THE MAN WHO MAKES RATS LAUGH

Jaak Panksepp

Jaak Panksepp has taken on many unusual roles in his storied career, but none so memorable as rat tickler: He learned how to stimulate the animals to elicit high-frequency chirps that he identified as laughter. Panksepp's interspecies game-playing garnered amused media coverage, but the news also stirred up old controversies about human and animal emotions. Since the 1960s, first at Bowling Green State University and later at Washington State University, Panksepp has charted seven networks of emotion in the brain: SEEKING, RAGE, FEAR, LUST, CARE, PANIC/GRIEF, and PLAY. He spells them in all caps because they are so fundamental, he says, that they have similar functions across species, from people to cats to, yes, rats.

Panksepp's work has led him to conclude that basic emotion emerges not from the cerebral cortex, associated with complex thought in humans, but from deep, ancient brain structures, including the amygdala and the hypothalamus. Those findings may show how talk therapy can filter down from the cortex to alter the recesses of the mind. But Panksepp says his real goal is pushing cures up from below. His first therapeutic effort will use deep brain stimulation in the ancient neural networks he has charted to counteract depression. Panksepp recently sat down with DISCOVER executive editor Pamela Weintraub at the magazine's offices in New York City to explain his iconoclastic take on emotion. His new book, *The Archaeology of Mind: Neuroevolutionary Origins of Human Emotion*, will be published in July.

PHOTOGRAPHY BY GREG RUFFING

Q+A

Your interest in emotion was sparked by an odd job you had in college. What happened there?

Putting myself through college at the University of Pittsburgh in 1964, I did night work on the side and ended up a night orderly in the psychiatric hospital. I came in when it was dark and people were starting to settle down and go to bed. Some of them were on heavy meds. Others were very disturbed and would wander all night unless they were put into restraints. Everyone who worked there had free access to the patient files, which were thorough in relating the life history of individuals. You really got to know a lot about the people. After that I decided to get into the field.

How did you get started in those early years?

I went to do my Ph.D. at the University of Massachusetts, starting in the clinical program. In my first year, I had the great fortune of becoming a Veterans Administration trainee and got a job in the electroencephalography (EEG) lab where they analyzed brain waves, mostly to diagnose seizure patients. The head of the lab was a psychologist, Arnold Trehub, who pretty much asked me, what do you want to do with your life? And I said, what I'm really interested in is brain stimulation and reward.

That was a rather precise and arcane interest for a clinical-psychologist-in-training during the 1960s. How did the idea occur to you?

A new faculty member at UMass, Jay Trowill, was interested in this exciting new technique: inserting electrodes in rat brains to create pleasure or excitement. After you inserted the electrode, you gave the rat the chance to turn it on or off itself by pushing a lever. Thanks to my experience in the EEG lab, Jay asked me to be his first student and run his lab. I had to build my own boxes that had levers that animals would press to turn on the electricity.


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What happened when you dropped a rat in one of those boxes you built?
He fell on the lever, causing the electrode to stimulate his medial forebrain bundle, a reward center. And he worked and he worked and he worked for hours. I didn't have to train the animal. I just dropped him on the lever, he got one taste and he started hitting it.

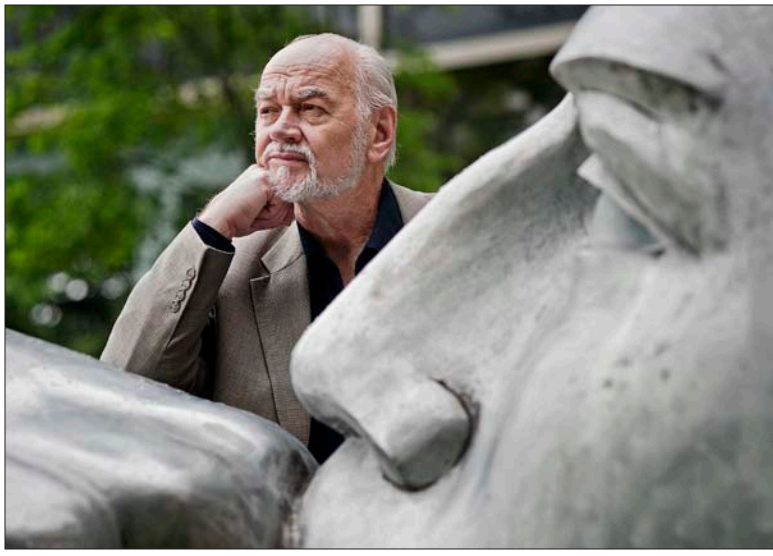
Those kinds of reward experiments had already been going on for years before you got to them. What insights did you add?
I observed that whenever the animal pushed the lever and got the motivating jolt, it explored its world energetically. That was very different than anything that happened when animals were working for food rewards, where they always stopped when they were full. To get at the difference between the two types of rewards, I designed an experiment that injected sugar water into the rats' stomachs whenever they pushed the stimulating lever. I put one animal in the apparatus and went out to get lunch. When I came back it had killed itself with too much sugar. It just kept pumping more and more until it went into osmotic shock. The next time I didn't walk away.

So even with a belly full of sugar, the rat was still craving something. What was going on?
I tried to answer that fundamental question through the behavior of my lab rats. It was clear that when I stimulated the reward center in the medial forebrain, they were not engaged in the kind of relaxation they felt when they stopped to eat or drink. It was just the opposite. It was the kind of behavior the animal showed when it was looking for food. So I started thinking in those terms: This was mother nature's way of allowing animals to explore the world. It was an exploratory system; it was about generating expectancies, seeking rewards.

You were describing a rat's experiences in terms usually associated with human experiences. That wasn't really the style of the times, was it?
I brought up the psychological issues, and my professor said, Panksepp, I've seen guys like you before, and they're not around anymore. Psychology was not on the table for animal research people. It's all just behavior, he told me. I said, well, I guess I'm not supposed to think here. This is like some kind of religion. You've got a certain view and you'd better say the mantra because that's how they're training you, and believe me, young scholars were brainwashed by the hordes. Most of them were ready for the brainwashing like sheep going to slaughter.

So how did you resist the academic brainwashing?
I learned to bite my tongue until they couldn't hurt me any more. I bit my tongue many times, but not hard enough usually. So gradually I became a radical without wishing to be a radical.

What were the radical ideas that motivated you?
My major question was, what are emotions? Since we could turn on the emotions with electrical stimulation, for my dissertation I decided to study rats for the anger and rage system already documented in cats. You could turn a peaceful pussycat into a raging monster by stimulating specific parts of the hypothalamus. It was much harder to turn lab rats rageful, because cats brought in from the street were predators. A predator needs that kind of attack system, whereas an omnivore like a rat needs a searching system.



Jaak Panksepp behind the *BG Thinker* at Bowling Green State University. Previous page: Panksepp communes with the rats in his lab on campus.

Did you eventually find the rage system in rats?
Yes, rats have this system in much the same areas of the brain as cats. Once I obtained aggressive behaviors in rats by stimulating specific areas of the brain, I started asking whether they liked or disliked the feelings by having them press a lever to turn the stimulation on or off. The answer depended on the kind of aggression I induced. Whenever aggression was predatory, marked by stalking and quiet biting attack, rats turned on the brain stimulation over and over again. I realized this predatory attack came from the seeking system. But whenever the aggression was agitated, resembling human anger, rats would press levers to escape the artificially aroused rage feelings. Anatomically and psychologically the two types of aggression were very different. More broadly, feelings of seeking, lust, care, and play feel good. Rage, fear, and panic feel bad.

You defined seven fundamental emotions, all spelled with capital letters in your academic papers. Why?
These are the emotional primes, the primary-process emotional systems associated with specific brain networks and specifically designated in the brain-stimulation studies of emotions. They are SEEKING, RAGE, FEAR, LUST, CARE, PANIC/GRIEF, and PLAY. These are capitalized because the evidence supports a category of evolutionarily homologous experiences, equivalent across different species of mammals.

In your next career move, you wound up at Bowling Green State University in Ohio in 1972. Why there?
It had a unique lab run by someone I found totally fascinating: John Paul Scott, a biologist in the psychology department who had done more work than anyone else on social attachments in

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dogs. Attachment is the bond of selective preference between a mother and a child, whatever the species. Mother dogs and their pups bond, mother sheep and their lambs bond, and so forth. When a real bond has been established, the young selectively prefer their own mother, and follow her around persistently in order to feel comfortable. Conversely, the mother will shower all her devotion on just her own babies. When this attachment bond is broken, the young cry and cry until reunited with the mother; this is the panic system in action. Animals that grow up crying the most because they are separated from their mothers for the longest are generally maladjusted. Scott insisted that attachment had to be studied biologically, but no one knew how.

Then you found a way to study attachment. How did you do it?

Serendipitously, that was the moment, in 1973, that scientists discovered the opiate receptor—the first neurochemical receptor in the brain. The day I heard that, I said, this has got to be the attachment mechanism. Opiate addiction is another phenomenon that creates a powerful bond. We call it by a different name, addiction, but it is activated via a molecule that produces good feelings, and mom produces a lot of good feelings in the young ones, too. They feel comfortable, they feel soothed, and opioids have that same property, psychologically.

How could you test the idea that social attachment is related to chemical addiction?

I had the insight that if you wanted to understand attachment, you would have to study crying. My first successful experiments used dogs. We took young pups and gave them morphine. Then we removed them from their mothers. The more morphine they got, the less they cried and the quieter they were. They sat alone and were satisfied, as if the mother was right there. Significantly, we could comfort the animals only with opiates like morphine, not with the types of agents often used to quell anxiety, the benzodiazepines. So we knew the crying wasn't a physical fear. As with aggression, there were two kinds of anxiety systems. One was fear that a predator would attack, and the other was panic over separation.

What was the response to your discovery?

We had to use emotional language to describe what we found, and the bottom line is we simply got rejected as being crazy. For the next 10 years, all we heard was, you're just sedating animals, what the hell? We don't have to pay attention to you. So we didn't get a penny for that work. When you don't have a penny to pursue research, that's a very expensive canine laboratory. After John Paul Scott retired, I was given the job of saving the canine research facility. We must have written at least half a dozen grant proposals, and the message was clear: We're not gonna get funded no matter what we do. Dogs were the perfect species for the study of social attachment, but no one got it. The best canine behavioral research laboratory, and the last one in the country, died with me. I was incredibly disappointed.

So what then—you turned back to rats?

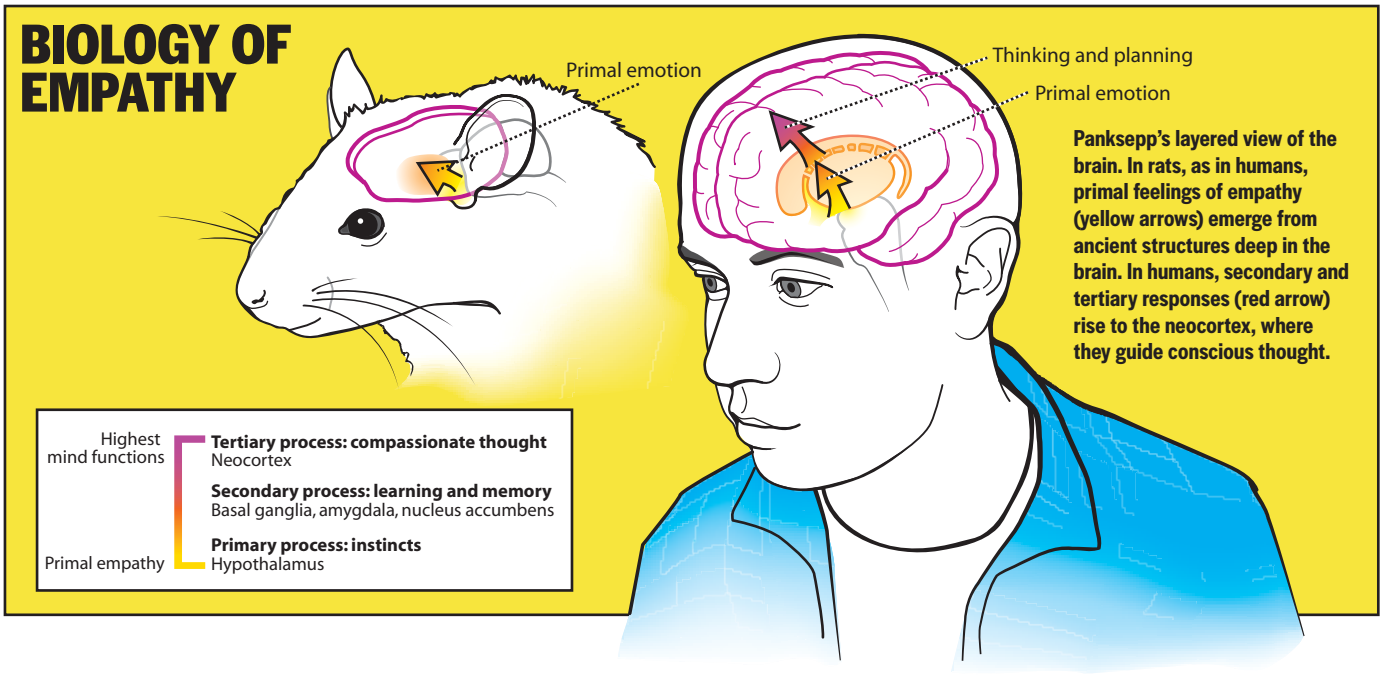
No, because rats don't cry. They give a distress call, but it's not about social separation; it's just, I'm cold, I'm out of the nest. But the guinea pig showed real vocalizations, and we found, yes, they also quiet down with opiates just like dogs. So Barbara Herman, one of my first Ph.D. students, took on the project of mapping the crying system in the brain of guinea pigs. That system converged in the periaqueductal gray area, an ancient area of the brain. By putting electrodes there, you could get the animals to make very intense separation calls. The calls continued as you put electrodes into the medial thalamus and the basal ganglia, areas seen as part of an anxiety system by fear researchers. I kept saying, this isn't fear, this is a different anxiety. They didn't care to listen because they never even thought about the separation call. But we mapped the anatomy. By 1978 we had mapped the attachment system in three species in all.

Today the bonding hormone is thought to be oxytocin, a chemical secreted after intense social experiences such as birth and sex. Is that an attachment molecule, too?

We studied oxytocin, and it turned out to be as powerful as the opiates in reducing separation distress. Every process in the brain has multiple chemistries. The three that had enormous effects on attachment were the opioids; oxytocin, which was superbly effective but had to be put directly into the brain because it does not cross the blood-brain barrier; and prolactin, the stuff that manufactures milk.

Then you made a U-turn: Instead of studying separation anxiety, you started to study play and laughter. Why?

It was the classic masks of theater, sadness and happiness. We had essentially done the work on the sadness mask. I wanted to move to the joy mask. Joy is social, so you're looking at play. Play is a brain process that feels good, that allows the animal to engage fully with another animal. And if you understand the joy of play, I think you have the foundation of the nature of joy in general. Part of its benefit is simply taking away the psychological pain of separation. Play is engaging in an attachment-like way with strangers, which you have to do later in life.



Time for another animal experiment, right?

To study attachment, we couldn't use rats or mice. They're laboratory animals bred inadvertently to live by themselves. But I noticed that rats in the lab are wonderful for play. Psychic pain reduces the inclination to play—but since rats don't feel it, they can be separated without panic and then when you put them together, bang! They play.

And the rats played with you, too?

After the experiments we'd dim the lights to make the rats more comfortable. That was our time to have fun. You see me sitting there and saying, come on, guys, come on—it's okay. I knew that if I could tickle them, they would get jazzed up more, and that's what happened, right in front of the camera.

How did you turn that kind of playing around into a rigorous experiment?

I thought about the hunger research I'd done in the past. If I wanted animals to eat, then the best way was to make sure they hadn't eaten for a while. If I want animals to play, I'd have to make them hungry for play. So I put them in a cage alone, apart from their family, first for 4 hours, then 8 hours, then 12 hours, and finally 24 hours. I was looking for a behavior that I could use to measure play, like jumping on each other. How often do they bounce and touch each other? Then they run around—it's too complex to follow unless you do slow-motion movies—and they end up wrestling. These behaviors were very easy to measure. We collected a lot of data on the response to social hunger.

Is play embedded deeply in the brain, the way attachment is?

Many experiments over the years suggested it was, but to be sure I removed the upper brain of the animals at three days of age. Amazingly, the rats still played in a fundamentally normal way. That meant play was a primitive process. We saw, too, that play helped the animals become socially sophisticated in the cortex. That's why it's so important to give our kids opportunities for play.

And yet it seems that childhood play has become much more controlled than it was when I was young.

I have gone to ADHD meetings to consider this childhood problem. But the doctors do not want to hear the possibility that these kids are hyper-playful because they're starved for real play—because they are giving them anti-play medicines. Teachers are promoting the pipeline of prescription controls as much as any other group, because their lives are hard. They are supposed to be teaching kids at the cortical level of reading, writing, and arithmetic, but if they've got kids who are still hungry for play, it's gonna be classroom chaos. And you can sympathize with them, because they should be getting kids that are sufficiently well regulated to sit and use their upper brains. But the kids' lower brains are still demanding attention.

What happens to animals if they are deprived of play over the long term?

They look normal and they eat normally, they're just not as socially sophisticated. Animals deprived of play are more liable to get into a serious fight. Play teaches them what they can do to other animals and still remain within the zone of positive relationships. If you have play you become sociosexually more sophisticated. Let's say you have the classic triangle: two males and one female, because males are competitive for sex. So if you've got one animal that's had lots of play and the other animal hasn't, guess who is successful? The animal that's had play knows how to stay between the female and the other male. The other guy's a klutz.

Did you ever find a way to track and measure the play response in rats?

Yes. I had a postdoctoral student, Brian Knutson, who asked

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me whether there was a play vocalization. I said, we know they don’t make any audible sounds but maybe there’s ultrasonics. We wound up buying the equipment so his study could be done. Brian came in the first day after it was set up and said, Jaak, there is a sound when the animals are playing. That was the 50-kilohertz chirp [at a pitch far above the range of human hearing].

What does the rat chirp mean?

We found it was most common in positive social situations—sexual, maternal, and play. They’re all in the 50-kilohertz range, but there are many subtypes. Animals start showing anticipatory chirps before access to play. They also chirp in anticipation of food. After Brian left, I woke up one morning—it must have been 1996—and I said, what if that sound is laughter? I got another student, Jeff Burgdorf, to work in the lab. Every morning I would get in at 9 a.m. He would be waiting for me, and I would say, Jeff, let’s go tickle some rats. I tickled the first rat and it worked beautifully, and the second, and the third. Eventually we developed a standard method where we were doing everything the same and then studying the 50-kilohertz chirps.

Isn’t that making the experimenter part of the experiment?

Yes, but you can’t tickle without it. We tried to get tickle machines—they were nothing like the human hand. Tickling has to be done in a joyful way. It has to have the characteristics of play, and since I had been immersed in play, I didn’t see that that was a big problem. The first animal worked and every animal worked. We got totally addicted to this. Give an animal a really good time, you know? They become so fond of you, it’s unbelievable.

But do the rats recognize you?

Oh, of course. The tickle is a way to the social bond in the rat—a friendship bond. That’s part of the function of play. So we have a psychobiology of cross-species friendship.

Does it cut both ways? Do the rats get mad if you do something wrong?

At one point we decided to ask, what happens to the rats when you put your hand in there but no longer tickle them? Our experiment was to have one hand deliver a tickle touch, and another, just a petting touch. The animals preferred the tickle hand enormously. When the animals came to my petting hand, I got my first bite ever. But it didn’t hurt; it must have been a play bite, like a puppy bite. Then we started measuring play bites. The more the animal wanted to play, the more it would nip, never breaking the skin. I said, whoa. This behavior is totally understandable for anyone who has a cat or dog: Rats give play bites that you could use as a measure of their desire to play. And now you’re getting into the animal’s mind in a fairly profound way.

You make a connection between rat brains and human brains through a concept you call nested brain hierarchy. What is that?

By nested hierarchy I mean a way of looking at the brain, looking at its layers and how they developed over the course of evolution. Humans go back to the Pleistocene [about 2.5 million years ago], but the emotional part of the brain goes back much further, all the way to the time when ancestral mammals evolved away from reptiles. Primary processes, based in deep subcortical regions, manifest evolutionary memories that are the basic emotional operating systems of the brain. Secondary processes, based on a series of way stations known as basal ganglia, are enriched with the mechanisms for learning—for linking external perceptions with associated feelings. Then on top, the tertiary level is programmed by life experiences through the neocortex, engendering our higher cognitive processes such as thinking, ruminating, and planning. Our capacity to think is fueled by our storehouses of memory and knowledge acquired by living in complex physical and social worlds. But the ancient feeling states help forge our memories in the first place. New memories could not emerge without the underlying states that allow animals to experience the intrinsic values of life.

Researchers have recently tried to treat depression by stimulating the brain with electrodes. The psychiatrist Helen Mayberg, for instance, has found a spot that, when stimulated, seems to relieve depression.

What Helen Mayberg has been doing is at the tertiary level [the neocortex, or center of thought]. We are evaluating similar manipulations at the primary level [ancient structures]. This should be more powerful. At the tertiary level, all you can do is dampen the psychological pain coming from deep down. We are going to that deep place, where we’ll try to do something more direct by amplifying eagerness to live.

You are going to address mood disorders by going straight to the source?

We plan to go smack into it. We think that depression is an underactive seeking urge that has been made underactive by too much psychological pain. We know that all the neural systems are still there, so our goal is to invigorate the primitive seeking urge to provide a positive affect to fight the negative pain. That’s what we’re gonna try.