DANNY LENNON: Greg Nuckols, welcome back to the podcast my man.

GREG NUCKOLS: Thanks for having me back Danny.

DANNY LENNON: So, with that the first paper that I want to turn to Greg is one you've outlined by Eddens et al from September 2017 titled The Role of Intra-Session Exercise Sequence in the Interference Effect: A Systematic Review with Meta-Analysis. Before we get into the study specifically maybe a good starting point for people might be to – obviously here we are going to be talking about concurrent training and having both resistance and endurance exercise element to that, and this whole issue around the interference effect. So just to get everyone on the same page, what is this hypothesized interference effect? How should we think about it? Where do they originate from, etc.?

GREG NUCKOLS: Yeah, absolutely. The work kind of demonstrating the interference effect dates back to the 80s with a paper by Hickson if memory serves. But essentially the interference effect is the idea that if you idea that if you only perform strength training, you are probably going to gain more muscle, gain more strength than you otherwise would if you performed a combination of strength and some sort of endurance training. So, a lot of ideas have been put forth to explain the interference effect. The most basic idea is just that you are going to be able to train harder when you are not as tired. When you are doing two different forms of training you will probably be a little bit more tired for them. So if you just had a hard cardio session yesterday, it may affect strength performance a little bit tomorrow for example. Or if they are being performed in the same day, if you do your cardio, lift weights right after, probably won't perform quite as well in the gym as he would have if you have done cardio beforehand.

So that's the most basic explanation that people put forward to explain the interference effect, maybe it's just fatigue and so you can't put quite as much effort into it in the gym. Then there are also molecular explanations. The signaling pathway that seems to do a lot of the heavy lifting, no pun intended, for aerobic adaptations starts with phosphorylation of AMP kinase and then all of its downstream targets, and with hypertrophy it's the mTOR signaling pathway. And those two pathways seem to be antagonistic to some degree so when you get elevations in AMPK signaling you tend to get decreases in mTOR signaling and vice versa to some degree.

So that can help explain the interference effect as well perhaps. And then there are neuromuscular differences as well. Just your nervous system is going to be activating the vast majority of your motor units and doing so synchronously for heavy strength training and for aerobic training rate coding is going to be lower, total fiber recruitment slightly going to be lower, just the neuromuscular effects of the training are going to be different. So that may kind of muddy with learning effects for trying to pick up and master strength exercises especially explosive ones, just because the way you would go activating your muscles is considerably different.

There's several more hypotheses to explain the interference effects but those are the main ones. In terms of kind of where the research is at, up to this point, there was a really good meta-analysis in 2012 by Wilson et al, and just kind of to summarize that very quickly, basically the more cardio you do, the smaller your gains are. I've found a negative dose response relationship with frequency, volume and I believe intensity for aerobic training and hypertrophy and strength. So basically in studies where people were doing aerobic training two days per week, the interference effects seemed to be pretty small and studies where people did aerobic training five days per week, the interference effects seemed to be pretty large. Same thing with total time spent doing aerobic training per week, etc. Basically, you lift weights, you get swell. You lift weights and you do cardio, you still get swell, but somewhat slower, and that's the interference effect. I should have just led with that. That would have been much better.

DANNY LENNON: Could have saved you some time, yeah. That gives us a good comprehensive roundup. And I suppose that brings us to this current study that we are looking at of based on what you said of where the literature has brought us to this point. What were they trying to look at in this particular study to add to that or what kind of new question were they trying to answer by doing this type of study and then maybe that might lead into what exactly the nature of the study was?

GREG NUCKOLS: Yeah, to this point, the basics of the interference effects are pretty well understood and summarized in that 2012 meta-analysis I mentioned. So now, people are looking at kind of more of the finer details. And so this was a systematic review and meta-analysis looking at the order of strength and aerobic training assuming you are having to do both of them in the same training session. So, essentially, if I do my cardio and then do my lifting versus if I do lifting and then do my cardio. Are there going to be differences in adaptations between those two training session orders? I am assuming most people listening to this probably care mostly about strength and hypertrophy, but it also looked at aerobic fitness as well. So changes in VO2 max. So this was a systematic review and meta-analysis meaning they sought out and pulled together all of the studies investigating this given question. And then pulled together their effect sizes and looked to see if there were significant differences between those two conditions. They found that their didn't seem to be all that much of a difference for hypertrophy or for measures of aerobic fitness, however doing strength training first and then cardio versus cardio first and then strength training, did seem to be significantly better for hypertrophy.

That was I guess really the only main important finding of this paper. But I think that's interesting for a couple of reasons. One, I think it kind of, to some degree, not discredits but would decrease the support of kind of the molecular AMPK and mTOR argument in support of the interference effect, and there was a study by, I believe, the researcher's name was Burklind, but 2014. They basically found that in the context of exercise, it didn't seem that mTOR and AMPK were antagonistic, so essentially, various things can elevate AMPK signaling. You have aerobic exercises and obvious one, but you are also going to get elevations in AMPK signaling if you just don't eat for example. And so it seems that in that context, like apart from training, if you are not eating and you get AMPK elevations that seems to mechanistically suppress mTOR signaling, but that 2014 paper I alluded to – and I can send that to you so you can put it in your show notes – found that in the context of concurrent training, the elevations in AMPK signaling, you would see with aerobic training didn't seem to suppress mTOR signaling to any meaningful degree.

And in this meta-analysis, if you were putting kind of all of your eggs in that signaling pathway basket to explain the interference effect, then what you would expect to see is do your strength training first, ramp up that mTOR pathway, get some hypertrophy juices following, etc., then you do some cardio, ramp up your AMPK signaling pathway, that's going to suppress mTOR pathway, and that's going to really decrease hypertrophy versus if you took the other approach, cardio first and then strength training, you'd expect to see initial elevations in the AMPK signaling pathway and then you start lifting and kind of shut that down and get mTOR ramping up and then that kind of be the predominant signaling pathway in the post-exercise period to determine adaptations. But what we saw here is that starting with strength training seemed to produce more strength and similar hypertrophy which I think kind of rains on the parade of arguing at least that that is the primary mechanism for the interference effect.

DANNY LENNON: Did you find any of the findings from this either that in some way surprised you, or if not, is there anything in the findings from this particular paper that you think have some clear implications for practice or is it more just building another piece of the puzzle of this whole area?

GREG NUCKOLS: I think the clearest implication for practice is that if you have to do aerobic training and strength training in the same session, it's best to always start with strength training if that's – okay, so just to put a caveat on that, regardless of condition and regardless of outcome measure they looked at, people improved on average. So, whether they did resistance training first and then endurance training or vice versa, people tended to get stronger, they tended to get bigger, they tended to improve their aerobic fitness. So, if for whatever reason, you've just – if you have to do strength and endurance training in the same session, and you just hate starting with strength training and you just want to start with endurance training, like that's fine, you will still make gains doing that. But if you are trying to maximize outcomes, then you are probably going to be better off starting with strength training, because you are going to go get similar endurance adaptations regardless and you are going to go get similar hypertrophy outcomes regardless, but it seems that starting with the strength training will net you larger strength adaptations. So yeah, that's just a little tweak to optimize your training.

DANNY LENNON: Yeah, and something that maybe goes beyond the scope of this particular study but maybe just asking you as what you've seen in practice with yourself and maybe others as well as just a general research on concurrent training, obviously one of the things within this study was I think they had, for the inclusion criteria that the two types of exercise modalities to be fairly close in nature, like not a big gap between them, so they were essentially done within the same session. In the more kind of real world scenario or like an ideal world scenario, if you had a client who was doing concurrent training using both modalities, are there other best practices that you've seen work particularly usefully in terms of programming in the broader sense of how to essentially get the best of both?

GREG NUCKOLS: Oh yeah, absolutely. So I am glad you asked that, because this meta-analysis was only looking at people performing both types of training in essentially the same training session. However, there's some evidence – I don't know if there's enough research yet to be worth meta-analyzing, but there's a fair amount of evidence at this point that shows that essentially you can dramatically reduce the interference effect or completely get rid of it, just by having enough time between your strength training and cardio. So, several of the papers that used that particular setup and didn't find a robust interference effect were cited in a brief review and perspective called negative evidence of the interference effect, I believe that was the title by Marak and Baglee in 2014-2015, I believe – and were actually reviewing another study looking at that specifically en masse this month with strength training and cardio performed in the same session versus separated by at least 24 hours.

And yeah, so essentially with that setup, you tend to see larger strength gains and more hypertrophy just by separating strength and endurance training by at least six hours or so. So yeah, like that's what I would personally do, that's what I would have my clients do. So, this meta-analysis kind of speaks to people who either due to preferences or just due to scheduling limitations, they just have to do strength training and cardio in the same session. But if you can do them in separate sessions, that's probably going to be the way to go.

DANNY LENNON: Awesome. We will move on swiftly to the second paper which is again a pretty interesting one. And for those listening again, this will be linked up in the show notes titled Fat-Free Mass Index in NCAA Division I and II Collegiate American Football Players. This is a 2017 paper by Trexler & Colleagues. So Greg, with this particular paper, I mean, probably the best place to start for again just to get everyone on the same page is what we are talking about when we referred to the fat free mass index and in addition to that – and this might lead into some tangent and get into more of the paper – but for those who are already familiar with that, why has this number 25 been on everyone's lips for so long?

GREG NUCKOLS: Yeah, absolutely. So, like I told you in the email, kind of leading up to this call, I mainly wanted to discuss this paper as a vehicle to discuss just how abysmally bad the fat free mass index paper that everyone cites is. So what is fat free mass index? Fat free mass index is essentially the same thing as BMI but it's only fat free mass instead of total body mass. So, BMI is body weight in kilos divided by height in meters squared. Normal values are between 18.5 and 25, overweight for BMI is 25 to 30 and then obese is a BMI of 30 plus. So that's looking at total body mass. Fat free mass index is essentially the exact same equation but it's just total lean mass in kilos divided by height and meter squared. So fat free mass index values tend to run smaller than body mass index, obviously because you have body fat as well.

And so what this paper did is they were looking at the fat free mass indices of Division I and Division II Collegiate Football Players, so for non-American listeners that would be American football, not real football. And so basically, they found that unsurprisingly American football players are pretty jacked. Yeah, that was really the primary finding. And the finding from this paper that got the most press I suppose is that a previous study by Corey, et al proposed that the highest fat free mass index someone could attain without the use of anabolic substances was 25.0 or that has been the interpretation of that paper at least. And they found that in this sample of football players who tend to be quite jacked, there were 235 of them, and 62 of them had FFMIs above 25, so more than quarter of them. And the mean fat free mass index – I need to look for it again – I believe, it was like 24.2 or something like that. So pretty close to that proposed "fatty limit". And I believe the highest one in this dataset was like 31 or something like that, so basically TLDR football players are super jacked.

And then of course, just for the findings of this paper, specifically fat free mass index tended to vary by position unsurprisingly. So, for example, quarterbacks aren't as jacked as running Backs or Titans, offensive lineman, defensive lineman and running backs and linebackers tend to be the most jacked positions in football you know basic stuff that I feel like most people would come away with if they'd watch the football game.

DANNY LENNON: I was going to make one observation when you said about how jacked these guys were, just like big like – to be a Division I Collegiate Footballer you are kind of a fairly big athlete and there was one line in just the method section where they are talking about DEXA scans and just something like for individuals with shoulders too wide for the scanning area we had to do X, Y, and Z, like that's pretty cool when you get literally too big for DEXA.

GREG NUCKOLS: Yeah, that's going to feel good.

DANNY LENNON: Yeah, you already made it then. So turning our attention to – so like you say, findings of these high levels of fat free mass indexes with these players, many of them were over 25, the average was very close to 25 and then there were a few that were extremely high, close to 31 or 32. So, that going back to the previous paper, you had alluded to in some small part of how – maybe not even the findings of the paper but how at least it's been interpreted, so what is it about this previous Corey paper that is so incorrectly either interpreted or what people take from that?

GREG NUCKOLS: Yeah, so, the Corey paper I think this was an example of a paper that was somewhat shoddy begin with and the subsequent interpretations of it have been even worse quite honestly. So, basically what they did in the study is they'd already recruited a fairly large sample, I think like a 154 or so, drug-free and drug using lifters from a couple of gyms in, if memory serves Boston and LA. And they had recruited these people I believe to study the psychological effects of anabolic steroids, but they realize like, hey, we have this data on hand, let's see if we can get anything else interesting out of it – which is a totally legitimate thing to do as long as the data you have are adequate to answer the question you are asking.

So, the reason that that caveat is important is what this paper claimed to be trying to do is propose an upper limit of muscularity for drug-free lifters. And the reason that's problematic is the way they recruited is they put out flyers at gyms in Boston and LA and basically said, hey guys, come take part in our study, we are just going to assess your body composition, ask you a few questions, we will pay you 60 bucks. So they weren't going to like hardcore bodybuilding gyms or weightlifting clubs or anything like that. As far as the methods of this paper read, they just went to just normal gyms to recruit people. And importantly, the only inclusion criteria were that people had to be at least 16 years old and to have lifted weights for at least two years. So that's your first red flag right there.

If you are looking to assess the upper limits of drug-free human muscularity, it would make sense to me that you would want to recruit people that perhaps approximate the upper limit of drug-free human muscularity. They didn't mention that a couple of the people in their sample had been reasonably successful at powerlifting and weightlifting and bodybuilding. So there very well could have been maybe 10, 12 people or so – that's just a random number, I have no idea how many, but there were a few people who may have been approaching their own muscular potential. But of the 74 drug-free subjects they had, it's a near certainty that the vast majority of them were nowhere close to their own muscular potential, much less any sort of theoretical human drug-free muscular potential. So essentially, this was just a reanalysis of some data they had on hand and the data they had on hand was not the type of data you would want to use to attempt to answer the question that they were asking.

So then the second issue with this paper is it attempted again to provide an upper limit of drug-free human muscularity and their sample size of drug-free people was 74 people, which for exercise science, like that's a pretty decent sample, that's bigger than the vast majority of people you are going to see. But the thing is, 74 people, that's a very well powered study to assess a mean and provide a good confidence interval. 74 people is not nearly enough people to attempt to define an upper limit to any human trait. So like just think about this – you go to an NBA game, the NBA tends to attract very tall people, you find 74 NBA players, you measure all of them, the tallest person is maybe 7'2". We say like, oh, that's it, humans can't get taller than 7'2". Like obviously that's idiotic. No one would do that. You go to a collegiate track meet, people run the 100-meter and someone runs in 9.9 and that's the fastest. You are going to say, like, “oh we saw 74 good-level sprinters here, 9.9 is the fastest 100-meter we saw, that's the fastest anyone can ever go”. That's obviously ridiculous. But that's essentially what they did here. They took 74, just random lifters from a couple of gyms, just looked to see how jacked they were and said, boom, that's it, that's the limit. That's not a statistically rigorous way to go about doing that.

The results were bound to be kind of silly from the get-go and then from there it kind of gets even more slapdash as we go. So that part is bad, but then where it gets ridiculous is since they recognize like hey we are probably not going to be able to see the upper border of any human trait in a sample of 74 people – which is a good thing for them to recognize – what they did is they then tried to estimate the FFMIs of Mr. America winners between 1939 and 1959. And essentially up until, I believe, 1948 or so, there weren't steroids in America, at least that we are aware of, and then up until about '53, '54, there were steroids but we don't know of them being used super frequently. Yeah, they got the FFMIs of these Mr. America winners to kind of get an estimation of what the upper limit of drug-free FFMIs were.

And so two huge issues here, huge issues is one, they took the heights and weights from a book called Super Athletes by Willoughby and I have that book and I checked it. And they don't actually provide any kind of source or documentation for it, like Willoughby just lists down the heights and weights, and just kind of have to take them at face value. So I am not sure I trust the data to begin with. But then heights and weights aren't enough, it's fat free mass index – you need to get the body fat out of the equation. So obviously, we don't have a time capsule to go back to 1940 and see how much body fat John Grimek had. So what they did is they found photographs of the Mr. America winners from around the time they won and based on photographs from like magazine covers they tried to estimate their body fat estimate to calculate FFMI. This is bodybuilding.com forum type stuff. This isn't...

DANNY LENNON: Scientific rigor right there.

GREG NUCKOLS: What is that? What even is that? So yeah, they found pictures of these guys in bodybuilding magazines from the time. So like looks like about 10% fat – and that's how they calculated it.

DANNY LENNON: That's amazing.

GREG NUCKOLS: God damn it! I still can't get over this. Like how did this get published. So anyway, that was issue number one. Issue two, if we ignore that enormous issue, in this dataset there were – so from 1939 to 1959, there were 20 Mr. Olympia winners. 13 of them had FFMI above 25, eight had FFMI above 26, three had FFMI of 27 and the peak was 28. The average for those 20 people was 25.4.

DANNY LENNON: So just based on that, given how many people have liked to cite this and talk about that number of 25, is that purely just because it's nice and convenient, it gives someone that clear distinguishing thing to say, this person is not here, this person is not, and it's a nice little narrative to go along with it. Do you think that's part of the popularity of why it's so easy for people to refer back to it or how did a paper that on the surface seems so terrible, actually get that much use?

GREG NUCKOLS: Well, I think it's one part intellectual laziness. Like you said, people like clear lines in the sand and not having to think too much about stuff, and they like yes and no versus probability. So yeah, I think it's in part intellectual laziness and one part just people not actually reading the paper. They see that like someone they like or trust or respect has interpreted the paper in a given way and then they just assume that that's correct interpretation and just roll with that instead of actually reading the paper for themselves and realizing the plethora of issues with it.

DANNY LENNON: Sweet. So with that we will start wrapping this thing up. Greg, thank you so much for taking the time out. I really do appreciate your time in all honesty and you've done a great job in bringing some daily dose of science to people's day, and I appreciate you taking the time out to do so.

GREG NUCKOLS: Thanks for having me Danny. It's always a pleasure.