# How Creatine is Disrupting a 2 Billion Dollar Anxiety & Depression Market | Dr. Darren Candow



(0:00 - 4:39)

When people think brain, when people think mood, depression, anxiety, probably the last thing that comes to their mind is creatine. But there seems to be some interesting new research happening in this area. I've got Dr. Darren Kando, who is one of the leading researchers in the world of creatine.

What is going on as far as mood disorders, anxiety, depression with creatine, and what's potentially happening mechanistically there? Yeah, it's exploded probably in the last decade. So the theory here is that when individuals are clinically diagnosed with depression or anxiety or even PTSD, there's evidence that those ailments or conditions decrease brain creatine stores. The brain is very bioenergetic and it seems to rely on or eat up a lot of brain creatine stores.

So there's some evidence to suggest that individuals that have depression, anxiety, or other similar ailments, when they consume creatine supplementation, it may offset some of the negative effects or decrease some of the symptoms of depression and anxiety, to put it a better perspective. However, please note though that those individual studies, those individuals were still on medications. There hasn't been any studies to look at in humans, creatine by itself, decreasing depression, anxiety, or PTSD.

But the theory and evidence is there and it's extremely promising, especially post COVID where I think a lot of people develop some of those mental health issues by being locked in their homes or being scared of everything going on in the world. So these are some of the areas that I think you'll start to see a lot of new evidence with that coming out. There's good evidence in road models in those areas, but with humans, it's still in its infancy and emerging, but there's a lot of potential.

I put a link down below for Thrive Market. I know this is a relevant pitch for them, but at the same time, it makes sense. There's a 30% off discount link down below.

Thrive Market is an online membership-based grocery store, and it literally is their mission to make healthier food more available for people in areas that cannot get healthier food. They really wanted to make sustainability a real thing and be able to get real good, unprocessed, and even healthier processed food options into people's hands. So that link down below is a 30% off discount link for whatever you choose.

You can fill up your grocery cart using that link. 30% off plus a free $60 gift. So 30% off whether you choose some beet chips or whether you choose siete tortilla chips instead of regular corn chips, or if you want jerky snacks or this or that.

And a lot of the times, it's going to be much, much cheaper than you would find at many grocery stores. So that link is down below. It's in the top line of the description underneath this video.

And again, 30% off and a free $60 gift. Now, as far as brain energetics and actually cognition, memory, there's some pretty decent data there, right? There is. So again, the area that we see the best results are in older adults compared to younger adults.

And then the best overall results are when the brain is stressed. So hypoxia, sleep deprivation, or if you give an individual a very mentally fatiguing task, creatine seems to improve memory or recall. And that seems to have some of the greater beneficial effects.

But we did a meta-analysis and show that memory was substantially improved in the combination of creatine in older adults, more so than in younger individuals, but primarily when the brain is taxed or stressed. And I use sleep deprivation as a very common example. Now, I mean, the brain, we always say the brain is a glucose hog, right? So there's probably very little beta oxidation really happening in the brain, I would imagine, right? Is it just strongly a heavy anaerobic environment that when you, like if I were to strain really hard mentally, I think, am I tapping into the creatine phosphate system for that task? I mean, how do you see that? Do you look at fMRI? Yeah, it's exactly as you point out.

So you still use the creatine phosphate system. There's some anaerobic metabolism, but although it is aerobic primarily, one of the interesting things with creatine is it shuttles to the mitochondria. So the theory or the mechanism with brain bioenergetics is it decreases reactive oxidative species, or think of this as inflammation in the brain, and it seems to improve mitochondrial health as well.

So just like your muscle, the brain is very similar, and that's where some of the main mechanisms. So it almost decreases stress or oxidative stress in the brain, which could translate into more health or performance benefits. Have you actually seen that measured in the brain, that there's a decrease in reactive oxygen species in the brain? It's been primarily in the rodent model, primarily in rats as well as mice, and then there's just some evidence potentially in humans looking at that as well.

Very difficult to look at that in humans, of course. You can't just be tapping into someone's live human's brain. That's right.

(4:40 - 6:10)

So I mean, with that, it's like you look at the rodent model data, and then you probably look at sort of more objective data in humans and kind of see like, okay, well, we're actually having improvements in memory, improvements in cognition. You kind of interlace that with what you see in the rodent models to kind of come to a somewhat of a hypothesis? Yeah, somewhat. And then there's a couple labs in the world that have this magnet called magnetic resonance

spectroscopy and a good colleague, probably one of the world's leaders in this that can measure brain creatine content is in Norway.

And by giving humans creatine supplementation, he's been shown that it elevates brain creatine stores. And so the theory is with depression, anxiety, or any type of neurological condition that reduces natural brain creatine stores. So if creatine can increase or sort of countermeasure that decrement, that's maybe why these populations might have some beneficial effects.

So there's a lot of promise and potential there. And again, the dosage might play a role, you probably have to take it for longer periods of time, multiple weeks, if not months, and probably a dose around 10 grams a day from a whole body perspective. But focusing on the brain seems to be very viable.

Do you tend to see and don't want to put them on the spot and think but people that eat maybe a low meat diet or vegan or vegetarian that might have lower creatine stores? Do you tend to see that manifest in the brain as well as lower creatine in the brain through that technology? Yeah, that's an excellent question. And the theory was all it must be different. You know, how can it not? So regarding muscle, yes, vegans and vegetarians have a lot less creatine in the in the muscle compared to someone on a carnivore diet or an omnivore diet.

(6:10 - 6:46)

And therefore, vegans and vegetarians respond very favorably from a muscle perspective with creatine. But the ironic thing is the brain is different. There's been a good study of a few years ago from Brazil where they actually looked at that exact question.

Females as well as males, young and old vegans compared to omnivore diets. And yes, there's huge differences from a muscle perspective. But when they look at the brain, dietary creatine intake had no effect or relevance.

So therefore, vegans had the same level of brain creatine stores compared to non vegans or individuals on an omnivore diet. So the brain is very unique. It likes to protect itself more than muscle.

(6:46 - 7:01)

So therefore, it's a totally different tissue. And that's why we think there's maybe the reason why different tissues require different dosages. Interesting.

And you said the brain can actually create its own creatine. That's correct. So perhaps it's requiring less from a supplement.

(7:01 - 7:34)

Or since it's requiring or making us more, you may require higher dosages, longer periods of

time to overcome its natural barrier or production. Interesting. And the way that I think of it is like, okay, if you have taxation on the body, that's requiring a certain level of demand from your body, then the brain might be taking a back seat to that.

Or maybe even vice versa, where it's, I would imagine that the brain probably takes a high precedence in terms of priority for the body taking care of it. Right? That's correct. And when we consume creatine, 95% is stored in our muscle.

(7:34 - 9:15)

So that means less than 5% will go to other areas of the body. And one of those areas is the brain. So that's probably why brain accumulation will take a lot longer, maybe higher dosages, because the muscle likes to take up the vast majority of dietary creatine or what we're creating in the body.

Are you seeing anything in younger adults as far as maybe cognitive performance versus maybe staving off cognitive decline? The only, in healthy children and adolescents, we actually see some beneficial effects from a performance perspective, and there's no adverse effects as well. So children, adolescents, teenage years, and young adults can benefit. But the interesting thing is in the two studies that looked at concussion, they were in young children, and it actually seemed to decrease the risk or incidence of post-concussion syndrome in those children as well.

So again, across the age spectrum, creatine seems to have some potential therapeutic effects across the wide ranges. This may seem like a very newbie type question, but you have neuroinflammation and you have different kinds of inflammation, obviously, in the body. Since creatine seems to post some potential anti-inflammatory effects in the body, the inflammation that it's potentially reducing in the body, could that cross over and potentially reduce neuroinflammation? Or is neuroinflammation really happening in isolation? No, it's their length.

So that's one of the theories, and that's how we think it can have a muscle, bone, and brain interacting effect. Inflammation from all three of those areas seems to play a role, and creatine seems to have promise in all those areas. And from decreasing neuroinflammation, oxidative stress, that's some of the most potent theories or mechanisms why we think it can have an improvement in brain bioenergetics or function.

(9:16 - 11:11)

Wow, so wow. It makes me really change my school of thought from an ergogenic aid to more of a recovery aid. Ergogenic aid, recovery, and overall health aspect as well.

It's sort of blossomed into this trifactor of things to look for, yeah. OK, so there's some interesting evidence on sleep. You can talk about that data, and obviously that can have an indirect effect on cognition.

But are the benefits potentially mechanistically? Are you thinking that they're coming from the inflammation side of things? Because right now, you can look at some pretty decent data that suggests that it's going to help if you're sleep-deprived. And we know that when you're sleep-deprived, there's usually an increase in neuroinflammation as well as a number of other things. So is that the potential mechanism there? It's 100% correct.

So when you look at a group that's had proper sleep the night before and you give them creatine or measure them, we don't see any greater effect from creatine versus placebo because the brain is probably not stressed. But when you measure them in a sleep-deprived state and you measure a TASA of memory and cognition, and then you look at the mechanisms, it seems to always come back to decreasing the inflammatory environment somehow or oxidative stress. Interesting.

And just to pivot for one second, I know we're talking about brain, but I've seen some older literature that suggests that short-term sleep deprivation doesn't necessarily affect the physical body as much as people may think, but it definitely affects that mental motor. Have you seen any literature on creatine helping the body versus the brain in times of stress and sleep deprivation? Can someone perform equally good if they're sleep-deprived but they're on creatine versus not? Yeah, there is some data that suggests it has some small muscle performance benefits by being able to engage in more exercise even when you're sleep-deprived. But as we talked about, the vast majority seems to come from the neck up, more of a cognitive memory perspective.

(11:11 - 12:01)

That's so wild. So at the end of the day, is there a dosing strategy for the brain given that you might need more to get into the brain? So there's only about a handful of studies that have looked at this directly. And when you look at all the studies, and if you take the studies that looked at depressive populations or anxiety on medication, it seems to be that on average, 10 to 20 grams a day for multiple weeks is required to get an increase in brain content, which could lead to some of these beneficial effects.

So on average, it's maybe 10 grams a day for at least four weeks before they start to get some beneficial effects over time. You may get an acute effect on brain creatine content, but to lead that into performance or health effects, it takes multiple weeks. So we propose longer, higher dosages as needed for brain overall health.

(12:02 - 12:22)

I've seen a lot of things floating around Instagram that'll talk about even one, two gram doses. And I've always been questionable about those, especially because they specifically talk about for the brain. But I haven't, and I know there is some benefit to just two, three, four grams per day, low dose, but it sounds like for the brain, I mean, you really need to be getting it up there a little bit more.

(12:22 - 15:28)

Yeah. And we think because geez, if the majority is going to your muscle and maybe now bone, maybe there's hardly anything left for the brain. So that's why you need to take a lot more.

And again, the blood brain barrier really restricts what's coming in. So if the blood brain barrier stops uptake, there's not a lot of transporters in the brain. And of course the brain makes its own, you may need a lot more to get in those little areas or to accumulate to have some beneficial effects.

So overall 10 grams or more seems to be a viable dose for bone, brain and muscle perspectives. So if someone is like super deficient in creatine, then I would imagine that at least as far as the body's concerned, even a low dose might make an impact for them because they're super low, but it sounds like the brain is still kind of operating a little bit in isolation, creating its own. That's a hundred percent correct.

So the lower they have in the amount, if they have some inborn illnesses or errors in creatine metabolism, vegans, vegetarians, or most people are adopting a plant-based diet, they're going to have a lot less coming into the diet. So now they need to rely on what's being produced in the liver as well as the brain. And again, the brain is a little bit different than the muscle is sort of is not reliant so much on the diet.

It sort of makes its own. So that could have some implications as well. The other argument is someone on a carnivore diet, people say, I'm not going to respond to creatine.

I'm like, well, we know that from a muscle perspective, but we have no idea about a carnivore diet or a pure meat diet with a lot of dietary creatine on bone or brain. And that needs to be looked at from a research perspective. Yeah.

Well, and additionally, I mean, a carnivore diet, that's maybe eating a lot of chicken and fish might not get as much as if they were saying, you know, eating tremendous amount of red meat. That's a hundred percent correct. Yeah.

So it's very kind of difficult and how much you're training, right? Like a lot of people that are into that kind of diet are also training pretty hard too. So there's a lot of different kind of questions there coming back kind of just directly to how the brain would function. I mean, first of all, how is creatine actually made in the brain? I know this might be a little bit nerdy and it might be something that goes over my head, but I mean, how is it? I mean, okay.

I know we can manufacture it in the liver. I know we can get it from our food, but how is it being made in the brain? Yeah. It's identical to what's the processes that start in the kidney and made in the liver.

So basically you have two amino acids, arginine and glycine. They sort of come together and hold hands through an enzymatic reaction and they form a compound called guanidinoacetate.

And then guanidinoacetate actually will leave the kidney, travel to the liver and combines with another amino acid, methionine, and they combine to form creatine.

So it's not an elaborate process. It takes two enzymes and three amino acids to form together. And that actually is identical to what's happening in the brain.

So the interesting thing is from a muscle perspective, it's the kidney and liver that sort of do the work, but the brain has its own unique ability to do that as well. And how much does the body produce per day, say in the liver versus the brain? Right. So excellent question.

On average, about one to three grams is produced naturally in the average 70 kilogram human per day. The brain we think is a little bit less that's produced or a little bit more depending on the individual. So there's more variability in the brain compared to what we think is happening in the kidneys and liver.

(15:29 - 16:02)

Wow. So at the end of the day, when you look at creatine for the brain, so what I'm hearing is there's no real way to say, okay, I'm going to have a high cognitive demand today, so I'm going to take more creatine. That's not going to necessarily.

So using it as sort of a nootropic in an acute setting is kind of misleading. It is. Unfortunately, it doesn't give you that instantaneous boost that we would all hope, especially if you know a day that you're jet lagged or sleep deprived.

So it is an accumulating effect. And again, it accumulates a lot slower in the brain than it does the muscle. So if this is something that the person is considering, they need to just sort of take it and be patient.

(16:03 - 16:18)

You get a whole body perspective. It's going to take a lot longer time to probably produce significant results in the brain compared to what we might think in the muscle. Perfect.

Well, as always, keep it locked in here, my channel and Dr. Kando, where can everyone find you? Probably the easiest is at Instagram at Dr. Darren Kando.