Welcome to the Huberman Lab Podcast,
where we discuss science and science-based tools
for everyday life.
I'm Andrew Huberman,
and I'm a professor of neurobiology and ophthalmology
at Stanford School of Medicine.
Today, we are discussing MDMA,
sometimes referred to as ecstasy or molly.
MDMA stands for Methylene Dioxymethamphetamine.
That's right, you heard the word methamphetamine in there.
And MDMA has properties similar to methamphetamine,
but also properties that are very distinct
from methamphetamine.
Just as a side note, methamphetamine
is a commonly used drug of abuse.
It is an illicit drug,
and it produces some of the greatest and fastest increases
in the neuromodulator dopamine
of any available drugs on the street or in the clinic.
And believe it or not, methamphetamine is prescribed
as a prescription drug in some very limited clinical uses.
MDMA, Methylene Dioxymethamphetamine,
has properties similar to methamphetamine
in that it powerfully promotes the release of dopamine,
and it is a stimulant.
And yet it also powerfully controls the release of serotonin,
and in doing so makes MDMA a distinct category of compound
from either classic psychedelics like psilocybin or LSD,
which largely work on the serotonin system,
and tend to produce mystical experiences.
And it's also distinct from pure stimulants,
such as methamphetamine,
because MDMA, by producing big increases
in both dopamine and serotonin,
acts as what's called an impathogen.
It actually can increase one sense of social connectedness
and empathy, not just for other people, but for oneself.
And in that way,
MDMA is commonly used as a recreational drug,
but also is now being tested
and is achieving incredible early results
in clinical trials for its use as an impathogen
for the treatment of PTSD in clinical therapeutic settings.

I want to be very clear that at this point in time,
June 2023, MDMA is still a schedule one drug.
That is, it is highly illegal to possess or sell
in the United States.
And today we are going to talk about some of the path
of legality that's underway.
We are also going to talk about the history of MDMA
and why it became illegal.
And we are going to talk about the key difference
between recreational use and therapeutic use
and the important components of the studies exploring MDMA
in the clinical setting for the treatment of PTSD.
So during today's discussion,
we will talk about what MDMA really is,
how it works at the level of neurons,
which brain circuits it activates and deactivates.
And in doing so, you will come to understand
why it is so exciting as a treatment for PTSD.
Well, you will also of course talk about the results
of these clinical trials using MDMA
for the treatment of PTSD.
They are incredibly exciting.
In fact, the field of psychiatry has never before seen
the kind of success in treatment of PTSD
with any other compound that they are seeing and achieving
with the appropriate safe use of MDMA.
And when I say appropriate,
that means in conjunction with nine therapy sessions.
So this is an area that really deserves some time
for us to discuss.
Because again, there is a distinct difference
between the recreational and the therapeutic use of MDMA.
We will also talk about the toxicity of MDMA.
This is a very important issue
because many of you have perhaps heard that MDMA
quote unquote puts holes in your brain
or kills serotonin neurons or kills dopamine neurons.
And indeed MDMA because of its similarity to methamphetamine,
which is highly neurotoxic,
MDMA can be neurotoxic.
However, there are ways to use MDMA therapeutically
that avoid its toxicity.
And yet there are still questions about its toxicity

and its long-term effects both after acute use,
meaning just one to three times,
as well as chronic use,
meaning people who have taken it many, many times.
So we'll talk about the spacing between sessions of MDMA.
We will talk about dosages.
We will also talk about things that people do
and that can be done to offset
some of the potential toxicity of MDMA.
So by the end of today's discussion,
you will have a thorough understanding
of what MDMA is, what it isn't,
what is known about what it does,
what is known about what it doesn't do,
as well as some of the still outstanding questions
about MDMA that remain to be resolved.
Before we begin, I'd like to emphasize that this podcast
is separate from my teaching and research roles at Stanford.
It is, however, part of my desire and effort
to bring zero cost to consumer information
about science and science-related tools
to the general public.
In keeping with that theme,
I'd like to thank the sponsors of today's podcast.
Our first sponsor is Helix Sleep.
Helix Sleep makes mattresses and pillows
that are the absolute highest quality.
I started sleeping on a Helix mattress over two years ago
and since starting to sleep on a Helix mattress,
I've had the best sleep of my life
and that's because the mattress is tailored
to my unique sleep needs.
Everybody has unique sleep needs
and if you go to the Helix website,
you can take a very brief two-minute quiz.
We'll ask you questions such as,
do you tend to sleep on your back, your side,
or your stomach?
Are you somebody who tends to run warm
or cold during the night, et cetera?
Perhaps you don't know the answers to those questions.
That's fine.
You can simply put that response

and Helix will match you to a mattress
that's ideal for your sleep needs.
This is so critical because sleep is the foundation
of mental health, physical health, and performance
and when we are sleeping well and consistently,
everything in life goes that much better
and when we are not sleeping well consistently,
everything suffers.
There's a ton of science to support those statements.
So if you're interested in upgrading your mattress,
go to helixsleep.com slash huberman,
take their two-minute sleep quiz
and they'll match you to a customized mattress
and you'll get up to $350 off all mattress orders
and two free pillows.
Again, if you're interested,
you can go to helixsleep.com slash huberman
for up to $350 off and two free pillows.
Today's episode is also brought to us by Roka.
Roka makes eyeglasses and sunglasses
that are the absolute highest quality.
The company was founded by two
all-American swimmers from Stanford
and everything about Roka eyeglasses and sunglasses
were designed with performance in mind.
I've spent a lifetime working on the biology,
the visual system and I can tell you
that your visual system has to contend
with an enormous number of different challenges
in order for you to be able to see clearly.
Roka understands those challenges
and has designed their eyeglasses and sunglasses accordingly
so that you always see with perfect clarity.
Their eyeglasses and sunglasses were initially designed
for sports performance
and as a consequence, they are very lightweight,
which is great.
They also won't slip off your face if you get sweaty.
However, even though they were designed
for sports performance,
they now also include a lot of styles
that are designed to be worn to work,
out to dinner, essentially recreationally

so that you could wear anywhere.
If you'd like to try Roka eyeglasses or sunglasses,
go to Roka, that's R-O-K-A dot com
and enter the code Huberman to save 20% off your order.
Again, that's Roka R-O-K-A dot com
and enter the code Huberman at checkout.
Today's episode is also brought to us
by HVMN Ketone IQ.
Ketone IQ is a ketone supplement
that increases blood ketones.
I know most people are familiar with
or at least have heard of the so-called ketogenic diet.
It's used for weight loss,
it's used to control epilepsy,
it's used for mental health reasons.
However, most people, including myself,
do not follow a ketogenic diet.
Nonetheless, increasing your blood ketones
can improve the function of your brain
and the function of your body
and that's because ketones are a preferred use of fuel
for the brain and body.
So even though I follow an omnivore diet,
that is I'm not in a ketogenic state,
I use ketone IQ to increase my blood ketones
prior to doing preparation for podcasts
or writing grants or doing research,
as well as prior to workouts,
especially if I wanna work out fasted,
I'll take some ketone IQ to increase my blood ketones,
which gives me a lot of energy during workouts
or during bouts of cognitive work,
even if I haven't eaten in the preceding hours.
It really increases my focus and my energy levels.
If you'd like to try ketone IQ,
you can go to hvmn.com slash huberman to save 20% off.
Again, that's hvmn.com slash huberman to save 20%.
Let's talk about MDMA.
MDMA or ecstasy is a fascinating compound.
And I say fascinating from the perspective
of its chemical structure, which is highly unusual.
I say fascinating because it has an incredible set
of subjective effects in terms of how it makes people feel

and it has a fascinating history.
So let's just briefly start with the history of MDMA.
MDMA was synthesized by the drug company Merck
in the early 1900s, but it actually was never applied
to any particular clinical use
and it wasn't really explored much
in any laboratories at all.
And then it was later rediscovered
by a guy named Alexander Shulgen,
who was a bit of a renegade drug chemist,
who was designing different drugs
for the purpose of understanding
their subjective effects on humans.
So there's a long history of Shulgen designing drugs.
He was after all a chemist
and then taking those drugs himself.
And then if he liked the effects of a particular drug
or rather if he thought that it had
potential clinical utility, he would give it to his wife.
Then she would give him her notes about those drugs
and then they would share them with their friends.
And it was a small group of friends
who consisted of therapists and physicians.
So this was a really underground kind of operation.
It was technically not illegal when it started
because MDMA wasn't illegal when it started,
but over the several decades
that Shulgen and his wife and this group
were doing this kind of exploration,
MDMA did become illegal and he fell under,
well, let's just say scrutiny by the DEA.
Now, here's the important thing to understand
about MDMA and its history.
First of all, MDMA is a synthetic compound.
As far as we know, it does not exist anywhere in nature.
So unlike similar compounds, such as mescaline,
because MDMA and mescaline are very similar
in their chemical properties
and to some extent their subjective properties.
Unlike mescaline, which can be found in the plant kingdom,
or LSD, which comes from ergot or psilocybin,
which of course can be found in magic mushrooms.
MDMA is a unique chemical in that, again,

as far as we know, only exists in its synthetic form.
It is human made.
And as we get into the chemical effects
and the subjective effects of MDMA
a little bit later in the episode,
I think you'll understand why it is such a unique
and to some extent exciting compound
from the perspective of clinical treatment.
Put differently, there's really no other compound
that we know of in nature
or in the pharmaceutical industry shelf
or options of drugs that are prescription drugs
that produce the kinds of effects that MDMA does.
And by the way, if you're interested
in the story of Alexander Shulgen
and the drugs he synthesized
and the group that he built up to take these drugs
and try them and actually had several members of this group
using these drugs in therapy with their patients
for a long period of time, both before and after MDMA
became illegal.
There's a wonderful book called PECOL
that stands for P-I-K-H-A-L.
PECOL is the title of the book,
which Shulgen wrote, which describes his discovery of MDMA.
I confess it also describes the synthesis of MDMA.
And for that reason was a book
that for a long time was not available
but is now available again in audible form
and in printed form.
PECOL stands for phenylethylamines.
I have known and loved.
Phenylethylamines is the category of drug
for which MDMA belongs to.
And it's a long book, but a very interesting one,
both from the perspective of understanding
the history of MDMA and what MDMA is
and the effects that it produces.
But it's also an interesting book
because it will teach you a lot about
the history of the pharmaceutical industry,
the war on drugs in the United States
and the interaction between illegal drug exploration

and drugs for clinical treatment of psychiatric challenges.
So right now this is a very important issue
because MDMA is currently granted breakthrough status,
which means it's now something that scientists
and clinicians can study if they have authorization
to do that.
It is, as I mentioned earlier, still a schedule on drugs.
So it's illegal to possess unless you are one of these scientists
who has been granted permission to study it
in the clinical setting or the laboratory setting.
And right now we are on the cusp of MDMA becoming legal,
but again, it is not yet legal.
And this is something I'm going to touch back on
a few times during today's episode.
Later, for instance, when we talk about
the potential toxicity of MDMA,
its ability potentially to kill neurons.
And the neurons it has been hypothesized to kill
are neurons of the serotonin and dopamine type.
So this is something you would not want.
Let's just recall that killing off of or death
of dopamine neurons is the underlying basis
for Parkinson's disease, which is a movement disorder
where people have difficulty generating smooth movements
and in very severe form, they can't move at all.
They sort of become locked in to some extent
and it also has cognitive effects.
So you don't want to lose dopamine neurons
and loss of serotonergic neurons
is known to impact mood negatively,
mood regulation negatively, et cetera.
The story of MDMA and its potential neurotoxicity
comes slam right up against this issue of legality.
And what we'll get into a little bit later
is that there has been a sort of race
in the scientific community consisting of two groups.
One set of groups trying to establish
the toxicity of MDMA so that it does not become legal again.
And another group trying to establish the utility
and the lack of toxicity in MDMA
so that it does become legal again
for the treatment of PTSD.
So even though the story Peacall relates to events

that took place largely in the 1970s, 80s and 90s,
right now MDMA and its toxicity or lack of toxicity,
its legality or lack of legality are really key issues.
So as you're listening to this,
I'm giving you a real-time blow-by-blow
of what led up to where we are now,
but we will also want to think about
how what's happening right now,
including the description of these data on MDMA,
may or may not impact the potential legal status of MDMA.
Okay, so what is MDMA?
MDMA is 3, 4 methylene dioxide, methamphetamine,
but unless you're a chemist,
that's not gonna mean much to you, nor should it.
MDMA has some very interesting properties,
the first of which is that methamphetamine component,
which because it's a methamphetamine
and acts like other amphetamines,
what it does is it blocks the reuptake of dopamine
from neurons after dopamine is released.
So for those of you that heard the episode that I did
on drugs to treat ADHD,
I discussed the biology and mechanisms of drugs
like Adderall and Vivants,
which basically are either combinations of amphetamines
or single type of amphetamines
that have either a quick release or a long release.
Now, MDMA, because it has this methamphetamine component,
prevents the reuptake of dopamine
and in doing so creates net increases in dopamine.
So for those of you that don't have a background
in neurobiology, let me just briefly explain,
I'll make this very simple,
neurons or nerve cells release chemicals
at their sites of communication,
which are called synapses.
Synapses are little gaps between neurons
and what happens is the neurons spit out
these little spherical balls,
which we call vesicles or vesicles,
depending on where in the world you live,
they'll either be called vesicles or vesicles
and those little vesicles contain neurotransmitter

or what's technically referred to as a neuromodulator.
Dopamine is a neuromodulator,
it can modulate the activity of other neurons,
it can either increase or decrease
the activity of other neurons.
Now, at the end of the neuron,
that what we call the axonal buton, okay,
axon is the wire component of the neuron
that can reach to another site in the brain
and then release the neurotransmitter
or neuromodulator there.
At those axonal butons, which are the sites of release,
the vesicles literally fuse with the edge of the neuron
and vomit their neuromodulator out into the synapse
and then the neuromodulator, in this case dopamine,
will bind to receptors on the postsynaptic side.
That means to another neuron
and then depending on how much binds
and depending on what else is going on
in that local neighborhood of neuronal connections,
the neuron will either increase its neural activity
and itself release neuromodulator
or neurotransmitter someplace else,
so sort of a chain reaction
or else it will suppress its activity
and the flow of communication from one neuron
to the next will be stopped, okay?
So MDMA doesn't prevent the release of dopamine
at the synapse, it does quite the opposite.
It actually prevents the sucking up of the dopamine
that's been released and that does not bind to the receptors.
So basically what it does is it blocks these things
called dopamine transporters
and the transporters are the things that suck back up
the dopamine that's been released
that has not bound to receptors.
So because it blocks that sucking up process,
there's more dopamine around in the synapse
to hang out and then bind to receptors
once some become available, okay?
The other thing that the methamphetamine component
of MDMA does just like methamphetamine
is that it actually gets into

what we call the presynaptic neuron,
the neuron that releases the dopamine
and it interferes with the repackaging of dopamine
into those vesicles.
Now you might think, oh, it interferes
with the repackaging of dopamine into vesicles
and therefore less will be released
but actually what happens is,
as a consequence of that,
a bunch of dopamine builds up in the presynaptic neuron
so that when an electrical impulse
comes down that neuron and dopamine is released,
a huge amount of dopamine is released.
And this is one of the characteristic properties
of methamphetamine and of MDMA,
which is that it leads to enormous increases
in the amount of dopamine released
and the amount of dopamine that hangs around in the synapse
and therefore it increases what we call dopaminergic tone
or dopaminergic drive.
That's just a bunch of different ways
to describe increases in dopamine, okay?
So that's the main way that MDMA and by extension,
methamphetamine increase dopamine.
However, MDMA is not just methamphetamine,
it's methylene dioxide methamphetamine
and it has another incredible property,
which is that it doesn't just lead to huge increases
in dopamine, it also leads to huge increases in serotonin.
And that's because there are other neurons
that release serotonin and they have serotonin transporters,
which are sometimes called CERTS, S-E-R-T-S's,
serotonin transporters,
and they work very much in the same way
that dopamine transporters do, right?
They basically control the sucking back up of serotonin
that's been released into the synapse
and that has not bound to serotonin receptors
on the other neurons yet.
And in doing so, allow more serotonin to hang out
and have its effects as those receptors become available
for serotonin to bind to them.
The other thing MDMA does is it also gets

into the presynaptic neuron to impact the packaging
of serotonin into something called
the vesicle monomine transporter for serotonin.
And in doing so, it leads to a big buildup of serotonin
in the presynaptic terminals
and then massive increases in serotonin release, okay?
So what we've got with MDMA is a really interesting compound
unlike methamphetamine or other amphetamine
such as Adderall, Vyvance, et cetera,
that cause increases in dopamine by blocking reuptake
and increasing release of dopamine.
MDMA does that, but it also does the same thing
for serotonin and here's a really key point.
The increases in serotonin that MDMA creates
are at least three times and maybe as much as eight times
greater than the amount of dopamine release
that MDMA causes, but when you put those two things together,
what you basically have is a drug that causes huge increases
in dopamine and even bigger increases in serotonin.
And remember earlier when I said that MDMA
is a purely synthetic compound,
as far as we know, it does not exist in any plants
or fungus or anything else in nature.
Well, this is a very unusual circumstance
of having big increases in dopamine
and big increases in serotonin caused by the same compound.
And that combination of big increases in dopamine
and big increases in serotonin are what lead
to these highly unusual and yet what seem to be
potentially clinically very beneficial effects
of having people feel a lot of mood elevation
and a lot of stimulation from the stimulant properties
of the methamphetamine component.
So that's the dopamine effect,
the dopaminergic tone goes way up.
So it's a stimulant, people feel really alert,
they feel like talking a lot, they feel very excited,
they feel a lot of positive motivation.
These are classic effects of drugs
that promote the release of dopamine,
including amphetamine, cocaine, et cetera.
But ordinarily that's not such a good thing
because what happens is there's then a crash

in the dopamine levels and then people feel depressed,
they feel lethargic, they don't feel good at all.
MDMA seems to cause these increases in dopamine
and all the accompanying effects I just described.
But by also causing big increases in serotonin,
it activates neural networks that are associated
with feeling more socially connected.
In fact, we'll talk about data in a little bit
where people have had their brains imaged
while under the influence of MDMA.
And it's very clear that people who have taken MDMA
look at faces that ordinarily they would rate as fearful
and rate them as less fearful.
They see faces that are smiling
and they rate those smiling happy faces
as more positive than they would off the drug.
The big increases in serotonin
create what we call a prosocial effect.
And that combined with the dopaminergic increase in mood
and the stimulation effect creates this thing
that we call an empathogen, where,
and this is very important,
the empathy isn't just for other people.
It's also for oneself and one's own experiences
happening in the moment,
as well as empathy for experiences from the past,
which, as you can imagine,
could be very beneficial for the treatment of PTSD.
Okay, so hopefully the way I described the biology
of MDMA makes some sense.
If you didn't get anything out of the description
I provided, except the understanding that MDMA is unusual
in that it causes big increases in dopamine
and even bigger increases in serotonin,
and you have more in your knowledge base now about MDMA
than you need in order to understand
the rest of our discussion.
Before we go any further,
I do want to separate MDMA out from some other compounds
which are referred to as psychedelics.
And I recently did a podcast episode all about psilocybin
and its therapeutic exploration
and its chemical basis, et cetera.

You can find that like all episodes at hubermanlab.com.
I also did an episode with expert guest,
Dr. Robin Carthardt-Harris,
who's at University of California, San Francisco,
who's pioneering a lot of the studies
on the clinical application of psilocybin.
psilocybin and LSD are mainly going to increase
serotonin activation in the brain.
In fact, they very closely resemble serotonin itself,
and they activate what's called the 5-HT2A,
or serotonin, 5-HT just stands for serotonin,
5-HT2A receptor to create very mystical type experiences.
They are considered classic psychedelics
and are very introspective.
And as I described in those episodes,
are being explored extensively now
for the treatment of major depression.
A different compound that's being used
for the treatment of depression is ketamine.
I will do an entire episode all about ketamine.
Ketamine is actually a N-methyldiaspartate receptor blocker,
that shouldn't mean anything to most of you,
but it is a dissociative anesthetic,
not unlike PCP, what used to be called angel dust
on the street.
Ketamine is being used as a treatment for depression.
It is currently legal.
So unlike psilocybin and LSD,
which are granted breakthrough status
for the study of depression, but are not yet legal,
they are still illegal.
And of course, as I mentioned earlier,
MDMA has breakthrough status, but is still illegal.
Ketamine is being used for the treatment of depression,
and it does so, as its name suggests,
a dissociative anesthetic by creating
a sense of dissociation from emotions.
Okay, now I raise this distinction
between psilocybin and LSD,
which are mystical in their effects.
Ketamine, which is dissociative in its effects,
with MDMA, which is an empathogen,
or sometimes called an anactogen,

but as an empathogen or an anactogen,
it's creating more affiliation.
It's affiliative, okay?
So it's a very distinct compound.
And I think this is important to understand
because when we hear the word psychedelic,
a lot of people tend to lump together
LSD, psilocybin, and MDMA.
If you talk to researchers in these areas,
they will tell you that MDMA really isn't
that much of a psychedelic.
It's an empathogen with stimulant properties,
and it also has this serotonergic component
that makes it an empathogen or an anactogen.
So MDMA is very different than the other psychedelics.
And my hunch is that over the next few years,
we will stop talking about MDMA as a psychedelic
because it does not tend to produce visual hallucinations
or auditory hallucinations of the sort
that classic psychedelics do.
And in general, it is more of a mood impacting drug
than it is mystical, okay?
So we'll get into some of the brain networks
and which ones are activated
while under the influence of MDMA.
But I do think it's very important to segment out MDMA
from the other so-called classic psychedelics
and also segment it out from ketamine.
Thanks to some really terrific studies,
both in animal models and in humans,
we now understand a lot of what makes MDMA
produce these incredibly unique effects.
And when I say unique, I mean unique from drugs
like psilocybin and LSD and ketamine
and from methamphetamine for that matter.
And it's really the combination of big increases in dopamine
and even bigger increases in serotonin
that create a situation where people have more energy
and yet despite having more energy,
they don't feel irritated, they feel a lot of pleasure.
They seem to want to be in the state
of having a lot of energy.
This will become important as we talk about anxiety

and the anxiety symptoms of PTSD.
It also because of the big increases in serotonin
produces a sense of emotional warmth
towards others and towards oneself.
That's the empathogen component.
And for reasons that we still don't understand,
it seems to increase trust.
And the increases in trust turn out to be vital
because as you will, you will also learn later
when we look at the clinical trials exploring MDMA
for the treatment of PTSD.
The major effect of MDMA for the treatment of PTSD
is not to cure PTSD, but rather to make the therapy,
the talk therapy for PTSD much more effective.
This is a very important point.
In fact, so important I'm going to repeat it at least three
times during today's episode.
MDMA taken on its own does not cure PTSD.
MDMA can augment or boost the effects of talk therapy
for PTSD.
And it does that through the engagement
of specific neural circuits.
But before we talk about what those neural circuits are,
I want to emphasize that the increases in serotonin
that MDMA produces seem to act on different receptors
than the big increases in serotonin
that LSD and psilocybin produce.
So if you listen to the episode that I did on psilocybin,
we haven't done yet one on LSD,
but the mechanisms are very similar for psilocybin and LSD,
whereby psilocybin and LSD very closely mimic
the molecule serotonin itself,
but seem to have a more selective activation
of just the so-called serotonin 2A receptor,
abbreviated 5HT2A.
And that leads to more interconnectedness
between different brain areas,
more consideration of new possibilities about events
from the past, present, and future.
And also the opening of so-called neuroplasticity
of rewiring of neural connections that persist
long after the psilocybin or LSD effects have worn off.
Now, MDMA can activate the serotonin 2A receptor,

but it seems that it largely activates
the serotonin 1B receptor.
What does that mean?
Activation of the serotonin 1B receptor
seems to be what gives MDMA its very strong impact
on the neural circuits of the brain
that relate to trust and to social engagement,
not just the willingness to engage socially
and to confide in a therapist or another person,
but the intense desire to do so.
And when I say intense desire,
that takes us back to the dopamine system.
Remember, dopamine, even though when increased
in the brain can increase our mood,
it is largely responsible for increasing our sense
of motivation and desire for something and to do something.
So the increase in dopamine that's created by MDMA
seems to make people what I call forward center of mass.
They want to do something.
They're very motivated to do something.
And the increases in serotonin acting
on the serotonin 1B receptor seems to be what creates
this desire to bond or create trust
or to have a discussion of real things,
both things that are positive,
but also to explore things that are difficult.
And this I realize is going to be a little bit
of a mind bend for people to understand,
but one of the key things that quality MDMA therapy consists
of is not just having a very good rapport
and communication with the therapist
that's guiding the PTSD treatment,
but also rapport and a willingness to engage
in conversations with oneself.
And I think that most of us can relate to the fact
that we have experiences, some of which are hard,
some of which are great and everything in between.
Trauma is, I believe, best defined by the words
that a former guest on this podcast
who's a world expert in trauma, Paul Conti,
explained as trauma is an event
that fundamentally changes the way that our brain works
for the worse.

Okay, so not every bad event of our past is trauma,
but events that change the way that we think,
our emotional tone or our behavior
in ways going forward that are not adaptive for us.
They don't serve us well,
either because they are highly distracting
or because they create anxiety
or because they disrupt sleep
or any number of different things
that are maladaptive consequences.
That's what really defines trauma.
And when under the influence of MDMA,
because of those parallel increases in dopamine and serotonin,
people seem far more willing to both trust the therapist
that they're talking about that trauma with,
but also to trust their own ability to, quote unquote,
go internal and think about the challenging thing
for things, because oftentimes trauma
can consist of many events, not just one event,
and the thought patterns around that
and the context around that,
and they're in to be able to explore new possibilities
to essentially rewire their relationship to that trauma.
So I promised that a little bit later,
we'll talk about the direct application of MDMA
for the treatment of PTSD,
but now I'd like to shift off of the chemical changes
that MDMA produces and some of the subjective changes,
these increases in trust and pleasure and energy
and emotional warmth to some of the brain circuits
that are activated and modified by MDMA use.
And then we will explore the toxicity issue,
and then we will explore the clinical studies
of which I can promise you are extremely exciting,
but until we understand the neural circuit phenomena,
and of course, until we consider the neurotoxicity issues,
I don't think those clinical findings
can be appreciated in their full value.
But now I'd like to talk about what MDMA
really does in the brain, both in the short term,
while someone is under the influence of the drug,
and in the long term, what sorts of neuroplastic
or rewiring changes does MDMA produce,

and how can those be beneficial or perhaps not beneficial?
I'd like to take a quick break
and acknowledge one of our sponsors, Athletic Greens.
Athletic Greens, now called AG1,
is a vitamin mineral probiotic drink
that covers all of your foundational nutritional needs.
I've been taking Athletic Greens since 2012,
so I'm delighted that they're sponsoring the podcast.
The reason I started taking Athletic Greens
and the reason I still take Athletic Greens
once or usually twice a day is that it gets to be
the probiotics that I need for gut health.
Our gut is very important.
It's populated by gut microbiota
that communicate with the brain, the immune system,
and basically all the biological systems of our body
to strongly impact our immediate and long-term health.
And those probiotics in Athletic Greens
are optimal and vital for microbiotic health.
In addition, Athletic Greens contains a number of adaptogens,
vitamins, and minerals that make sure
that all of my foundational nutritional needs are met
and it tastes great.
If you'd like to try Athletic Greens,
you can go to athleticgreens.com slash huberman
and they'll give you five free travel packs
that make it really easy to mix up Athletic Greens
while you're on the road and the car on the plane, et cetera.
And they'll give you a year supply of vitamin D3K2.
Again, that's athleticgreens.com slash huberman
to get the five free travel packs
and the year supply of vitamin D3K2.
So in order to understand what MDMA does to the human brain,
we need to take a step back
and really define the sorts of experiments
that one could do.
So for instance, you could take a person
who's never ingested MDMA
and put them into an fMRI machine,
which is functional magnetic resonance imaging,
put them into the fMRI machine
and just have them sit there with their eyes closed,
what we would call resting functional connectivity

or resting state functional connectivity
and simply look at how interconnected
certain brain areas are, which brain areas are active,
which brain areas are less active at rest.
This is an important thing to do,
not just to provide a baseline for understanding
what the drug MDMA will subsequently do,
but also because it addresses
what's called the default mode network.
The default mode network or DMN is the network
that is active in our brains
when we aren't really attending to anything specific
outside us and we're not trying to think
about anything specific or accomplish anything specific.
It actually relates to our sense of imagination
and daydreaming.
It has a lot to do with our self-referencing.
What we're thinking about ourselves,
this may come as no surprise,
but if you're just sitting there on the bus
or around the dinner table
and you're not paying attention to what's going on,
in large part, your brain is in this default mode network
and you're thinking about yourself.
So we can get a sense
of what the default mode network activation is.
We can get a sense of which brain areas
are more or less active,
simply by putting somebody into an FMRI machine.
Then of course, you could give somebody MDMA
while they are in the FMRI machine
and see how the activation
of different brain networks changes.
And then of course, you could analyze
how the default mode networks
and other brain networks change in the days and weeks
and even years after the drug has worn off.
So-called neuroplasticity effects.
What changed in a permanent or pervasive way?
Okay, so that's one basic paradigm
for exploring the effects of drugs like MDMA on the brain.
The other way that you can explore the effects
of MDMA on the brain is to ask people

in the general population,
hey, who out there has taken MDMA?
How many times have you taken it?
And come on into the laboratory
and we will image your brain
and compare people who have, for instance,
taken MDMA zero times
to people who have taken MDMA one time or five times
or believe it or not,
there's some studies sitting right here in front of me
on my desk of people who have taken MDMA
more than 200 times
and ask the same sorts of questions.
Which brain areas are more or less active?
Those studies have been done as well.
And of course, one can do studies
where you give people different dosages of MDMA
as well as giving people MDMA
and then giving them specific stimuli,
meaning not just asking them to sit there
in the fMRI scanner with eyes closed,
looking at the resting state functional connectivity,
but also how the brain responds
to the presentation of happy faces or sad faces
or images of oneself or even images
that recall memories of traumatic events and so on.
So fortunately, all of those sorts of studies
have been done in humans.
And there are also a large number of studies
in animal models exploring how the social activity
of laboratory mice changes
when they are under the effects of MDMA.
There are even studies, believe it or not,
on the effects of MDMA in cephalopods.
Cephalopods include octopuses as well as cuttlefish
and other aquatic animals
that are known for having complex behavior.
Some people believe that the cephalopods
are extremely intelligent.
The obsession with cephalopods
is something that really intrigues me.
I actually used to have cuttlefish in my laboratory.
We did not put them on MDMA.

But there is a study that's been published
in the journal Current Biology.
It's a self-press journal, excellent journal.
This is from Google Dolan's laboratory
at Johns Hopkins School of Medicine,
showing that if you give octopuses MDMA,
they like to spend more time with other octopuses
than they do if they are not on MDMA.
And that might sound like kind of a playful experiment
just done in order to entertain oneself
and the octopuses perhaps.
But actually in that study,
they identified the serotonin transporter
in octopuses and show that it has a lot of homology,
similarity to human serotonin transporter receptors.
And so what that really speaks to is the fact
that the pro-social effects of MDMA
that are observed in mice and in humans
and in octopuses all have a common basis,
which is the activation of more serotonin release
in particular brain networks.
Okay, so that interesting study on octopuses aside,
I think what most of us are interested in
is how MDMA impacts the brain.
And so I'm going to spell out the three major ways
in which MDMA changes the activation of the brain
in the short and long term.
And here I'm pooling across a number of different studies.
But one of the key sets of studies in this area
comes from what I consider very beautiful work
of Harriet DeWitt.
Harriet DeWitt runs the Human Behavioral Pharmacology
Laboratory in the Department of Psychiatry
and Behavioral Neuroscience at the University of Chicago.
And her laboratory has a long history
of giving people certain drugs in very specific dosages
and then measuring their effects on the brain
using different types of imaging, including FMRI.
And one particular study that I'll highlight
is entitled Effects of MDMA on Sociability
and Neural Responses to Social Threat and Social Reward.
So what the study looked at is how MDMA impacts
people's perceptions of others' emotional expressions

on their face.
What they found is that when people are on MDMA,
their response to threatening faces
or other threatening stimuli is reduced.
And it's reduced in a very specific way,
which is reductions in activity of the amygdala.
The amygdala is a structure that some of you
may be familiar with.
It is known to be involved in the threat detection systems
or networks of the brain.
It is sometimes called the fear area of the brain,
although I want to caution people
against assigning any one particular subjective experience
to any one particular brain area.
The amygdala is actually a complex.
It's actually called the amygdaloid complex
and has a lot of different sub areas
and it's involved in a lot of things
besides fear and threat detection.
Nonetheless, when people are under the influence of MDMA
and you show them a face that is grimacing
or would otherwise be rated as quite threatening,
they tend to rate it as less threatening.
In addition, they tend to respond to happy faces
or even slightly happy faces as more kind
or more generous or happier than they would
when they are not on MDMA.
Again, the faces that are being shown
are not of people on MDMA.
That would be an interesting experiment,
but that's not what they did here.
What's happening here is people are being given MDMA
and then they are rating in a subjective way
the friendliness or the level of threat
that they detect in these facial expressions.
And of course they have extremes of friendly
and threatening, but then they also grade them, right?
They titrate them so that they also have mildly threatening
and mildly happy faces, et cetera.
So everything from a grin to a smirk to a giant smile,
everything from a sort of, you know,
somebody looking a little bit of scance at somebody
to really, you know, wide-eyed and looking angry

like they're, you know, gonna attack you
and things of that sort.
So what's discovered in the study is that MDMA
has a bi-directional effect on our perception
of others' emotions, making people more likely
to rate something as positive if it's initially positive
or even a little bit positive
and less likely to rate a threatening face
as more threatening.
Now, one thing I have not mentioned thus far
are the dosages of MDMA used in this and in other studies.
Unfortunately, despite the studies that we're going to talk
about using a lot of different types of people,
different ages, different sexes, so male and female,
located in different parts of the world even,
some with PTSD, some not with PTSD, et cetera,
there's been fairly tight dosage control
of MDMA in these studies.
It's not perfectly matched from study to study,
but it's pretty darn close, which makes interpreting results
across studies a lot easier for me and therefore for you.
The typical dosages of MDMA used
in these neuroimaging studies and in the clinical studies
of PTSD that we're going to talk about later,
range anywhere from 0.75 milligrams per kilogram
of body weight to 1.5 milligrams per kilogram of body weight.
So for somebody like me, I weigh 220 pounds,
that's 100 milligrams, 1.5 milligrams per kilogram
of body weight would therefore be 150 milligrams
in a single dose, okay?
A dosage of one milligram per kilogram of body weight
would mean 100 milligrams for my 100 kilograms, okay?
Somebody lighter than 100 kilograms
would obviously take less MDMA in one of these studies.
But in general, the range of MDMA that's been explored
is 0.75 to 1.5 milligrams per kilogram of body weight.
The exception being in the clinical studies
that we'll talk about a little bit later,
there's a tendency to explore both an initial dose
of 1.5 milligrams per kilogram of body weight.
So again, for a 100 kilogram person,
there'll be 150 milligrams or so,
and then a so-called booster of half that amount,

about 90 minutes to two and a half hours into the session.
So another 75 milligrams later.
And I should point out that there is not always
the inclusion of the so-called booster.
And in some cases, lower doses of MDMA,
such as the 0.75 milligrams per kilogram dosages are used.
Why am I getting so into the details of dosages?
Well, if we are going to talk about toxicity of MDMA,
we absolutely have to talk about dosages
because like any drug, the toxicity of MDMA
does scale with the dosage that's applied,
not just the frequency of MDMA use.
We hear a lot about that.
Somebody has taken MDMA one time or four times
or 200 times, we hear about frequency of use,
but rarely do we hear about the specific dosages
that are taken in any one particular session.
So when we talk about the subjective effects
or the brain networks that are activated
when people take MDMA, in general,
we're talking about dosages somewhere
between 0.75 milligrams per kilogram of body weight
and 1.5 milligrams per kilogram of body weight.
Although typically you're going to see studies
both clinical and more research explorative
using anywhere from one to 1.5 milligrams of MDMA
per kilogram of body weight.
So that's important to highlight.
I told you about the subjective effects of MDMA,
engaging the responses of people's faces,
but I didn't tell you about the brain areas
that are responsible,
except for the reduction in amygdala activity.
Now, one of the key features of PTSD
seems to be that there is a heightened connectivity
between the amygdala and a brain area called the insula.
The insula is a brain area that's very important
for something that's called interoception.
Interoception is one's perception of our feelings,
both pure sensations, but also our emotional states
and our feelings of wellbeing or lack of wellbeing
for everything from our skin inward.
Okay, so that's interoception.

You actually can interocept now,
even though you're always interocepting a little bit,
you can interocept now to a great degree.
If you were to, for instance, close your eyes
or simply focus on the contact points between your body
and any surface that you happen to be contacting.
So maybe the backs of your legs against a chair
or your feet against the floor
or the bottoms of your shoes or sandals.
Your nervous system is constantly
sensing those contact points,
but normally they're not under your conscious awareness
unless you direct your interoceptive capacity to them,
which is just fancy nerd speak for saying,
you normally don't notice what's going on
from your skin inward unless you focus on it.
That focus is interoception.
It can be about the fullness of your gut,
it can be about how happy or sad you are,
it can be about how tired or alert you happen to feel,
but that's interoception and it is distinctly different
from exteroception, which is your ability
and tendency to focus on things
beyond the confines of your skin.
So this could be visual attention, auditory attention,
it could be paying attention to events like birds flying by,
whether or not your Uber is showing up,
these kinds of things.
And we are always in a balance,
a push pull of interoception and exteroception.
The insula is a brain area
that is absolutely critical for interoception,
so much so that it has a map of the complete body surface,
including our internal organs.
In other words, if you put somebody into an fMRI machine
or you were to record from the insula with electrodes,
as has been done in humans many times now
during the course of neurosurgery for other purposes,
what you would find is that if you stimulate neurons
in one end of the insula, the person will say,
oh, you know, I feel something going on in my gut
and on my left side.
And then as you were to march that stimulation

across the insula, you would find that they would now
be paying attention to their legs or just to one leg
or to their whole body or to the sensations
in their face or their head.
So there's a systematic map of interoception in the insula.
And there are direct connections
between the amygdala and the insula.
And the amygdala, despite getting this reputation
as just being a fear center or a threat detection center,
is actually part of a much larger set of networks
that include inputs from the hippocampus,
area of the brain that's involved in memory formation
and storage.
And what is observed is that people who have PTSD
tend to have greater or rather stronger connections
between the amygdala and the insula
than is normally observed in people who do not have PTSD.
Okay, so there seems to be heightened input
from the threat detection centers of the brain
to this area of the brain, the insula,
that is responsible for our sense of interoception,
which provides a logical explanation
for why people with PTSD often will feel the memory
or sense the discomfort or just feel agitation
or even other types of bodily sensations like back pain
or just perhaps just a sense within their body
that's more generalized.
It doesn't even have to be pain.
It doesn't even have to be negative,
but that's associated with the negative memory
of some traumatic event or series of events.
Okay, so this is a really interesting brain network
that I should mention exists in everybody,
but that in people with PTSD
seems to have heightened connectivity.
And those brain networks can be revealed
by putting people with PTSD
into functional imaging machines,
getting them to recall a traumatic event
or even looking at the resting state of connectivity
between the amygdala and the insula.
So those experiments have been done
and what's also been done is to give people

1.5 milligrams per kilogram of MDMA
and to look at the connectivity
between the amygdala and the insula
and between the hippocampus, the amygdala and the insula.
And so what's observed over time
in people that have been given MDMA
and this is a very important and,
and have done therapy for PTSD,
both before, during and after the drug,
there's a weakening of connections
between the amygdala and the insula.
And that scales very directly
with the relief of symptoms from PTSD.
So this is really exciting
because it's one thing to see a brain network
get activated or inactivated or you say,
okay, in one person, a certain connection
between threat centers
and the interceptive centers of the brain
was let's say arbitrary units,
let's say it was level eight out of 10 for that person.
Are you, these things are normalized
for a particular person.
And then after taking MDMA and doing PTSD therapy,
it was five out of 10 or four out of 10.
That's a good experiment,
but what's far more powerful is to observe that
in that patient or that person
and then to see a change that's perhaps less dramatic.
So a shift from eight out of 10 to seven out of 10
in another person
and to see less shift in brain connectivity
in the same network.
And then perhaps in the person that went
from full blown PTSD to full remission of PTSD,
something that believe it or not
has been observed in single sessions with MDMA.
If that person demonstrates an even greater reduction
in the connections between the amygdala and the insula,
well, then that gives even more confidence
that this connection between the amygdala and the insula
is actually perhaps causally related
to the reduction in symptoms of PTSD.

Or even if it's just correlated
with reduction in symptoms of PTSD,
the fact that the degree of reduction
of connection of this circuit scales
with the reduction in clinically relevant symptoms,
that's a very powerful finding
because it moves things away from pure correlation
of oh, this brain area is active or less active over time.
And this person has more or fewer symptoms of PTSD
to something that starts to look like a mechanistic
and logical framework for understanding PTSD
as well as the effects of MDMA
and for understanding how changes in the brain
underlie relief from PTSD.
Okay, so again, even if you just could grasp the idea
that you have a brain area, the amygdala
that's involved in threat detection
and it provides inputs to another brain area
called the insula, which is involved in this thing
called interoception, and that reductions in those
connections between the amygdala and the insula
scale with or correlate with reductions in PTSD symptoms
as a consequence of people taking MDMA.
So if you have that under your mental belt,
I promise you you understand far more
about how MDMA impacts the brain in the short and long term,
the 99.9% of people out there.
However, it's also important that you understand
a few other things that MDMA does to the brain
as well as what it doesn't do to the brain.
First of all, classic psychedelics like psilocybin
and LSD, as I mentioned earlier, are known to create
more lateral connectivity between different areas
of the so-called neocortex.
And these are long lasting changes that are thought
to underlie both some of the relief from major depression,
but also some of the enhanced creativity
and some of the other things that have been observed
with psilocybin treatment.
And again, if you're interested in psilocybin treatments
and psilocybin itself, please check out the episode
I did on psilocybin and the guest episode
with Dr. Robin Carthart Harris.

Those episodes, like all other episodes
of the Huberman Lab podcast can be found
at hubermanlab.com.
It's a fully searchable site.
You can put keywords into the search function.
It will take you to specific timestamps.
Every episode is timestamps.
You can navigate to topics of particular interest to you.
Feel free to go there and listen to those episodes
about psilocybin.
MDMA, by contrast, does not seem to produce
long lasting increases in lateral connectivity
between those same brain networks,
probably because it impacts different serotonin receptors.
It does, however, seem to change resting state
functional connectivity within these limbic structures
like the amygdala and related structures
that are associated with threat detection.
Now, this is interesting and it actually was highlighted
very nicely in a study I'll provide a link to
in our show note caption, which actually has Dr. Robin
Carthart Harris as the first author.
So not only has he done incredible work on psilocybin
and LSD and DMT in ayahuasca in his laboratory,
but also on MDMA.
And the particular study I have in mind here
showed that people who take MDMA
at more or less the dosages that we talked about earlier
report mark increases in positive mood
as well as decreased blood flow to the amygdala
and hippocampus.
So again, these threat detection centers of the brain
and brain areas associated with memory.
And those changes are seen both while under the influence
of MDMA and afterwards when the brain is simply at rest.
So it really does appear that MDMA creates neuroplasticity
that changes the overall level of activation
of these threat detection networks
and their connections to memory systems
in a way that's pervasive over time
and that doesn't require any particular probe
with a negative stimulus.
Now translate to English, what that means is that

during the MDMA session, people report feeling
less threatened, more prosocial towards others,
more empathic towards others and themselves.
And then after the session, they have less of a threat
response to memories that before the session
were more troubling and those changes in the brain
do seem to be pervasive.
So there are both short-term and long-term effects of MDMA,
all of which point in the direction of lowered levels
of threat detection, heightened levels of positivity,
prosocial components of the brain,
more active threat detection centers of the brain, less active.
Now, earlier we talked about MDMA as a drug
that potently increases dopamine
and even more potently increases serotonin,
largely acting through this serotonin 1B receptor.
Now, without getting into too many more details
before moving on to issues of toxicity around MDMA,
I do wanna touch on what I think is perhaps the finest
of the animal model studies of MDMA
that explored which brain networks
and which chemical that is serotonin or dopamine
is responsible for say the motivational components of MDMA
versus the prosocial effects of MDMA.
And then it also raises a really important point
which I haven't mentioned yet in this episode,
which is the role of oxytocin,
something that many of you have perhaps heard of.
The paper that I'm going to describe
is from the laboratory of Dr. Robert Malenka.
He's a colleague of mine
at Stanford University School of Medicine,
Psychiatry and Behavioral Sciences.
He is both a pioneer and luminary in the field
of neuroplasticity of how the brain wires
and forms memories and can change itself over time
in response to experience,
as well as the study of drugs of abuse,
as well as the study of drugs like MDMA
and now additional compounds
that can provide therapeutic support in certain conditions.
The study, which I will provide a link to
in the show note caption,

is entitled Distinct Neural Mechanisms
for the Prosocial and Rewarding Properties of MDMA.
And I'm just going to summarize
the major results of this study.
It's a study that was done on mice
and I realized that a lot of people will hear that
and think, ah, what relevance does that have to humans?
But when thinking about the effects of dopamine
and serotonin in the types of circuits
that we've been talking about thus far,
these circuits that are subcortical,
as we refer to them.
So these are limbic circuits.
These are hypothalamic circuits.
These are what are called mesolimbic circuits.
These are all names for circuits
that are highly conserved between mice and humans.
And so results in mice really do translate quite well
to results in humans,
at least in so far as the effects of MDMA
and which neurochemicals are involved is concerned.
So what they found in this study
using a huge array of beautiful techniques
such as inactivation of specific brain areas,
activation of specific brain areas,
drug antagonists to prevent oxytocin function
or drug antagonists to prevent specific receptors
involved in the serotonin pathway,
lots and lots of tools in their toolkit.
What they found is that MDMA,
causing the release of dopamine,
is what really establishes the rewarding effects
of an experience.
This isn't really a surprise.
We've known that MDMA, just like cocaine
or methamphetamine or Adderall for that matter
or Vivance for that matter,
creates big increases in dopamine
that tend to couple an experience with a sense of reward
and lead to changes in the neural circuitry
that make the animal or human more likely to seek out
that same experience again.
Okay, these are the rewarding

or sometimes called reinforcing properties of dopamine
that take place in the so-called mesolimbic reward pathway.
If you wanna learn about mesolimbic reward pathways
and dopamine and how they control everything
from your level of motivation
to your tendency to procrastinate or overcome procrastination,
I've done two episodes about dopamine.
You can simply go to hubermanlab.com,
put dopamine into the search function
and you'll find at least two episodes on that topic.
And you'll also find a number of different tools
related to how one can better regulate
their own patterns of dopamine release,
forsake of motivation, et cetera.
So MDMA is increasing dopamine
to increase reward to a particular experience.
What's the experience?
Well, this paper beautifully parses the fact
that it is serotonin release
within a structure called the nucleus accumbens,
which is part of the reward pathway,
which is rewarding the experience of social interaction.
They do this by putting mice in arenas
where they have the option
of either spending time with other mice
or not spending time with other mice
and blocking the activation of certain brain areas
and again, using drug antagonists, et cetera.
And what they find is that it really is the activation
of the serotonin 1B receptor in the nucleus accumbens
by MDMA that leads to this pro-social effect of MDMA.
So that's really nice to know
because there's always been this conundrum of,
okay, psilocybin and LSD are basically like serotonin.
They activate the serotonin 2A receptor.
MDMA has this huge serotonergic component,
tons of serotonin released when one takes MDMA,
but very different effects in the short and long term.
Very different subjective effects,
very different patterns of change activity in the brain
in the short and long term.
Well, that's because MDMA is activating
the serotonin 1B receptor, not the serotonin 2A receptor.

And it's doing so in a completely different set
of brain networks as is LSD and psilocybin.
So what happens when an animal or a person takes MDMA
is that social connection is strongly rewarded
and reinforced, making social connection more likely
after the drug wears off.
Now, that's one component of social connection,
but in addition, people who take MDMA
in the clinical therapeutic setting
for the treatment of PTSD often report feeling more empathy
and compassion for themselves during the session,
but also for long periods of time,
maybe even indefinitely after the session.
So it really seems that the addition
of this huge release of serotonin by MDMA
on top of the release of dopamine
sets in motion two parallel circuits,
one for rewarding something, anything.
That's the dopamine component.
And then fortunately, because the increase
in serotonin caused by MDMA increases empathy
and sociability for and with others,
but also for oneself.
The motivation that's reinforced,
that's wired into the brain seems to be a motivation
to perceive others as more kind,
but also to be kinder to oneself.
Now, I realized that for some of you who are listening
to this, you're probably saying, well, of course, right?
You know, serotonin is pro-social
and dopamine is motivation.
So you put the two together
and people become more motivated to be social
and kinder to themselves.
Ah, but it didn't necessarily have to be that way, right?
It is very hard to go from a statement
like drug A produces effects B, C and D
to neurochemicals, B, C and D cause motivation
and sociability.
And therefore, when you take that drug,
you're gonna get all of that stuff.
In fact, we have to go back to our understanding
that MDMA, despite causing a big increase in serotonin,

also causes huge increases in dopamine.
And it does so with this molecule that is methamphetamine.
Now, methamphetamine is not known to be a pro-social drug.
In fact, the study I just referred to,
as well as some human studies,
have explored how the application of methamphetamine,
so not MDMA, but pure methamphetamine,
impacts social interactions.
And what it does to social interactions is very profound.
It dramatically reduces one's tendency
to engage in social interaction.
So this really speaks to the polypharmacology,
as it's called, of MDMA.
The fact that serotonin and dopamine are released together
has distinctly different effects
than if just dopamine or just serotonin is increased.
So much so that it's worth taking a step back
and talking about another class of drugs,
which dramatically increases serotonin,
which are the SSRIs,
the Selective Serotonin Reuptake Inhibitors.
SSRIs such as Phloxatine, Prozac, as well as Zoloft,
and of course, there are many other SSRIs out there,
Citalopram, et cetera,
they block the reuptake of serotonin
and thereby lead to net increases
in the amount of serotonin.
And yet, those drugs are not known to create
even close to the same sorts of effects as MDMA.
In fact, there have been human and animal studies showing
that if you give somebody an SSRI prior to them taking MDMA,
you actually block the prosocial
and empathogenic effects of MDMA.
Now, you might say, why in the world would that be?
Aren't these drugs just increasing serotonin
and the increase in serotonin is prosocial, et cetera?
Well, that speaks to the complexity
of all this polypharmacology and the fact that
it's really the activation of serotonin
at particular receptors, in this case,
the serotonin 1B receptor, in particular brain areas,
in this case, the nucleus accumbens,
a brain area associated with motivation and reward

that largely explains the effects of MDMA
in making people and animals and octopuses included,
for that matter, more prosocial
and more empathic towards themselves.
It's not just an issue of raising the levels
of one neurochemical, it's really about raising levels
of a particular neurochemical,
acting at particular receptors in particular brain areas.
And in the case of MDMA, the fact that there's also
dopamine increased in those very same brain areas, right?
I don't think I mentioned this before,
but the nucleus accumbens is part
of that mesolimbic reward pathway
that is essentially establishing a reward
for whatever is happening at the moment.
So the way to conceptualize MDMA and its effects
on the brain, both subjectively and mechanistically,
is that it's an empathogen for which empathy
and social connection is very strongly reinforced
while under the influence of the drug,
and in a way so intense and powerful
that those neural networks get stronger
and persist in being more active for long periods
of time after the drug has worn off.
I'd like to just take a brief break
and thank one of our sponsors, which is Element.
Element is an electrolyte drink
that has everything you need and nothing you don't.
That means plenty of salt, sodium, magnesium and potassium,
the so-called electrolytes and no sugar.
Now, salt, magnesium and potassium are critical
to the function of all the cells in your body,
in particular to the function of your nerve cells,
also called neurons.
And we now know that even slight reductions
in electrolyte concentrations or dehydration of the body
can lead to deficits in cognitive and physical performance.
Element contains a science-backed electrolyte ratio
of 1,000 milligrams, that's one gram of sodium,
200 milligrams of potassium and 60 milligrams of magnesium.
I typically drink Element first thing in the morning
when I wake up in order to hydrate my body
and make sure I have enough electrolytes.

And while I do any kind of physical training
and after physical training as well,
especially if I've been sweating a lot
and certainly I drink Element in my water
when I'm in the sauna and after going in the sauna
because that causes quite a lot of sweating.
If you'd like to try Element, you can go to drink Element,
that's lmnt.com slash Huberman
to claim a free Element sample pack with your purchase.
Again, that's drink element lmnt.com slash Huberman.
Now, one of the things that's been explored
in both the animal literature and the human literature
is that MDMA doesn't just increase dopamine
and doesn't just increase serotonin,
but it also profoundly increases levels
of oxytocin release in the brain.
Now, oxytocin is considered what's called a neurohormone
because it acts as both a neurotransmitter
or I guess if we were going to be really specific,
we'd say a neuromodulator
because it tends to modulate the activity
of a bunch of other circuits and a hormone.
How can we say it's a hormone or a modulator or a transmitter?
Well, hormonal effects tend to be effects
that act not just locally,
but on many sites within the brain and body as well.
And oxytocin is known to do that
as well as to work locally.
So that's why we call a neurohormone.
It activates neurons and is associated with neural networks
related to pair bonding,
both between parent and child,
both mother and child and father and child
or caretaker and child, not just biological parent,
as well as bonding between friends, bonding between lovers,
and it's thought to actually be involved in the process,
that is the painful process of breaking of bonds
when people are no longer available to us as caretakers
or as partners either by way of breakup, death,
departure, et cetera.
In fact, there are even data suggesting
that humans can have strong oxytocin responses
to their pets, in particular dogs,

and their dogs can have strong oxytocin patterns of release
in response to their owners.
I think for any dog lovers or dog owners,
certainly includes me, I'm raising my hand.
That comes as no surprise.
Anyone that's ever had to put down a dog
or has lost a dog and hear no disrespect to the cat owners,
but I'm just referring to the studies
that have been done on humans and dogs,
you can certainly relate to the incredible pain of that loss.
Oxytocin is thought to be involved in bonding
between people and other creatures,
as well as the breaking of those bonds.
MDMA is known to powerfully increase oxytocin release.
In fact, there's a really nice study on this done in humans.
This is a study I'll provide a link to
in the show note captions entitled
Plasma Oxytocin Concentrations Following MDMA
or Intranasal Oxytocin in Humans.
Nowadays, oxytocin is available by nasal inhaler.
To be honest, I don't know the legality around it.
I don't know if it's gray market or,
but what I'm about to tell you will basically discourage you
from wanting to take it because what they found
in this study was people given either 0.75 or 1.5 milligrams
per kilogram of body weight of MDMA experienced increases
in oxytocin.
However, it was only the group that took 1.5 milligrams
per kilogram of body weight of MDMA that experienced
the really big significant changes in oxytocin.
And when I say really big,
really highly statistically significant,
what they observed is that in the placebo group,
because of course they include a placebo group,
the amount of circulating oxytocin was 18.6 picograms
per milliliter, which to you probably means nothing.
And to me also sort of means nothing
because those units of oxytocin can't be directly related
to any kind of direct experience of feeling bonded
or not bonded, that's just a number.
But nonetheless, it provides a baseline to compare
to the average levels of oxytocin in the bloodstream
of people that were given 1.5 milligrams

or kilogram of MDMA, which is 83.7 picograms per milliliter.
That equates to nearly a five-fold increase
in the amount of circulating oxytocin
when people are under the influence of MDMA.
Now, this study had a bunch of different conditions,
not just MDMA of different doses, not just placebo.
They also had people take oxytocin by nasal spray,
which we know can change levels of circulating oxytocin.
And indeed, when measured in the study,
it did change levels of circulating oxytocin.
And the endpoint in the study was to have people
give subjective ratings of their feelings
of connectedness to one another, as well as rate.
And here I'm just drawing directly from the paper
of how much they like the feeling, how much they felt high,
they measure their heart rate, their systolic pressure,
their diastolic blood pressure, et cetera.
And they looked at how social people felt.
They looked at how insightful people felt.
And the key takeaway from this study,
for sake of our discussion here today,
is that it does not, again, it does not appear
that the increases in oxytocin produced by taking MDMA
are the source of the prosocial effects of MDMA.
And that's also what was found in the animal studies of MDMA,
where in those studies mice were given MDMA
at comparable doses.
We're a little bit higher than used in the human studies,
but at comparable doses,
big increases in oxytocin were observed,
increases in sociability of those mice were observed,
just as they are in humans that take MDMA.
But in those mice, they were also given a drug
to block the oxytocin receptor.
And lo and behold, no changes in sociability were observed.
In humans that take oxytocin by nasal spray,
you can see big increases in oxytocin.
That's not surprising, gets across the blood-brain barrier,
oxytocin goes up, and levels of sociability do not increase.
So what this points to is a situation
where MDMA is increasing dopamine to increase motivation
and to reward something, what gets rewarded.
Well, what gets rewarded is the serotonin activation

of particular brain networks associated with sociability.
And the dramatic increases in oxytocin
that are very, very real when people take MDMA
do not appear to underlie any of the known short
or long-term subjective effects of MDMA.
Now, a conclusion like that needs to have a caveat.
And the caveat is that as far as we know,
the big increases in oxytocin that are produced by MDMA
aren't doing anything for the sorts of effects
that we've been talking about here,
sociability, empathy, et cetera.
But there could be other effects of oxytocin
that we're just not aware of.
That said, the data from both animal models and in humans
really point to the fact that the increases in oxytocin
that are produced by MDMA are not directly related
to any of the short and long-term effects of MDMA
that we are most familiar with, namely motivation,
sociability, increased empathy,
or the longstanding changes in neural circuitry
that underlie, for instance, reduced threat detection
or reduced connectivity between threat detection centers
of the brain and interoception.
So is the big increase in oxytocin produced by MDMA
completely irrelevant in the context of this discussion?
We don't know.
It appears that it's not very relevant.
Is oxytocin a meaningless molecule?
Right after all, they gave these people nasal infusions
of oxytocin, oxytocin went way up.
It didn't observe anything very interesting or significant
in the context of sociability.
But we do know that oxytocin can play a powerful role
in pair bonding and in human, human, human animal bonding
of various kinds from other experiments that have been done.
So I don't want to diminish the incredible power
that oxytocin has in our brains and bodies,
but it doesn't appear that the MDMA induced increases
in oxytocin, which are enormous,
have much to do with anything related to the value of MDMA
as a treatment for PTSD or for its subjective effects
on empathy, sociability, or any of those other factors either.
Now, perhaps the one caveat to that

is that Harriet DeWitt's laboratory,
which I referred to earlier,
has looked at how variations in oxytocin receptor genes
vary between people.
So it turns out that some people have an allele,
basically a version of the oxytocin receptor
that is different from other people
that makes oxytocin work differently
and actually less effectively
in activating certain brain networks.
And it does appear that when those people take MDMA,
they actually experience less of a pro-social effect
of the drug.
Now that spits in the face of everything I just said
about oxytocin not being involved in the effects of MDMA
on prososciability and empathy.
I think the bulk of the data really point to the fact
that it's the serotonin increases
combined with the dopamine increases caused by MDMA
that lead to most of the understood effects.
And that oxytocin, if it's playing a role,
is going to play a more minor role.
Let's talk about the safety
and potential neurotoxicity of MDMA.
And here I really want to highlight
that our discussion today is couched in a discussion
about the application of pure MDMA to animals or humans
in the context of laboratory or clinical studies.
This is really important to point out
because I would be remiss if I didn't note
that there is a lot of recreational use of MDMA.
In fact, it was the recreational use of MDMA in the 1980s
but really that took off, even exploded in the 1990s
with so-called rave culture
that created the massive attention on illegality of MDMA
and put the drug enforcement agencies onto MDMA as a drug
that they wanted to and indeed do restrict.
In fact, just today in anticipation of this episode,
I put MDMA into the search function on Google
and clicked news and there were at least two reports
of major MDMA seizures and busts.
So again, I want to highlight the fact
that MDMA is still illegal to possess or sell

and certainly to traffic.
I also want to highlight the fact
that nowadays all recreational drugs
but certainly MDMA included are often,
in fact, very often contaminated with fentanyl
and while fentanyl has certain clinical uses,
fentanyl is highly deadly.
The current estimates are as much as 60%,
maybe even 80% of drugs that are sold on the gray market
are being repackaged or reformulated with fentanyl
and there have been a lot of fentanyl related deaths
both in kids and adults.
So the sourcing of MDMA is extremely important
and the safety issues simply cannot be overlooked.
And I say that not to protect me,
I say that to protect you, right?
The last thing any of us want is for someone
to take a compound thinking it's one compound
and it contains another compound
and them getting hurt or even dying
and that is happening a lot, a lot
and it is certainly happening a lot for people
that think that they're buying MDMA.
The use of MDMA in the laboratory
or in the clinical setting with pure MDMA
has also been explored for the potential neurotoxicity
of MDMA.
So how would methamphetamine and MDMA be neurotoxic?
Well, that's because they increase dopamine
in the case of methamphetamine
and dopamine and serotonin in the case of MDMA
and they do so to a very high degree.
The big increases in dopamine and serotonin
but in particular the big increases in dopamine
tend to promote electrical activity of other neurons.
Remember, these are after all, neuromodulators.
They modulate up or down the activity of other neurons
and dopamine tends to modulate the activity
of other neurons up.
So dopamine itself is not neurotoxic
but when a lot of dopamine is released, it is neurotoxic
and it's well known that even a single dose
of methamphetamine can be neurotoxic

not just for dopamine neurons
but for other types of neurons as well
including serotonergic neurons.
Put differently, we know that the brains of people
that take methamphetamine degenerate to a small
or to a large degree depending on how often
they take the drug, how potent the drug is
and whether or not they combine it with other drugs.
And yes, if you heard that combining caffeine
with amphetamines can increase the neurotoxicity
of amphetamines such as methamphetamine, that is true.
If you've heard that taking caffeine within the hours
or same day as MDMA can increase the toxicity of MDMA
that does appear to be true based on animal studies.
Now, there are not a lot of studies looking
at the toxicity of MDMA in humans but there are a few.
There are also studies looking at the toxicity of MDMA
in animal models including non-human primate models.
Now, this is a very complex literature.
A lot of results, not all over the place
but they're scattered in a number of ways.
First of all, some of the animal studies
have used dosages of MDMA as high as two milligrams
per kilogram of body weight, as high as three milligrams
per kilogram of body weight and even in upwards of that.
But even for the animal studies that used a range
of dosages from 0.75 to 1.5 milligrams
per kilogram of body weight, there is some evidence
that in laboratory mycer rats,
there can be some loss of serotonergic tone
in the brains of animals that have been administered MDMA.
Now, notice I said serotonergic tone,
I didn't say serotonin neurons.
Because of the way that MDMA works in encouraging
or promoting big releases in dopamine,
big releases in serotonin, it's not surprising
that if the animals that were given MDMA
are subsequently sacrificed, say later that day
or the next day or maybe even a week or two weeks later.
And those brains are stained for proteins
that are related to the synthesis or release of serotonin.
It's not surprising that there would be reductions
in those sorts of proteins.

After all, a lot of dopamine and serotonin is released
and it can be depleted.
But I should point out, depletion of a neuromodulator
in the short term is not the same thing
as depletion of that neuromodulator in the long term,
nor is it the same as loss of the neurons
that release dopamine and serotonin itself.
So there are data pointing to the fact
that repeated administration of MDMA
at dosages that are very much within lines
with what we're talking about today,
1.5 milligrams per kilogram of body weight
can lower total amounts of serotonin
or other proteins in the serotonin synthesis pathway
or dopamine or proteins that are in the dopamine
synthesis pathway in specific areas of the brain
related to reinforcement, related to mood,
related to motivation, et cetera.
However, the primate studies
or I should say the non-human primate studies,
which are the sorts of animal studies
that most closely mimic what one expects to see
in the human brain, because after all,
mice and the effects of these drugs and mice
do translate to humans, but it's thought
that non-human primates provide a model
that's far more similar to humans.
There the data start to get kind of complicated
in a way that suggests that MDMA might not be
as neurotoxic as is thought based on the rodent studies.
And this gets into a whole history of back and forth
between different laboratories and governing bodies
who are trying to keep MDMA illegal as well as people
such as the Sasha Shulgens of the world
and people in the therapy community
that are excited about the potential
for MDMA becoming legal for the treatment of PTSD.
And it really centers around one or two studies,
both of which were published in very high profile journals.
And the one that I'll highlight
because the results are now very clear and conclusive
is a study that was published back in 2002,
which was entitled severe dopaminergic neurotoxicity

in primates after a common recreational dose regimen
of MDMA or ecstasy.
This paper was published in the journal Science,
which is one of the three APEX journals
for publishing scientific research.
So there's Science, Nature and Cell,
those are the top, top journals,
most stringent journals to get scientific manuscripts into.
The paper received a lot of attention
because as you can imagine based on the title,
it suggested that even recreational doses of ecstasy,
even if it's pure ecstasy and it doesn't have contamination
from additional methamphetamine or other things in it
is neurotoxic to serotonergic and or dopaminergic neurons.
This is largely where MDMA got the reputation
for quote, unquote, putting holes in your brain.
However, this study came under a lot of scrutiny
for a couple of reasons.
First of all, and I'm certainly not saying this,
but it was argued that the authors of the study
were perhaps trying to prevent the legalization of MDMA
for the treatment of PTSD.
As far as I know, there's no direct evidence
that that statement is true,
but you will actually find that
in some of the scientific journals.
In fact, I was able to find an editorial
that was published in the biomedical journal in 2003,
which argued somehow that Dr. Riccarte
was accused of quote, rushing his results into print
because of legislation designed to curb ecstasy use
before US Congress.
So, you know, there were some connotations
or rather there were some strong suggestions
that there was a political backing
to try to get this study done quickly and into print
and so forth.
I don't think that ever really got resolved.
What did get resolved, however,
is that the very study in question was retracted.
Okay, so the authors themselves publish a letter
of retraction that unfortunately is not as well recognized
as the paper that stimulated this idea

that MDMA is neurotoxic in primates.
And keep in mind that we are human primates,
non-human primates being the closest model
to human primates that we are aware of.
But to make a long story short,
there were some issues of labeling of MDMA
versus other drugs in the laboratory.
There were some issues of mislabeling,
all of which were eventually acknowledged
by the authors of the study.
And they concluded, in fact, they verified
based on some very detailed analysis
that what these monkeys were injected with
was not actually MDMA, but rather was methamphetamine itself.
So what's not often acknowledged is the retraction
of the paper on neurotoxicity.
And unfortunately, the neurotoxicity issue
is often what's mentioned.
Now, keep in mind, there are studies in rodents
showing neurotoxicity of MDMA,
perhaps even at recreational doses.
But to date, at least to my knowledge,
there don't seem to be any data
in either non-human primates or in humans
showing toxicity of MDMA at clinically relevant doses,
provided it is pure MDMA.
I want to be very clear.
I'm not saying that if you can get pure MDMA
that you should take it or that it won't be neurotoxic.
Certainly we can expect that because of the huge
known variation in dopamine receptors,
in serotonin receptors, and of course,
because of the known interactions between MDMA
and other compounds in particular caffeine,
but also drugs such as cocaine or other stimulants
that some people might experience more toxicity
to a given dose of MDMA compared to somebody else.
And there's really no way to detect that susceptibility
to neurotoxicity.
Now, what we do know is that there are people
in the general population that have taken a lot of MDMA
anywhere from one to 200 or sometimes even in excess
of 400 doses of MDMA.

And they're now our studies that have explored
the neurotoxicity and perhaps even more importantly,
the neurocognitive and behavioral effects
of taking MDMA either zero times, one time,
five times, 40 times, 200 times, et cetera, et cetera.
And one of the, what I would consider landmark studies
in this area is a study entitled
residual neurocognitive features of long-term
ecstasy users with minimal exposure to other drugs.
And those words with minimal exposure to other drugs
is really key in the context of this conversation
because as I mentioned before,
interactions between drugs, what's called polypharmacology
can create neurotoxicity.
It's unclear if MDMA is neurotoxic,
but we know methamphetamine on its own is neurotoxic.
We also know that people often will combine MDMA
and methamphetamine.
We also know that a lot of so-called MDMA out there
is mostly methamphetamine with only a little bit of MDMA.
So a study of the sort that I'm about to describe
where it is essentially confirmed
that people were taking pure MDMA
and not taking any other drugs is of immense value.
This study has been a little bit controversial.
In fact, I've talked about it before.
I talked about it on the Joe Rogan podcast.
I've talked about it briefly with a guest on this podcast,
Dr. Nolan Williams, who's a triple board certified physician,
psychiatrist and neurologist at Stanford School of Medicine.
And it's an interesting study and a little bit controversial
because it relied on a population of people
who have taken MDMA anywhere from one to 200 times
and who've not taken any other drugs, including caffeine.
And the population in mind here is a population of people
living in Utah who self-identify as members
of the Church of Latter-day Saints,
sometimes referred to as Mormons,
sometimes referred to as LDS
or of the Church of Latter-day Saints.
The Church of Latter-day Saints, as I understand,
does not allow for taking of certain compounds,
certain drugs, certainly most recreational drugs,

alcohol, even caffeine.
And I'm sure there's some variation on some of those themes
depending on where people live
and the certain communities that they happen to be in.
I am in no way, shape or form,
declaring that I'm an expert on Latter-day Saints.
I have a couple of friends who are LDS.
Happen to be very nice people.
As far as I know, they were not the people in this study.
But this study really emphasized ecstasy users,
as they're called, who have not taken other drugs,
who self-identify as LDS.
And the major takeaway of this study
was that for moderate, meaning people who have taken ecstasy
anywhere from 22 to 50 times in their lifetime,
as well as heavy users of MDMA.
So these are people who have taken MDMA
anywhere from 60, 60 to 450 times in their lifetime.
There was little evidence of decreased cognitive performance
in standard assays for cognitive performance.
Now, there were some effects showing poorer,
here I'm quoting from the findings,
poorer strategic self-regulation,
quote, possibly reflecting increased impulsivity.
However, when you see a conclusion like that,
you should immediately be thinking chicken versus egg, right?
It could be that people that are more impulsive
and that have less strategic self-regulation
are more likely to take ecstasy 450 times.
You could conclude that or you could conclude
that people who have taken ecstasy 75 times
or 25 times, et cetera,
are degrading their levels of self-control
and thereby increasing impulsivity.
The direction of the effect is not known.
These are purely correlations.
Nonetheless, this study and a few others like it,
really stand as our best evidence, believe it or not,
as to how ecstasy taken many times,
because after all these people are taken anywhere
from 22 to 450 doses of ecstasy in their lifetime,
is producing severe detriments in cognitive performance
and that simply does not appear to be the case.

Now, unfortunately, there are no data looking at
the brains of these individuals,
looking at, for instance, which brain structures are active
or less active or perhaps even looking at
levels of serotonin or dopamine,
all things that can be done with
positron emission tomography imaging,
functional MRI, et cetera.
Hopefully those studies will be done
in the not too distant future.
But if we were to just take a step back from all the data,
the data in mice and rats and non-human primates,
the retraction of the study in non-human primates
would show that the primates that showed neurodegeneration
were not given MDMA as was thought by the researchers,
but rather as later was acknowledged,
were actually given methamphetamine.
And we take into account these moderate and heavy users
of MDMA who, as far as we know, are being honest
and haven't taken any other drugs.
And we look at the clinical studies
where people who have never taken MDMA
are given one or two or three defined doses of pure MDMA.
We'll talk about those studies in a moment.
I think the Gestalt, the top contour,
the overall view of those studies
is that provided it is pure MDMA
and provided the individual is not consuming other drugs
which have the potential to be neurotoxic
and provided that it's being done
in a controlled clinical setting,
the risk for toxicity seems quite a bit lower
than the popular press has promoted.
And yet there is still the risk of neurotoxicity
if people are taking high doses of MDMA
or taking it very frequently
or certainly if they are taking it in conjunction
with other drugs or, or I should say,
and or taking MDMA in settings
that can promote neurotoxicity.
And the settings I'm referring to
are any settings in which blood pressure or body temperature
have the propensity to be greatly increased.

Every study in mice and non-human primates
and in humans in which MDMA is administered
has observed significant increases
in blood pressure and heart rate.
MDMA is after all a psychostimulant.
It's a sympathomimetic.
Talk about sympathomimetics and what that means
in the episode on Adderall and Vivance and ADHD.
But basically it's ramping up the activity
of the sympathetic nervous system
which is your fight-or-flight system.
This is why people who take these drugs get big pupils,
big pupils of the eyes.
This is why they feel agitated, they wanna talk a lot,
they feel like they wanna move a lot.
This is why people take it to dance at raves, et cetera.
But when people take sympathomimetics,
whether that's MDMA or amphetamine or cocaine
or even caffeine, there's an increase
in blood pressure and heart rate, but also body temperature.
And if that's done in an environment
in which there's very little temperature regulation.
So people aren't, for instance,
drinking enough fluids and electrolytes.
It's very hot in the room.
You can get neurotoxicity based on temperature effects
and that's because serotonin and dopamine
also act on the so-called medial preoptic area
of the hypothalamus which is involved in temperature regulation.
If you're curious about temperature regulation,
I covered a lot of that in the episodes
of the Huberman Lab Podcast on deliberate cold exposure
and deliberate heat exposure.
This is an area I used to work on many years ago
as a research scientist
before moving on to other topics to research
in my laboratory.
Big increases in body temperature are not good.
The body and in particular your brain
can tolerate decreases in body temperature
that are pretty robust and you can still stay safe.
You're not gonna kill neurons,
but even an increase of three or four degrees

in body temperature can start to kill off neurons.
So when thinking about the potential neurotoxicity of MDMA,
the conditions that is the environmental conditions,
the behavioral conditions under which somebody takes MDMA
are vitally important, at least important, I would argue,
as any other compounds they might be ingesting with MDMA.
So that's something really serious to consider.
So if somebody says MDMA puts holes in your brain,
you would be correct in being skeptical
or at least giving them some counterarguments
for that statement.
But if somebody says MDMA is not toxic,
well, then you would be equally valid in saying,
ah, wait, but we need to think about the conditions
under which MDMA is being taken.
Is it pure MDMA or is it mostly methamphetamine?
In which case it would be very toxic.
Is it MDMA alone or in conjunction with caffeine
within that same 24 hour period?
Is it MDMA while moving around a lot or being outdoors
or being in an environment,
perhaps a rave or dance type environment
where temperature is going up?
Well, in that case, it could be very neurotoxic.
So pharmacology of MDMA counts,
but so does polypharmacology,
the ingestion of other compounds,
not just during the MDMA session,
but also in the 24 hours before and after that MDMA session
and behaviors will certainly impact temperature
which will impact whether or not MDMA is neurotoxic or not.
And despite my efforts, I couldn't find out
whether or not the LDS community
has officially sanctioned the use of MDMA.
Certainly that's one possibility,
but I have no evidence for that.
Or rather, whether or not certain people
within the LDS community have allowed themselves,
given themselves permission to use MDMA
and they are not using other drugs.
What I do understand to be the case
is that people within the LDS community
are discouraged from using drugs like caffeine

or cocaine or alcohol.
And this particular population of people
that was explored in this study,
self-identify as LDS and self-identify
as having taken MDMA anywhere from 22 to 450 times.
But where they got permission for that,
whether or not it was from someone else or from themselves,
I do not know.
What I do know is that within the acknowledgments
of the paper, there's actually a thank you
to the person that identified
this quote unique population for our study.
So I welcome you to take a look at the paper
and if any of you know more about
if and how a particular subgroup within the LDS community
is allowed to take MDMA,
perhaps you wanna put those in the comment section
on YouTube.
Before moving to our discussion about what MDMA is doing
and the effects that people are seeing
in the clinical studies for the treatment of PTSD,
which by the way are extremely exciting.
I can't wait to share these data with you.
I do wanna touch on something that anyone who's heard
about MDMA or perhaps used MDMA is familiar with
and that's the so-called crash
that people experience after MDMA.
There are a lot of myths about the post-MDMA crash
and there's a lot of lore out there on the internet
about how to offset the crash and a lot of lore
about how to prevent the potential neurotoxicity of MDMA.
Earlier we talked about some of the major points
around offsetting neurotoxicity.
So certainly making sure that any MDMA
that one takes is in the legal clinical setting,
that it's therefore pure MDMA,
that it's not cut with other things,
which certainly can increase toxicity,
controlling the temperature of one's environment,
restricting caffeine intake,
at least on the day of MDMA ingestion,
but certainly the day before and the day after
would be advantageous.

Well, simply because of the way that caffeine
and activation of the adenosine receptor
as well as caffeine's effects on dopamine receptors
can interact with the potential,
again, potential neurotoxicity of MDMA.
But the crash that one experiences after MDMA
is actually a phenomenon very common
to the crash that one experiences
after ingestion of any type of stimulant,
cocaine, amphetamine, et cetera.
And the crash that we're referring to
is a drop in mood, increase in lethargy,
feelings of lack of motivation.
Many people have wrongly assumed
that the crash was due to, quote unquote,
depletion of serotonin or depletion of dopamine
or maybe even death of serotonergic
and dopaminergic neurons.
And while certainly that could be the case,
it's very unlikely that that would be the case
in the immediate 24 or 48 hours after MDMA ingestion.
That said, you will see protocols
that people have put out on the internet,
such as, oh, after taking MDMA,
you should take a bunch of five-HTP
or other precursors to serotonin or dopamine,
which come in amino acid form.
So L-tryptophan, for instance,
is the amino acid precursor to serotonin.
It's in the serotonin synthesis pathway.
You'll hear that people will take L-tyrosine,
which is the amino acid precursor to dopamine
as a way to try and buffer or increase dopamine
during the so-called period of the crash.
There's really no evidence
that any of those things can be beneficial.
And there is actually some reason to believe
that it might be detrimental
because if anything, taking L-tryptophan
and taking L-tyrosine
would actually further deplete serotonin and dopamine.
So the logic there is simply not very good.
What is clear, however,

is that MDMA can cause not just profound increases
in dopamine, serotonin, and oxytocin,
but that anytime there's a big increase in dopamine,
there is going to be a post-dopaminergic increase
in prolactin release.
And prolactin is a hormone,
sometimes considered a neurohormone,
but it's really a hormone
that's involved in a lot of things,
milk let down in lactating women.
It's involved in setting the refractory period
to sexual arousal and erection and ejaculation in males
after ejaculation.
It's involved in lots of different functions
in the brain and body,
including the laying down of body fat stores.
And it's also associated with increases in lethargy,
decreases in dopamine.
This is why drugs that increase dopamine
are known to decrease prolactin,
at least in the short term.
This is why drugs like cabragoline, for instance,
that increase dopamine are used
as ways to suppress prolactin.
Now, MDMA ingestion is known
to dramatically increase prolactin.
And people are starting to realize
that it perhaps is the increase in prolactin
that occurs both during and for some period of time,
probably hours or days after ingestion of MDMA
that leads to at least some components
of the so-called crash,
that feeling of lethargy and lack of motivation,
maybe diminished mood, et cetera.
And for that reason,
some people have started to explore the use
of things like P5P,
which is essentially a metabolite of vitamin B6,
which is known to suppress prolactin
as a way to try and buffer some of that crash.
To my knowledge, there are no human data yet exploring
the use of P5P or other vitamin B6 derivatives
or cabragoline or things of that sort

to reduce prolactin in a controlled,
standardized clinical trial kind of manner.
But I've spoken to some of the clinicians
that are using MDMA legally
within the context of the treatment of PTSD.
And this is an area that's starting
to receive some additional attention.
So I just mentioned it briefly here
because for instance, there's a lot of ideas out there
that people should be taking L-triptophan,
they should be taking L-tyrosine,
they should be taking magnesium,
other things, et cetera,
after taking MDMA in order to recover
from the post-MDMA crash more quickly.
But it's really the increase in prolactin,
which speaks most directly
to the subjective effects of the so-called crash.
So by my read of the mechanisms of MDMA,
the neurochemicals it releases,
the neurohormones that it promotes
the release of prolactin in particular,
this P5P suppression of prolactin
is perhaps the one that's most intriguing
and that really has any kind of mechanistic basis.
So I promise that going forward
as the scientists and clinicians that are using MDMA
for the treatment of PTSD and other conditions
such as alcohol use disorder, et cetera,
start to explore the use of post-MDMA session P5P
and other modes of suppressing prolactin
for the hours and days after MDMA,
promise to update you on those findings.
Throughout today's episode,
I've been referring to clinical studies,
that is clinical trials,
exploring the use of MDMA
in order to augment treatment for PTSD.
So let's just take a moment
and talk about what PTSD is.
PTSD is post-traumatic stress disorder.
Trauma is anything that modifies the brain
to function less well going forward.

You can have physical trauma,
you can have emotional trauma.
Typically PTSD is used to refer to emotional trauma
caused by either single events.
So you can imagine car accident, sexual assault.
These can be first-person experiences.
So things that happen to somebody
that leads to trauma and then PTSD.
These can also be third-person events
where someone observes something that is traumatic to them.
Maybe somebody being killed, dismembered,
any number of different things
that could be very traumatic in the immediate and long-term.
And of course, PTSD need not be caused
only by single event traumas,
but by multiple event traumas,
entire relationships, entire childhoods,
wartime experiences,
combinations of different traumas, and on and on.
There are so many different forms of trauma.
If any of you are interested in trauma and its treatment,
I highly recommend the book Trauma by Dr. Paul Conti.
He's an MD, medical doctor, psychiatrist.
He was featured as a guest on this podcast.
He's been on a number of other prominent podcasts.
We will provide a link in our show note captions
to the book Trauma.
I consider that book to be the best book
in terms of describing what trauma is and isn't
and how it leads to PTSD.
It also describes some of Dr. Paul Conti's own experiences
with trauma and his own treatment of trauma
in his patient population,
which is quite wide-ranging men, women, young people,
older people, and a variety of traumatic experiences.
So excellent book for those of you interested in trauma.
Now, the treatment of trauma has been met
with some degree of success through quality talk therapy.
Let's define quality talk therapy
in the way that Dr. Paul Conti did on this episode.
That's talk therapy for which the patient
sometimes referred to as the client,
but more traditionally referred to as the patient

and the therapist.
So a psychologist or psychiatrist has good rapport.
And as a consequence of that rapport,
there is the feeling of support,
that there is a safe place in which to explore the trauma
and what's happening in one's current life
in order to understand how that trauma is fitting in
to adaptive and maladaptive behaviors and emotional states.
Now, in addition to rapport and support being critical,
there's a third component of effective talk therapy
for trauma, which is insight,
where one's ability to come to an understanding
of why one feels the way they do,
and to link that to some larger context
that brings about some degree of relief.
And that's where things start to get a little bit abstract.
And that's also where we start to see that
while trauma therapy in the form of talk therapy
can be very effective,
about half of people that undergo talk therapy
and talk therapy alone for the treatment of PTSD
achieve no long lasting relief of symptoms
and an even smaller number of them
undergo complete remittance of their PTSD.
So their symptoms can lessen,
they can get some improvement,
but that improvement is often slight or is transient.
And for those that do achieve relief,
it's often not complete remission of the PTSD itself.
Now, in addition to talk therapy for PTSD,
there is of course prescription drug therapies.
And most often these fall under the category of SSRI,
selective serotonin reuptake inhibitors.
And it's well known that SSRIs can be
in limited circumstances,
effective for the treatment of PTSD.
It has been shown, for instance, that as many as 40,
maybe as many as 60% of people that take SSRIs
for the treatment of PTSD get some symptom relief.
Now, that is not to say that SSRIs don't have side effects.
They can have side effects.
Some of you are probably familiar with these side effects.
Things like blunting of libido,

blunting of appetite or increases in appetite,
in some cases disruption of sleep wake rhythms,
motivation, et cetera.
So there's often an exploration
for the so-called minimal effective dose
that provides some symptom relief to PTSD,
but that doesn't introduce unwanted side effects.
And of course, there's a third situation
where people are taking SSRIs
and doing talk therapy for PTSD.
And what's very clear is that anytime you add quality
talk therapy to a drug treatment,
you're going to improve the outcomes
for that drug treatment.
The reverse is not always true.
It's not always the case
that adding prescription drug treatment
to talk therapy improves outcomes for talk therapy,
although that has been observed in a number of studies.
Now, the whole idea of exploring the use of MDMA
for the treatment of PTSD stemmed from the fact
that even in people who are getting quality talk therapy,
and again, we can define quality talk therapy
as good rapport between patient and clinician,
as well as feelings of support,
as well as potential insight.
And even when SSRIs are combined
with that quality talk therapy,
there's still a large number of people
who simply do not achieve significant
or long lasting relief from their PTSD,
and even fewer number who go into full remittance
of their PTSD.
That is despite being diligent
and hardworking in their talk therapy,
despite the therapist being very committed,
despite the use of SSRIs in conjunction
with that talk therapy,
those people often still qualify as having PTSD.
And the goal, of course, is for somebody
to receive treatment that allows them
to no longer meet the criteria for having PTSD,
not just in terms of a clinical evaluation,

but that they themselves report feeling much better,
not feeling overwhelmed with the symptomology of PTSD.
Now, the symptomology for PTSD is vast,
and it's far too vast to go into a lot of detail right now.
I think most people are familiar
with the stereotyped example of PTSD.
This is the soldier that comes back from overseas
that has been in gunfights or in battles of different kinds,
has likely seen casualties and severe injuries,
and that upon return to a safe environment,
is still experiencing a lot of anxiety
and sometimes panic attacks that occur seemingly at random,
or that can be sparked by the classic stereotyped example
as a car backfires and then the person
suddenly feels as if they're back in battle.
That sort of thing does happen, certainly,
but there are a whole other category of symptoms of PTSD,
which include dissociative symptoms of PTSD.
People who have PTSD from very intensely traumatic
experiences that are checked out,
they don't feel like they can engage,
they have brain fog, they are distracted,
they go from feeling anxious to feeling exhausted,
they have sleep issues, not surprisingly then,
people with PTSD of either the dissociative type
or other symptomology of PTSD,
and keep in mind that one can have both dissociative
and non-dissociative symptoms of PTSD,
such as anxiety and panic,
are at a far greater risk of substance abuse.
So the current estimates are that people with PTSD,
no matter what type of PTSD, dissociative symptoms
or otherwise, you know, panic attacks or both,
are at a much greater risk of having addictions
to either illicit drugs or prescription drugs or both.
So things like alcohol use disorder is very common
in people with PTSD, opioid use disorder is very common,
stimulant use disorder, and on and on.
So people with PTSD suffer at a number of different levels
and there are all these what are called comorbidities
with PTSD, including addiction,
but also depression, anxiety,
and so you can start to see how PTSD sets up

a whole cascade of things that make
living life extremely problematic
at the level of basic relationships
functioning in the workplace.
And even when mental health appears to be in check,
oftentimes people are holding a lot in,
so they have cardiovascular and cerebral vascular deficits
that cause a lot of problems in their immediate
and long-term physical health.
So PTSD is a very serious issue.
The current estimates are that as many as 8% of people
in the United States have PTSD,
and again, the estimates around comorbidities
range anywhere from, you know, 17 to 46
or as high as 65% of people with PTSD having comorbidities
for other mental health issues and addiction in particular.
So finding lasting relief to PTSD is extremely important
and made even more important by the fact
that many people with PTSD sadly end up committing suicide.
So suicide rates are far greater in people with PTSD.
The exact rates of increase in suicidality
in people with PTSD are a little bit hard to arrive
at in the statistics because of all the comorbidities,
but suffice to say that suicide is far more likely
in people with PTSD along with all the other issues
that PTSD brings about.
Now PTSD creates all the problems that it does
largely through changes in brain circuitry
as well as neural communication between the brain and body.
Many people have perhaps heard of the book
The Body Keeps the Score, which is a very successful
and popular book about the idea that trauma can be
quote unquote stored in the body.
To be clear, traumas can't actually be stored in the body.
You don't actually store memories in the body.
What you store are activation of neural circuits
that include brain and body,
and they all seem to center back into the insula,
that structure that we talked about earlier,
this structure in our brain
that has a map of our body surface.
So contrary to popular belief,
we don't store memories in the body or trauma in the body

in a way that for instance, working out a knot
or a pain in one's lower back will relieve the trauma.
It sometimes can activate a memory of the trauma,
but when one is doing that, what you're really doing
is activating neural circuits that reside within the brain,
within the insula that correspond
to sensations within the body.
Now, I don't want to diminish the role of the body
and the formation and the persistence of PTSD.
And I certainly think the book The Body Keeps the Score
is a pioneering book, it's in fact an important book,
but I want to emphasize that the modern neuroscience
really points to the fact that PTSD is caused
by the exact sorts of brain network activations
that we were discussing earlier.
Things like heightened levels of activation
in the amygdala to insula pathway,
which of course would exacerbate bodily sensations
related to the trauma or heightened activation
of the hippocampus, this memory center in the brain,
to amygdala to insula circuitry.
Now, therefore it should come as no surprise
that if MDMA can reduce the levels of activity
in the hippocampal to amygdala to insula circuitry
and can do so both while someone is under the effects
of MDMA, but then lead to persistent long lasting reductions
in the activation of those brain networks.
Well, then it stands to reason that MDMA could be
a valid therapeutic for the treatment of PTSD.
And of course, this has been explored.
And here we can really give a nod and a large debt
of gratitude to the so-called maps group.
The maps group is a group that's operating mainly
out of Santa Cruz, California, but they have a number
of different satellite laboratories and clinical groups
both in the US and Canada and abroad,
where they've worked with government organizations
to get legal authorization to give MDMA to patients
who have PTSD to also give them talk therapy
and then to compare the effects of talk therapy with MDMA
to talk therapy with placebo alone.
And there are about three to five studies in this area now
that stand as large scale clinical trials

that are showing what can only be described
as remarkable results for the treatment of PTSD.
So rather than going to any one of those studies
in immense detail, I'm going to summarize across those studies.
I will provide links to those in the show note captions.
The two that I think are most interesting
are the study entitled MDMA assisted therapy
for severe PTSD, a randomized double blind placebo controlled
phase three study, as well as the study entitled
the effects of MDMA assisted therapy on alcohol
and substance use in a phase three trial
for the treatment of severe PTSD.
So as the title suggests, both clinical trials
involve giving people talk therapy and MDMA
or talk therapy and placebo.
Talk about exactly how that was done in a moment.
And then to look at relief of PTSD symptoms,
but also relief of some of the addictive symptoms
that are commonly associated with PTSD.
So just to give you an overview of what's happening
with these trials and why there's so much excitement
and why we really are on the cusp of legalization of MDMA
for the treatment of PTSD
in the sorts of clinical context I described.
When people are given just talk therapy alone
or talk therapy with SSRIs, they will often,
as I mentioned earlier, experience reductions
in their severity of PTSD symptoms.
And rarely they will experience complete remittance
of their PTSD.
That is they will no longer qualify for PTSD
after receiving a number of talk therapy sessions.
So let's compare that to what happens
when people do talk therapy in conjunction with MDMA.
And I'll explain exactly what that means in a moment,
but it essentially means taking MDMA while doing talk therapy.
However, this is a very important, however,
the people who are taking MDMA in these trials
have already done talk therapy without MDMA.
Then they're doing talk therapy under the influence of MDMA
and then they are doing sessions of talk therapy,
not under the influence of MDMA.
And the entire time they're doing that

with the same two therapists.
In the placebo group, people are doing talk therapy
with two therapists, but they're not taking MDMA.
So they're doing the same number of therapy sessions,
but they're not taking MDMA.
So to just get to the key numbers first,
the overall rate for clinically effective response
to MDMA assisted therapy is 88%.
That's what's emerging from these trials
versus 60% for the placebo and therapy alone.
So on the face of it, you might say, okay, wow,
88% of people who do talk therapy,
and here I might as well just finally explain
how this is done.
Patients are selected because they have PTSD.
They meet the clinical criteria for PTSD.
They do three 90 minute therapy sessions with two therapists
talking about their PTSD symptoms,
talking about to the extent that they can,
or incidents, the life events that led to that PTSD.
None of that is done under the influence of any drug.
Okay, so everyone in the experiment does that.
Then the group divides into two
where half are taking MDMA.
They take that three times.
During those three times, they are also receiving
therapy sessions with the same therapists
that they were working with before they took MDMA.
The first session, they're taking 80 milligrams of MDMA
and then a 40 milligram booster
about an hour and a half to two hours in.
The second session, they are taking a higher dose of MDMA.
It's 120 milligrams.
And then if they elect to,
they can take a 60 milligram booster
about an hour and a half to two hours into the session.
And then there's a third session where they take,
again, 120 milligrams of MDMA
and have the option to take a 60 milligram booster
about an hour and a half to two hours into the session.
Again, anytime they're on MDMA,
they have therapists there
that they're talking to about their trauma.

They are either spending time
with their eyes closed lying down,
sometimes in an eye mask and thinking about the trauma,
thinking about their current state and experience,
also thinking about what happened before,
then they're exiting the eye mask
or talking to the therapist.
Therapist is taking notes, asking questions.
Remember, they've established a strong rapport,
supportive relationship with these therapists
prior to taking MDMA in the therapy session.
And then they also undergo three 90 minute therapy sessions
with the two therapists spaced one week apart
after the final MDMA session.
Now, those that were placed into the placebo condition
do everything exactly the same as I just described.
So three 90 minute sessions as prep,
then three eight hour sessions with those two therapists
and then three 90 minute follow-up sessions one week apart,
but they take a placebo, not MDMA.
So you can see that in these so-called MAPS studies,
these clinical trials for PTSD,
the conditions are very similar
except for the inclusion of the drug MDMA.
So those rates of success with talk therapy and MDMA,
again, overall rate for clinically effective response
to MDMA assisted therapy was 88% compared to 60%
for therapy and placebo.
What's even more impressive, however,
is that 67% of the people in the MDMA
plus therapy treatment group,
no longer met the criteria for PTSD
by the end of the treatment.
So in other words, their PTSD went into remittance.
We could say they are quote unquote cured,
but typically for things like PTSD,
that's not the language that's used.
Rather what's used is statistical evaluation
of how the different symptoms like dissociation
or anxiety or sleep disorders are explored.
So while to some of you,
a difference between 60% success with talk therapy
and placebo versus 88% success with talk therapy

plus MDMA might not seem like that big of a difference.
It is indeed quite an enormous difference.
In fact, to my knowledge,
there is no other example of a treatment
for a psychiatric disorder
that is successful to the same magnitude.
I could be wrong about that.
I'm sure some psychiatrists out there
are gonna jump on me about this.
And please do, I would encourage you
if you are aware of any therapy plus drug treatment
that is effective at rates of greater than 88%
for the treatment of a major psychiatric disorder,
please do put that information in the comments on YouTube
and perhaps a reference to a study would be even better,
but even if not, just put a reference to that.
That would be great for sake of future episodes, et cetera.
But nonetheless, an 88% success rate,
and here I'm referring to success rate
as a significant reduction in clinical symptoms for PTSD
and 67% of those people going into full remittance for PTSD
by the end of the treatment is pretty spectacular,
which is why you're hearing so much these days
about the potential transition of MDMA
from a schedule one drug for which there quote unquote,
no clinical applications to potentially a legal
within the context of clinical use application of MDMA,
which it does appear the legislature
is at least considering for as early as 2024,
maybe even later in 2023, it remains to be seen.
Now, a number of other important results have emerged
from this and other clinical trials.
For instance, remember earlier,
I talked about how many people with PTSD also suffer
from alcohol use disorder.
What's interesting is that for people
that were in the MDMA plus talk therapy group
in this and other studies who also had patterns
of alcohol use disorder
and even some other substance use disorders,
the MDMA plus talk therapy treatment in many cases
resolved their addiction to alcohol
or other symptoms as well.

And perhaps that shouldn't be surprising
if we think about the addictions as stemming directly
from their PTSD, but it is surprising
if you think about the fact that alcohol use disorder
and some other addictive disorders oftentimes will stem
from disruptions in neural circuitry
that are the same disruptions in neural circuitry
that occur in PTSD, but often are the consequence
of entirely other brainwiring phenomenon.
What I'm saying here is that just because addiction
and PTSD are often comorbid with one another,
it was not necessarily the case that treating
and resolving PTSD would resolve the alcohol
or substance abuse disorder.
And yet that seems to be the case often, not always
but often in these successful treatments of PTSD.
So that's very exciting.
Some of the other particularly exciting results
from these clinical trials on MDMA plus talk therapy
is that the dissociative form of PTSD
has traditionally proved to be especially hard to treat.
And that's thought to stem from the fact
that successful treatment of PTSD,
whether or not it's by talk therapy
or talk therapy combined with SSRIs
or talk therapy combined with any drug treatment
or behavioral treatment like EMDR,
eye movement desensitization, reprogramming
or other forms of treatments that are designed
to rewire neural circuitry almost always involve
the patient getting very close to
or at least reporting the traumatic experiences
in a lot of detail.
And you can imagine why for somebody who's dissociating
from that very experience who's quote unquote checked out
and can't really seem to access the emotional states
and the memories because they're blocked off from them
or because they're unwilling to access those memories
and really think about the full emotional capacity
of those memories that it would be particularly hard
to bring them through any kind of treatment for PTSD.
So it appears that MDMA in providing this pro-social empathic
again empathic for others and empathic for self

chemical and mental environment
as well as the presence of two trusted therapists
which one has a really good rapport
allows patients with PTSD to really get close
to those experiences that were traumatic
to talk about them and to think about them
and in many ways to reframe them in a context
that often involves empathy for others and empathy for self.
Now here we're not necessarily talking about
forgiveness of perpetrators
although that's sometimes the case
that people will forgive the person
that inflicted the trauma on them.
But more often than not it's about tying their feelings
of trauma and their feelings of depression,
anxiety, dissociation, et cetera
to some sort of larger context that allows them
to see themselves in the role of agency
to be in the role of knowing that yes, these things happened
and yet by getting close to the emotional load
of those things and really being in many ways
unafraid to get close to the emotional load of that
and having support around that
that the emotional load seems diminished
and that they experienced the emotional load
of those experiences as diminished
both within the MDMA treatment session
and afterwards for long periods of time.
So essentially what happens is these people feel
that once burdened them, they can still remember
but it no longer burdens them.
It no longer feels like it's in their body
and in their mind or on loop or on repeat
in a way that's invasive and in a way that interferes
with other aspects of normal functioning.
So when one hears about these kinds of results
and when you hear about some of the patient reports
and I invite you to do that, you can go to the map site
which by the way is recruiting subjects
for these clinical trials and you'll also find reports
of individuals who participated in these clinical trials
and of course we will provide links
to these incredible clinical trials

that maps has spearheaded.
What you find is that the combination of MDMA
and talk therapy in many ways is not about the drug
having a particular effect.
It's really about the drug having a particular effect
that allows the motivations and the results
of talk therapy to really be heightened.
And I think that's a really key point to make
because up until now we've really been talking
about the neurochemistry of MDMA,
the potential toxicity or lack thereof of MDMA.
We've been talking about the brain networks, et cetera.
But when one thinks about the valid clinical use of MDMA
for the treatment of PTSD and I should mention
it also had some success in dealing
with not only alcohol use disorders
and other use disorders associated with PTSD
but also relieving the depression associated with PTSD.
So now MDMA is being explored for treatment
of not just PTSD but also for depression,
for alcohol use disorder and for eating disorders as well.
MDMA seems to be a compound that produces
the right kind of subjective and neurochemical milieu
in the brain that allows therapy to be that much more potent
within a limited number of sessions.
And when one thinks about the cost of mental healthcare,
how expensive it is to get therapy over and over
and over again, which in ideal circumstances
people are able to do that either by way of insurance
or by their own finances or I don't wanna say
that the cost of therapy should be reduced
because of course therapists have to survive also.
But the idea here is that people who are suffering
would be able to achieve relief from their PTSD,
their depression, their addiction and to be able to do so
by hopefully persisting in their therapy
over whatever period of time is required.
But also to assume a circumstance in which somebody
only has 10 or 15 or maybe even just three opportunities
to undergo treatment for PTSD and nonetheless
is able to achieve tremendous relief during the session
and after the session.
And it really does seem to be the case

that for reasons that you now understand,
the activation of particular brain networks,
the suppression of other brain networks,
in particular this amygdala to insula pathway
that when people are under the influence of MDMA
in these very safe and therapeutic supportive settings,
they're able to look at traumatic events
and the ways that those traumatic events impact them
in ways that really allow them
to cognitively reframe those events
and somatically reframe those events
to really change the way that it lives in their body and mind
so that it's no longer invasive
and then they can go on and lead productive adaptive lives.
And as a final point related to these clinical studies,
I of course it would be remiss
if I didn't touch on some of the so-called adverse effects
because anytime there's a drug or talk therapy
for a mental health issue,
adverse events have to be considered.
And I think it's quite reassuring
that in the case of MDMA therapy,
there were no increases in the number of suicide attempts
or suicidality or obsession with suicide.
Contrast that with the group that received placebo
where there were a certain number of baseline
and predicted obsessions with suicide.
Fortunately, at least to my knowledge,
there was no actual suicide attempt
or successful suicide, thankfully.
But the point being that the addition of MDMA drug therapy
to PTSD talk therapy does not seem to increase
the quote unquote side effects
that are sometimes associated with PTSD talk therapy
because indeed there can be side effects
to exploring PTSD and trauma as one would expect.
So overall, I would say it's very exciting times
for the exploration of MDMA as an augment to talk therapy
for the treatment of PTSD and these other conditions.
Again, I think the maps group has done a remarkable job
of keeping this within the realm of legal
and trying to move things forward in terms of legislation
to make sure that MDMA isn't simply made legal

and then abused recreationally.
I know people out there have different views
on whether or not drugs like MDMA should be legal or not.
That's not what this episode is about.
What I am very excited about, as you can probably tell
and what I think a lot of people in the psychology
and psychiatry community are very excited about,
you say the mental health community at large
is that these compounds that for many years
were only associated with their recreational uses
and therefore were not well understood
because they were often contaminated
or taken in combination with other things
or by people that never should have been taking them
in the first place, taken by young kids
which is a whole other matter.
A lot of issues and problems associated with these compounds
and yet we're now seeing from these clinical trials
when used, let's say properly
because really when safety protocols are obeyed,
when there's clinical support,
it is very clear that when MDMA is combined
with quality talk therapy
that the outcomes are looking tremendously positive.
It's by no means a miracle cure,
it is by no means perfect and time will tell
what problems if any arise
from the short or long-term use of MDMA in this context
but I think it's remarkable that anywhere
from two to three sessions with MDMA and talk therapy
have been shown to significantly reduce PTSD symptoms
and in some cases completely eliminate PTSD symptoms
in such a wide range of patients
and in patients that have experienced both PTSD
and these other comorbid disorders.
I think it's really remarkable, it's very exciting
and I look forward to seeing
what the next round of data produce.
So as is often the case on this podcast,
today we went into a lot of detail about a subject.
MDMA is this incredible compound synthesized
as far as we know, first by humans, not by plants,
not by aliens but by humans

and that produces big increases in dopamine and serotonin
to create these highly motivated prosocial empathic states
meaning both empathy for others and for self
and that when applied in the context
of psychiatric challenges like PTSD and addiction
is proving to create a lot of relief
for a lot of people where other forms of drug therapy
or combination drug and talk therapy had failed before.
We talked about some of the potential neurotoxicity issues.
I don't think that is a resolved issue just yet
although the bulk of data in humans
and non-human primates point to the fact
that at reasonable doses
and we talked earlier about what those are
at reasonable doses when not combined with other drugs
does not appear that MDMA is exceedingly neurotoxic
and it may not be neurotoxic at all.
Of course, one needs to be exceedingly cautious
when thinking about the use of any sympathetic,
they of course can be neurotoxic,
anything with methamphetamine in it
has the potential to be neurotoxic
but of course dosage matters, context matters,
we talked about that and of course
the purity of drug matters.
And again, I just wanna reemphasize
the fentanyl contamination of MDMA that's sold on the street
and that is being used recreational
is of very serious potentially lethal concern.
I also expect that there will be a lot of interest
in these clinical trials that MAPS is doing.
So again, you can find links to that
in the show note captions.
And I think in general, we should acknowledge
that we are a very interesting and important time
in human history for the treatment of psychiatric disorders
and for neuroscience generally
because whether or not we're talking about psilocybin
or LSD or ayahuasca or ketamine
or today's topic of MDMA,
regardless of what drug and neurotransmitter
and modulator systems are involved,
what we're really talking about

are ways to access neuroplasticity,
the nervous system's incredible ability
to modify itself in response to experience,
ideally to be modified in adaptive ways
that make it function better.
So that's really the crux of what talk therapy
and drug therapies are about.
That's what the goal of using MDMA
as a clinical tool is all about.
And in that sense, I find MDMA to be
an incredibly interesting and important topic.
And I hope you did as well.
If you're learning from and or enjoying this podcast,
please subscribe to our YouTube channel.
That's a terrific zero cost way to support us.
In addition, please subscribe to the podcast
on both Spotify and Apple.
And on both Spotify and Apple,
you can leave us up to a five star review.
If you have questions for me or comments about the podcast
or guests that you'd like me to interview
on the Huberman Lab podcast,
please put those in the comment section on YouTube.
I do read all the comments.
Please also check out the sponsors mentioned
at the beginning and throughout today's episode.
That's the best way to support this podcast.
Not so much during today's episode,
but on many previous episodes of the Huberman Lab podcast,
we discuss supplements.
While supplements aren't necessary for everybody,
many people derive tremendous benefit from them
for things like improving sleep,
for hormone support and for focus.
The Huberman Lab podcast is proud to have partnered
with Momentus Supplements.
If you'd like to see the supplements discussed
on the Huberman Lab podcast,
you can go to livemomentus spelled OUS.
So that's livemomentus.com slash Huberman.
If you're not already following me on social media,
I am a Huberman Lab on Instagram, Twitter,
Facebook and LinkedIn.

And at all those places,
I discuss science and science related tools
for mental health, physical health and performance,
some of which overlap with the science and tools
that are discussed on the Huberman Lab podcast,
but much of which is distinct from the information
covered on the Huberman Lab podcast.
So again, it's Huberman Lab
on all social media platforms.
If you haven't already subscribed
to our neural network newsletter,
the neural network newsletter is a monthly newsletter.
It's completely zero cost,
where we provide podcast summaries as well as toolkits.
The toolkits are short lists in PDF form
of things that you can do to improve, for instance,
sleep or neuroplasticity or dopamine regulation
or deliberate cold exposure or fitness and on and on.
Again, all of that is available at zero cost.
You simply go to HubermanLab.com, go to the menu,
scroll down to newsletter and provide your email.
We do not share your email with anybody.
So if you're interested in those toolkits
and the neural network newsletter, again,
that's available at HubermanLab.com.
Thank you again for joining me for today's discussion
all about MDMA.
And last but certainly not least,
thank you for your interest in science.