Historic Denial of Consciousness in Other Animals

JAAK PANKSEPP: Well, it's a pleasure to be here. I think most of you are freshman. When I entered University of Pittsburgh as a freshman, I started in electrical engineering. That didn't last for more than a year, and then I went through a couple other majors trying to find what I was really interested in. So just consider the university as a place where you can find your interest, and then really focus on it, and educate yourself. After all, that's your job. We just help you on the way.

And what really brought me to my interest was working myself through college, and working in the back wards of a psychiatric hospital as a night orderly, and finding these human beings whose emotions had gone astray. They'd lost their center of gravity, and since I was a night orderly, I had lots of time to read their case reports, which were wide open for consumption as long as you were working there, and I became fascinated. Then wondered how I'd get into the field. I didn't have the prerequisites for medical school, so I was not about to pay for another year of college, and I decided that I could get into the field by being a clinical psychologist.

So the last year I just took psychology courses like crazy, and I was fortunate enough to be accepted into clinical psychology at University of Massachusetts. And the first year there I was a little bored again, because I thought people would be talking about the emotional problems, and how they emerge, and what we know about them, but that was an era of behaviorism, and the main kind of therapy was behavioral modification. So if you modify the behavior, you supposedly modify the mind.

That didn't seem to suit me, but I was fortunate enough to have a trainee-ship in a Veterans Administration hospital with all the wounded soldiers. And my training there was to go to three stations in the hospital of my choosing and finally decide where I wanted to stay. And I did autopsy for my first rotation, and I did psychotherapy for my second rotation. It was behavioral modification, and I wasn't all that intrigued by it.

And then I ended up in an electron cephalography lab, and the director of that laboratory, who was measuring brain waves and people who had brain damage or epilepsy-- that seemed fascinating. One was now in touch with the organ of the mind, and I thought you could not understand emotions unless you understood the brain, and the emotions were barely being discussed in those days in the early '60s, long before you were born. And it turned out that he had a laboratory in the back, an animal laboratory, and he was measuring visual processes and how the cortex handled all these signals coming into the world.

And he asked Panksepp, what do you want to do with your life? I said I'm really interested in emotions. He said, emotions? Can you even study that? And I said, I think I can. And he said, well, go ahead then, and gave me free run of the lab. That was the best education I ever had. Here are resources. Use them if you think you can do it.

So you can't understand human emotions without understanding animal emotions, because things are way too deep in the nervous system to be able to access them in humans, except on the surface, and the surface is important, but that's a really higher process. So here's this little symbolic picture I had a friend draw of the evolution of the mind. We still have the other creatures inside our minds. We're brothers and sisters with the other mammals, and our ancestry goes way back. If we understand those ancient minds, if they have emotional feelings, they certainly have emotional behaviors, but you can't read a behavior and say there's a feeling there. That's the scientific dilemma.

And I want to share this journey with you of half a century as quickly as possible. If you want the longer story, this book came out last year, and I'm currently using it in my affective neuroscience class. So here's a picture, a slightly different title. I'm going to relate this to psychiatric disorders, my main interest. So of those two creatures on your left there, which is the picture of science, and which is the picture of reality? Of course the guy on the right is science.

Science is an approximation of reality, and we often go astray, and we often sustain our mistakes for very long periods of time. So the issue of feelings has become very contentious. Do other animals have feelings? That's the most important question for psychiatry, because if you're going to develop new medicines, new treatments, you've got to understand it, as opposed to just kind of approximating things. You have to get down into the details, and then you can perhaps discover some new medicines.

And most people say obviously they do, but as I asked you earlier, that is an argument from empathy. And even though I respect empathy, empathy is not science. We can do science on empathy, and that's a hot area these days. I've done some work there myself, but it's an argument from sympathy as opposed to scientific knowledge. So the question is why can't scientists just believe things? Well, we have three primary values.

We are the ultra skeptics. We are the doubters. We will not believe something unless you can provide the weight of evidence, the facts, and every fact has to be interpreted, and there are multiple interpretations. That's always a problem, but without the weight of evidence, you're just in the land of make believe as far as we're concerned. That helps keep us honest.

And finally, we accept that there is no absolute knowledge in this world. There's a lot of people out there that pretend there's absolute knowledge. I'm sorry. They're just making it up. There is no absolute knowledge. There never will be. All our knowledge will be approximations. So Kathryn Schulz said it all in her wonderful reading book. "Where certainty reassures us with answers, doubt confronts us with questions," she said, coaxing us to recognize and live with quote, "the unconsoling fact that nothing in the world can be perfectly known by any mere mortal."

So probing the animal mind is very popular these days. The science is relatively early, so we're having provisional ideas. So scientifically, do animals have emotional experiences? I will argue

the science has been done, and the weight of evidence is that they do, and now we can begin to use that knowledge for human as well as animal welfare, but we've got a barrier, a historical barrier-- behaviors and the thing I didn't like, behavioral modification.

BF Skinner said these emotions are excellent examples of the fictional causes to which we commonly attribute behavior. All we can see is behavior. We cannot see the animal mind. It's best to bite our tongue and not go there. James Watson was essentially the father of this movement, starting about 1920, and it lead to radical behaviorism, which is alive and well today in my field, psychology. It's loosened up a little bit, but when it comes to animals, we say the animal mind is impenetrable. Impenetrable.

There were two schools of thought-- behaviorism and ethologist. Here's one that got a Nobel Prize, and he wrote the subject that experience should be left out of the analysis. We can never go there. We can neither support nor deny their existence in this famous book, because we are going to put our own emotions on the animal, and that's anthropomorphism-- giving animals human qualities-- and that is not kosher. So Marian Dawkins, the most famous of the Tinbergen's living students-- she's at Oxford-- wrote a book last year, Why Animals Matter, and she pretty much show repeated her mentor's advice. He said there's nothing to say that the emotion of fear has to be consciously experienced in animals.

Book was Why Animals Matter. They only matter because they make choices, behaviors. They don't matter because they have feelings. So it's very alive and well, this behaviorist bias. Now, Temple Grandin, who was here last year, the most famous autistic person in the world, who was a professor at Colorado State University, Fort Collins. She had written wonderful books where she's used my science to support what we are doing. We're not doing anthropomorphism. We're doing zoomorphism, and zoomorphism is returning animal motions to humans, because we share them.

They're evolutionarily related for sure. We get addicted to the same drugs. We learn more about human pain by studying animals. So surely we will also learn about our emotions in this way. So here's a couple illustrations. A little fawn had been injured. A friend sent these a couple years ago. The dog of the house took a great interest, and the problem is pretty clear. What is the dog feeling right now? Is the dog feeling you smell good, or you're an interesting guy? Different mental states.

Here's the second picture I'll share. Is the dog saying I like you, or I want to eat you, or I love you? There is no way to separate these possibilities scientifically. As a matter of fact, dogs don't talk. So I shouldn't have said what is the dog saying, what is the dog feeling? So why try to scientifically determine if animals have the emotional experiences?

Well, we understand their basic feelings. We will finally begin to understand our own. Wow. We don't understand the source and nature of our own feelings yet scientifically. This is a big ticket question, and I think it can lead to new minds medicines. At the end, I'll share three treatments that we are currently evaluating in human beings as a result of studying animals.

An artist who I love bought this rooster picture. She took it off a photograph-- Lonnie Rosenberg-- so how shall we ever understand experience of other animals? We have not the sadness system, the separation distress system even in birds, chicks, and the anatomy and the chemistry say the same as our own. Isn't that remarkable? There are differences in detail.

So let's go to the weight of evidence for the position I've been advancing for 30 some years. Again, just summarizing. Why study them? We're all curious about our own powerful feelings. Animal brain research is the only path to substantive understanding, causal understanding. Most animal lovers-- those that raised the hands here myself-- are committed to the idea that they have feelings. Most scientists are skeptical.

I showed you some. The most famous fear researcher in America, Joe LeDoux, last year said we will never know what animals feel. So you can imagine the resistance in the field that one might have to battle with, but feelings evolved. They're a natural part of all our minds, and we are animals, sophisticated animals cognitively, but emotionally rather stupid at times. And you'll find that in your own life-- how many stupid emotional mistakes you make. I've made my share.

An affect of feelings, a feeling aspect of emotion-- affects always feel good or bad to humans. And animals can tell us whether certain brain systems are rewarding or punishing mainly good or bad, feel good or bad. We can test whether circuit in the brain means something to the animal objectively.

If we understand their basic feelings, we will finally begin to understand our own. So what the heck are we waiting for? Well, we're waiting for these people to perhaps discuss all the evidence, which they wish not to do because they've taken strong positions. Again, we don't have rewards or punishments-- water when you're thirsty, food when you're hungry, et cetera, et cetera. They always feel good or bad to us, and we can ask whether these brain systems feel good or bad to animals using deep brain stimulation, which is a common procedure in human therapy these days for Parkinson's disease, and we recently tested this idea with a new target in the human brain-- people that had not gotten any benefits from anything else.

So the lower part of our brains guides the upper part. A lot of people think the lower part is unconscious. They're wrong. The unconscious is somewhere else in the brain. It's not at the basement. At the basement, you've got feelings.

So we take a Spinozan view. Dual aspect monism-- namely, nature has many faces. Think about physics, light-- it's like a particle, like a wave, particle wave dynamics. Physicists don't know how to bring them really together. They simply accept they're two parts of nature, and we have found that angry behavior reflects angry feelings. When we elicit rage in any mammal-- I worked on rats-- the animal has an experience, an angry type feeling.

So a fact-- wherever in the brain we evoke emotional actions with deep brain stimulation, animals always treat those states as rewarding or punishing always. It's a law of nature. It's a law a psychology. It's barely recognized. This indicates the states of the brain feel good and bad

to the animals. So how many emotions can we elicit this way? We actually use a specialized terminology capitalizing every letter because the common words have too many meanings, too much access, too much ambiguity.

So there's a seeking system that leads the analyst to explore the world with a great energy. What is the feeling like? Well, I think it's enthusiasm. Enthusiasm. And the university here is to focus your enthusiasm for knowledge, and you're responsible for that. The university is not responsible. It just gives you the resources to find your enthusiasm. Do find it. This is the time. Rage-- you're pissed off. Everyone knows that feeling.

What shall we call fear? Well, there's lots of words-- anxiety there. What should we call lust? Yup. Well, if you can find a better word, let me know. Care is tender and loving. Tender, sweet, love-- that maternal care that females have much more than males. Males better learn that message.

There's a panic system we call that we mapped for the very first time that we think is the source of the psychological pain of loneliness and sadness, the things that lead you down the path of depression. And play is an ancient process. It's amazing all these are under your neocortex. The hardware for these is under your neocortex, and then it allows the top of the brain to learn things about the world. It's like the cortex is like random access memory-- empty when you're born. So every feeling has a dynamic-- try to get the feeling of maternal caress there. Anger is like that. Pow. Projectile.

So all of these systems are rewarding and punishing. Yellows are positive. Blues are clearly negative. Rage is a negative emotion in the pure form, but if it works for you, at the top of the mind, it can become a useful strategy, but the top of the mind has no feelings independently of the lower mind. So all the heavy duty data were summarized in this book in 1998, and that's why they invited me to this wonderful university we're at. So always rely on the weight of evidence for any position.

So what's the history? Well, Descartes gave us dualism-- that mind and matter are separate things. We cannot study the mind by studying matter. Well, it turns out we can study the mind by studying the matter of the brain. His young colleague, Spinoza, said, now hold on, Rene. I think it might be unified in some way-- mind and matter. I think that's a wiser choice. We've got lots of types of neuroscience and psychology-- cognitive neuroscience. You might have even heard of some of these people. Joe LeDoux said we'll never know what animals feel. Behavioral neuroscience-- heavily in American England, but not the continent, continental Europe, and the rest of world.

And affective neuroscience, which I'm part of-- the remaining part right now. These folks said feelings are irrelevant. That's nonsense talk. These people said feelings are deeply subcortical based on a mountain of evidence, and these people said feelings are neocortical, and they're still saying so. Well, what's that about?

So the question I hate and I love-- can one tell me why science never answers why questions? I'll give you my answer for why-- because they're useful. They help us survive. They're automatic heuristics, ancestral memories that tell us what is supporting our life. Every negative of motion it tells you you're on the path of possible destruction. Every positive feeling tells you you're on the path of thriving and survival. That's the why, but science doesn't answer why questions. In answers how questions.

So how do we have a feeling. Well, it comes from the subcortical terrain. Here's just one evidence for that. If you're mapping rage, as I did back starting in the late '60s, you can produce-- turn a peaceful animal-- I was using rats-- into a raging monster by stimulating the right part of the brain, and all the areas are deep and subcortical. The lowest one is the most important because the PAG there.

You can produce rage there always regardless of how much brain you damage. The other ones in the hypothalamus rely on the lower one, and when you go to the amygdala, that's high up. It relies on the hypothalamus and the PAG. So the bottom line is you can take the whole neocortex away, and the animal still shows rage. They call it decorticate rage. Neocortex is there to control your behavior in complex ways, most of them learned.

How about humans? Does this apply to humans? There are children that are born congenitally decorticated. Here's a child-- MRI scan. If she's been brought up well, still in a family, she's got emotion. She has likes and dislikes. Likes certain foods. Likes certain people. Dislikes certain foods, certain music, certain people.

Here's another paper we wrote saying, listen, you know the cortex is not needed for emotions. It's the bottom of the brain that generates emotional feelings. Look at that powerful emotional response that a child without a top of the brain can have, but if we grow up and we lose that brain, we will be goners. It's only in the beginning the bottom can do all these magical things. It trains the rest of the brain to think, to feel, et cetera.

So we have to take a level of control. The primary process is the most important one to study. It's enormous in early development. Little babies-- they laugh and cry at a snap of a finger. The secondary process, the learning and memory mechanisms, in the brain-- call that secondary process-- and our top of the brain is empty. The cortex actually learns how to see. That's amazing. Our visual cortex learns how to see. If it's surgically taken away in utero-- as [INAUDIBLE] did at MIT-- the mouse is born and I learns how to see with the remaining cortex. So again, it's the bottom that is so critical. You can't have a house without a foundation.

These primary processes are capitalized because it's a scientific terminology. I'm talking about a circuit in the brain that you have to understand in order to understand the feeling. So we know where to go, and we know lots of the chemistries. As we grow up, it almost seems to disappear because of learning and memory. Learning and memory fill the top of the brain with all kinds of knowledge, and all kinds of nonsense, and fun. If these powers of the mind get imbalanced, excessive, I think you have psychiatric problems.

Here's where the unconscious is-- the learning and memory mechanisms are the unconscious, deep unconscious. You do not experience learning and memory. You only experience the results of it. So you can apply yourself, and it works better, but you don't feel it operating. It just does its magic, and up here you might have awareness, knowing you will experience. At the bottom, you've got experience without knowing. On the top, you have experience with some understanding and knowledge. So neuroscience is a wonderful discipline. Here's those seven again with slightly different names.

Where does depression come from? We think it comes from too much separation, too much sadness. And when you have this, it does a number on your enthusiasm system. It suppresses it, and we've actually measured this, and it's true. If we overstimulate the separation distress system, enthusiasm goes down. It's a long story, and play can be a rejuvenator of enthusiasm and counteract psychological pain. Then there's an ancient system like this, and we think that, if we can identify molecular pathways for social joy, we might have new antidepressants. One of them is in human testing right now.

So there's no absolute knowledge, and if I'm sounding too absolute for you, I'm just trying to convince you that the evidence is pretty heavy. Not a proof. Science is not a matter-- some people say you can't prove that. I say, hold on, you must not have taken a philosophy course. Scientists never aspire to prove anything. That's for logicians and mathematicians. We only collect evidence for a certain argument. So it's supposed to be more humble than proof.

So the separation system, the psychological pain that it creates-- it's enormous. We thought there might be a relationship between mother infant attachment-- that loving bond-- and opiate addiction. They've got similar characteristics. The first receptor, neurotransmitter receptor, discovered in the brain was the opiate receptor. Three labs published it in 1972, and everyone said now we have the explanation why it controls pain, why it controls coughing. And it has one other medical use. Opiates-- pain, coughing-- anyone know what the other one is used? To save children when they've got life threatening diarrhea, like the children are having right now all over the Philippines as a consequence of the storm there and all that bacteria. That diarrhea can be brought in control with opiates.

So brain opioids were discovered, and we think that's the bonding process between mother and child. If we recognize this-- and it's a heavy duty your assertion based on a lot of evidence-- if we had this clear in our minds, we would not be putting addicts to jail. We would be giving-- insisting upon therapy as the first order of business for every one of them, but we're still primitive in our discussions.

It turns out that brain opioids are superb in quelling psychological pain. That's why people usually get addicted. They find they're self-medicating themselves. Then we found that oxytocin, the molecule that releases milk from the breast when it's touched just right by a baby-- it also in the brain controls psychological pain. And prolactin, the molecule that allows our body to manufacture milk-- the female body to manufacture milk, also suppresses psychological

pain. So the physiology, the neurochemistry, the body chemistry of caring for a baby are also the chemistries for caring for the baby psychologically. That's a miracle almost.

Here's how we tested separation distress. We had beagles, some other breeds, and we separated from the mother for 15 minutes in a warm room, no physical distress, just being by yourself, and the little puppies cry almost 800 times. Peep, peep, peep. Oh, that's a chicken. Sorry.

[LAUGHTER]

And here's [INAUDIBLE], and they had slightly different responses. These are behavioral effects with opiates that are the lowest in the scientific literature. In other words, this is the mechanism in the brain that is most sensitive to opioids, the psychological pain mechanism. The animal doesn't like this feeling. Because we mapped it in the guinea pig brain using deep brain stimulation, we know where the circuitry is anatomically, and then we went to chickens. That's why I was making chicken sounds. The chemistries in the chicken are the same as in the guinea pig, and the dog, and human beings. That's why I say we're brothers and sisters under the skin.

We also map the chick separation system, and it was anatomically the same as guinea pigs. And then along came human brain imaging. There's our summary of a guinea pig down below, and when PET imaging, where could actually monitor feelings with brain imaging-- the anatomy of human sadness was very similar, and the anatomy of human sadness was also a low opioid state.

And then the people at University of Michigan, where I taught for a year, found that depression was low opioids in the same brain areas. So the psychological pain of depression partly a low opioid state. Wow. That's why people are often getting addicted. They've got too much psychological pain, and they're self-medicating themselves.

We found that touch and social contact alleviate psychological pain. A little chick is born, and it's crying for it's mother when it's born. Peep, peep, peep, peep. And we decided we would just pretend that we're the mother, and we picked them up, put them in our hands. The crying stops immediately. The chick settles down. His beak goes down and falls asleep. If you block the opioid system, the animal cannot settle down as readily. It does settle down. It still has oxytocin, prolactin, but it takes the animal much longer to settle down.

So the comfort of being with others is partly an opioid phenomenon. So this gives us the animal's secure base. This is social bonding, social attachment. You love your mother because your mother has released so many wonderful chemistries in your mind hopefully. Maybe there's too little in depression. So again, that's why this kind of research is important. This is what I wanted to learn when I first went to graduate school, and it turned out I had to do the work myself. Thank goodness for universities that permit that.

So we have three treatments for depression now. One is using safe opioids, namely opioids you can't kill yourself with. They would never get to respiratory depression for various interesting scientific reasons. One is buprenorphine. And we have a project on suicide going on in Israel. So now again, contact, comfort alleviates the psychological pain by releasing opioids. Touch alleviates pain. It releases opioids. Opioids should reduce depression and suicidal thoughts.

We tried to get a depression study going in America, but we were closed down. For some reason, we have a culture that cannot tolerate the thought of using opioids psychiatrically. We had to go elsewhere, but we'd already seen that here's the picture of opioids in the brain, and we had shown back 30 some years ago that animals playing are releasing opioids dramatically.

So again, safe opioids are much underutilized in psychiatry. Buprenorphine can help alleviate psychological pain for sure. Perhaps then it would reduce suicide. We have no medicine for suicide. We have no way of pulling a person back with any medicine that has been approved. So we're doing a study in Israel. This is Yoram Yovel, and I helped him start the Institute for the Study of Affective Neuroscience there-- a psychiatrist with a kind heart and courageous. Initially we just did four people, and this is Beck suicide inventory-- how many ugly thoughts are running through your mind to kill yourself.

During the first week, the placebo was just as good as buprenorphine, but we know now that the placebo effect is very much release of opioids because you trust your doctor. Trust is releasing opioids, but by the second week, that short term effect disappeared, but buprenorphine was still reducing suicidal thoughts. Now we've had people for 30 some weeks. We have more than 60 people in testing right now. The codes haven't been broken, but I can be pretty confident it's going to be a substantial effect. It might be the first medicine for suicide. It will have a tough time being approved in certain countries.

This is an old idea. It goes back to the father of biological psychiatry who wrote the first modern textbook on psychiatry, Emil Kraepelin, at my hometown University of Tartu. He said back 100 years ago the treatment of the malady cannot-- this is depression with suicidal thoughts-- be carried out, except in asylum. The treatment being opioids, because thoughts of suicide are almost always present. So in severe cases, we did this in the hospital.

Opium is employed to combat the apprehension in gradually increasing doses, which are then by degrees reduced, and he said this remedy has often done very good service. So this is all. We're doing ancient history that disappeared off the map, and you have to have great care in discharging, but buprenorphine is much safer, much more effective. So we'll see what happens within a couple of months.

Use of deep brain stimulation of the enthusiasm system-- people just call it the brain reward system. That's a placeholder. No one thought that was a proper description psychologically. Well, we proposed in a paper that we can stimulate the seeking system, and there's a human map of the fiber pathways for panic namely-- this system in gold orange-- and then the seeking system that's very near underneath it. And we said, why don't we consider a person that's been

depressed, has gone through every treatment, including electroconvulsive shock, and give them the option of participating in the test of a new therapy?

The first seven patients were finished. The idea is too much psychological pain. That gets too large. It suppresses the seeking enthusiasm system, and that's dysphoria, just feeling ugly all the time. If you stimulate the seeking system, you should be able to counteract that psychological pain.

So six of seven individuals that have been tested so far that have been resistant to all depression exhibited very robust antidepressant effects on the first treatment during the first day of treatment, and then it got larger and larger across the days. One did not respond. There's a story there, but I don't have time to tell it. And it's published in Biological Psychiatry a couple months ago.

So finally we've done a genetic analysis of play, looked at the gene patterns and the cortex that change as a function of rough and tumble play in rats. We started this area of research. Young rats love to play, and it turns out it would be quite easy to measure, quite easy to study in the laboratory. Why it took until we started for science to come of it, I'm not sure, but it's probably because of behaviorism.

Playful behaviours reflect joyful feelings, because we have I have an indicator of the joy, which is a rat laughter, 50 kilohertz chirp that's outside our hearing range that really-- the sincere rat laugh looks like this frequency modulated. If you just have the flat little thing, chevron, that flat one does not indicate positive affect. That's just social communication. Anyone out there?

So we've done 30 years of work on play. We've measured practically everything we can imagine, so we know what we're dealing with, and then we wanted to get the genetics and the circuits for play. After I finished in Ohio, I joined a drug development group at Northwestern, and they were working just on brain cancers, treating brain cancers, and they asked me start a new psychiatric drug development program. And I said let's focus on play as the way to identify joy promoting molecules, hopefully ones that are not addicting.

And if I'm hooked up to the sound system, I'll show you a video of me tickling rats in 1998. I couldn't publish this stuff, but the BBC heard about it, and they came out from England with a full filming crew to see it for themselves, and they had a documentary entitled Beyond a Joke, because we were advocating play for the treatment of ADHD because of its powerful effects on the nervous system in beneficial ways. It's only two minutes. If you're really interested, just Google tickle rats or laughing rats. I'll be the first hit.

[LAUGHTER]

We developed the first psycho assay. Usually animal work is considered behavioral assay. We have psychological assays, namely how good do you feel? And we tickle animals, and that film shows how you tickle animals. And here is two minute psycho assay-- works as good as

biochemical assays. You've got male and female rats being tested. 15 seconds of no tickle followed by 15 seconds of tickle repeated four times. 2 minutes and you can identify how happy the animal is. The happier they are, the more resistant to depression. The less they laugh, the more susceptible to depression they are.

Here's two experimenters, me, experimenter one, and my senior female lab person. We produce exactly the same results. That's what assay is supposed to do. Play does not come from the cortex. We have eliminated the neocortex, and animal's show normal play, super normal play. Play-- even though the cortex is not needed for play, the cortex lights up like a Christmas tree when the animal is playing.

Here's a picture on the left, an empty cortex. This is a test for looking at nerve cells that are firing. It just measures where are the cells that are firing a lot. Look at that expression of firing in the cortex. That's not needed for play. So get plenty of play while you're in college, too. Sure that'll be no problem for most.

[LAUGHTER]

So I was at the Fox Center for Molecular Therapeutic. Joe Moskal is the chief there. When I got invited to WSU, I was finishing one more student in my retirement, and he was my last PhD student. I gave him the post-doc to fill in for me because he knew everything I knew, and he's young and energetic.

So can we find molecules that can promote social joy and depression? That was the question. We did the generics on the cortex. It's a darn long story, and you'd be falling asleep fast if I went into details, but basically one third of the genes that we measure in the cortex-- we measure 1,200 genes and how they're up or down regulated. One third of them were influenced by half an hour of play one hour later. At six hours, there were still 33, 17, 73 in the front, and back, and the overlapping regions. Now we have 17 candidates as possible treatment modalities, so we had to figure out what they do in the brain. That's harder than the genetics, and it turned out that it modified a receptor.

You can see the messenger RNA was elevated significantly. The protein was coming out like gangbusters. So this NR2B subunit of the glutamate receptors within a package that is very enticing as a target for depression-- a lot of people know that, but it's too powerful to modify. So we developed a very gentle way to modify this either up or down, and the results were quite remarkable in our psycho assay, tickling psycho assay.

This molecule, GLYX-13, dramatically elevated joyfulness. We also could block that molecule, and that reduced joyfulness. It turned out to be totally safe. No toxicity at all. Now the hard job becomes attracting venture capital during the last recession that we're still in, and lo and behold Joe has got such a good mouth on him that he convinced-- after four years of chatting, he convinced four higher risk venture capital groups to pony up $4 million apiece to do the phase 2a clinical test, namely does it have antidepressant effects?

The phase 1 is merely toxicology, and he had to pay for that himself. That's very expensive, human toxicology, but it had no toxicity. The Food and Drug Administration said you can go and test it in humans because you've gotten to such outrageous doses with no bodily problems. Lo and behold, the phase 2a proof of concept was finished a year and two months ago, September of 2012.

It beat the best antidepressants on the market. It was twice as good. Our molecule had effects in the first day, and one treatment lasted a week. That allows you to go into phase 2b. Phase 2b is, does it sustain an antidepressant effect? And that is ongoing. Venture capitalists sold off, made 100% profit in a year, but fortunately it's in the hands of small pharmaceutical companies, so we don't have the fear that some powerful agent will put it on the shelf until they need it, because they don't want to close off ongoing pipelines, money pipelines.

So the conclusion-- taking the emotional feelings of animals seriously may yield more rapid understanding of our own emotions and promote progress in psychiatric medicinal development. Before you take off, let me highlight for you the modern psychiatry era has been with us for 60 years. It started in 1954 with a serendipitous chance discovery of an anti-psychotic called Thorazine. Since then, every psychiatric medicine that we have has been discovered by chance, and serendipity, and not human knowledge.

Why has that been such a big problem when gazillions of dollars have been thrown down the chute? My answer is because we as scientists have not taken the emotional feelings of animals seriously. All we've had are behavioral models. So use your time here wisely. It's really the only chance you get. Thank you.

[APPLAUSE]