#399_ Prof. James Betts – Does Fasting Have Benefits Beyond Those Caused By Calorie Restriction

DANNY LENNON: And here we are. Professor James Betts, thank you so much for joining me on the podcast, it's a pleasure.

JAMES BETTS: Thank you for inviting me on.

DANNY LENNON: There's lots that I want to ask you about, and, in particular, a variety of different areas that you've discussed, we'll probably dip into. But to start off, specifically to talk about the concept of fasting, I think is a good one, given not only its popularity, but probably the mismatch sometimes between certain claims and the actual evidence we have. And I know your group has been at the forefront of trying to answer some of these questions. So we have this situation, I guess, with fasting where several studies have shown benefits, but often we see in the context of those, participants may have lost a degree of body fat mass, and there are changes associated with that. And so, the interesting question then comes to ponder, how much of the effects are down to weight loss or caloric deficits, and how much are separate to those, and how do we tease those apart. So, before I may be ask about the randomized controlled trial that your group recently published, from an overview level,

what do you perhaps see as the most coherent hypothesis that people have put forward as to why fasting may have specific health benefits, or, what are some of the main that are put out there?

JAMES BETTS: Yeah, so if we're asking about a hypothesis on there, the question we're asking is, how and why does it work. And I always think there's two routes you can go with that when we ask how-why type question is one is kind of why should it work, so you can be more philosophical and say, well, why would we expect this to work. And the other why-how is when we're really getting into mechanisms. So to take the first part of that, about the kind of philosophy, I mean, you'll read this in plenty of the mainstream books on how to do fasting, and they will hark back to kind of archaeological evidence and say, well, fasting is natural, and this is a natural thing for humans to do. It's unnatural for us to wake in the morning and have a chilled refrigerator full of ready to eat food. So you could say that's part of the hypothesis is that the way humans are intended to eat is not little enough, and it's long periods with uncertain food supply, fairly random chaotic food availability. And then when you get hold of food, you have larger amounts, and we know that that's true for humans relative to some of the smaller mammals that much more science is done on. We know that rodents need to eat pretty much continuously, whereas arguably, humans are designed to accommodate these longer periods without food.

So you could have a hypothesis and justify these studies and these diets based on that, or, the other side, as I said, was the how question can be how does this work mechanistically, and what is it about our bodies that expects this. And then a lot of the talk you see then is people arguing, well, you adapt your body to shift away from using carbohydrates, using fat sources, ketones as an alternative, and maybe there's health benefits of that. And certainly,

going into the trial we did, there had been an idea in recent years that perhaps even the weight loss might somehow sustain lean tissue mass is better, so that fasting might make you lose more fat and less muscle, which is, I guess, we'll come to later, isn't what we've seen at all.

DANNY LENNON: Sure. So again, before we touch on that trial ahead of going into that, and I suppose, in the formulation for potential research questions answer, at that point, what were some of those unanswered questions that you were hoping to address, or, maybe put another way, what were some of the claims you were hearing about fasting that you were either not convinced about or thought we actually don't have evidence for this yet, let's go and work that out?

JAMES BETTS: Yeah, well, nutrition is an area that I always think is just rife with myths and misconceptions. It's not like other areas of science, where non-experts just say, well, I'll ask an expert. Everyone thinks they know. So I kind of like that, that there's so many things that everybody thinks we have the answer to, or they just say, well, we know that if you fast, you're going to eat more later, and you can actually go back to the evidence when you know how to search the literature and then ask "well do we know that?" And, in fact, you find that that's a good example of saying that really isn't true that even if someone fasts in quite a substantial way, they really don't make up for that by eating more later or the next day. So yeah, there's a lot of misconceptions that you need to go back to basics and say, well, do we really know the answer to this, and fasting is a real classic area of nutrition, where there's so much we think we know, whether it's about the effect of fasting on eating behavior, whether we're thinking about metabolic effects. So off the top of the bat, people will say, well, you need to eat to kick start your metabolism, and there's some feeling that if you fast, your body's going to go into this emergency starvation mode and cut your metabolic rate. And again, these are things that if you look back into the

actual science, that's really not a clear, quantitatively important effect that we're going to see.

So I really wanted to get into some of those things, and do the trials necessary to do that, and I think the point related to that, that is helpful to get out of the way, early on in a conversation like this, is about definitions of terms. And I'm sorry if I bore anyone, always going back to definitions, I bore myself sometimes always doing this, and I know the undergraduate students know all my lectures start with saying, well, let's just define our terms before we start. So yeah, before we go into a big discussion about what fasting might do, it's always important to just discuss what is fasting, because sometimes two people will be arguing about the effects of fasting, and you come to realize that they're actually, the way they had defined fasting was so different that they don't disagree at all. So some people will say, is fasting just not eating, and, of course, we all don't eat at some point in a day, none of us eat continuously like a mouse would. So is fasting not eating or is fasting going a certain time without food such that, I mean, this would be my own personal definition then would be to start saying, well, your physiology would have to move into a fasted or post absorptive state. And definitely, I think I look through the literature and some studies on fasting supposedly, which people throw in and say, well, this fasting study showed things that disagree with that conclusion, I would look at and say, well, if people were eating 600 calories spread through a day, I wouldn't call that a fasting day, because they may not have been in the fasted state at any point in that period.

So that's an important thing I think that I wanted to get to is having clear definitions of what a fast is, and sometimes that means doing some quite extreme things. So case in point is our trial, some have criticized it, saying that this isn't the kind of fasting people would do in real life. But we weren't trying to develop a diet

book to sell a fasting protocol, we were trying to do something which is undoubtedly fasting, and then we get to see whether true fasting does what we think.

DANNY LENNON: Yeah, I think that's such a crucial point, because, again, what you're talking about here is we can be very clear on there's a certain metabolic state that is characterized when someone is truly fasting, rather than just the absence of food for an arbitrary period of time with some of these protocols. And as you were talking through that, you kind of mentioned, I suppose, three different parameters that could affect the type of fasting. You mentioned we could think about the length of time that someone spends fasting, how frequently then they go and repeat that, but then also the degree of restriction of food. So if we take some of those protocols that you might see in alternate day fasting or 5:2 diets, for example, where you said, you could have days people eating 600 calories or so, that might not necessarily put them in that same physiological state that you are trying to assess here. So I think that's really key for people to take away. And so, if we do then shift the focus specifically to the recent study that your group published – and for people listening, I will link to this in the show notes – the study is titled a randomized controlled trial to isolate the effects of fasting and energy restriction on weight loss and metabolic health in lean adults. So from that perspective, given what you've just said, James, how did you go about designing that study in terms of addressing the things you actually wanted to address based on what we just discussed?

JAMES BETTS: On one level, it's very simple what I knew we needed to do. But then, as always, the devil's in the detail, and it gets complicated. So very simply, it doesn't matter if a trial is about fasting or anything else. But if you've got two variables, A and B, that you want to isolate and test the effects of, which in this case is fasting and weight loss we want to separate out, you

need to do an experimental design, which applies them separately and in combination. And sometimes that's impossible to do with fasting and weight loss, it's very difficult to do. But that's the simple concept is we knew we needed one trial where people would fast without losing weight, one where they would lose weight without fasting, and then another way they would do both. I mean, there's many more combinations we could have had and other treatments, but that was ultimately what we wanted to do. So to do that, our group who are going to lose weight without fasting, well, that's standard dieting. So we just took the general recommendation that you'd say, a general control diet for hypocaloric diets would be cut 25% of your calories, and that's going to give you the kind of gradual steady weight loss that might be recommended and desired by people. So you might call that our control group. These people ate every single day in a regular meal pattern, three square meals with snacks, but they were going to get 25% less than they would do normally at every single eating occasion.

The second group, I guess, I deal with is the opposite, the group who were going to fast, but without weight loss. And for them, we wanted to ensure that their baseline energy requirements would be met as precisely as is possible, but we needed them to fast. And as we've just talked about, I really wanted to make sure that as a kind of first study to do this, you need proof of principle. So I didn't want to finish the study with noisy data and have people saying, well, maybe they didn't fast long enough. So what we wanted here was to have a method of fasting, which at the very least nobody can say to us that was not severe enough fasting. If there are fasting mediated mechanisms, this is going to flip the switch on, and so, we wanted a full 24 hours without food. The data that I'm aware of suggests that once people get to 16 to 19 hours, you can be confident that fasting mediated mechanisms are activated. So yeah, we wanted 24 hours at a

time, and so, alternate day fasting fit the bill there. The slight complexity there is that most people day to day think of alternate day fasting as in fast Monday, eat Tuesday, fast Wednesday, which doesn't quite work actually, because once you take sleep into account, you end up with quite variable fasting times. So we didn't define our days as Monday-Tuesday-Wednesday, we were basing it just on a turn of the earth. So at three o'clock each 24 hour cycle, so three o'clock in the afternoon you switch to the other eating pattern, and the challenge there, not for us, but for the participants is if you've gone without food for 24 hours every other day, but you need to not lose weight, then it's obvious, you're going to have to eat double for 24 hours, and a consistent observation of the participants was that that was harder than the fasting.

Those are our two groups where you have weight loss without fasting and fasting without weight loss. And then, of course, in the middle, we have our group that are going to get the combination of the two. We had a group who were fasting every other day, but only eating 50% more energy on the fed periods, which therefore, matches the first group for a net 25% daily deficit.

DANNY LENNON: Brilliant. So yeah, just to recap for people, we have those three groups of the control group, the 25% calorie deficit, the alternate day fasting without weight loss, so that's 24-hour periods without food, then alternating with feeding twice that amount, and then the alternate day fasting in a 25% calorie deficit on the net. So given that setup, it's really nicely and eloquently done. In terms of what you were expecting to see, and then maybe some of the initial results to come out, what were the, I suppose, the biggest first initial data point that you were excited by or that you thought were the most important, rather than the study?

JAMES BETTS: We had a number of primary outcomes in a study like this as a basic science study where

we're interested in mechanisms. It's not like a clinical trial where there is one outcome of survival or a certain health outcome. All of our outcomes are interrelated. So many people push you to say, what's the primary, but we had a number, since you're asking which ones I had the greatest interest in, I think, yes, I was interested to see what happened to weight loss, but particularly, the composition of that weight loss. It was very interesting to me to know, are people going to lose fat or muscle, or at least fat free mass, which we can tell using DEXA scans, which separate out bone, fat, and non-fat mass.

I actually have a personal interest in the behavioral response, I find that fascinating. So when people are losing weight, or doing any kind of diet, what's going to happen to their non-exercise activity, thermogenesis, so essentially, all the body movements and activities we have outside of our structured activity. That was interesting to me, because past studies, we and others have done, show that there's some effect of fasting on these outcomes, and then the metabolic control aspect is fascinating too. So we measured a whole range of different appetite regulatory hormones and metabolites, and it was interesting to me to understand how those things changed, both in terms of what that means as a health indicator, but also in terms of regulation, are we seeing changes in blood glucose or insulin over the time. So yeah, there was a lot of unknowns at the start for sure.

DANNY LENNON: Great. Yeah, so maybe let's start working through some of those. You mentioned there the differences in body composition, and at the outset of this discussion, you also mentioned, this is an area where various people have pointed to potentially benefits in some cases and other people you see potentially point to as a harm of fasting. So within this particular study, what type of differences did you see, if any, between body composition amongst those groups?

JAMES BETTS: As you say, there were suggestions in both directions, some arguing, like I said, earlier, based on the philosophy of it that, well, if fasting induces fat oxidation, then maybe you lose more fat, but then others saying, well, long periods without food is catabolic, and maybe you lose more muscle. So there were both perspectives out there, I have to say that by the time we came to write up this study, but when we started conducting it, those were two kind of contrasting suggestions. By the time we wrote up, I would say that the feeling generally in the field was that probably lean mass would be more lost with fasting; all those studies were not showing that by the time we published. And so, that's what we've shown, the weight loss that we observed with standard dieting, to start with a positive, a good news story is people who are not doing anything fancy are just trying to eat less at every meal, it's not a kind of clever diet to follow. But if you do that, the great news was that pretty much all the weight loss they experienced was from a reduction in body fat mass. So you don't need to invest hundreds or thousands of pounds in DEXA scanners at home; your bathroom scales, if they're showing you losing weight, you can hope that that is mostly body fat that you're losing, which is what most people are hoping to lose.

The worst news from some perspectives is then that with the alternate day fasting induced weight loss, that resulted in a similar amount of weight loss, slightly less, but the bathroom scales will be showing you a couple of kilos of weight loss over those few weeks. But unfortunately, half of that was fat, which means half was fat free mass. We can't specifically say it's muscle, that's a bit of a misconception that DEXA is measuring muscle. But certainly a large part of that is going to be due to reductions in skeletal muscle mass, and that's not what people want to hear – when they're celebrating the drop on the bathroom scales, they don't want to think that that's muscle, because not only does it mean

it's not fat you lost, it also means you're losing a functional tissue that most people would rather retain or build on. So I think that's the thing that jumped out at a lot of people is the fact that fasting might not be great for losing weight, if you're hoping to hang on to muscle mass too.

DANNY LENNON: That is a really important observation for people to look at, especially given the confusion that there's been in this area. One of the other aspects of, I suppose, the fat loss, given that we've said, per unit of weight loss, the linear dieting seems to have been more effective, because all of that was from fat loss. I know that you also looked at changes in visceral fat, and this is something that can have consequences for metabolic health. In that area, did we see differences between any of the groups?

JAMES BETTS: Yeah, it was interesting considering that would normally mirror the total drop in body fat, but we didn't see that. So actually, visceral fat was more similar, I mean, it is always worth remembering that DEXA scans are not the greatest thing in the world for measuring all of these outcomes. So I think lots of people aspire to have a DEXA scanner, and when you've spent your money on one, it's nice to think of all the wonderful information it gives you. But it's worth remembering that it's really intended for looking at bone density, and although we can get body composition data, when you're seeing small changes in particular depots of fat, you need to take that with a pinch of salt. So these were very small changes, albeit similar between groups. It is interesting though, because the visceral fat mass should, in theory, mirror the total body fat losses, and also is particularly responsive to changes in activity levels, supposedly, which we saw differences in activity, which we'll come to, but that wasn't reflected in the changes in visceral fat either.

DANNY LENNON: Just before we move away from the body composition changes, on reflection afterwards,

what did you feel were maybe some of the most likely explanations for seeing those – is it simply a function of we're having this extended amount of time without protein feeding or muscle protein synthesis and this anabolic effect, or there are other mechanisms that could also be contributing to those differences?

JAMES BETTS: The one that you first suggested there I think is K, is just a very simple relationship that a prolonged catabolic period, so a period where we're having to draw upon reserves and liberate energy, it makes sense to me that that is going to favor the loss of muscle tissue. We know that part of the response to going without food is going to be to draw upon reserves, which would include gluconeogenesis from proteins and that fasting state, especially with very prolonged and repetitive fasting can draw upon bodily protein reserves. So you know a decent percentage of our – so it could be 10 to 20% of the sugar that is then emerging from the liver to support energy requirements, because we still need blood sugars is going to be derived from gluconeogenesis of proteins which you're now not ingesting. So even if you're then doing physical activity, if you're doing resistance exercise, but not eating afterwards, you can have a net catabolic state. So I think, yeah, it's the long periods without energy, and particularly without the stimulus of amino acids arriving in the system is going to favor a net catabolic or proteolytic state. So we're losing muscle. We know that these participants in that group reduced their physical activity levels too, so they don't even get the stimulus to the muscle to actually hang on to any of its protein either.

DANNY LENNON: So on that point and something you touched on a bit earlier as well, if we think about energy expenditure, this is really interesting to consider because I think this again addresses many claims that sometimes people might have that, okay, even if we hold calories consistent, and in this case, either a 25% calorie deficit or at a maintenance level of intake, there might

still be differential impacts or benefits for certain interventions, if it has an impact on energy expenditure that causes that to change. So in relation to energy expenditure, what did you see in this particular study?

JAMES BETTS: We measured all the major components of energy expenditure. So, just as a recap for anyone who needs it, the main things we're thinking about here is resting metabolic rate, which is largely just driven by your requirements just to sit there at rest, mainly then just due to how much of you there is with a slight caveat that your body composition might change that, i.e., people who are more, a greater proportion of muscle might have a higher metabolic rate than people who have more adipose tissue. The second component would be diet induced thermogenesis, which is the energy you expend processing foods, which obviously is zero if you're fasting. And then lastly, the one that I really think is very interesting is physical activity thermogenesis. That's the one that can vary the most. Everybody focuses on resting metabolic rate and saying, well, this will kick start your resting metabolism or your resting metabolism will compensate by going into starvation mode, but we really have very, very little capacity to adjust resting metabolic requirements, they pretty much are what they are and are dictated by your body size and morphology. Whereas the physical activity thermogenesis has huge capacity – if we think about the difference between a very active day and a day of bed rest, we can clearly modify that. That was the one that we hypothesized would be responsive, because we've seen that in various other studies with less extreme fasting.

So our guess was that when people were fasting, they would restrict their physical activity levels. And so, although I think it's an interesting finding, it wasn't surprising to us to find that resting metabolic rate was incredibly stable between groups and from baseline to follow up. Maybe that is surprising given that

some of the groups lost weight here that their metabolic rate was so stable, but needless to say, we're not seeing a metabolic adaptation in that sense. The adaptation was all behavioral that when people were losing weight through fasting, they cut their physical activity levels. And as we've seen before, the tool we use is an Acti Heart monitor. The big advantage of that is that you don't just get one number of, here's your daily energy expenditure, we also get to know when that occurred, so was the individual cutting their energy expenditure in the morning or evening or in the fasting period and so on. And we also get to know the intensity. And that I think is interesting, because it tells you a little bit about maybe why that's happening. And this isn't a certainty, but I would suggest that if someone's vigorous activity is changing, that's probably something they're more consciously at least aware of, even if they didn't make the decision. So if they suddenly are expending 400 kilocalories a day extra through vigorous exercise, they probably made a conscious decision to run or go to the gym. Whereas if we're seeing a change in their low to moderate level activity, this is the more spontaneous type of movement that people are not maybe thinking about or even aware that is happening. And again, that is what we saw changing that it was a reduction in the light and moderate level activities, and mostly, during the actual fasting period, although interestingly, that was also happening on the days that they were fed too.

DANNY LENNON: Fantastic. So given that we've talked a bit about these changes in energy expenditure, body composition, then I suppose, another part of the discussion that people tend to bring up with fasting is, okay, it's not something that we're really concerned about, body composition per se, but it has a raft of health benefits, and again, they can point to various mechanisms. So in terms of some of the health markers that you looked in this particular study, I know, you looked at things like blood glucose, insulin, cholesterol, etc., can you

maybe talk about those metabolic health markers you did look at, and then what you are actually able to observe in this particular study?

JAMES BETTS: Yeah, so just to start with the health markers, we did the kind of standard raft of measures that you might go, if you went to a physician and just said, can I have a health MIT, metabolic health MIT. So we're looking at metabolites and regulators of those like insulin. And we also did meal tests, I should say, so not to downplay the workload here, if you went to your doctor, you'd get fasted values. What we're really always interested in, in our lab, is to look at the response to meals, because although we appreciate that on the NHS your fasted value is probably all that can be stretched to, we spend the majority of our time in a fat state, and you get a lot more information about the physiology by looking at that. So the data we have is for all the outcomes you've mentioned, but critically, not just fasted, but the response to a meal, and a particular thing that we are interested in our lab is a second meal response too. So it's a lot of work for the participants and for our researchers, but we do test people in their response to breakfast, and then lunch, which is an interesting carryover from breakfast.

What we found though, in this group, in this recent publication was in lean individuals, which I'll come back to, but there was no really meaningful or significant change between groups in these responses. A couple of them improved slightly, so some of the cholesterols might have reduced slightly, but ultimately, these were quite healthy individuals to start with. So it's perhaps understandable why you don't see dramatic improvements with fasting or weight loss. Just to say one more thing on that though, because there's been some critics online about the study saying, well, why the hell would you test somebody who is lean in a weight loss trial. And I think that more reflects the fact that some people who are very sold on

fasting feel that this trial is almost a slight against their worldview. But I wouldn't say that that is at all the case, because ultimately, the fasting in this trial did result in weight loss. So it was effective in that regard, but I should also say that although we describe these individuals as lean, we mustn't fall into the trap of thinking this was a study of skinny people. The term lean is just the scientific term for someone whose BMI is less than 25 kilogram meter squared. So there's plenty of people whose BMI is in the upper end of that range, who still attempt diets, who still attempt fasting, and who still would benefit from weight loss. So there were certainly capacity for individuals in this study to lose weight because they did, and to improve health, but this type of fasting or even just daily dieting didn't result in that in the short time.

DANNY LENNON: So given all that we've discussed here, what do you think are the most significant takeaways from this, because I think there's been – I don't know if there's any other really – I can think maybe of one other trial that attempted to do similar, I think it was out of maybe Leonie Heilbronn's lab where they looked at alternate day fasting. But this was very kind of novel in terms of the way you set up to try and answer this question. So from this, what do you think that has added to our understanding of this area of the literature, and what are the main takeaways from people from this particular trial?

JAMES BETTS: Yeah, I'm glad you asked that, because, in retrospect, I look back at the conclusions and maybe some of the press releases I've put out, and I feel I could have done things differently to get across that clear take home better, because so many have I think misinterpreted, they look to a study like this and think are we putting this in the box of supports fasting or in the box of don't do fasting. And happily in some ways, life isn't that simple binary. This trial wasn't conducted to tell people whether to fast or not, and I wouldn't want it to be put in

the box of is this a trial that says you shouldn't fast then. We can use the information more intelligently than that I think, and we can say, this just tells you that fasting was effective, it resulted in weight loss. It's not telling you don't fast. It's saying, what do you need to know if you're going to try that effective method of fasting. And I just want to know that, okay, so there was some weight loss from muscle, what can I do about that. So, for future studies and for future application, I would just be thinking, right, well, maybe we just need to think, let's try and get the benefits, and there were benefits of fasting, but to mitigate any of the risks, and if we look at that kind of cost-benefit ratio, we know what some of the strategies would be. Maybe just a trial I would love to do would be to do alternate day fasting with alternate day resistance exercise, and then decide whether we have the resistance exercise happening in tandem with the fasting days or when alternate days, having some protein feeding maybe at key points in the fasting days.

There's all sorts we can still do with research, but yeah, the takeaway now for the non-researchers is just to be aware of those effects; be aware that when you're fasting, you're going to have this natural propensity to cut down your physical activity levels, and that's something that you are completely in control of. So you just think, well, when I'm on my fasting days, I'm likely to just be a bit more sedentary than usual, but that's not uncontrollable for me. I can make sure I insert activity into my day on top of the fasting and get the best of both worlds.

DANNY LENNON: Thanks for clarifying all that, James. And just as you were speaking there to those differences we see in physical activity thermogenesis, and this is something we obviously don't have time to get into in depth now, but it certainly reminded me of some of the data that you would publish from the Bath Breakfast Project, a couple of studies that you did a number of years ago, where we saw that on an intraday

perspective, I guess, whether someone had consumed breakfast in the morning or had fasted until 12:00 p.m., and that led to changes in that physical activity thermogenesis across that time period or across the day. I think there might have even been differences again in the study where it was in lean people versus people with obesity. But it's just interesting to note that we're seeing impacts then on activity, like you mentioned, in some way that at least mirrors this study.

JAMES BETTS: Yeah. And when that breakfast study came out, we saw that in the lean participants, and it was such a clear finding that when they were fasting, they'd cut their physical activity levels, I really interrogated those data, because it was like, is there some issue with the measurement tool, is this, you know, it was just so obvious. Even though we'd hypothesized it, I wanted to make sure I wasn't just confirming my own suspicions. The finding look clear, and I'm really happy to say that we then replicated that finding in overweight and obese cohort, we've replicated that with pilot work we've done looking at Ramadan fasting, other versions of alternate day fasting – other groups, more importantly, have independently verified that effect, and there's correlations at a population level showing this link between eating patterns and activity. So yeah, so I was less surprised by our current study, and also kind of feeling vindicated that this has now been independently verified so much, I think we can be confident that there is a link between fasting, eating patterns and physical activity that needs to be taken into account in future research, and taken into account by anyone trying fasting diets.

DANNY LENNON: Yeah, for sure. And maybe I should just clarify for people listening, and again, I will link to the full studies in the show notes of this episode, but here we're talking about a trial where – and you can correct me if I'm wrong in this James – the morning period, one group either had more than 700 calories versus a group that fast until

12:00 p.m., and those changes in physical activity, thermogenesis, like you say, were quite stark, I think it was 850 versus 450 thereabouts calorie difference. And so, quite large, and I think what struck me there is where this kind of fits into another area that I'd just like to ask your general thoughts at the moment is we're starting to see more and more work being done on, obviously, time restricted feeding, and, in particular, seems to be a lot of interest around early time restricted feeding for some of the metabolic impacts potentially on glucose, insulin, and glycemia seems to be the main area. And this is something that, if someone wanted to, could probably add some weight in that where we're seeing a benefit maybe to eating more of that food earlier in the day, if that influences greater energy expenditure, although my question is more so, as it currently stands in the area around time restricted feeding, and specifically early time restricted feeding, what is your current sense of where we are with the human trials in the area if it's something that you've been keeping a focus on. And yeah, what are kind of general feelings around at the moment?

JAMES BETTS: Yeah, the short answer is I have absolutely been monitoring that field. It's a really emerging field. Every week, there's more time restricted eating papers coming out. It's another one where we need to watch our definitions, because ultimately the whole phrase, time restricted eating, is just the kind of umbrella term for just making sure that feeding happens at a certain time of the day. It definitely seems to be coming through as something feasible that people like time restricted eating, it's a sweet spot where it's not too extreme, it's something you can adhere to; and importantly, it does seem to have benefits. We haven't yet got studies like the one we've been talking about today to show whether those benefits are above and beyond weight loss, but the public using it, don't care about that. If it has benefits and it's doable, then all good. And yeah, my take on the emerging

literature is it does seem to be case that the fasting later in the day is better than earlier in the day. And that would be consistent – I think that's what you're getting at with this link to physical activity. Right? If you fast later in the day, and the fasting is going to reduce your activity, well, that doesn't really affect your overall energy expenditure if you're asleep anyway. So if you frontload your normal nocturnal sleeping period with the fasting, you may then not lose your activity. I mean, if you're someone who does a lot of activity in the evening, then it might be better for those people to fast earlier in the day and then eat before they train. But yeah, that's why I think it's so important that we look at the mechanisms through which fasting can affect overall energy balance, because for some people, it might be better to fast during the waking hours, and allow the kind of knock-on effects of fasting to affect your eating and your activity and your metabolism; for others, it might be more important to schedule the fast in the evening and overnight, because then it can't affect those things, and often people then wake up the next day, and they've kind of reset their hunger and their lethargy, and they can just bank the deficit from the day before and move on with a net negative energy balance.

DANNY LENNON: Yeah, for sure. And I think that's why probably up to this point, at least, to me, it seems that the strongest data in the area seems to just relate to the glycemic markers like glucose and insulin, because we have a clear mechanism there of change in insulin sensitivity or beta cell function. But when it comes to energy balance and body composition, we don't really seem to see that yet with any of these fasting protocols, which I guess is what your work is confirmed with alternate day fasting. So, James, this has been fantastic. Before I get to my final question, for people who are interested in keeping up to date with what you're doing, either on social media or work that your lab is putting out, where are some

places on the internet you'd like to send their attention towards?

JAMES BETTS: So I work as part of the Centre for Nutrition, Exercise and Metabolism at Bath. We've really just formed that Centre quite recently, but we have a website at the university, which we could link to, along with this podcast. And then, I mean, my Twitter is purely work related, so anyone who finds me on Twitter, I'll make sure that any paper from any one group is highlighted on there.

DANNY LENNON: Great. And for people listening, I'll link to both of those in the show notes, and you can go and find those there. So James, that brings me to the final question I always end the podcast on, it can be completely separate to what we've discussed so far, and it's simply: if you could advise people to do one thing each day that would have a positive impact on any area of their life, what might that one thing be?

JAMES BETTS: Immediately, when you asked it, my tip of the tongue response would be, be physically active. And then I'm thinking well, is there – if we're thinking about health, then it could be things not to do. The only thing that would be being active would be to stop smoking, if you do that already. So we'll assume they're doing that. But the more philosophical answer would just be, be nice to people. That's going to be the most important thing for all of us if everybody was a bit nicer nowadays.

DANNY LENNON: For sure. That would certainly help a lot of issues I think that we currently face. James, thank you so much. I've really enjoyed this discussion, and more than that, I've really enjoyed consuming your work and your publications for a number of years now. So this has been an absolute honor for me to be able to talk to you, and your work has certainly informed a lot of things I think I've hopefully come to understand, so I want to thank you for that, and then for taking the time to do this today.

JAMES BETTS: Oh, thank you very much.

DANNY LENNON: There we go. Fantastic.

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