

WEBVTT

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NOTE Confidence: 0.8856081366539

00:00:04.050 --> 00:00:10.910 Welcome to a series of net casts brought to you by Yale University.

NOTE Confidence: 0.930757641792297

00:00:11.600 --> 00:00:36.840 Most addictive drugs come with a combination of pleasant and unpleasant effects. Robert Mallison wants to understand exactly how cocaine produces that mixture in the human brain in hopes of developing better treatments for addiction. This is Colleen Shaddix for the Yale Office of Public Affairs and communications talking with Doctor Mallison about how that work is progressing. So tell me specifically what you're trying to learn.

NOTE Confidence: 0.927197515964508

00:00:37.430 --> 00:01:08.680 Well, you know for a long time, I've been impressed how some individuals who are exposed to a drug of abuse like cocaine experience it as a love at first sight experience an overwhelming pleasant effect, with little or no downside or negative effects. Well, I've talked to other people who've done and experience just the opposite that they found it intensely unpleasant or dysphoric and it struck us that maybe one of the factors that contribute to whether somebody is at risk for going onto addiction.

NOTE Confidence: 0.913351058959961

00:01:08.680 --> 00:01:41.330 Now the chronic use and abuse of the drug so if you gain all the pluses and none of the minus is all the more reason to keep going So what do you want to know more specifically about how those pluses and minuses lighting up different brains? Well, you know we're taking a convergent approach. I guess using a variety of different methodologies were relying on some of the clues. We've gotten from basic science research in laboratory animals about the ways in which drugs influence the brain the way genetics influences the ways animals, either prefer or don't.

NOTE Confidence: 0.928674817085266

00:01:41.330 --> 00:02:11.620 Prefer a drug and taking some of those clues and bringing them into humans. So we're using a pharmacologic approach looking at the way patients. People who use cocaine actually respond to the drug. We're using genetics based on some of those animal clues looking at genetic variation that mimics that variation we see in animals that influences their responses and then we're using some state of the art research tools that allow us to peer inside the brain noninvasively to get a sense of what neurochemical factors.

NOTE Confidence: 0.923454523086548

00:02:11.620 --> 00:02:42.570 Are associated with positive and negative effects of the drug and are those pet scans. Those chips cans. Positron emission tomography? Thank you very much and can you tell me a little bit about yells capacity to do that you know we're really fortunate here at Yale. We have probably one of the world's leading if not the leading pet center its head by Rich Carson and they have a wonderful staff of talented radio chemists radio physicists Technical Support staff and they enable us to do these.

NOTE Confidence: 0.933382391929626

00:02:42.570 --> 00:03:12.840 Rare opportunity type studies looking at neurochemicals in the brain that are present in oh. Gosh, nanomolar I guess infinitesimally small levels in the brain in particular, a particular neurotransmitter receptor, a dopamine receptor in the brain that is thought to underlie very much. The addictive properties of cocaine and what if you been able to learn so far well. We're just at the start of these studies, but based on some clues from these genetic studies in animals.

NOTE Confidence: 0.929660737514496

00:03:12.840 --> 00:03:47.850 We have a hypothesis that people who are going to respond positively to drugs experience them as pleasurable are going to have very low levels of these dopamine D2 receptors and and more specifically those dopamine. D2 receptors are like a light switch they can exist in an on state or an offsite and using some very clever radiotracer is the pet center has helped to develop we can look for the first time it just specifically the receptors in that on state. The state that we think is going to dramatically influence whether somebody experiences, these effects as pleasurable orp.

NOTE Confidence: 0.944192349910736

00:03:47.850 --> 00:03:54.870 Positive or unpleasant and negative so if you could somehow figure out how to flip that switch.

NOTE Confidence: 0.921205818653107

00:03:55.570 --> 00:04:26.060 Absolutely so we have some clues from clinical studies in humans that have shown that a medication disulfiram medication used to treat alcoholism. For many years. Turns out to be affective, but mildly so in cocaine users people had presumed. It was because there was a lot of comorbid alcohol use in the cocaine addicted population. But some subsequent studies by Kathy Carol and others here at Yale have gone to clearly show that disulfiram works in cocaine users who don't drink alcohol.

NOTE Confidence: 0.928416430950165

00:04:26.060 --> 00:04:56.390 At all, and so the mechanism of disulfiram actions a mystery to us, but one of the things that we suspect strongly as its influencing the state of these D2 receptors whether they exist in this honor off form and if we can confirm that in some of our studies in humans, then that

might lead to the development of more selective and effective medications actually for the treatment of the disorder so pet scans must be incredibly important in developing medications. They very much are I mean?

NOTE Confidence: 0.932443857192993

00:04:56.390 --> 00:05:29.300 We use them in academia, they're very much utilized now by industry, an industry collaborations between our pet center specifically aimed at trying to develop better medications to treat not just neuro psychiatric disorders, but a whole range of medical conditions now. You started out on this path with a \$15,000 pilot grant from the Yale Center for clinical investigation. What have you been able to leverage that into you know that's a great great point? We actually were fortunate enough to get a sort of a seed money to start some of this work.

NOTE Confidence: 0.919832348823547

00:05:29.330 --> 00:06:00.040 Seed money from the YCCI that actually was generously matched by an equal contribution from the L pet center and then using that money. We were able to collect some preliminary data what we would call feasibility data show that we can do this work here at Yale and we can recruit the subject. So we can do the brain scans in them and we can see some encouraging results and in the current era of federal funding the mainstay of most of our research. One can't get large scale grants to really underwrite this research in the absence of such preliminary data.

NOTE Confidence: 0.917595326900482

00:06:00.150 --> 00:06:33.520 So fortunately with that preliminary data. We were actually successful in getting a larger grant to grant that was part of the stimulus funding that will actually now help us for the next 2 years conduct. This work in a more definitive way. We hope now that's true even for somebody like yourself a scholar with some reputation. You couldn't just salute. Lee reputation only goes so far at a certain point, scientific review panels want to see not just do you have a good idea and are you a good person but what's the evidence that this idea is really likely to be the case.

NOTE Confidence: 0.940079092979431

00:06:33.520 --> 00:07:04.270 You've treated people with cocaine addiction does that play a role in motivating you in your research. Oh, absolutely I mean, the the dream. The goal for all of us who see people who suffer with this is to find a way to more effectively alleviate their suffering addiction is just a huge public health problem that impacts everybody from society to families to loved ones to of course, the individual that's most severely affected themselves and the goal is for us to develop better treatments.

NOTE Confidence: 0.929194569587708

00:07:04.270 --> 00:07:36.960 That will help everyone in that regard because for most of the history of treating it's it's just been really behavioral right?

That's all I mean, I think the mainstay of our treatments. Currently absolutely have been behavioral for addiction and the good thing is that we do have some behavioral interventions that work and work very well. But we also know that there's large large numbers would dare to say maybe a majority of addicted individuals that are left Unhelped by the best treatments. We currently have and so we really do believe in there's evidence for that now in the fields of alcoholism.

NOTE Confidence: 0.93749463558197

00:07:36.960 --> 00:07:58.420 Opiate addiction nicotine dependence that medications are likely to help us that will likely play a major role in us being able to help people get back on the road to leading better lives again. Thank you. That was doctor. Robert Mallison, talking about his research aimed at developing new treatments for cocaine addiction.