# Science AMA Series: I'm Niklas Ivarsson, co-author of the recent "why High Intensity Interval Training works" paper, AMA!

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April 17, 2023

**Abstract**

Hello redditors of /r/science. I am Niklas Ivarsson, PhD student at Karolinska Institutet, Stockholm, Sweden. Yesterday you showed a great interest in our work regarding why high intensity interval training works. In the article we found that free radicals produced during high intensity interval training (HIIT) react in particularly with the ryanodine receptor, a critical calcium channel in excitation-contraction coupling. The reaction causes the channel to leak calcium from the specialized subcellular compartment (sarcoplasmic reticulum), into the cytoplasm. This causes a prolonged period of increased basal levels of calcium in the muscle cell. Increased baseline calcium acts as a signal for transcription factors important for mitochondrial improvements (e.g. Peroxisome proliferator-activated receptor gamma, coactivator 1 alpha (PGC-1α). HIIT, which is extremely intensive, causes a greater production of free radical than 'regular exercise'. This results in the 'damage' to the ryanodine receptor, and subsequent 'leak' is more severe, and last longer than after a marathon. The ryanodine receptor modification and leak can be prevented if the exercise is done with strong antioxidants. Explaining why antioxidants prevents the positive effects of exercise (Ristow M. et al 2009) A little bit about me: I have a background in biomedicine. For my master thesis I decided to leave the world of cell culture and try my best in, what to me was a great unknown, physiology. For the master project I focused on insulin signaling in skeletal muscle. From there I kind of just stuck around in the research group of Professor Håkan Westerblad. During my master I got kind of bored. As per usual with large lab groups, there are often several "unfinished" projects laying around waiting for someone to come along. One of those side project eventually led us to applying for research money, namely 'How does a muscle cell know it need to improve after endurance exercise'. We already knew calcium had to be involved somehow. Now 4.5 years later I am about to present my PhD thesis, which includes 6 (4 published, 2 waiting) different manuscripts around the subject of calcium's role in training adaptation. Tl;dr I am a biomedical lab rat who stumbled onto the discovery that free radicals produced during exercise stress the muscle cell, which teaches the it to improve for the next shower of free radicals, resulting in improved endurance. I will be back later today to answer your questions, Ask me anything! edit: I will start answering your questions around 4pm USA East Coast Time edit: ok, you guys seem really interested so I'll try and squeeze in some answers early edit: Thank you everyone for your questions. It is very late over here and time for me to go. Hope my answers satisfied your curiosity. //Niklas

the WINNOWER

REDDIT

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NIKLAS-IVARSSON R/SCIENCE

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Tl;dr I am a biomedical lab rat who stumbled onto the discovery that free radicals produced during exercise stress the muscle cell, which teaches the it to improve for the next shower of free radicals, resulting in improved endurance.
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//Niklas

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CORRESPONDENCE:

DATE RECEIVED:

I admit I don't understand this at all - are people supposed to avoid antioxidants when exercising?

And is there an ideal schedule for these intervals? I've seen people suggest everything from 15 seconds to 5 mins. Thanks.

November 08, 2015

**DOI:**
10.15200/winn.144690.01009

**ARCHIVED:**
November 07, 2015

**CITATION:**
Niklas-Ivarsson , r/Science , Science AMA Series: I'm Niklas Ivarsson, co-author of the recent "why High Intensity Interval Training works" paper, AMA!, *The Winnower* 2:e144690.01009 , 2015 , DOI: 10.15200/winn.144690.01009



chimpscod

We and the other studies showing antioxidants preventing training adaptation use ridiculous amounts of antioxidants. You are unlikely to get anyway near those concentration by eating fruit. However, I still think the current dogma that if you live an active lifestyle you have to pop pills to stay healthy is a bit ridiculous.

As for ideal schedule, I would say, use what works best for you. But, based on numbers, the 'best', although the differences aren't big, is the so called Hickson protocol. Training was 6 days a week with both HIIT and continuous training on alternate days. The HIIT protocol consisted of 6x5 minute close to VO2max on a bike, with 2 minute rest in between.

Could you explain this in ELI5 terms? It would be great if you could give practical examples. Do this: it is good for you. Don't do this because it is bad or doesn't work. Thanks.

english_major

To improve your general health, do this: be active, worst thing you can do is to do nothing.

Exercise stress the muscle. The muscle reads this stress so the next time it happens it is prepared. The greater the stress, the greater the improvements. However, be sure to give your muscles time to recover from the stress (48h). If you are interested in better endurance: train in short intervals (30s-5min) at your maximal speed, it is the most time efficient.

Don't over consume antioxidants. Antioxidants reduces the stress from exercise, which means there will be less improvements. Follow NIH guidelines for nutrient and vitamin consumption, no need to go above.

Hi Niklas,

Do you have a description of the routines studied and their effectiveness? I'm interested if specific movements had the tendency to be more effective.

Thanks.

space_monkey13

This is a really good article comparing different types of HIIT: (Bacon A.P. et al 2013)

We used the most common style of HIIT, namely repeated Wingate tests. Which is 30s maximal cycling with 7% of the subjects body weight as resistance. This was repeated 3-6 times with 4 minute rest in between.

However, as I posted to /u/chimpscod it would seem that a combination of low intensity continuous work and high intensity intervals is the "most effective".

I do intermittent fasting (up to 3 days each week) and continue to work out. It has been amazing - strength increasing and fat disappearing. Do you have any thoughts on fasting and if it acts as a stressor, like HIIT?

matt2001

There is evidence which shows that caloric restriction is very health beneficial. Prolonged fasting can

reprogram muscles a bit, although I don't have much knowledge to what and why. In the end, it wouldn't surprise me that the second law of thermodynamics apply to our body as well. i.e. if you want to say healthy, you need to balance energy intake with energy expenditure.

My tip for you is to be careful and not overdo it. Having body fat is not a bad thing. Too much, and especially located in the wrong place is the danger.

For maximal ryanodine receptor damage, and subsequent leak, was there a measurable floor level of vitamins C&E dietary intake?

I think it would be agreed that vitamins C&E are beneficial and necessary for a healthy body. Though how much intake is enough to get the greatest impact from HIIT while avoiding negative effects of vitamin defeciency?

edit:: for those below, this is discussing the least amount of these vitamins necessary to allow the greatest training effect, so the opposite of an excess. A goal of consuming less vitamins C&E to maximize training effect, but not so much as to negatively affect other bodily function.

doubleweiner

Unfortunately, we did not measure the participates vitamin C and E levels before the exercise.

However, most studies which have seen a reduces training adaptation because of antioxidants, including ours, use a very high dose. You are not going to reach those levels by eating fruits.

As per my recommendation to the others who asked similar questions, stick to the NIH guidelines for vitamin consumption. Vitamins are necessary for other essential functions. Just don't over consume them.

Does the 7 minute scientific workout qualify as HIIT?

dilirst

They don't really state any quantitative value for intensity. If the exercise raises your heart rate close to your theoretical maximum, I would call it high intensity.

In light of your findings, what further research do you believe should now be done to improve exercise recommendations to the public?

kapnkerrunch

The benefits of "everyday" activity. The more evidence and real numbers we can attach to "taking the stairs" type of activity, the easier it would be to convince the largest risk groups. The most important thing is that you do something.

Hi Niklas,

I have a question : should antioxidants ,like vitamin C or E, be taken before, during or after exercises or is it better to not take them at all? Or should it be taken "after burn effect" subsides eg. 16-20 hours after workout?

Bloomsey

If you want to take them, I would suggest some time after and not before exercise.

Also, personally I don't see the point in consuming more vitamin C and E than the current NIH guidelines.

I'm sure readers will be most interested in the benefits this training can give them, not in the causal factors that explain how it works.

What's the overall benefit that HIIT brings? Muscle strength, cardio, heart health?

I used this 7 minute workout last year and saw benefits to overall muscle growth, but I never thought I was burning much fat away or at all benefiting my ability to run a bunch.

And to show I'm not a scientist, around my workouts, should I be avoiding anti-oxidents?

mike-kt

There is evidence that HIIT is more effective than moderate exercise even for people with coronary artery disease Liou K et al 2015. The overall benefit is increased endurance. Generally, higher endurance means reduced risk for heart disease and metabolic disorders.

That 7 minute workout seemed focused on general muscle health, i.e. combination of strengths and endurance. In terms of burning fat I'm sorry to tell you that there probably aren't that many shortcuts. However, I think we have been overly focused on fat when we should be focusing on activating the muscles. There is evidence that exercise repogram the fat tissue for the better (Stanford K.I. et al 2015.

You should actively try to avoid antioxidants. The concentrations needed for any effect in muscle tissue is enormous. So just don't over consume them. Also worth mentioning: when you increase your endurance, you also increase your bodies internal antioxidant capacity.

Are there differences between a HIIT cardio workout and a HIIT weights workout? Or is it just HIIT workouts in general that are beneficial?

skuttle64

I would imagine the level of resistance. But I am not so well read up on HIIT weight workout.

The eccentric contraction is also an important component in strength training. Something you generally don't get with traditional HIIT on a bike.

I have not read the study yet but release of calcium in the cytoplasm would cause increased transcription factors associated with mitochondrial development. From a nutrition standpoint would it make sense to routinely have a high antioxidant diet, berries, nuts , and leafy green vegetables and a tums to sequester calcium intracellularly to produce the elements needed to get the most out of HI IT? It would be a jump start to the process. Likewise there are quite a few cardiac drugs that target calcium transport in the heart. Would low doses of these effectively increase mitochondrial development thus increasing metabolism?

Gallifreyggle

In order to get most out of HIIT, or exercise in general, you want to allow the production of free radicals during the exercise. So antioxidants would actually have a negative effect. However, it doesn't hurt to

make sure your body has an ample supply of essential amino acids and vitamins when the muscle recovers from the stress.

What we see is that baseline intracellular calcium need to hit a concentration threshold in order to signal for improvement. So it's not the shift in concentrationgradient, but rather hit that threshold. There is an interesting genetic mutation causing a-actinin-3 deficiency. This deficient creates a constantly higher level of baseline calcium (Head S.I. et al 2015). What is even more interesting is that the mutation is far more prevalent in Olympic endurance athletes, and almost non-existent in sprinters.

In terms of leafy green vegetables, we know if you eat them regularly, you increase calcium stored in the sarcoplasmic reticulum (Hernández A et al 2012). Having more calcium stored improves your internal signaling for contraction. If this effects the outcome of HIIT I can't say, but it does make mice voluntary run faster on a running wheel.

I'll referrer to /u/omgbiscuit awnser regarding drugs that affect calcium transport.

In terms of playing around with drugs that causes an increased baseline intracellular calcium concentration: to be continued, stay tune ;)

Hi,

Thank you for taking the time to do an AMA. I am interested in taking the other side of the debate, since I believe LISS and HIIT of are equal importance to improving health.

The mitochondrial ROS production was mea- sured with the fluorescent indicator MitoSOX Red in single FDB fibers from sedentary control mice and mice that had free access to a running wheel in the cage. The lat ter mice performed voluntary endurance training by running ~ 20 km each night for 40 d ( SI Appendix ,Fig.S12 A ). The isolated fibers were activated with elec- trical current pulses and a stimulation scheme mimicking the acti- vation pattern during the all-out cycling bouts (six 30-s periods of 250 ms tetanic 100-Hz stimulation given every 500 ms with 4 min of rest between the stimulation periods). At 5 and 10 min after the simulated HIIT exercise, the MitoSOX Red fluorescence was in- creased by ~ 200% in the sedentary control mice, whereas the in- crease was significantly smaller (by ~ 80%) in the endurance-trained mice

Do you think this and your findings that elite endurance athletes didn't have the same RyR1 fragmentation support that LISS can result in similar adaptations to HIIT?

In addition, what is the amount of antioxidants needed to take to simulate your 20mM concentration? assuming an extracellular fluid volume of 16L (12L interstitial + 4 L plasma), this would mean one would need to take **87 of these NAC pills**, and assuming 10% bioavailability, more like 870 pills to achieve the same antioxidant concentration you exposed muscle to. **Did you do a lower concentration, and find that it had a lower effect? Did you feed mice an antioxidant and find that it also had no effect?**

Thanks!

halodoze

Good question. What can be seen in the literature is that a combination of both produces the greatest outcome. However, HIIT is better than LISS when just comparing the two.

What we see with running a marathon is that it also does affect the ryanodine receptor, although not as severe. So the subsequent calcium leak last longer after HIIT than the marathon.

more like 870 pills to achieve the same antioxidant concentration you exposed muscle to

Yes, the antioxidant needed to have any substantial effect on tissue is ridicules. Ristow et al used something like 1g of Vitamin C per day, which is ~10x NIH recommendations. The point of the experiment was to answer the question "what happens if we have no free radicals". You are very unlikely to reach those concentrations via diet, especially if you are keeping it natural.

Things to also consider is that experiment you quoted. If you exercise, you improve your own antioxidant capacity.

Exercise and diet are two realms of knowledge that fall victim to a lot of misconceptions and pseudo-science.

Do you anticipate an increase in scholarly research concerning exercise and fitness? Do you think HIIT is here to stay or do you think it might be treated like a fad?

Enshaedn

I certainly hope we can increase the research into both diet and exercise. IT is quite obvious that both are extremely relevant factors when it comes to "western diseases".

The problem we currently are facing in sports science is that most research surrounds the 'what if', not the 'why'. We have known that HIIT is more efficient than moderate intensity for more than a decade. We have tons of data on which is the better protocol, does it work for patient groups etc. Which is all great, but if we are to be able to apply all of this data to a general understanding of health, we need to start asking the "why".

As for if HIIT is just a fab or not is hard to say. I personally think you should combine HIIT with prolonged low intensity training and even strength training. The skeletal muscle has turned out to be an extremely complicated tissue, so it is probably best to train it for the multiple types of usage.

Do HIIT workouts produce diminishing returns after awhile the same way doing the same lifting routine can be less effective over time even with increasing weight?

Geeoff359

Yes, this is what we see with elite athletes. As your endurance increases, your bodies own antioxidant capacity also increases. This means that the "damage" done by free radicals is reduces the better endurance you have.

I am a weight lifter and I lift 4 times a week. When should I do HIIT for maximum fat burning? Right after lifting, same day later or non-lifting days?

What training do you recommend for maximum fat burning?

Thanks.

SunSage

I don't think HIIT is going to be the most effective training for fat burning. You probably should look into a more prolonged low intensity exercise

1. There's presumably more to fitness than muscle density or power lifters would be excellent

marathon runners? Does this really replace the need for the long run, given the necessary improvements in cardiovascular performance, which result in greater oxygen provision?

2. Existing science already tells us there are two broad types of muscle fibre (fast and slow twitch). Are you seeing results in both fibre types or just one?

3. To what extent is this merely a confirmation of the existing interval training done by runners like Lydiard involving track repetitions mixing pace, fartlek training etc. In other words, how much of HIIT is marketing spin for stuff that coaches have been talking about for years?

4. How much have you learned about the way results from an important, but fairly small study on specific chemical reactions are interpreted by society and the mainstream press by this experience?

philipwhiuk

1: yes, you have a strength component and an endurance component of your muscles (white (fast) or red (slow) muscle fibers). These are not necessarily mutually exclusive, I have seen marathon runners with really explosive muscles and vise versa. For strengths training I certainly would recommend you focus some on endurance as well.

2: I really can not say if one fiber type is more affected than the other. All measurements were done with mixed. However, slow twich fiber do generally have a greater oxidative capacity and antioxidant defense, so presumably HIIT has less on an effect on them.

3: I am not really familiar with Lydiard work. But there are numerous peer-reviewed articles showing a host of different HIIT protocols are more effective than low intensity: here is a good comparison article (Bacon A.P. et al 2013). * Interval training estimate +0.5 L/min VO2 Max after 6wks
* 'conventional' (30-40 min jogging) +0.4 L/min VO2 Max after 20 wks

4: The response to this article has actually been interesting. There's a lot of interest, and people are actually quite well read up. A couple of years ago we had another article were we showed what nitrate from green leafy vegetables does to the skeletal muscles and well, the press kind of sensationalized the results a bit.

In the abstract it states the following:

recreationally active human subjects performed highly demanding HIIT consisting of 30-s bouts of all-out cycling with 4-min rest in between bouts (≤3 min total exercise time). Skeletal muscle biopsies taken 24 h after the HIIT exercise showed an extensive fragmentation of the sarcoplasmic reticulum (SR) Ca2+ release channel, the ryanodine receptor type 1 (RyR1). The HIIT exercise also caused a prolonged force depression and triggered major changes in the expression of genes related to endurance exercise. Subsequent experiments on elite endurance athletes performing the same HIIT exercise showed no RyR1 fragmentation or prolonged changes in the expression of endurance-related genes.

Don't you think this is more related to the fact that elite endurance athletes have already achieved the majority of the benefits they can get from 30 second high-effort bouts on an exercise bike with 4 minutes of rest inbetween? I've never met an elite endurance athlete that *hasn't* been doing interval workouts for years, *in addition* to lower-intensity aerobic efforts, higher-intensity tempo efforts, etc., a la Jack Daniels. It seems to me it's more likely than that they're simply at a performance level that can't be improved by *this particular interval workout*, or else elite endurance athletes all around the world wouldn't bother incorporating interval workouts into their training, which we both know is wrong.

It seems more to me like this study suggests that in under/averagely trained individuals, 30 second high-effort exercise bouts show more muscular improvements than those same bouts do in very elite

individuals. Because the elite individuals have already gained all the muscular benefits they can achieve through such a workout, so they need to incorporate interval work differently, which they've been doing for years.

Eibhlin_Andronicus

Don't you think this is more related to the fact that elite endurance athletes have already achieved the majority of the benefits they can get from 30 second high-effort bouts

yes, because the elite athletes, even though the exhaust them selves to a force depression similar to the recreationally active, simply do not produce the same concentration of free radicals. Good endurance = good endogenous antioxidant capacity. So in order to improve at that point you need to focus more on activating other metabolic signaling pathways.

Hi, I wanted to know who you wouldn't advertise this kind of training to. I understand the appeal for athletes, due to the fact that it prevent them from having to jog for hours to get the heart going, but is it better for someone starting sports after a long break, or even starting sport completely, than for exemple going to the gym, or running/walking long distance? Taking the case of someone whose goal is to simply get fitter, be it good looking or just less likely to wheeze to death after climbing 5 set of stairs. Thank you for your time, and good luck on your thesis.

Sexygrizzly

This is the interesting thing with HIIT, it is most effective for those who start out with an already low endurance. So by doing this, you can actually catch up to the well trained quite fast. For elite athletes this type of exercise isn't that impressive. They really do not see any big difference from their regular training regime.

Your paper shows that the response to free radicals changes after HIIT. What do we know about the connection between this response to free radicals and:

1. Long term health
2. Athletic performance (for example, when are the free radicals a performance bottleneck in practice?)

Thanks!

danielv134

The better your endurance is the better your internal antioxidant capacity is going to be as a consequence. So in terms of the free radicals produced during exercise, I don't think there is any negative long term health problems, but rather to the contrary. By exercise you strengthen your own antioxidant capacity.

For athletic performance there is the state of 'over training' to worry about. Which consequently is the ugly side of the calcium leak coin. There is evidence which shows that a large prolonged calcium leak is actually damaging. So there seems to be a threshold: little stress = improvement; too much stress too often = 'I give up'. That is why I recommend you give your muscle ample time to recover after HIIT.

What else are the free radicals reacting with within the cell?

Is there an increased likelihood/consistency with them only reacting with this calcium channel?

Does the level of exercise relate to the concentration of free radicals, and, assuming that this is the case, does this offer a baseline for what can be considered high intensity training?

maxillz23

What else are the free radicals reacting with within the cell?

We don't know. In all likelihood they are produced by the mitochondria closest to the sarcoplamic reticulum (SR), since there is where the greatest ATP demand is going to be at submaximal(force) exercise. The ryanodine receptor just happens to be the largest and protein in the SR membrane. But there might be other proteins affected.

Does the level of exercise relate to the concentration of free radicals

Although we don't have the strongest evidence for this, it is what makes most sense. With higher energy demand, more free radicals are going to be produced as a byproduct of oxidative phosphorylation. And the 'damage' seen is much greater with the more stressful type of exercise.

Very cool read! Thanks for doing this AMA.

My question: Looking back now at your study, what are some changes you might consider making to the experiment to improve it? Or maybe there are other burning questions now that you have your results?

BUDDZILLA

There are a couple of experiments not included in the study which I would have liked to improve. For instance, what happens if you block the muscles internal antioxidant system. We also wasted a lot of time trying to extract mRNA from stimulated mouse toes, we finally have a protocol working, but it was way to close to the deadline. Also in hindsight, the training mice and see if there is a difference in ROS production with HIIT was a reviewer question. If I had more time I would have liked to compare the trained mice with untrained mice in terms of calcium leakage and mRNA response after HIIT.

For weight loss, should I eat anything before and/or after a HIIT workout?

ln00

You really do not want to eat anything before a HIIT. After: just keep to a varied diet and follow the NIH guidelines on vitamins and nutrients.

If you want to optimize your weight loss you should really combine HIIT with some days of prolonged low intensity exercise.

Hi Niklas! Thanks for doing this AMA!

What is considered HIIT? I do 1-1.5 minute sprints and rest for a min, which I repeat for 6 times. I have seen some people do HIIT of various types and some last for 3 minutes. I have been wondering if that is too long to be considered HIIT since even at 1.5 minutes, my pace starts to wear off quickly and I am unable to keep up the high intensity.

So I'm curious as to whether there is a specific work:rest ratio to follow when we are performing HIIT workouts to experience the proper gains.

CircusManTheFirst

It's unfortunately a bit of a mess with no clear definition. In my opinion it is not high intensity if you are not over 80% VO2max/maximal heart rate. Then whether each interval is 30s or 5 minutes isn't so important.

However, the more effective styles seems to be longer intervals and shorter rest in between (e.g. 5 min with 2 min rest). But the difference in gain is quite small between the different styles I could find.

Serious question, ISE or HIIT? Why limit yourselves to high intensity only, there is significant evidence supporting moderate intensity interval exercise Do you believe your results would be relevant to MIIT, if so at what intensity would you see diminishing effects?

ReAvenger

I would say that there likely exist some either linear or sigmoidal relationship between intensity and adaptation. I can't say what really is "optimal". However, a combination of both seems to be better than either / or.

If I eat an entire box of Oreo's in five minutes is better for me than if I had taken a week to eat them?

3029064

If I eat an entire box of Oreo's in five minutes is better

I guess you'll have a very interesting bathroom experience.

1. Is there any reason simple strength training wouldn't work as well as the exercises used in the paper?
2. Do you think this interaction with calcium has anything to do with lactic acid and anaerobic metabolic buildup.

*Disclaimer; english as second language and no education in biomedicine*

ups1dedomn_1

1: The improvements from strength training generally comes as a consequence form mechanical damage during weightlifting. Whereas HIIT generates more of a metabolic stress on the muscle.

2: lactic acid no, but calcium can react with the free organic phosphate which accumulate during periods of extreme energy expenditure. This forms calcium-phosphate crystals, resulting in temporary muscle weakness.

Can you explain the effects of different interval and rest lengths? Some intervals can be 20s, 30s, 1+ minutes, etc. Same for rest periods. What effect do different lengths have?

Also, it seems like there is a lot of misinformation on the internet about HIIT. Some HIIT routines will be 30s of bodyweight squats, 30s rest, 30s situps, 30s rest, etc. I am skeptical of these types of HIIT routines because I doubt the intensity will be there. It seems like a lot of the benefits of HIIT come from the fact that it is so intense. I usually do it on a stationary bike to ensure that I can give it 100% each interval. Do these easier/less intense routines give the same benefits as a more intense HIIT routine?

IAmDavidGurney

Can you explain the effects of different interval and rest lengths? Some intervals can be 20s, 30s, 1+ minutes, etc. Same for rest periods. What effect do different lengths have?

Not a super big difference. Combination of HIIT and low prolonged low intensity seems to be the best though.

My definition of HIIT is that each interval has to be as close as possible to your VO2max (max heart rate).

Should I avoid excessive vitamin C if I want to get the best results of my training? How much is too much?

Unidan18

No, you should still take vitamin C. You need it for other processes than its antioxidant effect. Just follow the NIH guidelines, anything above that is excessive.

What common things containing antioxidants should be avoided then (green tea, wheatgrass juice?), and for how long before the workout?

Turkishfigs

There is no need to actively avoid natural products containing antioxidant. I find it very unlikely you'll reach the concentration needed to have any major effect. (we are talking in the order of like 300 oranges)

Interesting work Niklas! I think that this ties in nicely as an exercise approach that is concurrent with work already done from a nutritional standpoint, whereby high-fat diet can induce mitochondrial biogenesis through mito derived ROS-activation of CAMKII (Jain SS et al. 2014; Nature). I think this would confuse a lot of the general public, as to why our physiology can adapt similarly when perturbed by a 'healthy' stimuli like exercise, or 'unhealthy' high-fat diet. Of course both have drastic effects on influencing ETC flux and ROS-formation.

Just curious, why no direct protein (eg. western blots) quantification of mito proteins? Are you attempting to link an increase in ROS and RyR fragmentation with mitochondrial protein increase?

Also, would you agree that considering mito bio increases can hit a ceiling/capacity, HIIT vs. endurance from this perspective would be equally as effective if done over a chronic time-frame (i.e. the best is whichever people can adhere to)?

Overall, how big of a player do you think mitochondrial content is for exercise performance?

I'm currently a graduate student in Canada, and share a lab with a few exercise-driven labs. I find your research very compelling! Thanks for partaking in this AMA.

SciGuy29

whereby high-fat diet can induce mitochondrial biogenesis through mito derived ROS-activation of CAMKII

That is very interesting. Is it high-fat-low carb or "western"?

The original aim of the study was to try and find where the calcium comes form necessary to activate either CAMK or calcineurin pathways already proven to increase mitochondrial biogenesis. I did do westerns for mitochondrial proteins like VDAC and cytochrome c oxidase, but did not really see any thing happening, which isn't that surprising since we are looking at the direct effect of HIIT.

HIIT vs. endurance from this perspective would be equally as effective if done over a chronic time-frame

yes, HIIT would probably reach the point faster but eventually you would be able to catch up with regular low intensity exercise. I still think a combination of both is still preferential since you will have a greater caloric expenditure with a more prolonged exercise.

Overall, how big of a player do you think mitochondrial content is for exercise performance

For endurance I think it is the major limiting factor. Atleast to a point.

I'm currently a graduate student in Canada

good luck on your own studies :)

Hey you may be done- but if not - will this type of exercise work for weight loss? What type of cycle do you recommend?

AusterMcEwan

It will work, but not be the most optimal. I would suggest a combination. HIIT 2-3 times a week, and some low intensity prolonged style of exercise in the days between.

Niklas - thank you for doing this AMA, and congratulations on your novel findings! I am a first year Exercise Physiology PhD student and I was hoping you could tell your adviser thank you, on behalf of the entire ExPhys field.

Related to your recent findings, I'm curious as to your thoughts on the role of actively transporting Ca2+ back into the SR post Ryr leak. Theoretically, could the increased metabolic cost (ATP) of active Ca2+ transport account, at least in part, for the observed effects of your intervention?

In your opinion, what can we do to further our understanding of the effects of resistance training, aerobic training, or the mixture of both, on the human scale.

Lastly, do you have any plans to attend any conferences in the states this year? Would love to talk more over a pint.

Thank you again, all the best.

Joshua_trees

Theoretically, could the increased metabolic cost (ATP) of active Ca2+ transport account, at least in part, for the observed effects of your intervention?

Possibly. There is a study showing that basal fatty acid metabolism is up by 60% 24 h after HIIT (Whyte L.J. et a.).

In your opinion, what can we do to further our understanding of the effects of resistance training, aerobic training, or the mixture of both, on the human scale.

Ask the "why" followup questions. There is a tremendous amount of difference training papers showing

various protocols giving various improvements to various patient groups. But more researchers need to stick with it and focus on to why certain training protocols are better than others.

Lastly, do you have any plans to attend any conferences in the states this year? Would love to talk more over a pin

no plans, sorry, was at the latest ACSM in San Diego. I'll actually need to start looking for jobs soon :P

Your paper mentions that HIIT produces large amounts of free radicals that, ideally, would not be neutralized by antioxidants.

Does this mean that exercising this way could have implications as far as early-aging and/or cancer?

killedbyhetfield

No, probably the opposite. You only create a short but intense shower of free radicals. This is the stress your muscle responds to. Resulting in improvement to both endurance and the cells own antioxidant defense. So by exercising and allowing your muscle to recover you actually strengthen your defense against free radicals.

Would it be possible to develop a drug that could mimic the effects of these free radicals or perhaps target the ryanodine receptor in a similar manner? In simpler words, could this lead to a workout pill?

roybo

too be continued ;)

I just trained for and completed my first trail ultramarathon (50k, or 31 miles) following a traditional training plan that steadily increased my weekly mileage and long runs. To be honest, the training was more difficult than the race; I had to re-organize my life around training and was in a state of near-perpetual fatigue. I did incorporate HIIT in the form of speed work and hills and feel like they were very beneficial in building strength. Based on time, my overall training was 90% distance/10% HIIT.

Your research leads me to believe that if I train for another ultra I could probably reduce my overall training mileage and "Time on feet" if I incorporate more HIIT into my routine. What do you think? Am I interpreting your research accurately?

Thanks for doing this AMA and for your research. I have been a "weekend warrior" for 25+ years and am amazed at how training methods have evolved over the years based on research like your.

johnmflores

if I train for another ultra I could probably reduce my overall training mileage and "Time on feet" if I incorporate more HIIT into my routine

That's the idea. But for running such a long distance there are also other aspects to consider. Like simply getting your feet used to the constant impact of long distance running. So don't reduce your long distance to much.

What was the maximun heart rate levels you used to do your experiments?

casaboza1912

We measured around 90% of maximal at the end of both first and last interval.

My problem with HIIT studies tends to be the fact that A) they almost always compare exclusively HIIT to exclusively steady state (which is not a realistically how people train if they have performance goals), and B) they tend to be short term (and therefore can't address diminishing returns or the benefits of periodization), which can be misleading to people trying to apply their results.

Do you think that there are ways that exercise scientists can improve the studies to make them more applicable to real life, given funding and measurement constraints?

fdw3sn

The general problem when designing studies is to make sure you can make sense of the data in the end. That is why we like do design studies with few variables.

I agree on the problem with most HIIT studies tending to be short. The best I've seen went for 10 weeks and still had a linear increase in VO2max.

Our aim was to look at what happens inside a muscle after just one HIIT. We have a current study running where we are going to look at the changes in the muscle when training with HIIT.

Does this apply to untrained athletes or everyone?

I've read that hiit is more effective for untrained athletes while longer steady state cardiovascular is better for trained athletes in sports like running an rowing.

GenericUsername017

Yes, there is diminishing return as your endurance improves. So think of it as a way to "catch up".

So...all of the beverages that tout their "anti-oxidant" ingredients... could those be inhibiting the benefits of interval training?

I_make_things

Really depends on concentration. If you stick to natural products like fruit or juice you won't get the antioxidant dose necessary for any real effect beyond your GI tract.

What was the control group for this study? Just interested in what "regular exercise" was considered in contrast to HIIT and what their respective results were

Relativelygrave

Running a marathon :)

So not really "regular exercise", we just wanted something which was still energy demanding, just not as intense as HIIT.

Within the subset of Different HIITs workouts, is there a large (or slight) variance in effectiveness or is the difference negligible?

p0rt

differences are quite negligible, do what works best for you. However, a combination of both HIIT and low intensity continuous exercise every other day works the best.

I've seen mention of exercise like this contributing to faster aging. Is there any truth to this?

HangryHungryHippo

That is an old assumption based on telomere length. It hasn't really stood the test of time as more research are emerging suggesting exercise reduces some of the problems related to ageing.

Hello Niklas,

Thanks for doing this research! My questions are:

If someone has an autoimmune illness, doing HIIT coupled with antioxidants intake will still be beneficial in terms of improved cardio health, or should they steer clear of it?

Also, the free radical load seems to be high, how much antioxidants should someone with chronic inflammation take to reduce the damage by these free radicals?

Is it better to take them before or after the workout?

tookie_tookie

I really don't know much about the use of antioxidants to treat autoimmune illnesses.

The point we get to in the article is that the short, but intense, burst of free radicals is essential for muscle improvement.

I know there are some research being done on the effects of endurance and strength training on chronic inflammation, but I think it is to early to give any form of general conclusions.

Hey! Great job on that paper, and good luck in your future career :)

My question is: did you do the statistics of your paper? I am writing my second paper now (radiology), and since my mentor did stats for me last time, now I want to try my hand at it. We had an introductory course in it at uni, but that proved rather insufficient for the real thing. What is the best program currently to start (R, SPSS, Stata...) and how difficult will it be to learn the basics?

DoctorThackery

The stats we did were fairly simple since we were either comparing two groups or repeated measures. I.e. unpaired t-test or repeated measures ANOVA.

It is fairly easy to learn the basics. And with the most modern programs you just need to make sure your data is formatted correctly and know which test is most appropriate.

Thanks for doing this AMA! My main question has already been asked an is decently high up, so i'd like to ask a side question if that's alright. You mention that you've studied insulin signaling in skeletal muscle. Does that tie in at all with this? My understanding is that contraction exercises can prime the

muscles for greater energy intake. I've gained a fair bit of leg mass from doing air squats 15 minutes before cheat meals.

Fedwinn

You mention that you've studied insulin signaling in skeletal muscle. Does that tie in at all with this?

both yes and no. I was looking at ways to improve insulin sensitivity in insulin resistant muscle. What I did find (unpublished unfortunately) is basal glucose uptake is increased by ~40% 20h after extremely fatiguing an isolated mouse muscle.

After reading your article my girlfriend pointed out that she was under the understanding that free radicals are not necessarily a good thing. Is this assumption correct and can you expand on what they do? And now that you have explained HIIT, do you recommend it?

Secularnirvana

Yes, there is a strong correlation between free radicals and diseases such as cancer. However there are some major difference. First, exercise generated a short burst where as in disease is generally a chronic increase. There is also a question of which type of free radical and where in the cell it is created (still some large unknown there).

Also, the short burst of free radicals you train your body to handle increased levels of them. So by exercising, you get a better protection from future free radicals.

Niklas, do you know if free radicals somehow connected to ageing? We have a scientist here in Russia who develops a mitochondrial "upgrade" that neutralises free radicals and he says it prevents ageing. What do you think of it?

zzz0

There has been some suggestions free radicals enhances ageing. The difference is that with HIIT, or training in general, the generation of free radicals is really short. As apposed to the more chronic problems with free radicals in ageing and diseases. There you have the interesting findings of Safdar A. et al 2011. They exercise mice suffering from premature ageing and manage to rejuvenate their mitochondria.

What are the factors which would imply that Andrew Marr's stroke wasn't attributable to High Intensity Training?

Which factors could have contributed?

Not a troll, would really like to know from an expert, who is able to describe all sides of the argument.

Thanks.

sgmctabnxjs

This is the problem with underlying condition vs triggering events. Things like stroke, either if it is brain bleed or blockage have an underlying problem with the blood vessels by which the cause isn't fully understood. The stroke can then be triggered by a stressful even. But at that point it is already an inevitability.

Does the effectiveness of HIIT suffer if one is to perform it in a fasted state? Such as immediately upon rising in the morning or if following an intermittent fasting diet?

PPCLI_OR_DIE

I have no idea. I still think it will be effective

If adaptations that produce cardiovascular fitness happen inside the muscle cells, rather than in the respiratory-cardiovascular system itself - this is how I understand your results - does it follow that the benefits of HIIT are muscle dependent?

In other words, will training endurance (with HIIT or regular cardio) on a stationary bike leave your upper body "unfit", because you haven't caused the ryanodine receptor damage in your arm muscles?

TheConnivingPedant

While you would not have the same gain in your upper body. There is evidence suggesting that the positive effects of exercise spread through the body.

What's your stance on all the bro science and amateur nutritionists out there? Is there a way for us normal people to sort through all of the misinformation that's thrown our way, while still staying informed on how to eat and train? Is it even worth our time to research an optimal routine when the goal is just to stay healthy?

thehenkan

It can be a bit of a mess. In the end, as long as you stay active and have a moderate and varied diet is the most important part.

When it comes to 'bro science' with grand claims of massive effects: ask for numbers. Preferably absolute and not relative.

For one that prefers smth like tabata swings (medium weight, 20s/10s) vs running (medium pace) is there an overall benefit/deficit or it's only situational in the type of anaerobic glycolysis/aerobic conditioning ?

Also, have you seen some difference in Hiit type results ? i.e. Hiit body weight (e.g. mountain climbers) vs Hiit +weight (e.g. KB swings)

condumitru

We haven't measured different forms of HIIT.

You can take a look at this article for some comparison of different HIITs:
http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0073182

Very interesting, thanks for taking the time to do an AMA! As a runner and swimmer, I've been a slave to interval workouts (with less intensity as I age :)).

Have you explored the evolutionary aspect to your research? Does this seem to benefit human

development? Have you seen the same mechanism in other species?

OfficialBloke

We can replicate the same effect in isolated mouse muscle. I think it is a general function for all animal species.

so what kind of HIIT routine would you recommend to get this optimum basal Ca2+, & just wondering what you mean by mitochondrial improvements?

birelbirel

See my response to /u/chimpscod for "optimal protocol".

Mitochondria are the power stations of your cell. The signaling seen after HIIT increases the machinery in the mitochondria responsible for producing the energy needed to sustain repeated contractions.

So can you mimick this effect of HIIT exercise with ryanodine receptor agonists?

Are you already doing this study?

deadpanscience

There are a few studies out showing that using high concentrations of caffeine increases the oxidative capacity of isolated muscles.

I do have a study ongoing using another drug to achieve increased calcium leak. To be continued ;)

Would you refer someone to Cross Fit workouts as a form of high intensity training? I feel as if Cross Fit workouts target all of the scientific evidence behind working out but that there's a stigma behind it that prevents people from actually taking part and utilizing the training program.

maximus9966

I don't have much practical experience with Cross Fit, so I can't really say much.

In the end though, I think the most important thing is that you do something. So do what ever exercise works best for you.

If I want to lose weight, what sort of hiit plan would be best? I'd like to incorporate weight training along with cardio about five days a week--not necessarily on the same days.

biggreenfan

I would recommend a combination. HIIT 1-3 days a week and more of a low-mid intense continuous exercise the other days.

Are the anti-depressant effects from aerobic exercise the same or more for HIIT as well?

TheLegendaryTakadi

That is an interesting question. I don't think anyone has tested that. But the anti-depressive effect did correlate to PGC1a expression and endurance, so possibly.

What positive or negative effects does activation of mitochondrial transcription factors have?

Schnooks

Positive effect is greater energy capacity and greater antioxidant defense. I don't think I have ever seen a negative effect of increased mitochondria.

What did you guys define as HIIT?

2muchedu

We used repeated wingate tests. 30s "all out" cycling with 7% body weight as resistance. Repeat 3-6 times with 4 min rest in between repeats.

How does age and sex affect this?

Teachu2x

I haven't seen any major differences. Although I can't find any direct comparison either. But HIIT does work for both men and women

I went from 145kg to 95kg using a mixture of good diet, HIIT, normal endurance cardio and light weightlifting.

It took me years to get that far, but all of it works. HIIT is by far the best weightloss and stamina exercise universally provided your diet is clean. That and endurance cardio in a fasted state (i.e. first thing in the morning).

Just my own experience.

As for asking you anything, I'm on a more weightlifting intensive plan at the moment and am sticking to either 2-3 sessions of some sort of cardio workout. If my goal is strength training, am I better off with endurance cardio or HIIT?

Also I am presently isolating my cardio workouts, so at most one or two compound lifts (deadlifts and squats usually) before I head into the cardio session. Is this generally a good idea? Or could I get more effective results by omitting the weight session entirely on cardio days?

jon6

I went from 145kg to 95kg

Congratulations!

I am not particularly well read up on strength training. But if strength is the goal I would imagine focusing on weight lifting and squeezing in HIIT 1-2 times a week would be the way to go.

Hi Niklas Some how all my fat stiks to my belly, and not else where. How should i train to get a

sixpack?

flyveren

I'm suffering from the same disorder unfortunately.

What about the effects of HIIT on the central nervous system?

Th3MadScientist

I have no idea. We could not detect any problems with signal transduction in the periphery.

Sorry if I'm late to the game and somewhat "vague" (it's late in Melbourne!), but... is there any relationship between the calcium channels mentioned in your study and other recent reports that endurance athletes such as cyclists should consume calcium prior to commencing extended exercise sessions? Or are the two uses of calcium unrelated/on different orders of magnitude?

Also, as someone who unwittingly used an approximation of HIIT (single speed bike in downtown stop-start traffic) to go from fat to fit, thank you from the bottom of my happy and healthy heart for ... well, giving us all ($7x10^{9)}$ the depth and background to grok ourselves better and be better off for it.

HeathenCyclist

recent reports that endurance athletes such as cyclists should consume calcium prior to commencing extended exercise sessions

I had not heard of this. However, the calcium homeostasis inside the skeletal muscle is very tightly regulated. So I doubt taking supplemented calcium would do much to intramuscular signaling.

to go from fat to fit,

congratulation

Thank you for taking the time to come to Reddit, and interact with the people, as it were, freely sharing your knowledge. I've been planning some time to do a much more thorough read of all this recently brought to light information, but, as it has to to with HIIT, (of which I am a habitual, daily practitioner), I was curious if the calcium leaks might induce cases of Calcific Tendinitis, the cause of which is still largly a mystery, or even other such calcium deposited ailments. The last few years has seen my training regeme increased by quite a margin, and I've since had one in my left shoulder (last year), and this year in my right. After doing a cursory read of the topic, I couldn't help but to wonder if there may be some connection here.

StrangeInsight

The calcium leak we see is in to the muscle. Calcific Tendinitis is accumulating calcium in the tendons. I can't say if they are or aren't related, but it seemes unlikely. Some sort of chronic inflammation seems more likely.

I'm running my first marathon tomorrow. I get that for training (either endurance or strength) I may want to avoid excessive antioxidants, but what about for performance at an event? Would it be a good idea to try and eat a bunch of antioxidant rich foods the day before to help prevent damage to ryanodine

receptors?

Also, would consuming a lot of antioxidants the day before be useful for endurance events because they would help protect against damage to muscles caused by free radicals? As I understand, muscle fatigue after low intensity long duration events is due more to damage to the muscle rather than a failure to produce adequate ATP

o0eagleeye0o

Would it be a good idea to try and eat a bunch of antioxidant rich foods the day before to help prevent damage to ryanodine receptors?

The idea has been floated around. I honestly can't say if it will make any difference. It might be something worth studying.

This study seems flawed. 45 minutes is hardly "endurance," and could still be classified as "steady state," which is a much higher intensity. Basing it on HR can also yield subjective results.

I'd consider a proper endurance comparison to be 2 hour rides vs. your 21 minutes. And I'd use power, not HR.

Why not HR? Who says the day your "control" HR was measured, you weren't tired, or slightly sick? Who says the day you do an exercise, you aren't tired, or slightly sick (resulting in an artificially higher HR)? How do you account for HR decoupling, and its decrease as you become fitter?

1q2w3

hu? Where are you getting 45 minutes from? We compared 6x 30s wingate tests versus running a marathon.

I'd like a HIIT program comprised of everyday household chores please, 2 birds 1 stone etc. Totally serious, laundry basket stair running for instance.

argumemtatarian

How many floors? Does is take you more than 30s max speed to reach the top?

Does age factor in on the effectiveness of this training?

target51

I have no idea. But, exercise reduces age related problems.

Thanks for doing this AMA.

In my daily training I am focused on improving my time in 5k races. I haven't done any HIIT yet, but it seems I should give it a try. What interval timings should I aim for? Short 15 sec burst interspersed with 3-4 minute low intensity exercise? Or should the intervals be selected much longer? Should the total duration be comparable with or longer than the 5k time I am aiming for?

Kapede

Hi The the so called Hickson protocol seems to be the more effective I could find. It involves training 6 days a week with both HIIT and continuous training on alternate days. The HIIT protocol consisted of 6x5 minute close to VO2max on a bike, with 2 minute rest in between.

How well would this training incorporate into training for ultramarathon length (6+ hour) events? Would it serve better as a compliment instead of a main training method?

Are you familiar with the swimming training methodology of ultra short race pace training? If so, what is your opinion on it?

Thank you

ohintxla

oh, that's a hard question. I think that if you can complete an ultra-marathon in 6 hours you already have a really great endurance. So I wonder if HIIT really would be super effective. But maybe incorporate it one day a week.

Probably a bit late for this - does the leaking calcium cause any cross bridge cycles to occur? And does having damaged receptors reduce muscle power noticeably during the recovery period?

hughligen

And does having damaged receptors reduce muscle power noticeably during the recovery period?

This is the weird thing. There is fatigue in the hours following HIIT. But at 24h the muscle weakness is virtually gong. But the ryanodine receptors are severely fragmented at that time point. So we have fragmented, leaky but fully functional channels.

It's been 13 hours and I see no questions answered. What's the breakdown in layman's terms for endurance vs. weight training in HIIT?

9babydill

The little we have done on weight training doesn't show any major effects on ryanodine receptors of calcuim handling. The mechanism affected seems to be limited to the contractile proteins.

So for endurance the stress is on the signal for contraction (so many fast repetitions the cell struggles to keep up)

Strenght training puts mechanical stress on the proteins which actually generate the force.

Would an unfit/weak person aiming to change that benefit most from HIIT provided they knew what they were doing? Take two average couch potatoes with one doing HIIT and the other not - the one doing HIIT will see improvements faster?

BuffKunkka

Yes, the person doing HIIT would see the best gain

- Interval training estimate +0.5 L/min VO2 Max after 6wks
- ‘conventional’ (30-40 min jogging) +0.4 L/min after 20 wks

(http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0073182)

Does HIIT carry a higher risk of heart attack compared to lower intensity aerobic exercise?

Should people complete an "Exercise Tolerance Test" (aka Stress Test) in a medically supervised context before stepping up to a HIIT program?

vtjohnhurt

There are some studies showing that HIIT works for people suffering form Coronary Artery Disease. But yes, if you are over 40 and haven't been near a training bike since your 20s, you might want to get a checkup before going full speed.

Hi Niklas, thanks for doing this AMA! Your research looks at ryanodine receptor in the SR membrane - does the a-actinin-3 mutation affect other proteins or is it isolated to that one receptor?

threehundredandnine

Why a-actinin-3 deficienty causes increased baseline calcium is still largely unknown. There are some evidence pointing towards the sarcoplasmic reticulum caclium ATPase (i.e. the mechanism which pumps calcium back to the sarcoplamic reticulum)

I understand this research shows the effect of HIIT on fat loss and muscle gain. What about for heart health? Does it have better or worse impact on blood pressure and resting heart rate?

shireboy

While evidence is still not perfect. Those studies done show that HIIT does have benefits for people with Coronary Artery Disease (Liou K. 2015)

Not sure if this was asked already but are there any long term studies about this and the effect of the increased radicals on cellular stress, possibly leading to DNA damage, cancer, aging...?

lokizzzle

The problem is that most studies which ave looked at "long term" exposure to free radicals are done so with chronic exposure. With exercise you get a short burst, and then a recovery period.

Is it possible to get injured doing these exercises? I have hypermobility and sometimes if I train too hard I'll strain a muscle. Is it possible do do these exercises by yourself (no trainer, at home)?

bananawtf

Remember to warm-up and stretch. Also it is important you let your muscles recover afterwards. Doing HIIT every day is most likely going to lead to a state of "over training"

Can you comment about how PGC-1a and CREB interact? What PDE enzyme variants are usually involved in breaking down CREB activating cAMP in skeletal muscle? Thanks!

abelard_lindsay

I don't really know much about CREB signaling in skeletal muscle. Looking at pubmed, research seems fairly limited to hepatozytes and other cell cultures.

Hi Nikas! As a lab rat, what's your favorite kind of cheese? Also, does high intensity training before sleeping have negative effects? I'm a student and find that the best time for me to exercise is a couple hours before I sleep. How does this compare to exercising during other times of the day? Thanks!

Tennispro1213

Brie and red wine.

I don't think time of day affect the outcome that much. There will be a short period of fatigue an hour or so after HIIT.

Antioxidants prevent the beneficial effects of exercise? What about people who eat a diet high in fruits which have antioxidants like blueberries, are they not getting the benefits of exercise? Would antioxidant supplements negate the benefits of exercise?

Five_Decades

The article I linked in the description from Ristow et al used 1000mg/day Vitamin C and 400 IU/day of vitamin E. That is quite a lot. One orange has around 50mg Vitamin C.