Jason Anthony: Welcome to Proto, a new podcast that explores the frontiers of medicine. I'm Jason Anthony.

Sarah Angler: And I'm Sarah Alger.

Today. We'll explore what we know so far about the effects of pot smoking on the teenage brain and what new research may have to tell us.

Eden Evans: What she really showed for the first time is that kids who use cannabis have trouble acquiring new information. And that's the job of school.

Sarah Angler: That's Eden Evans of Mass General Hospital talking about a new study that should be of great interest to school administrators and parents too.

Jason Anthony: And we'll meet a woman with type one diabetes who felt limited by the therapeutic options available to her, so she and her husband have created what they call an artificial pancreas by hacking existing technology.

Dana Lewis: So with diabetes, there are a lot of innovations that are coming out through traditional clinical trials, but it takes a really, really long time for them to come to market. And the diabetes community to be honest, is really fed up with waiting.

Jason Anthony: Stories, news and commentary from the frontiers of medicine, welcome to Proto.

Sarah Angler: For our listeners who are new to Proto, Our first order of business should be an introduction. I'm sitting next to Jason Anthony, who is the current editor of Proto Magazine.

Jason Anthony: And next to me is Sarah Alger, who is a former editor for Proto, and currently the Director of the Russell Museum at Massachusetts General Hospital. Proto was published by Mass General to bring a broader public awareness about what's happening in medicine.

Sarah Angler: And we cover those frontiers wherever they happen, at top research hospitals in the United States and around the world.

Jason Anthony: Not just at Mass General.

Sarah Angler: Yes, but sometimes at Mass General. We have an editorial board of researchers and clinicians there, many of whom have been working with the magazine since it's start 11 years ago.

Jason Anthony: And as a result, we have a good relationship with a lot of the physicians and researchers on the MGH campus, many of whom are on our editorial board, and they often lead us to fascinating research happening at MGH.

Sarah Angler: And that was the case with our first segment today, two researchers from the Center for Addiction Medicine at Mass General Hospital found a new way to study a most puzzling and important topic, how cannabis affects the developing brain.

Jason Anthony: About 38% of Americans have tried marijuana, according to a recent Gallup poll. And for many, the experience is a kind of coming of age, an experiment. And you might say that cannabis policy in the United States is also in a try anything stage. After decades of decriminalization and medical use, a handful of states are now trying something new, full legal recreational use. The financial side of that story has been making headlines. Last year, the revenues for legal cannabis in states like Washington and Colorado was $5.4 billion. By 2020, four years from now, the number's on track to be almost $22 billion. And those numbers are driving part of the conversation about what happens next with cannabis in the United States. But of course health concerns, that's another part of the story, a big part. The Vermont Legislature, for instance, is considering legalizing marijuana for recreational use. And they're asking questions like, does cannabis have long-term effects, which we, the state will have to pay for?

How addictive is this substance? And what does it do to the brain? Another important question about unintended effects, what happens when cannabis gets into the hands of teenagers? Our guests today are Eden Evans and Randi Schuster from the Center for Addiction Medicine at Massachusetts General Hospital. Eden Evans is the Director for the Center and the Cox Family Chair in Addiction Medicine at Harvard Medical School. Eden, thank you so much for being with us.

Eden Evans: My pleasure.

Jason Anthony: And Randi Schuster is a neuropsychologist who's recently launched a pioneering study to look at the effects of cannabis in the teen brain. Randy, welcome.

Randi Schuster: Thank you so much for having us.

Jason Anthony: So I want to read something from the RAND report that was just commissioned for the Vermont Legislators who were thinking about one of these kinds of laws, basically saying that persistent cannabis use is associated with small, but meaningful, long-term impairments in cognitive functioning, but the possibility remains, the report says, that the associations are partly or wholly spurious.

Eden Evans: We certainly need more research, but the data that we have so far of longitudinal studies does indicate that persistent, heavy use is associated with a decline in cognitive function, a decline in IQ. And what Randi's study really seeks to do is to put in place an experimental design, which will allow us to draw cause and effect conclusions.

Randi Schuster: What we're hoping to do with this project is enroll kids who use and don't use marijuana at local high schools in the Boston area, and we're incentivizing some of them to stop smoking for 30 days with the idea of looking at the time course of cognitive recovery when kids stop smoking. So the question is, we do believe that marijuana hampers cognition, but the question is for how long? So our kids who are smoking on the weekends up to par for their trig test on Thursday, and that's the question we really hope to address with this project.

Jason Anthony: Let me ask you about that experimental design. It's got to be challenging to sort of approach a high school with this idea that we'd like to answer this very important question of what cannabis does to a child's brain? How do you set up a study that answers that question, but doesn't put the children themselves at risk?

Eden Evans: Randi designed this brilliantly, I think, in which that she'll take a large number of kids, whether or not they smoke pot. So participating in this study does not imply anything about your drug use. And so one group will be people who don't use pot who we monitor over time, and that'll be the control group. And then those who do use pot will be randomly assigned to receive payment for quitting or no payment for quitting. So no child will be encouraged to use cannabis, but half of those who do use any way will be paid to quit for a month, which we don't think will be harmful.

Randi Schuster: Another key part of this is of course the parents. So we consent all of the parents before any of the students are enrolled. And it says very clearly in the consent form that we are not sharing any of the information that the student provides during the course of the 45 day study visit with them. So parents need to be okay with that. But I think that's really important so that the kids feel comfortable talking to us and sharing openly with us their experiences with marijuana and with other behaviors that might get them in trouble with their parents.

Jason Anthony: We're talking about effects on the childhood brain, on the learning brain. What ages should these effects of cannabis, this inability to sort of pick up, and learn and process information, how long is the brain in that stage?

Randi Schuster: We know that regions of the brain that might be important for learning and these higher order cognitive abilities continue to develop well into the third decade of life. So we're really thinking that earlier use, again, confers risk for more vulnerability, but that the developing brain might extend well into at least probably late 20s, mid to late 20s.

Jason Anthony: So what are those impairments? Is there a research trail on what you might expect to find?

Randi Schuster: So what the literature seems to suggest most consistently is really speaks to impairments with memory. But myself with Dr. Evans and Dr. Jody Gilman here recently published a paper suggesting that those impairments in memory, that's again most commonly stated in the literature, is probably driven more by a learning deficit rather than a retention deficit. So memory in the way that we traditionally think about it, that it seems to be the broken link in that chain, we think is more in how kids in code information and how they learn information, not so much their ability to hold onto it.

Eden Evans: So Randi's paper that it will be coming out very soon, I think is very important. And it was very important to school administrators, because what she really showed for the first time is that kids who use cannabis have trouble acquiring new information. And that's the job of school is to learn new information, and then remember it, and apply it and all of those things, but first to learn new information. And what she showed was that that was where the deficit is.

Randi Schuster: Which is why we think it's really important that we're looking at this question in high schoolers, potentially middle schoolers, because that really seems to be where kids are taking the biggest hit, no pun intended.

Eden Evans: They're the most vulnerable. The younger and adolescents people start, the more vulnerable they appear to be to cognitive impairment caused by cannabis exposure.

Jason Anthony: As I was sort of preparing for this interview, I looked at the town where the high school is, and I think the third results was a Yelp page that said the best 10 cannabis clinics in, and then the name of the city, which was an interesting sort of result to get. I think it speaks to the fact that really cannabis culture has gone from something that is behind the dumpster in schools to Yelp and the state legislature. What do you see as the result of more relaxed laws around cannabis around the country?

Eden Evans: Yeah. Well, I think that cannabis has gone from a grassroots push to a corporate for profit business. And so those Yelp pages are sponsored and there's much money to be made from marketing an addictive substance. And what that will drive is far increased exposure for kids. We know that we have laws for that alcohol is only allowed for people over 21, and we've been not very good at enforcing that and having people under the age of 21 not be exposed to alcohol. Same for tobacco. So as you're advertising the product, that's against the law to advertise, say cigarettes and beer to minors, but you advertise to the adults and you get the kids for free because the kids want to be adult-like.

Adolescents want to be like adults. And so this is going to drive use. So we hear a lot about addiction to illicit substances, cocaine, et cetera, but the substances that cause the largest public health impact, that cause the most death, and early death and illness are legal substances. So alcohol and tobacco. And so shifting from, as you say, in the shadows to being listed on Yelp and becoming legal, you will increase the use of the substance, and to the degree to which it's use causes harm, you will increase the reach of that harm through our population.

Jason Anthony: Randi, I have one last question for you. You're working face-to-face with these kids now. What do they feel about this research? Are they excited to be a part of it? Are they worried? What messages are they getting? And is that changing?

Randi Schuster: Yes to all of those questions. So the kids that we've been working have been just awesome. They've been really delightful to work with. And we've been open and honest about kind of where we stand about the potential risks and dangers of marijuana use. But I think they feel excited to be a part of a project that is really relevant to policy questions today. They're confronted with it on the news and pop media just as much as we are. So I think that the reception has been much better than I expected.

Jason Anthony: Eden and Randi, thank you so much for joining us.

Randi Schuster: Thank you for having us. This was fun.

Eden Evans: It's our pleasure.

Sarah Angler: So what I find really fascinating is just how willing these kids are to be helpful in a study like this. I'm really surprised by that.

Jason Anthony: Yeah, it is surprising. One of the other things that we found really interesting, one of the reasons that we gravitated towards this story, in fact, was the way that this study created a way to actually capture teenagers who were using marijuana. Obviously you don't want to give teenagers cannabis and then test them and their abilities. But this is so cunningly constructed that they've invented a way to invite kids into the conversation, invite kids into the research and to really get their feedback.

Sarah Angler: And they're a population that is not talked about very much.

Jason Anthony: No. You hear an awful lot about cannabis laws and the progress of decriminalizing these substances, but what you don't hear about is the halo effect, that when it's sitting around the house, teenagers are going to pick it up. When it's legal in the community, somehow teenagers are going to get their hands on it. And if there are harms for these teenagers, then really we need to be thinking what those might be before these laws become very widespread.

Sarah Angler: It's fascinating stuff. And as you mentioned, you can read more about that research in the feature Pot and the Teen Brain, which you can find on our website, protomag.com.

Jason Anthony: I'm Jason, Anthony.

Sarah Angler: And I'm Sarah Alger. And you're listening to Proto.

Jason Anthony: Sarah, the idea of DIY medicine, do it yourself medicine, it's been an idea that we've talked about at Proto Magazine for years. How would you describe to our listeners DIY medicine?

Sarah Angler: I always understood it as patients taking things into their own hands, striking out on their own.

Jason Anthony: Right. When patients maybe look to fill the needs that drug makers or device makers haven't filled for them, right?

Sarah Angler: Yeah. And as I remember, sometimes it goes badly and sometimes it goes surprisingly well.

Jason Anthony: It seems like the history of medicine is filled with lots of unsanctioned experiments. Now let me try that bark, or let me put that berry in my mouth and see what happens.

Sarah Angler: Right. And when it works, hopefully medicine moves forward with it.

Jason Anthony: So we recently published a feature, The Accidental Innovator, about a number of these breakthroughs.

Sarah Angler: It turns out that a number of good treatment ideas start with frontline doctors and patients themselves. And we sat down with one of these innovators in the studio.

Jason Anthony: Dana Lewis has type one diabetes. That means her pancreas doesn't produce enough insulin, which is a chemical that regulates the glucose in her blood. So the glucose in her blood gets really easily out of whack. Dana, like many of the millions of other type one diabetics in the United States, needs to monitor her glucose. And for that, she depends on a medical device. These devices are pretty cutting edge. The one that Dana uses sits underneath her skin and it beams out information about her glucose levels every few minutes. But the device didn't do everything that Dana wanted, so she and her husband, Scott Lybrand, took matters into their own hands. They began to develop something they somewhat jokingly called DIYPS, a do it yourself pancreas system.

The two began to connect the information from her existing devices to automatically regulate Dana's glucose levels, making a kind of artificial pancreas. The project eventually led to something called OpenAPS, an open source platform that would allow other users to modify their own insulin devices. Dana and Scott, welcome.

Scott Lybrand: Thank you.

Dana Lewis: Thanks.

Jason Anthony: Dana, a number of years back, you had a dream about your diabetes and it wasn't a good one. Can you tell us about that?

Dana Lewis: Yeah. I had a dream about three years ago that I woke up in the middle of the night and suddenly felt like there was something wrong. My first thought was that somebody broke into my apartment, but there was no movement. It was just pitch black, and still and silent. And I gradually realized that maybe it was my blood sugar and I needed to test my blood sugar since I have type one diabetes. But I couldn't roll over and test my blood sugar. I felt paralyzed in the bed. Again, completely silent, completely still, but I was gradually feeling like something was really, really wrong and that I needed to drink juice on my bedside table, but I couldn't roll over and get it.

And so I gradually realized that if I wasn't able to achieve rolling over and getting to the juice box, that I was potentially going to die in my sleep. Thankfully I woke up and that was just a dream, a really, really realistic dream, but it kind of is my worst nightmare. And it's a reality that many people with diabetes face, is the potential that even if you do everything right and take the best possible care of yourself, you could still potentially pass away in your sleep or end up passing away due to the complications of diabetes.

Jason Anthony: And this then led you and Scott, who was your boyfriend at the time, but who's now your husband, this led you to sort of think about your monitoring device in a different way. Is that right?

Dana Lewis: Yeah. So I use a continuous glucose monitor, or a CGM, and that reads a blood sugar reading every five minutes from a sensor on my body to a receiver, which is great because it means I don't always have to prick my finger and get a blood glucose reading that way. And the device does have some alarms. If your blood sugar drops below a certain point or passes above a certain high range, it'll alarm. But the alarms weren't loud enough for it to wake me up in my sleep. And so as Scott and I talked more and more about diabetes as we got to know each other and I was teaching him about this, he asked the same question everybody else does, which is, well, why can't the data from this device go on your phone or go on your computer, and then maybe that would make a louder alarm and that would wake you up? But we didn't have a way at the time when we first started dating to make those louder alarms.

Jason Anthony: And so you came up with a way, is that right? As I understand it, you sort of hacked the data stream from these devices and you made it do what you want.

Dana Lewis: Yeah. And that's a really short hand way to look at it. But it's a longer story than that, in that we didn't actually hack the device. We actually found somebody on Twitter who shared a picture of the fact that he had gotten the data off the device of his son's device. And we reached out to him and asked him if he would share his code, and he said yes. And so with that code, we were able to get the blood sugar reading off in real time and use that first with a computer, and later with my phone to make louder alarms.

Jason Anthony: Is it fair to say that when you sort of decided that you wanted the data coming from your medical device, you found a world of other people who are sort of involved in that same work?

Dana Lewis: There were a couple of people out there who had ideas or had done different things, but it really never took off. But with the power of social media and people sharing so freely open source what they had done and what they had accomplished, it really enabled us to all get together as a community and build off one another's projects and each other's successes. And that's really what I think enabled this to help so many people so quickly.

Jason Anthony: And one of the things that it's led to, as I understand it correctly, is the DIYPS, which stands for the do it yourself pancreas system.

Dana Lewis: Well, DIYPS is actually what we called that louder alarm system jokingly, just because we wanted to name it as a thing. So we called it DIYPS. But what's cool is within a year, we actually managed to close the loop and allow it to automatically adjust the insulin levels on my insulin pump overnight while I slept. And that's what we call the DIYPS Closed Loop, but we decided to make that open source. And so what people often hear about is what we call OpenAPS, the Open Artificial Pancreas System, which is the open source iteration of that year, year and a half of work that Scott and I did to first create those louder alarms, build a predictive algorithm, and then ultimately close the loop so it could automate insulin delivery in our sleep.

Jason Anthony: So you mentioned two terms there, one was close the loop, and the other was open source. I wonder if you can talk about those a little bit more?

Dana Lewis: So closing the loop, a person with diabetes needs to test their blood sugar, and that might be with a finger stick and a meter. In which case you get the number, and you have to check and see how much insulin you've already given, think about how much food is in your body and what you're going to be doing for the next amount of time. And then with all that information, you can actually make a decision and then give yourself an injection. Or if you're like me, use an insulin pump. So closing the loop is about automating that decision-making process.

So getting the data from the CGM, automatically tying that in with data from your insulin pump about how much insulin you have, running a prediction algorithm to say, what is your blood sugar going to be and what action do you need to take? And then issuing a command to say, give more or less insulin than is being given currently right now in order to adjust what the blood sugar is going to be in the future, over and over and over again all while you're sleeping so you don't have to wake up and take action.

Jason Anthony: And the second part of that was open source. Now open source, as I understand, it means that it's maybe a coding language that anyone can can understand and change.

Dana Lewis: Open source means that the code is publicly available. It's on GitHub. So if somebody wants to come and review the code, they can. If somebody wants to use the code for themselves, they can. If they want to take it and tweak it or build upon it, they can. And that's what it means, is it's openly sourced so you can actually look under the cover and see what the code is and what it would be doing if you were going to run a system of your own.

Jason Anthony: I should share with our listeners that we're talking to you, you're in Seattle, and you're in that strip of where all of our technological companies are, sort of Seattle, and Portland and San Francisco. Scott, I think you actually were working in that tech industry. Is sort of being tech savvy, is that a prerequisite for doing this work?

Scott Lybrand: Definitely not. I did come at this from a background in network engineering. I wouldn't consider myself a programmer. Having decided that we wanted to do something like this, I knew that it was possible. But all of the skills that I needed to know to make it happen, I pretty much picked up as I went along. So we've seen this in a large number of cases. There are currently now about 50 individuals who are using their own versions of the OpenAPS, Artificial Pancreas System. And every one of those people had to build it themselves. They had to assemble all the hardware components. They had to install and configure all of the software. And a large number of those people actually started with very little technical ability.

Jason Anthony: Now I notice on the website where you talk about the DIYPS, there's also a hashtag, and that's #wearenotwaiting. What's that all about?

Dana Lewis: Well, it's this very point that living with diabetes is very challenging. Like I said earlier, even if you do everything right, you can still have bad outcomes, whether it's just a bad 15 minutes because you feel bad or something longer. And so with diabetes, there are a lot of innovations that are coming out through traditional clinical trials and through traditional manufacturers, but it takes a really, really long time for them to come to market. And the diabetes community, to be honest, is really fed up with waiting. And so this hashtag came out of a meeting two years ago by not us, but another group of people who had the same motivations of let's spur manufacturers to move faster, but let's do everything we can as individuals and as the community. And that's what this really is about. But Scott and I have really embraced it. There's artificial pancreas and closed loops that are going to come out in 2017 or 2018. But when we started this in 2013 and 2014, we didn't want to wait any longer, and so we didn't.

Jason Anthony: Have you had any response from the companies that manufacture these devices? What do they think about this?

Scott Lybrand: We actually have talked to with both of the companies that make the continuous glucose monitors and the company that makes the insulin pumps. And in all cases, they have been very supportive of us as individuals doing whatever is best for us using their devices. But more importantly, they've all come around to really appreciating that we play an important role in advancing medical device innovation and the regulation around that.

Dana Lewis: These companies in a lot of cases have their own closed loop artificial pancreas devices in clinical trials. They're going to come to market. It's just a matter of time. But what we're seeing is through our efforts, conversing with the FDA and showing the relative safety of a really basic device, the FDA has a lot more knowledge going into reviewing these new cutting edge products that are going to come from the companies and come out to market.

Jason Anthony: So I have to ask, how is your health today?

Dana Lewis: My health, just like it was when I started, was great, but the difference is it's a lot easier to achieve the outcomes I want to, and it takes less time and energy to do the diabetes stuff. So I can actually go hiking, and go running, and work and live the life I want to without diabetes taking away as much time as it would otherwise.

Scott Lybrand: And she can sleep all the way through the night. That's been a huge difference as we progress through the system, as we've built it. We started out with trying to make louder alarms and trying to wake up at night to make sure that the blood sugars could be kept in range. And as we progressed towards a closed loop, and now that we've completely closed the loop, we found that pretty much every night, the system can regulate the blood sugar all by itself without any help from a human. And so, Dana and I can both sleep through the night.

Jason Anthony: Dana and Scott, thank you so much.

Scott Lybrand: Thank you.

Dana Lewis: Thanks for having us.

Jason Anthony: If you want to hear more about Dana and Scott's story, go to protomag.com and read our feature about accidental innovators. You can also learn more about Dana and Scott's work at diyps.org and openaps.org.

Sarah Angler: Thank you for listening to the launch of the Proto Podcast. We hope you'll join us again. You can find us on iTunes or wherever you get your podcasts.

Jason Anthony: In our next episode, we'll look at the medical journey of transgender kids. Pediatricians, endocrinologists and a host of other medical professionals are grappling with some of the thorny issues around children and gender.

Sarah Angler: And I'll speak with Mass General Psychologist, Nancy Etcoff, about the history and psychological secrets of the white coat.

Jason Anthony: Until next time, join us at protomag.com, or follow us on Facebook or Twitter. And thank you for listening.