How Fasting & Caloric Restriction Impact Health | Dr. Satchin Panda & Dr. Andrew Huberman

So there is a famous experiment that was published last year by J Takahi Islam and it came out in science and that relates to caloric restriction And we kind of started with this idea Um We started discussing that the rat experiments were done with caloric restriction and researchers gave reduced calorie consumption by 20% or 30% and get that food the rats and then subsequently mice and they all lived longer What is interesting is um in all those experiments um the researchers came and gave this bolus of food at one time whereas they are lit on fed mice or rats they had access to food all the time So they were eating all the time and then these rats uh were given 20% less And what happens is this mice or rats Then I'm going to take that less food which is restaurant now and just eat a little bit of uh lunch and then snack after three hours or snack After three hours they gobble up all that food within 2 to 3 hours maximum four hours food is gone So they're sort of on the ed diet The one meal a day Yeah they're almost like one meal a day 3 to 4 hours food is gone Or you can sit that on four hours eating or feeding and 20 hours fasting Um So then the question became well the benefit of calorie castration as we know is it due to reduced calorie or time restricted feeling or time There is a timing component to it that they are eating all of that within 3 to 4 hours And then there is a long fasting and this is a difficult question to answer because now you have to ask these poor grad students or technicians to come and split that food into eight or 10 or 15 different small persons and then give them to mice in every two hours Um So Joe Takahashi who actually published the first paper in 2017 showing that most cal restrictions I mean he used the protocol that was used by CAL restriction field Uh it actually creates a condition of time restriction So he saw that and then he went back and worked with engineers to come up with a smart kids where um he could actually tell he could program how much food is given to mice at what time of the day or night completely programmed So then he took this uh for example suppose say the ad libitum fed mice its 5 g of chow in a day And if you want to reduce calories by uh 20% then the cr mouse should get 4 g of food and it divided this into nine or 10 meals and then gave them in every 90 minutes So in this case they're eating small meals throughout day and night So there is no fasting So you can say that well this mouse actually is not getting into fasting because in every few hours is uh

getting some food and then he measured how long the mouse is going to live Um And he used um it means this is a very standard protocol People count how many mice are dying on which day and then examine them to see whether they died because they there was an accident or they actually there was a natural cause and then they calculate at the end what is the um half uh life So 50% survival because that's on an average that's a good indicator because if there is an outlier that will live for a long time then that can skew So what was interesting was the alibi and fed mice of course they live a certain number of days And then this caloric restrictor mice that never got into super fasting but kind of eating snacking throughout day and night that also lived 10% extra 10% longer So that means caloric restriction extended lifespan by 10% I've wondered about this because recently you know there's been there were a bunch of news headlines about intermittent fasting and and frankly I was frustrated Uh If you looked at one major news outlet they would say time restricted feeding affords no additional benefit beyond caloric restriction for weight loss Then an another popular press venue let's call it that same study described as time restricted feeding doesn't work And then another 1 may be someplace um even more extreme you know time restricted feeding um uh only beneficial because of caloric restriction or something like that So what you've essentially got are three different interpretations of the same data All of which are well two of which are true one of which is false in my opinion But what I think people take away from that is oh time restricted feeding isn't valuable which is not the case And I think for many people it's a convenient way to eat because at least for people like me it's simpler to designate between portions of my day when I'm eating and portions of day my day when I'm not eating as opposed to eat Portion control for other people portion control can work But all of that is related to either maintenance or loss of weight None of it deals with the potential health benefits independent of weight loss Um And so I I think that um if we can segment those out um obviously in humans it's hard to know if a given treatment or experiment is extending life because you don't really know how long people would live anyway Right Whereas with mice you have some sense of when the mortality was likely to occur So what what can we say about time restricted feeding and longevity in terms of biomarkers or in terms of any other indication that people who start and stop their feeding window at a consistent time somewhere between eight and 12 hours per 24 hour cycle are tilting the scales towards living longer as opposed to living shorter This example of this news article that you mentioned is really

interesting because that relates to Jos J Taka's study because I described that if you split calories and eat throughout the day throughout day and night then the mice leave 10% extra But if you now give mouse the same calorie restricted diet and fit them during daytime whether within 12 hours or two hours then the mice live 10% extra beyond that So 20% So ok so let me make sure I understand so that uh so that I make sure I understand if you take a certain number of calories and you distribute them throughout the 24 hour cycle it's caloric restriction the mice will live 10% longer if you however restrict that to the active cycle of the So for humans the daytime then 20% then they live 20% longer So it's not just total caloric intake and meaning it's not just important to be sub maintenance and calories for the sake of longevity it also is important as to when in the 24 hour cycle you eat those calories Do I have that Right So now that's still this story is not over because these mice were fed during daytime when they're not supposed to eat That's right So for us it would be the equivalent of being on the night shift and only eating at night But a sub uh sub maintenance calorie diet I guess is the right way to say it But when they fed mice during night time when they're supposed to eat and they're seeing this getting the same number of calories within 12 hours or two hours And the mice live 35% longer than they control 35% longer So scale to human lifespan which you know we don't know but but a 35% longer would mean that um and again no one knows But um humans now what is the average mortality in the United States Somewhere around 80 Yeah So it's around 80 It used to be 80 now reduced a little bit because of COVID but let's take 80 Ok So people are then now living somewhere between 25 and 35 years longer but I'm putting some error bars on that So that was really profound But now you pointed out um biomarker and other stuff So now if you look at any given time within that experiment and actually Joe went back and um had a separate cohort of mice very similar and so that he could take tissue samples And of course in this case you have to sacrifice the mouse And he looked for um he did a lot of molecular analysis with non markers For example hemoglobin a one c equivalent of glucose control cholesterol all this stuff he could not find anything that predicted the benefit of caloric restriction So that means in this experiment whatever we know so far the predictor of longevity none of them could predict whether this um see our only mouse which at throughout day and night that mouse is going to live less than the night fed mouse that was going to live 35 25% extra Does that mean that there are biomarkers related to longevity that we just haven't discovered yet So that's exactly So that

means what we know so far about biomarkers Uh those he could not use to predict maybe there was a lot of noise maybe he wanted he had to use more number of mice to get that because you know biomarkers I'm not going to predict In every instance there is some error What is also very interesting is if you look at the body weight and body composition of all these mice there is no difference in body weight and body composition across all these different groups all these groups So it doesn't matter when they ate provided they were sub sub maintenance calorie intake so less fewer calories than is required to maintain their weight It didn't matter what pattern of eating they were the same weight So that in many ways seems to mimic the human studies where they say look it doesn't really matter whether or not you use caloric restriction or or you start your feeding window in the morning or start your feeding window in the evening or you um or you portion control for sake of weight weight loss because you're taking a snapshot of that And then another thing with the human study that we are referring to here um that in that human study people are actually already eating within 10 hours window habitually when they selected these people to have them enroll in the study So they are already eating for 10 hours and fasting for uh 14 hours All participants had to reduce their calorie intake and they reduced by almost 25% The cr group continued with 10 hours eating window and the cr plus time restricted group had to eat the same number of calories within eight hours So it's just a two hour difference It's just a two hours difference Ok So that people I just want to make sure people can understand So in in this human study which is the one that I felt that the popular press venues all except one venue um got either semi wrong or badly wrong in terms of their conclusion that was my interpretation anyway was that either people came into the study eating basically in a 10 hour feeding window which goes back to my first question which is that most people are not eating in the middle of the night or if they're on shift work and they are then they're sleeping during the day anyway So they're eating in a 10 to 12 hour feeding window anyway So you're saying they either did caloric restriction portion control within a 10 hour window or another group within the study eight sub maintenance calories So caloric restriction cr as we're calling it the acronym cr but restricted that to an eight hour feeding window and they didn't see any difference in terms of weight loss But but it's not all that surprising right I mean if it's just a two hour difference Yeah exactly So we have done that experiment in mice and we don't see um difference in not only weight loss many other markers And I was telling you about this um Jor Taka paper

where I told you that he allowed these mice to eat within two hours or 12 hours sub caloric diet two or 12 2 or 12 Yeah that's dramatic But still he did not see change in longevity even within those two So that means um when you do caloric restriction and then at least per miles and you are within 12 hours window um that's that is giving the mice the best benefit the optimum benefit and um 23 or five or 12 per mi doesn't matter at least for longevity