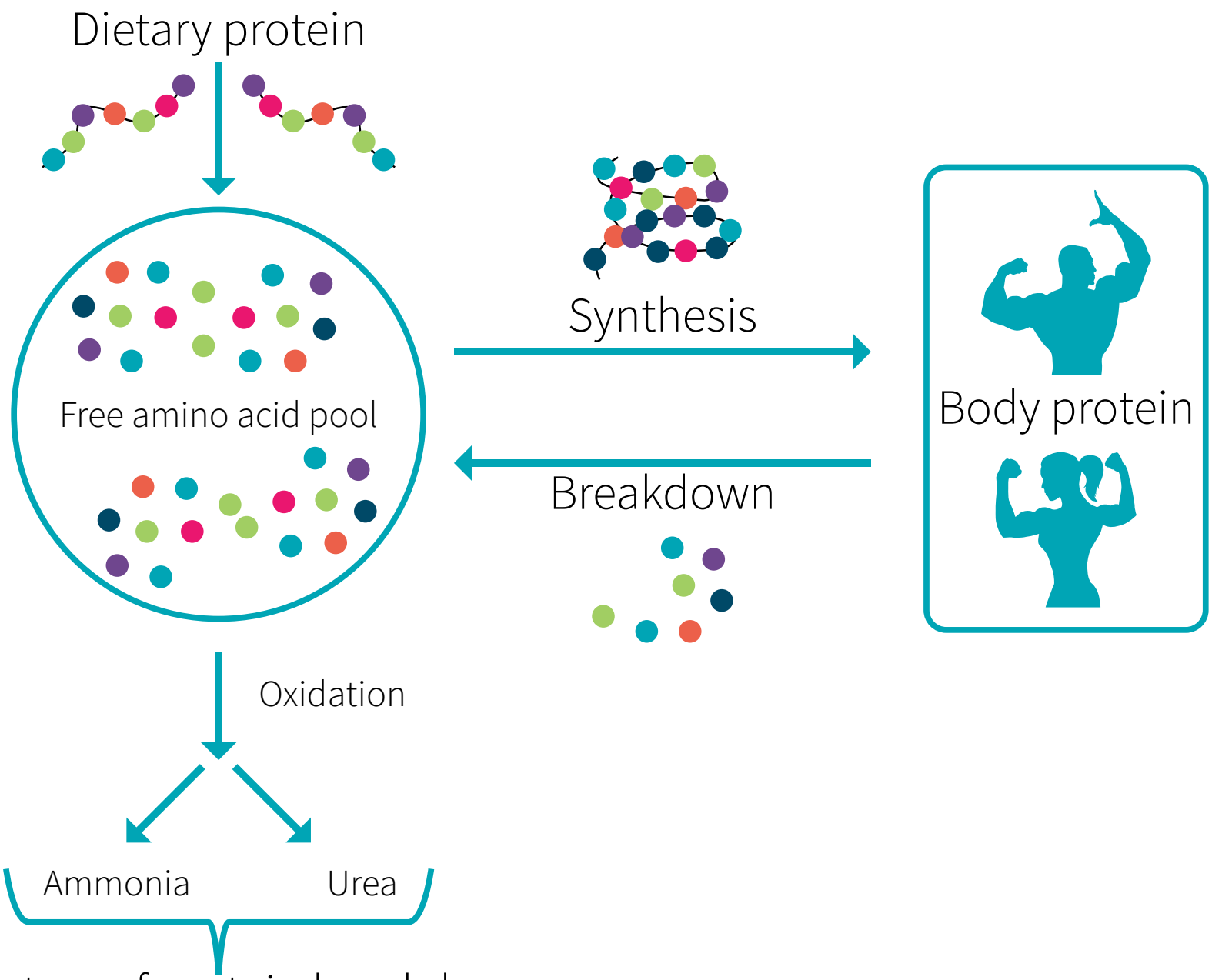
Contrary to the authors' hypothesis, whole-body net protein balance was not significantly augmented with a protein supplement over the 10-hour post-exercise recovery window compared to carbohydrate. However, the protein group did see better protein balance results at the 24-hour mark - possibly due to a synergistic effect of the protein timing plus the total amount of protein supplemented.

It is possible that the type of protein given was suboptimal for generating positive protein balance. Whey protein is digested and utilized by the body very quickly, whereas a casein or whey plus casein combination may have extended the time participants spent in an anabolic state overnight. Also keep in mind the participants had a habitual daily protein intake of about 1.9 grams per kilogram of bodyweight per day *before* the supplement was added on top of that. This is on the high end of what is typically recommended to athletes (about 1.2 gram to 2.0 grams per kilogram per day), so another possibility is that the anabolic effect of protein may have been blunted due to the athletes' already high protein intake (a.k.a the 'ceiling effect').

The protein supplement group did see a moderate improvement in performance recovery at the 10- and 24-hour marks. This is likely due to the greater protein intake mediating increased protein synthesis, as evidenced by the greater 24-hour net protein balance seen in the protein supplement group. While this acute change in protein balance and performance recovery may not seem like much, repeated acute improvements in protein balance may lead to long-term increases in muscle mass over time. However, this concept needs further evaluation as acute changes over a 24-hour period are not always predictive of long-term results.

One curiosity of the study was the lack of association between 10- and 24-hour whole body net protein balance and changes in performance compared to the post-exercise performance tests. This may be due in part to the way protein balance was measured. While the researchers were looking at whole body protein balance, skeletal muscle turnover, depicted on the right-hand side of Figure 3, only contributes to about 30% of this. This may have prevented the model used by the researchers to detect, with sufficient precision, the net muscle protein balance from the whole-body glycine tracer used in the study. Alternatively, it is possible that a dose-response relationship for muscle and/or whole body protein balance towards performance recovery does not exist, in which case inducing some as yet undetermined minimum net anabolism may be sufficient to enhance or maximize performance recovery. This is one aspect that will have to be studied in further trials, though.

Figure 3: Protein turnover



This study had some notable strengths. While the initial power calculation called for only 10 participants, the researchers enrolled 12, all of whom completed each trial. Compliance with the prescribed diets was very high, with participants consuming 98.4% of the calories and 98.4% of the protein provided. The study's blinding procedures were rigorous as well—only one of 12 participants correctly identified which supplement they were taking during all arms of the trial. Finally, the order of the exercise tests was set up from the least to most strenuous, with adequate rest periods in between. This helps minimize any carryover effect from fatigue that may bias the results.

It should be noted that funding and consultation for the study design were provided by Iovate Health Sciences International Inc. Iovate owns the brand MuscleTech, whose whey protein was used in this study.

Protein supplementation did not improve whole-body net protein balance at the 10-hour post-exercise recovery window, but did so the 24-hour mark. The participants already high daily protein intake may have attenuated any additional benefit of protein, or a larger dose of protein may be needed. While there were no statistically significant associations between 10- and 24-hour whole body net protein balance and changes in performance, this may have been due to a lack of sensitivity to measure muscle protein balance, which accounts for about 30% of whole body protein balance.

The big picture

This study contributes to a growing body of evidence that milk-based proteins consumed after exercise can preserve muscle strength and attenuate decreases seen in repeated sprint challenges up to three days after exercise. The present study complements these findings by demonstrating that whey can enhance muscle performance as early as 10 hours into the post-exercise recovery window and extending up to the 24 hour mark.

The mechanisms of improved markers of exercise performance with whey protein ingestion are not fully understood. It has been hypothesized that the greater muscle protein synthesis and repair driven by protein supplementation may facilitate a quicker performance recovery, although evidence backing this hypothesis up is lacking. It's also possible that the essential amino acids in protein supplements may attenuate inflammation, soreness, and muscle damage, which could also positively influence performance tests.

The study contributes to a body of evidence indicating milk-based proteins may aid in muscle recovery and preserve strength - something that would be of particular interest to athletes. It's possible that this performance-preserving effect is mediated by essential amino acids decreasing muscle inflammation, soreness, and damage.

Frequently asked questions

Does consuming protein before bed help improve muscle building?

In terms of protein timing strategies to maximize muscle protein synthesis (MPS), it is most important to consume enough protein each day and to spread your protein doses throughout the day - about 3 to 4 hours apart. For most people, the hours spent sleeping will be the largest window without a dose of protein to stimulate MPS. Pre-bed protein may help to narrow this window and to further optimize muscle protein synthesis or recovery. Studies have indicated that a 40 gram dose of protein is needed to yield a notable increase in MPS rates during overnight sleep.

Does the type of protein consumed before bed matter?

It is thought that casein (particularly, micellar casein), due to its slow digesting nature, may provide a longer anabolic stimulus during sleep than its fast-digesting counterpart, whey protein. This hypothesis has some conflicting research though. In ERD 32 volume 2 we covered a study that compared whey and casein, which found that muscle and strength adaptations did not differ between groups that underwent a 9-week resistance training program. However, there have not been any head-to-head trials comparing pre-bed whey and casein to determine if one could induce greater MPS over the other. For those interested, ERD 32 volume 2 also covers a study looking at pre-sleep protein.

What should I know?

A 25-gram whey protein supplement timed after an evening training session and again the following morning increased whole body net protein balance over the following 24-hour period in resistance-trained young men. This led to small to moderate improvements in exercise performance 10 and 24 hours post-training. More evidence is needed to see if if and how this effect hold over the longer term. ◆

Increase your gains in understanding by taking in a dose of discussion after reading this article in the ERD Facebook forum!

INTERVIEW:

Denise Minger

You once subscribed to raw food veganism. What made you transition out of raw food veganism and what advice would you give to folks who want transition into or out of such diets? Is it possible to be healthy on a vegan diet?

I first went raw as a wide-eyed 16-year old with no background in nutrition, human biology, anatomy, or any other relevant field—which made it easy to fall for the pseudoscience oozing from the raw vegan movement at the time. My transition out of that diet stemmed from two things: the rapid failure of my own health (a mouth full of cavities, hair loss, muscle loss, fatigue, impaired cognition, B12 deficiency, anemia, looking like Skeletor), and gaining enough scientific competence to realize the claims I'd bought were erroneous.

I don't recommend anyone transition into raw veganism (or even regular veganism) with long-haul intentions. People get duped by the initial honeymoon period, which feels incredible, but that high is impossible to sustain or recapture down the line. There's no compelling evidence that eliminating all animal products or cooked food from your diet is necessary—or even helpful—for obtaining good health. Even from an ethical standpoint, growing and harvesting plant foods inevitably causes animal death, whether through habitat destruction, mechanical carnage (e.g., plows and threshers decimating small critters), or pesticides (contrary to popular belief, even organic produce is grown with pesticides—just not synthetic ones). For those attracted to veganism for ethical reasons, financially supporting humanely raised animal products can probably have a bigger impact on animal welfare than dropping out of the consumer market entirely.

Basically, arguments for going vegan are tenuous from virtually every angle. Did I mention I don't recommend that anyone does it?

That said, if someone doesn't trust me on this and wants to try anyway, I'd advise going the supplement route (vitamin B12, algal oil for DHA, vitamin K2, and vegan vitamin D3, at the very least), avoiding processed vegan frankenfoods and prioritizing nutrient density (colorful veggies, mushrooms, fruit, root vegetables, seaweeds, legumes, some nuts and seeds, fermented foods), and supporting provitamin A absorption by eating beta-carotene rich foods with a little bit of fat. And this one's controversial, but I'd strongly encourage any current or prospective vegans to consider adding

bivalves—especially oysters—to their diet. Bivalves lack a central nervous system and consequently don't experience pain in the way most animals do. They can fill in a number of mineral gaps typical of vegan diets, including iron and zinc and B12. And for the adventurous: insects. Ick factor aside, they're a great source of protein and micronutrients, and from a cruelty standpoint, and there's a logical inconsistency if an ethical vegan is willing to eat plants grown with pesticides but not consume insects directly for nutrition.

For transitioning out of any form of veganism, there's no one-size-fits-all strategy. It's massively individual. Some people start craving animal foods so badly they'll mow down a steak and never look back. Others have extreme psychological hangups surrounding the textures, smells, visuals, and tastes of animal foods, and those hangups need to be addressed before un-veganizing can happen. My main advice is to take it slow: many long-term vegans have hypochlorhydria (low stomach acid), reduced liver enzyme activity (especially if their diet is low protein), or microbiome changes that make the initial reintroduction of meat a little gnarly. All those conditions are reversible, but some vegans misinterpret post-animal-food digestive distress as evidence that such foods are bad for them. This isn't the case. It does go away.

I won't say it's impossible to be healthy on a vegan diet, because all it takes is one exception to that statement to invalidate it. I think there's a small—very small—minority of the population with the right mix of genetics and gut bacteria to efficiently digest plant foods, make the necessary nutrient conversions or synthesis, and maintain a high degree of health for long enough to earn them a place in the "HEY LOOK IT'S A HEALTHY VEGAN" hall of fame. Especially if they at least supplement with vitamin B12. But when this happens, it's generally in spite of—rather than because of—the lack of animal foods, and has more to do with eating greater quantities of unprocessed plant foods than eating less meat, eggs, or dairy, per se.

For the nearly half of the population that struggles to convert beta-carotene into usable vitamin A (due to BCMO1 mutations), for people with compromised gut health that can't break down plant foods well enough to obtain all the goodness inside, for people without the right bacteria to synthesize vitamin K2—need I go on?—staying healthy as a vegan becomes increasingly difficult. That's why pointing to cherry-picked examples of thriving vegans (and yes, I do believe some exist, just like your grandpa who lived to be 114 smoking two packs a day and wrestling alligators on weekends) doesn't support the idea that veganism is adequate for the general public.

There are a lot of nutrition writers that have consistently been blogging for many years but many have also stopped. What first got you writing about nutrition and what drives you to keep writing?

I first started blogging after I'd abandoned veganism, gotten serious about researching nutrition, and wanted a platform to share my ideas without being censored by trigger-happy forum moderators. I'd been surreptitiously hanging out on raw vegan message boards for a while—mostly trying to help people who were going through the same trajectory of health problems that I'd faced—and got pretty tired of having to make new usernames from fake IP addresses every few days just because I'd said the word "egg" and gotten banned. My blog became my first amendment stompin' grounds.

I had no intention of turning nutrition writing into a career, but after the site started picking up traffic and I realized there were actual human people reading it, I wrote more things. And now here we are.

As for what drives me to keep writing, this pretty much sums it up.

How have your beliefs about food policy and nutrition research changed since you've written Death by Food Pyramid?

When I first started writing Death by Food Pyramid, I'd

been heavily influenced by the Paleo community, which pulled me into its fold after I'd written my China Study critique (probably under the guise of "the enemy of my enemy is my friend"—I don't know why else they'd want me; I hadn't eaten red meat in 16 years). As a result, I'd adopted a pretty harsh view of the grain industry (and sugar industry and vegetable oil industry) without applying equal criticism to the meat industry, dairy industry, and other industries that are rife with shady business but friendlier to the Paleo cause. The bias here became obvious to me after my book hit the stands, and I wish I'd taken better care to stay impartial.

Other than that, I'm much more open to the idea of high carb, low-fat diets working now than I was mid-manuscript. Speaking of which...

A few years ago, you wrote a blog post about how high carbohydrate diets may be particularly useful for managing insulin resistance and other conditions. How would you categorize the evidence for such a diet? Is it weak, moderate, or strong? What influenced you to write such a post?

This one's tricky. High carb, very low fat diets—when they're actually followed (none of this "low fat means 30% of calories" nonsense)—appear to benefit the majority of subjects in studies while predictably worsening the condition of a few. Identifying what factors land people in either of those categories is key for deciding when this kind of diet should be applied. When it does work, it can often do so spectacularly.

If I had to put my finger somewhere on the spectrum, I'd call the evidence just shy of strong. There's a surprising body of research out there already, but I'd love to see more studies directly comparing, for example, very low fat diets with very high fat ketogenic ones, as well as more controlled trials that specifically examine what mechanisms are driving the diet's benefits. Since many of the existing low fat ("real" low fat—10% of calories) trials are decades old and not as rigorous as we'd demand today, I fear some truly important research is getting swept under the rug.

As for what compelled me to write that post, I refer you back to Exhibit A

To elaborate, the massive explosion of articles, blog posts, and books blaming carbs for insulin resistance and obesity and other woes has not—in my opinion—received as much scientific backlash as it deserves. At least not from sources other than the Purveyors of Conventional Wisdom, which no one seems to care about these days anyway. So, I wanted to round up some research most people don't even know exists and present it as a challenge to the current anti-carb ideology. I'm pretty excited for "In Defense of Low Fat, Part 2" (ETA sometime before the year 2070) to fill in questions about mechanisms and drive the discussion even deeper. Stay tuned.

What are your favorite books on nutrition research and/or food policy?

There are surprisingly few books I recommend without doling out some caveats first. I'm much better at telling people what not to read and encouraging PubMed safaris instead. That said, these ones are pretty solid, or at least good starting places for the curious:

"Food Politics" by Marion Nestle
"Salt, Sugar, Fat" by Michael Moss
"Food and Western Disease" by the late, great Staffan Lindeberg
"Nutrition and Physical Degeneration" by the equally late, great Weston A. Price (this book is valuable for gauging the common denominators in successful traditional diets. I recommend reading Price's original writings rather than summaries by other sources, which tend to misrepresent his work)

What would you recommend to someone who's confused by the debate between low-carbohydrate diets and low-fat plant-based diets?

First, I'd frame it this way: if we have successful low carbers claiming low fat doesn't work, while also having successful low-fatters claiming low carb doesn't work, there's obviously a disconnect between theory and reality. Both these groups have some pieces of the puzzle, but not all—even though they think they do (ha ha, silly humans). We need to drop the rivaling-tribes mentality and get all those pieces dumped in one place.

The reality is that both of these diets have documented successes. Both diets are likely to work therapeutically for at least some portion of the population. Both diets can elicit surprisingly similar benefits, despite their menus being so radically different. And both diets are best used for reversing existing disease states, rather than serving as preventative programs for the general population (most of whom wouldn't benefit from such extreme diets simply because they'd struggle with adherence).

If someone switches to a diet based on minimally refined whole foods—rather than processed junk foods, isolated fats, and isolated carbohydrates—then their health will probably improve no matter what's being eaten, especially if the starting line was the Standard Western Diet. The "macronutrient extremes" can come in handy for healing from certain chronic diseases, but there's neither a need nor an ability to declare one side the winner. A diet that "wins" is the one that works for the specific individual.

What does your diet currently consist of? Do you take any supplements?

I live on sunshine and laughter. And also: seafood (salmon and oysters are my favorite), lots of fruit (berries are my favorite), root vegetables (jicama is my favorite), rice or legumes (lentils are my favorite), eggs (duck eggs are my favorite), organ meats (chicken liver is my favorite), seaweed (dulse is my favorite), and truly unfathomable quantities of vegetables (literal mountains; you'd be horrified). I rarely use isolated fats like oils or butter, and despite me talking smack about raw veganism, the majority of my diet is still raw and plant-based.

That's my diet at home. If I eat out or someone kindly makes food for me, my only hard rules are no gluten, no dairy, and no ultra-processed shenanigans, which actually still rules out almost everything so you probably shouldn't invite me to a dinner party.

I take vitamin D in the winter, vitamin K2 fairly regularly, and collagen. My other supplement experiments have been well intentioned but short lived. ◆

Denise Minger is an author, public speaker, and health consultant who specializes in critiquing bad science and questioning established dogmas underlying both alternative and mainstream beliefs about nutrition. Her book, "Death by Food Pyramid," was a Wall Street Journal bestseller and the recipient of several awards, including the 2014 gold INDIEFAB award for health books. She is a regular speaker at both national and international conferences, such as NUNM's Food as Medicine Symposium, the Ancestral Health Symposium, the Icelandic Health Symposium, the Eisenhower Wellness Center Speaker Series, the Nutritional Therapy Association Conference, and the Wise Traditions conference, where she also served as the 2014 keynote speaker. Along with sparking a viral online debate that first landed her name on the map, her analysis of "The China Study" by T. Colin Campbell has been featured in books such as "Wheat Belly" by William Davis and "Primal Body, Primal Mind" by Nora Gedgaudas. Currently, she divides her time between the Pacific Northwest and Arizona and maintains the website http://www.deniseminger.com, where she sporadically posts critiques of things that annoy her.

Remember what you see with vitamin D

Does high dose vitamin D supplementation enhance cognition?: A randomized trial in healthy adults

Introduction

Vitamin D has been suggested to play a role in numerous diseases outside of its established role in skeletal health. One of these areas is cognition. Observational evidence suggests that vitamin D deficiency has been linked to a 54% increased risk of developing dementia, 21% increased risk of developing Alzheimer's disease, and 139% increased odds of developing general cognitive impairment. These observations are also supported by experimental evidence in animals and cell cultures. Vitamin D receptors and the enzyme necessary to activate vitamin D (1α-hydroxylase) are located throughout the brain, and vitamin D and its metabolites have been shown to increase acetylcholine levels and neuronal density, enhance neuroprotection, and promote the clearance of β-amyloid. Vitamin D's possible interactions with cognition are summarized in Figure 1. Granted, researchers don't know whether these findings are relevant to humans.

Nonetheless, these observations raise an important question: can vitamin D supplementation improve cognition? One study in healthy young adults answered "no" when comparing 5,000 IU of vitamin D_3 to placebo over six weeks. However, only 10 of the 128 participants were vitamin D deficient at baseline and, as has been observed with changes in musculoskeletal health, changes in cognition may require more than six weeks to manifest. An analysis of the Women's Health Initiative reported that 400 IU of vitamin D_3 had no effect on cognition over eight years, but subsequent vitamin D levels were not obtained and the dose may have been too low to have an effect.

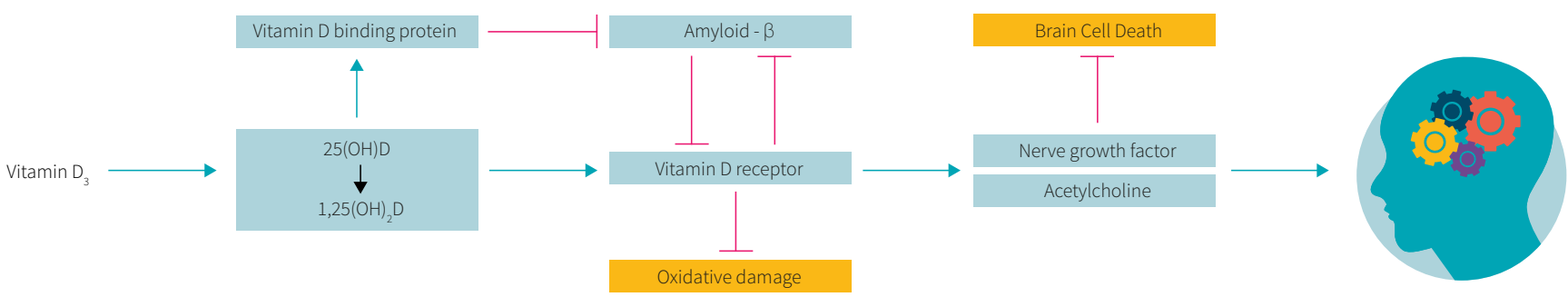
The study under review is a randomized controlled trial evaluating two doses of vitamin D_3, 4,000 and 400 IU per day, on a broad range of cognitive domains in healthy adults over 18 weeks. A predetermined subgroup analysis was also planned to assess only those individuals who were vitamin D insufficient at baseline.

Vitamin D has been associated with cognitive function in observational and mechanistic research, but supplementation interventions to date are scarce and have some limitations. The study under review was an 18-week randomized controlled trial evaluating the effect of vitamin D supplementation on a broad range of cognitive domains in healthy adults.

Who and what was studied?

This was a randomized controlled trial involving 82 healthy adults from Northern British Columbia during the winter and early spring (November to March) who had baseline vitamin D levels less than 40 ng/mL (100 nmol/L). The average age of the participants was about 55 years, with about 15% between 20-44 years, 40% between 45-59 years, and 45% between 60-76 years. At baseline, vitamin D supplements were taken by 57% of the participants at an average dose of about 600 IU

Figure 1: Interaction of vitamin D with Alzheimer's disease and cognition



Reference: Morley JE. Nat Rev Neurol. 2014 Nov.

per day. These doses were maintained throughout the study; additional vitamin D was added on to what these participants were already taking.

The participants were randomly assigned to supplement with either 400 or 4,000 IU of vitamin D_3 daily for 18 weeks. They were blinded to the intervention and were simply told they were supplementing with a nutrient. Although the assessor was aware that the intervention involved vitamin D, she too was unaware of the dose each participant was receiving until after data collection.

Primary outcomes were the differences between the low-dose and high-dose vitamin D groups for changes in cognitive test scores from baseline. Standardized cognitive testing consisted of the Symbol Digit Modalities Test (SDMT) to assess information processing speed, verbal fluency (VF) to assess executive functioning, digit span forward (DS-F) and backward (DS-B) to assess attention/working memory, and the Cambridge Neuropsychological Test Automated Battery (CANTAB), which includes measures of verbal memory (VRM), visual memory (PRM) and learning (PAL), working memory (SWM), and executive functioning (OTS). These tests were performed at baseline and after 18 weeks of vitamin D supplementation. Alternate test versions were used to minimize any learning or practice effects.

An intention-to-treat analysis was used to analyze the data and no correction for multiple comparisons was performed. Additionally, a predetermined subgroup analysis was performed with the same statistical methods using only those participants in both groups (n=50) who began the intervention with vitamin D levels less than 30 ng/mL (75 nmol/L), which is considered insufficient by several authoritative bodies like the Endocrine Society.

> “Vitamin D has been suggested to play a role in numerous diseases outside of its established role in skeletal health. One of these areas is cognition.”

This was an 18-week randomized trial involving 82 healthy adults that evaluated the effect of supplementing with 400 or 4,000 IU of vitamin D_3 per day on a broad range of cognitive domains, including information processing speed, executive functioning, attention and working memory, and visual and verbal memory.

What were the findings?

Both groups had an average baseline vitamin D level of around 25 ng/mL (64 nmol/L). Expectedly, the high-dose vitamin D group experienced a significantly greater increase in vitamin D levels than the low-dose group, with final values being 52 ng/mL (131 nmol/L) and 35 ng/mL (86 nmol/L), respectively. Overall, no one in the high-dose group was insufficient after supplementation, while 22.5% of participants in the low group still had vitamin D levels below 30 ng/mL (75 nmol/L). However, neither group contained people who

were deficient after supplementation (less than 20 ng/mL or 50 nmol/L).

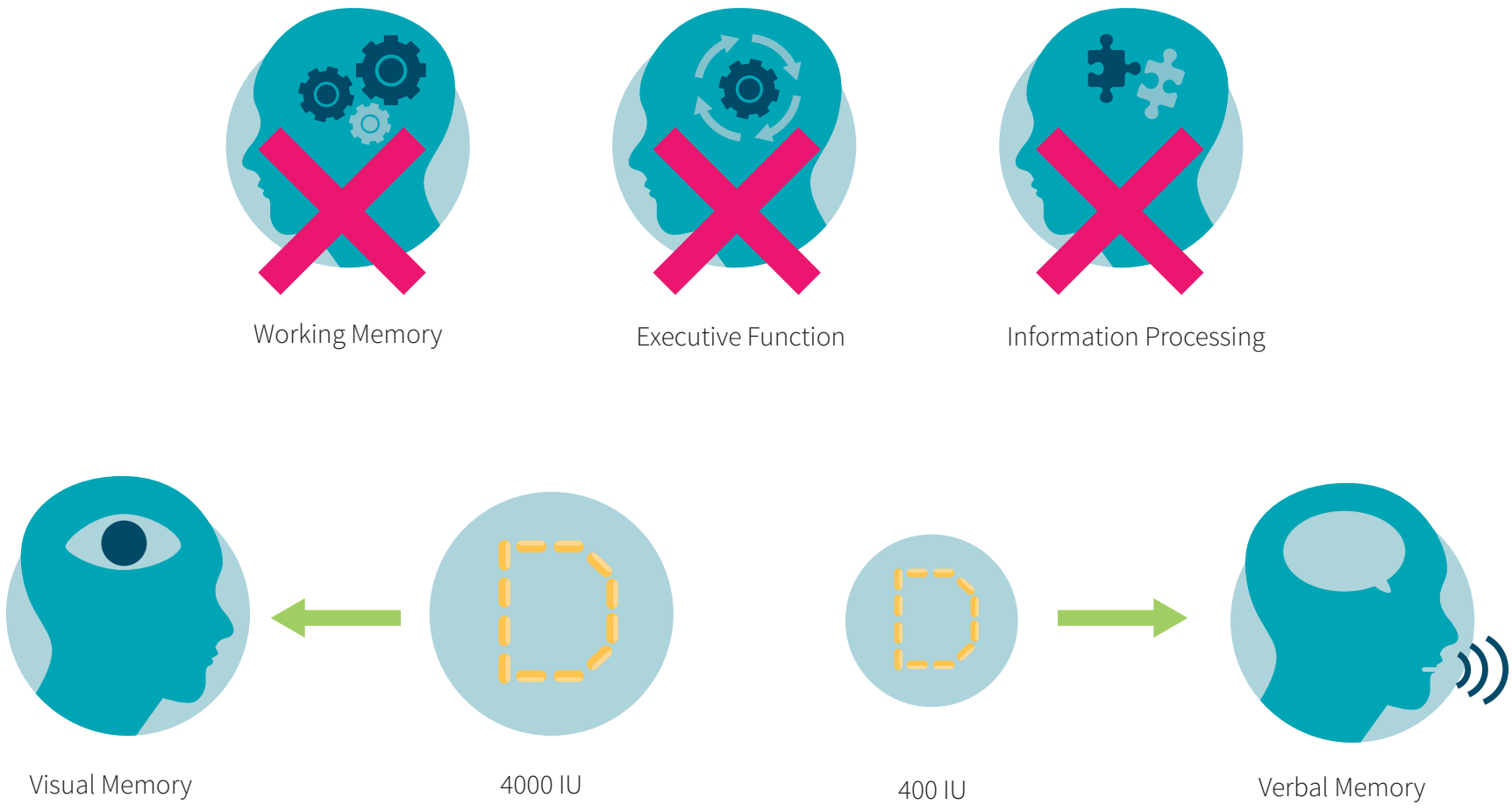
The results of this study are summarized in Figure 2. The only statistically significant finding between groups was a greater improvement on a test of verbal memory (VRM) in the low-dose group compared to the high-dose group. Within each group, most cognitive tests were unchanged after supplementation. The high-dose group significantly improved on two tests of visual memory (PRM & PAL) compared to baseline, while the low-dose group significantly improved on a test of verbal fluency (VF) and a test of verbal memory (VRM) compared to baseline. These within-group changes are, however, rather meaningless because they are simply observations of something that occurred over time and there is no way of knowing if they were the result of vitamin D supplementation or some other influence, such as the practice effect from frequent testing.

In the subgroup analysis of 50 participants with vitamin D insufficiency at baseline, average baseline vitamin D levels were just over 20 ng/mL (50 nmol/L) and the high-dose group experienced a significantly greater increase than the low-dose group, with final values being 49 ng/mL (120 nmol/L) and 32 ng/mL (80 nmol/L), respectively. The only significant finding was a greater improvement on a test of visual memory (PRM) in the high-dose group, compared to the low-dose group.

In both the full analysis and subgroup analysis, neither intervention significantly affected calcium or phosphorous levels, suggesting the intervention was safe. Parathyroid hormone was significantly reduced in the high-dose group only; the difference from the low-dose group was not significant.

Supplementing with 4,000 IU of vitamin D_3 per day for 18 weeks improves visual memory significantly more than supplementing with 400 IU. This occurs when looking at all participants and when looking at only those with vitamin D insufficiency at baseline.

Figure 2: Effect of vitamin D supplementation on domains of cognitive function



What does the study really tell us?

On the surface, the study under review suggests that vitamin D supplementation may improve visual and verbal memory in healthy, primarily middle-aged and elderly, adults. This conclusion was reached by the authors of the study who dedicated nearly their entire discussion of the results to putting these findings in context with other research. However, this study had important limitations that impede putting too much faith into the results.

First, depending on how the cognitive tests are counted, the study at hand had five to 10 primary outcomes listed, which really defeats the purpose of declaring a primary outcome in the first place. Having multiple outcomes increases the likelihood of false positives, or observing a significant effect by random chance. To help reduce the likelihood of this occurring, researchers will usually correct for multiple comparisons. A common method to do this is the Bonferroni correction, which divides the significance level by the number of tested outcomes. Dividing the p=0.05 significance level by five to 10 outcomes shows that the new level of statistical significance (p=0.01 at most) is not reached for any outcome, suggesting that the results could be due to random chance.

Random chance also easily explains many of the inconsistencies in the study outcomes, such as the odd finding that the only significant outcome was a greater improvement in verbal memory in the low-dose group compared to the high-dose group. Even if more vitamin D isn't better when it comes to improving this aspect of cognition, why would the high-dose vitamin D group not also experience a similar degree of improvement in verbal memory as the low-dose group? Additionally, why was this result not also observed in participants who were vitamin D insufficient at baseline, for whom it would be expected that vitamin D supplementation has a more notable impact?

Second, there was no true placebo group in this study. Both groups received vitamin D supplements. The low-dose group could have experienced marginally improved cognitive function, which would make it more difficult to observe a significant effect of high-dose supplementation when compared to no supplementation at all. Accordingly, the study under review cannot tell us what effect supplementing vitamin D has, it can only tell us if there is a difference between supplementing two doses of vitamin D. This is also why the observed within-group changes are difficult to analyze: there is no control group to compare them to, so these within-in-group observations remain just that, observations.

Regardless of these limitations, the study under review also shows that supplementing with 4,000 IU of vitamin D3 per day, in addition to self-supplementation of about 600 IU per day, is safe and has no effect on blood levels of calcium or phosphorous.

This study had several strengths, including the use of a comprehensive battery of established cognitive tests, a double-blind randomized design, and a long intervention duration. However, the sample size was at the low end of a power calculation finding that 40-60 people per group would be necessary to observe a moderate effect. This implies that small effects of the intervention could be overlooked due to a lack of statistical power.

When these strengths and limitations are considered alongside the strong possibility that the outcomes were owed to random chance, it's plausible that vitamin D supplementation has little effect on cognition in primarily middle-aged and elderly people without cognitive impairment. But it is still possible that a small effect does exists,. A follow-up study with a larger sample size that focuses on one or two cognitive outcomes in the visual domain is necessary to test this hypothesis. Similarly, whether different results would be observed in young and healthy or old and cognitively impaired adults requires further study.

The study under review had methodological limitations that impede our ability to put faith in its findings, such as not correcting for its many outcomes and not using a true placebo group. It is possible that any statistically significant changes in cognition were owed to random chance, rather than an effect of vitamin D supplementation. However, small effects, especially in visual domains, cannot be ruled out. A follow-up study with a larger sample size focusing on visual cognition is needed to confirm these findings.

The big picture

The role of vitamin D in cognitive function is not well characterized, and it is not known what level of serum vitamin D is optimal for cognition. It's also unknown if 25(OH)D is the right marker of vitamin D status to look at, considering that most of the neurological effects come from its metabolite, $1,25(OH)_2D$. Nonetheless, the study under review and others suggest that the benefits of vitamin D supplementation are, at best, minor in healthy adults. However, there may be a benefit of vitamin D supplementation in people who already have dementia, Alzheimer's disease, or some other form of cognitive impairment.

Animal models have shown that the disruption of vitamin D metabolism leads to a perturbation of pathways known to be altered in Alzheimer's disease and that supplementation with vitamin D restores cognitive function. For example, a vitamin D deficient diet in a rat model of Alzheimer's disease intensifies learning and memory deficits and increases amyloid-beta plaque and inflammation in the brain.

Unfortunately, vitamin D interventions in people with Alzheimer's disease are lacking. One study involving 32 people with Alzheimer's disease reported that there was no significant difference between supplementing 7,000 or 1,000 IU of vitamin D_2 on global cognition, functional abilities, or verbal memory despite a significant difference in vitamin D status between the groups after the eight-week intervention. This may be owed to the use of vitamin D_2, which has a lower binding affinity for vitamin D binding proteins and the enzyme responsible for converting it into 25(OH)D. Plus, vitamin D_3 metabolites also have greater biological activity toward the vitamin D receptor, and the aforementioned studies in rat models of Alzheimer's disease used $1,25(OH)_2D_3$.

Although the pathological characteristics appear similar between humans and animals, there are also some pretty big differences which make it is more difficult to model Alzheimer's disease. One major difference between humans and rodents is our genetics. Several polymorphisms that impact vitamin D receptor activity have been reported as potential risk factors for Alzheimer's disease. This is especially important because serum vitamin D levels may not accurately reflect an individual's ability to use vitamin D. Accordingly, trying to achieve an "optimal" level for 25(OH)D or other markers of vitamin D status may be futile.

The role of vitamin D in cognition is not well characterized and few interventions have assessed how vitamin D supplementation impacts cognitive function, especially in disease states such as Alzheimer's. Animal studies suggest a benefit to maintaining adequate vitamin D status, but the only human intervention suggests that eight weeks of supplementation can't reverse cognitive decline once it's established.

Frequently asked questions

What role does sunlight play in cognitive function?

As suggested in the study at hand, sunlight could potentially influence cognition through its effect on vitamin D status. Sunlight can also indirectly affect cognition through its effect on mood and circadian rhythms, at

least in susceptible populations, such as those who suffer from depression and seasonal affective disorder. Finally, bright light exposure has been shown to enhance alertness and attention, visual search ability, reaction time, and working memory.

Two observational studies have associated a lack of sunlight exposure with cognitive decline, and a series of experiments in healthy adults have shown that climate and season affect mood and cognition. But none of these necessarily imply a causal role of sunlight in cognitive function, and no controlled trial has been conducted to directly investigate this question. Even if such a trial were performed, it is likely it would only investigate the acute effects of sun exposure on cognitive function. This is problematic because cognitive decline can take years or decades before it becomes noticeable and there are ethical limitations regarding locking people in dark rooms for that long.

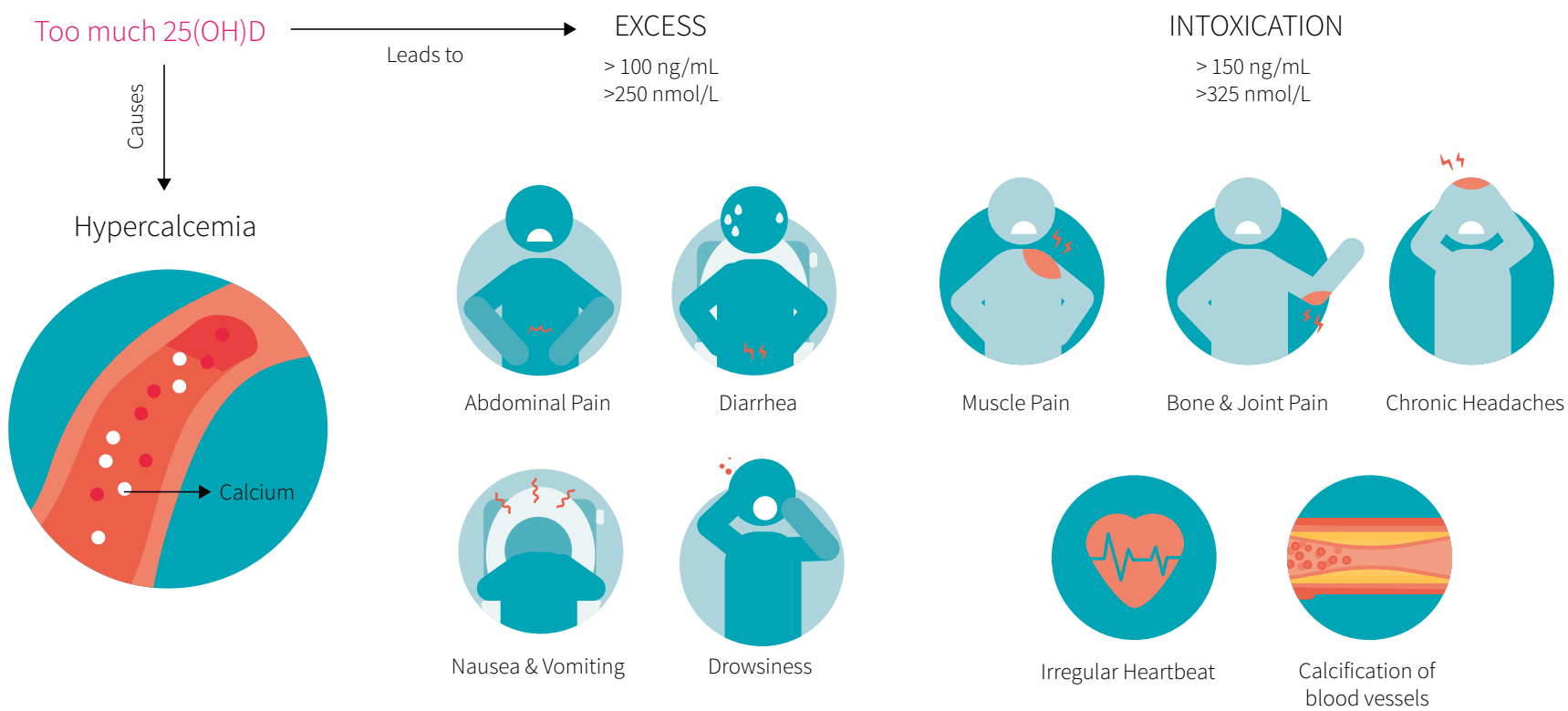
What about supplementing with the active metabolite of vitamin D, 1,25(OH)$_2$D$_3$?

Calcitriol, which is the common name of 1,25(OH)$_2$D$_3$, is used medically for the treatment of hypocalcemia in adults and rickets in children. It is also used in patients with chronic kidney disease because the kidneys are the primary site of its production, which means that blood levels of calcitriol will be lower when the kidneys are not functioning properly. However, calcitriol is not sold as a supplement for good reason. It is the most potent metabolite of vitamin D, which plays a central role in calcium regulation, so there is a high risk of inducing hypercalcemia and other signs of vitamin D toxicity that are shown in Figure 3.

What should I know?

Observational research has linked low vitamin D levels to an increased risk of dementia, Alzheimer's disease, and general cognitive impairment. Mechanistic research shows that vitamin D plays an important role in brain health and function. Yet, intervention studies with vitamin D are lacking. The study under review was an 18-week randomized trial involving 82 healthy adults that evaluated the effect of supplementing with 400 or 4,000 IU of vitamin D$_3$ per day on a broad range of cognitive domains, including information processing speed, executive functioning, attention and working memory, and visual and verbal memory.

Figure 3: Vitamin D excess and toxicity



Reference: Alshahrani et al. Nutrients. 2013 Sep.

This study reported that supplementing with 4,000 IU of vitamin D3 per day for 18 weeks significantly improved visual memory, while supplementing with 400 IU per day significantly improved verbal memory. Together with observational research, this suggests that vitamin D may play a larger role in visual memory than it does in verbal memory. However, due to the relatively small sample and the number of outcomes examined, this research does not provide strong evidence for vitamin D's efficacy in this case. Larger follow-up studies will be necessary to confirm these findings. This study was conducted in healthy adults and further research is also necessary to investigate how vitamin D supplementation affects cognitive function in people with dementia or Alzheimer's disease. ◆

Test out your verbal memory of this article at the private ERD Facebook forum!

Can fasted exercise increase fat oxidation in women?

Exercise before breakfast increases 24-h fat oxidation in female subjects.

Introduction

It's pretty common to see "fat-burning zone" or "weight loss zone" plastered on cardio equipment. This fabled aerobic exercise intensity is supposed to be the best for melting the fat away. The thinking behind the fat-burning zone has a little bit of science to back it up. The relative contribution of fat versus glucose to fuel activity reaches its peak at moderate intensities of exercise - this is the fat-burning zone. Here, the body is using more fat relative to glucose in order to fuel the exercise.

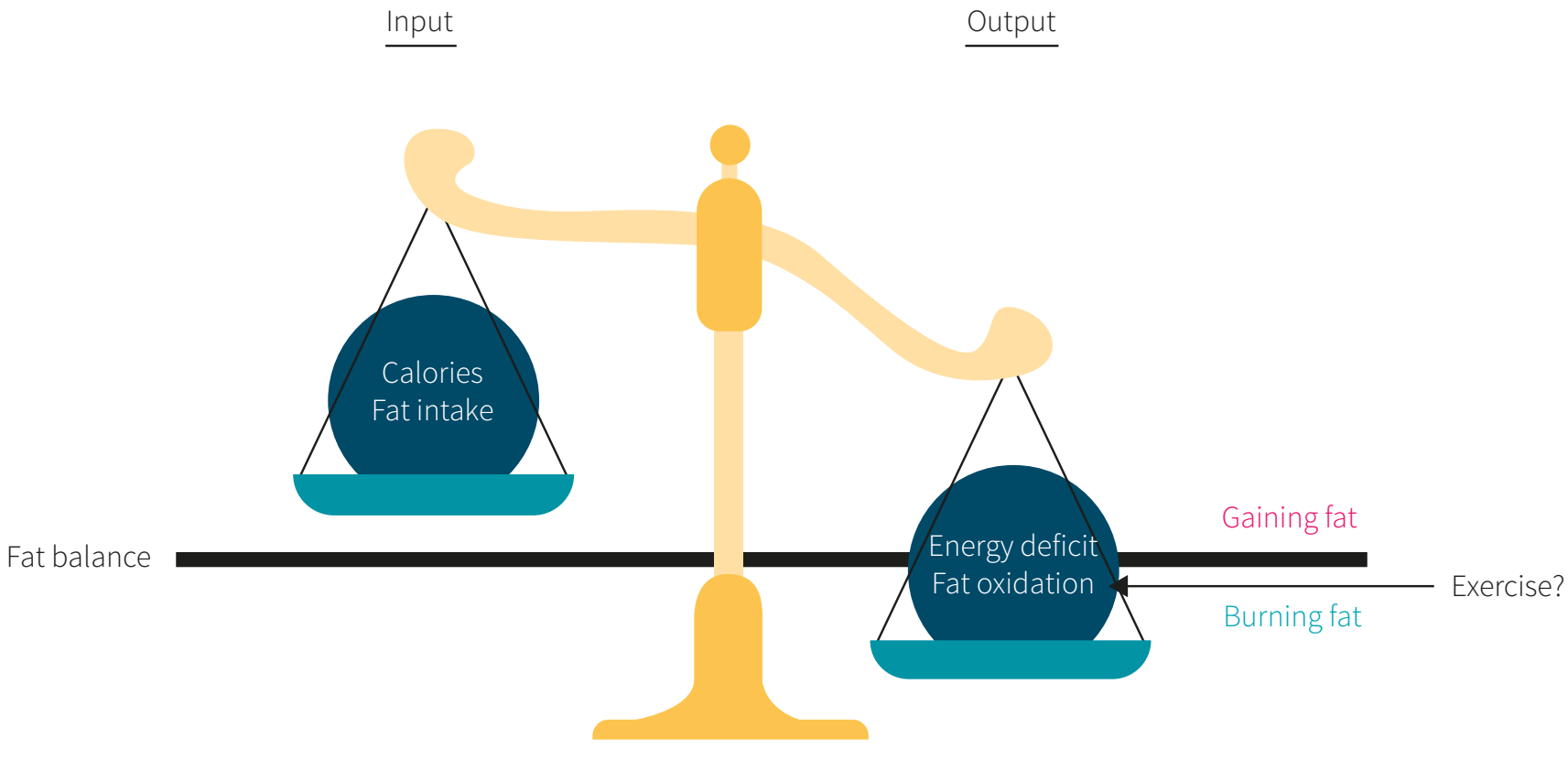
But fat burning *during* exercise doesn't tell the whole story. After all, it's not really the goal of people training in the "fat-burning zone" to switch up the ratio of fuel their muscles are using in the moment. Presumably, their goal is to lose fat mass. And here's where the science of the "fat-burning zone" starts to break down.

As shown in Figure 1, in order to lose body fat, the body has to be in a negative fat balance. One way to tip the fat balance scales could be to increase the fat oxidation rate. This concept has been tested, and at this point, the general consensus is that exercise does not affect 24-hour fat oxidation compared to sedentary controls, at least if energy balance is maintained (i.e., you eat just enough food to compensate for the greater energy expenditure from exercise). So, while the body uses more fat as fuel *during* moderate intensity exercise, over the course of a day, fat balance is the same as if the person just laid around all day. In other words, it looks like exercising does not magically make you lose fat. The key to fat loss is burning more energy than you consume.

The story doesn't end there, though. Recently, a series of studies have found that if moderate intensity exercise is done while fasted (i.e., before breakfast), 24-hour fat oxidation is indeed increased, even when energy balance is maintained. But there's a nuance here that limits generalizing these results: the studies were all done in men, which is a common problem in exercise science. This leaves open the question of whether these findings extend to women.

There are several physiological differences between the sexes, many of which are related to exercise and

Figure 1: Fat balance in a nutshell



Reference: Melanson et al. Exerc Sport Sci Rev. 2009 Apr.

fat metabolism. On average, women burn more fat than men during exercise, but less fat afterward. Men's and women's skeletal muscle also adapts differently to endurance training. Some of these differences involve how skeletal muscle utilizes fat as a fuel, and can be observed at the genetic level. So, it's far from clear that aerobic exercise in a fasting state could burn more fat for women. The study under review aimed to address this gap in the research.

Current consensus is that aerobic exercise in a fed state doesn't affect fat oxidation over a 24-hour time frame; fat balance is maintained, and so the "fat-burning zone" of cardio exercise doesn't live up to its name in practical terms. However, recent evidence has suggested that if exercise is done in a fasted state, fat burning increases. But this evidence has only been collected from studies involving men. Physiological differences raise the question of whether this effect would also be seen in women, and the study under review sought to answer it.

Who and what was studied?

Nine healthy women were enrolled in this randomized, controlled crossover study. They were all deemed to be moderately physically active (they exercised about 2.5 hours per week, on average). None of the women were taking any medication at the time of the study, including oral contraceptives. On average, their BMI was about 22 and they were around 24 years old.

The researchers determined the participants' baseline workload capacity by using a cycle ergometer to measure their maximal oxygen uptake capacity (VO_{2max}) and the amount of work on the bike that each participant could perform that corresponded to 50% of their VO_{2max}. The participants' average baseline VO_{2max} was almost 44 mL/kg/min, which puts them well above the 90th percentile for women their age.

The participants were then either randomly assigned to a sedentary or exercise condition. In the sedentary condition, the participants remained at rest for an entire day. In the exercise condition, participants pedaled on a cycle ergometer before breakfast for 60 minutes at 50% of their VO_{2max}, then remained sedentary for the rest of the day. Both conditions were performed in controlled conditions, ensured by a metabolic chamber, so macronutrient metabolism (how much fat, carbs, and protein was burned) could be measured using indirect calorimetry. In the chamber, participants were fed standardized meals containing 15% protein, 25% fat, and 60% carbs three times a day at regular times. Each meal contained about a third of the participant's calculated needs to maintain energy balance for the day, and the amount of calories each participant was fed depended on their baseline measurements and whether they were exercising or sedentary for the day. Non-exercise activity was taken into account using an activity monitor worn on the wrist.

From all that, net energy balance was calculated by subtracting energy intake (that was controlled through the meals) from total energy expenditure (which was estimated by indirect calorimetry).

After each participant completed the day-long experiment, they switched conditions. Those who were in the sedentary group exercised for an hour, and vice versa. Each experiment was done during the early follicular phase (during or right after menses) of the participants' menstrual cycles in order to control for hormonal contributions to metabolism. Additionally, each participant was asked to maintain their bodyweight between experiments to control for body composition differences. Also, the two experiments were done within a two-month time frame to minimize possible variability of results over time.

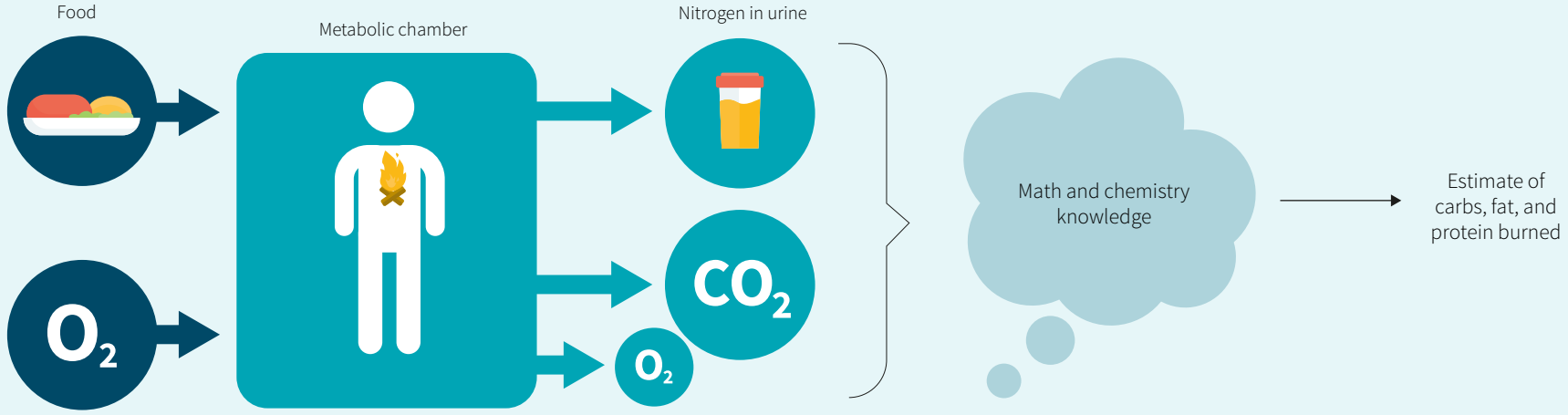
Indirect calorimetry and the magic of chemistry + math

Calorimetry literally means "the measurement of heat," so it may be surprising to learn that heat was not measured by the method of indirect calorimetry that was used in this study. Instead, three things were measured in this study: each participant's amount of oxygen consumed, carbon dioxide excreted, and the amount of nitrogen in urine over the course of 24 hours.

These three measurements, plus some math and basic knowledge of biochemistry, are enough to estimate the contribution of carbs, protein, and fat to the subjects' energy supply. This process is summarized in Figure 2. This is because basic chemistry dictates that burning these three macros in the presence of fixed amounts of oxygen yields fixed amounts of carbon dioxide and nitrogen. So, if you write out these chemical reactions, you have three equations and three unknowns that can be solved mathematically. Since urine nitrogen content comes mainly from metabolized protein and burning carbs and fat doesn't yield nitrogen, you can get a direct estimate of protein metabolism from urine nitrogen, and then calculate carb and fat metabolism using changes in carbon dioxide and oxygen in a sealed metabolic chamber.

With just three measurements and a little math and chemistry knowledge, researchers can estimate macronutrient metabolism indirectly.

Figure 2: Indirect calorimetry



The goal of this study was to determine how exercise before breakfast affects fat metabolism in women. Nine healthy, young women with normal BMI were assigned to two conditions in a metabolic chamber for a day: one where they did moderate aerobic exercise before breakfast for an hour and one where they were at rest. Their overall energy expenditure and their carb, fat, and protein metabolism was estimated.

What were the findings?

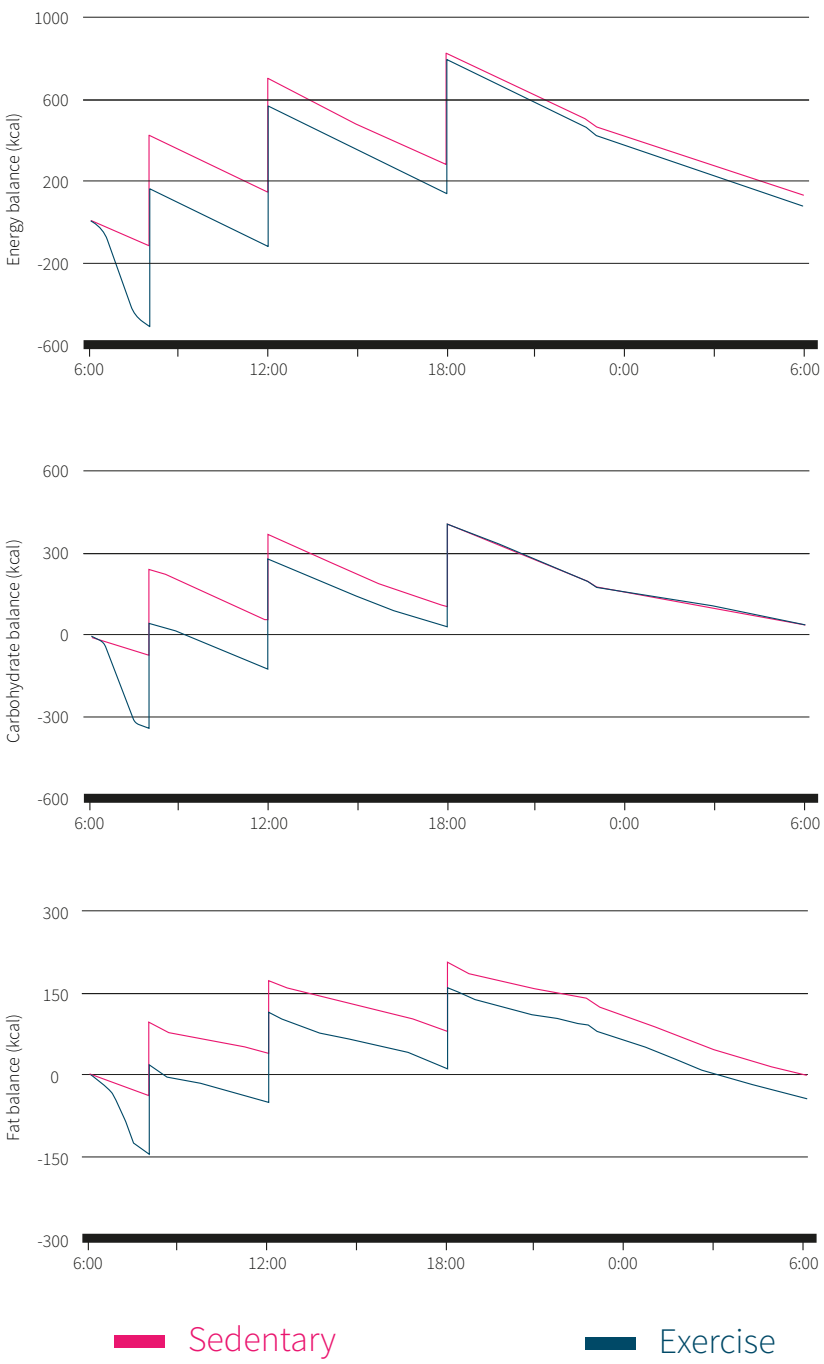
The exercise condition burned about 120 kilocalories more fat than the sedentary condition over 24 hours. Thus, fat oxidation increased over the course of the study. Also, about 235 kilocalories more carbohydrate were burned than the sedentary condition

The experiment was designed to keep total energy balance the same between participants and conditions by

providing extra calories as a proportion of the overall diet, as opposed to directly replacing the substrates oxidized during exercise. This seems to have succeeded, as no significant difference between the conditions was observed. Participants were also able to maintain body-weight over the course of the experiment.

The time courses for energy, carbohydrate, and fat balance can be seen in Figure 3. While transient differences between the sedentary and exercise conditions existed, the carbohydrate and total energy balance evened out between conditions toward the end of the study. However, a significant difference between the sedentary and exercise conditions remained for fat balance.

Figure 3: Energy, carb, and fat balance over 24 hours



Moderate intensity aerobic exercise before breakfast increased 24-hour fat oxidation in healthy, young, fit women relative to being sedentary.

What does the study really tell us?

When combined with other findings from previous studies, this study fills a gap in the research.

This gap arises from the previously described lack of effect of moderate exercise on fat oxidation in both men and women when overall energy balance is neutral. In other words, if you're eating as many calories as you're consuming every day and exercise in a non-fasted state, you won't burn more fat than if you just laid around.

But what about fasted exercise? This question was addressed by some of the same researchers as the current study under review, but only in men. They found that fat oxidation under energy-balanced conditions in lean, healthy men could be increased by moderate exercise, but only in a fasted state in the morning.

Together, these findings are quite interesting, but they do not answer the question of whether this fat-burning effect would also be found in healthy women of normal BMI. Due to the physiological differences between men and women mentioned in the Introduction, it cannot be assumed that these effects would carry over to women. And that's where the study under review comes in; it was designed and conducted to confirm that this fat-burning effect does indeed seem to apply to women.

One possible weakness of this study lies in the control group. The control in this study was women at rest, not women exercising in the fed state. Ideally, future research will include compare fasted to fed conditions to tease out the effects of feeding state more clearly.

The larger problem lies not with the study itself, but misinterpreting it. This study tells us something about how the body uses fat relative to carbohydrates as a fuel 24 hours after fasted exercise while in energy balance. What it does not tell us much about is body fat loss while in energy balance. This study justifies more research looking into whether the fat-burning properties of chronic pre-breakfast exercise could lead to body fat loss in the long term for people who take in as many calories as they burn. However, it does not demonstrate body fat loss.

What would fat loss while in energy balance look like? If energy balance is maintained and fat is lost, weight wouldn't be lost. That means that either protein or carbohydrate storage would offset the fat loss. But the carbohydrate pool in the body is too small to make much of an impact weight-wise, leaving increased protein stores, possibly in the form of muscle, as the main contender in maintaining weight in the presence of fat loss. Some people with training experience may raise an eyebrow at the suggestion that moderate intensity aerobic exercise could be a muscle builder. But some evidence indeed exists that aerobic exercise can influence muscle mass and hypertrophy. While there's much reason to be skeptical, the study under review does warrant more research looking into the effects of repeated bouts of fasted versus non-fasted aerobic exercise on body composition in the longer term.

Previous research has found that moderate aerobic exercise in healthy men of normal BMI in energy balance increases fat oxidation if it's done before breakfast. The study under review adds to the research by showing that the same effect holds for women. More research is needed to see if these effects last for chronic pre-breakfast exercise and to elucidate possible long-term effects on body composition in the presence and absence of caloric deficits.

The big picture

While the researchers of the study under review were mostly correct that there has been little research done looking at the effects of aerobic exercise on fat-burning in women, there has been some research that's at least somewhat relevant.

One such study looked at a population of young, recreationally active women fairly similar to those in the study under review. The participants consumed either water or a meal of rolled oats before exercising. The researchers did not use indirect calorimetry, but did measure blood lipids, and found that the meal suppressed plasma lipid levels, which is suggestive of using less fat for energy, although that's not certain since fat oxidation wasn't measured.

Another study, however, did use indirect calorimetry. This study also had a similar population to the study under review. In this study, fit, young women exercised 30, 60, or 90 minutes after consuming a test meal of chocolate chip breakfast bars and low-fat chocolate milk or consuming no meal at all. They then exercised on a treadmill for 30 minutes at around 60% of VO_{2max}. The study found that, during exercise, the women's total energy expenditure didn't vary between conditions. However, the women who had no breakfast burned about 20 kilocalories more in fat than women who had breakfast at any time. However, this study only performed calorimetry while the women exercised. The study under review, in contrast, extends this research by measuring macronutrient oxidation for a full 24 hours.

The two studies above were included in a recent meta-analysis examining the question of aerobic exercise's effects on fat burning. This study found that aerobic exercise in a fasted state burns about three grams more fat on average than exercise in the fed state. However, the population characteristics did slant heavily toward male and trained individuals. Subgroup

analysis found that most populations burned more fat when exercising while fasted, regardless of BMI, time spent exercising, sex, or training level. However, one pattern that stuck out in the analysis was training intensity: the authors did not see any difference in fat burning between the fasted and fed states when exercise intensity was at 70% of VO_{2max} or above. So, it seems that high intensity exercise while fasting may not burn a higher percentage of fat relative to carbs. Only moderate intensity aerobic exercise does the trick.

While the long-term effects of aerobic exercise while fasting and in energy balance have yet to be explored, exercise while in a caloric deficit has been. One study found that body fat was indeed lost in healthy, young women who exercised aerobically, but no difference was seen between exercising in the fasted versus fed state (for more information, see ERD Issue 3, "*Running on empty: can we chase the fat away?*"). High-intensity interval training in both the fasted and fed state also led to similar amounts of fat loss in women who were sedentary and overweight in another study. Caloric intake was not strictly controlled, though, so it's hard to tell if caloric deficit is what led to the fat loss. A third study compared the effects of exercise in the morning versus evening in women with overweight. The women who exercised in the morning lost weight and had a statistical trend for body fat loss was seen, while evening exercise didn't affect weight or body fat. However, it is not clear if the women who exercised in the morning did so before or after breakfast. In addition, the morning exercisers also seemed to take in fewer calories as the study progressed, further confounding the effects of the exercise alone on fat loss.

The study under review agrees with previous research looking at fasted aerobic exercise in women, although that evidence is limited. Overall, it looks like fasted aerobic exercise of moderate, but not high, intensity can burn relatively more fat regardless of training status, BMI, or sex. Whether fasted exercise while in energy balance can translate to body fat loss remains to be determined, but some evidence to date concerning exercise in a caloric deficit indicates no difference in body fat loss between people exercising in the fasted or fed state.

Frequently asked questions

Why does aerobic exercise on an empty stomach burn relatively more fat than carbs while exercising?

The authors of the study hypothesize that it comes down to reduced glycogen stores. The body's pool of carbohydrates available for use is relatively small compared to its fat and protein pools. Accordingly, the

"[...] some evidence to date concerning exercise in a caloric deficit indicates no difference in body fat loss between people exercising in the fasted or fed state."

body's metabolic reaction to changes in the carbohydrate pool tend to be more sensitive. So, it's reasonable to suspect that in the morning before breakfast, carbohydrate pools stored as glycogen are relatively low, making the body turn to fats for its energy needs. Indeed, it's known that skeletal muscle and the liver both turn to fat when glycogen stores are low. It's possible that circadian rhythms could play a role in fat burning as well. However, research in men speaks against this hypothesis, since exercise in the morning and evening burned the same amount of fat after an identical meal. Also, eating carbs stimulates insulin release, which in turn suppresses fat oxidation.

Does the menstrual cycle affect fat burning?

It seems so. Recall that the study under review was done in the early follicular phase, right around or shortly after the time of menses. The authors did this since a lot of other research also focuses on women in this phase. However, some research suggests that more fat is burned during the mid-luteal phase (after ovulation) compared to the early follicular phase due to higher levels of sex steroid hormones. Furthermore, since glycogen utilization is influenced by the menstrual cycle as well, further research is needed to see how fasted aerobic exercise affects fat oxidation during the luteal phase.

Given what was said above, would oral contraceptives impact the fat-burning effects of aerobic exercise in the fasted state?

One study found little difference in fat oxidation between women taking oral contraceptives and those who weren't. If there was any difference at all, it's swamped by the effect of exercising in the fasted state. However, oral contraceptive use does seem to increase the intensity of exercise needed to reach maximal fat oxidation, although it is not clear if this effect was found in the fasted or fed state.

So far you've focused on aerobic exercise. What about resistance training?

This area is less well studied, but some evidence exists for both men and women. In men, neither aerobic nor resistance exercise increases 24-hour fat oxidation in the fed state. And in women, fat oxidation is increased by resistance exercise in the short term, but not over 24 hours. This looks like the pattern seen with aerobic exercise. However, more research is needed to see if fasted resistance training affects fat oxidation.

What should I know?

The consensus is that aerobic exercise leaves the body fat-neutral throughout the day, at least if the amount of calories coming in each day equals calories going out. However, recent evidence suggests that aerobic exercise in the fasted state can actually lead to the body increasing the percentage of fat used as fuel over the course of a day, even in energy-neutral diets. Much of this evidence comes from studies in men, though. Due to several physiological differences between men and women in terms of fat metabolism and exercise adaptation, it's not clear if exercise in the fasted state would also lead to higher fat oxidation in women on an energy-neutral diet.

The study under review examined this issue, and found that women indeed do burn more fat over the course of a day when undertaking moderate intensity, pre-breakfast aerobic exercise relative to being at rest. However, this does not necessarily translate to repeated bouts of cardio affecting body fat. More research is needed to see if this effect actually translates to changes in body composition in the longer term. Ideally, future research would directly compare the effects of exercise in the fasted and fed states. ◆

Head on over to the ERD Facebook forum for some moderate intensity discussion about this study!

Credits

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