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SCIENCE DESK

How Brain May Weigh the World With Simple Dopamine System

By SANDRA BLAKESLEE (NYT) 2042 words

IN the ever increasing cascade of new information on brain chemistry and behavior, one substance seems to pop up whenever pleasure is involved. It is even called dopamine, a name that has no connection to the slang "dope" for drugs, but might just as well, considering that dopamine plays a critical role in the way animals and people respond to cocaine, amphetamines, heroin, alcohol and nicotine.

Dopamine has been shown to be a key modulator in an astonishing array of human behaviors. Get too much dopamine in the brain and you hear voices, hallucinate and wrestle with twisted thoughts. Get too little of it and you cannot move. Like Parkinson's patients, you are locked in your body, depressed and joyless.

Dopamine's broad influence is an irresistible lure to scientists. And based on a few new experiments, some researchers think they have the first glimpses of a simple reward system, mediated by specialized dopamine neurons active in all vertebrates, indeed in insects and crustaceans as well. Their ideas are still more hypothesis than theory and have yet to be integrated with the exceedingly complex waxing and waning of other neurotransmitters in the human brain, but the work has drawn the attention and excitement of other prominent researchers.

The dopamine story begins deep in the brain stem with several tiny clumps of cells, together no bigger than a grain of sand. These 100 million or so cells, the only producers of dopamine, form long nerve fibers called axons that reach out to billions of cells in almost every other part of the brain.

Like other neurotransmitters, dopamine allows neurons to "talk" to each other, facilitating the transmission of signals from one brain cell to another.

This is only one small system in an incredibly sophisticated brain. But its size seems to belie its influence. And the reason may be that the brains of humans and other creatures operate on some deceptively simple rules, said Dr. Terrence J. Sejnowski, a neuroscientist at the Howard Hughes Medical Institute and the Salk Institute in La Jolla, Calif.

An idea recently proposed by Dr. Sejnowski and others is that the dopamine system evaluates rewards -- both those that flow from the environment and those conjured up by the mind. When something good happens, the system releases dopamine, which, in essence makes the owner of the brain take some action. This account is vastly oversimplified, of course, but Dr. Sejnowski does suggest that the dopamine system works unconsciously and globally, providing guidance for making decisions, when there is not time to think things through.

Recent experiments on bees, monkeys and humans provide the basis of these ideas about the dopamine system, which are by no means proved. They are more in the realm of well grounded speculation, Dr. Sejnowski said.

Dr. P. Read Montague, a researcher at the Center for Theoretical Neuroscience in the Baylor College of Medicine in Houston, has collaborated with Dr. Sejnowski and others in modeling the way a dopamine-like system works in bees. The bee brain has only one dopamine neuron. (It actually releases octopamine, a close cousin to dopamine that serves the same purpose.) As in other creatures, this neuron sends projections to every nook and cranny of the bee brain.

Bees can find nectar-containing flowers under highly variable lighting conditions, from numerous angles and distances and during different seasons. There could be dozens of yellow flowers, of similar shape and size in a given field, yet only one or two might contain nectar. Bees can very quickly figure out which ones to sample and give the information to other bees.

How do bees do this? At the University of Illinois, Dr. Leslie Real, an experimental psychologist, has built enclosures with artificial flowers spread over the floor. Bees fly around, sampling various amounts of sugar placed in each flower by Dr. Real.

In one experiment, Dr. Real put out blue and yellow flowers. A third of the blues contained high amounts of sugar; the other blues were empty. Among yellow flowers, two-thirds contained a small amount of sugar; the other yellows were empty. The experiment was rigged so that the total amount of sugar in the blue and yellow flowers was identical.

But which foraging strategy would the bee prefer? Would it go for high payoff blues? It would get the most sugar for the least amount of work but it would have to tolerate hitting more "empty" flowers. Or would the bee go the "safer" route and sample the yellows, making more work for itself?

In papers published in 1991, Dr. Real reported that bees went to the yellow flowers 85 percent of the time. In seeking reward, they were averse to taking risks.

Fascinated by this finding, Dr. Montague, in collaboration with Dr. Sejnowski and Dr. Peter Dayan of the Massachusetts Institute of Technology's department of brain and cognition, wondered how the bees computed rewards. And so he built a virtual bee inside a computer, with a model of the dopamine system that might explain genuine bee behavior.

"We made a fake bee and let it fly over the blue and yellow flowers" with variable amounts of sugar, Dr. Montague said. Each time a virtual bee landed on a flower, its dopamine neuron was alerted. As in most animals, the dopamine neuron at rest fires signals at a steady, base-line rate. When it is excited, it fires more rapidly. When it is depressed, it ceases firing.

The virtual bee's neuron was designed to give three simple responses. If the amount of sugar was more than expected (based on what the bee knows about similar looking flowers), the neuron would fire vigorously. Lots of dopamine meant lots of reward and instant learning. If the amount of sugar was less than predicted, the neuron would stop firing. Sudden lack of dopamine, going to other parts of the brain, told the bee to avoid what had just happened. If the amount of sugar was the same, as predicted, the neuron would not increase or decrease its activity. The bee learned nothing new.

This simple prediction model -- the dopamine neuron "knows" what has just happened and is waiting to see if the next reward is greater or smaller or the same -- offers one explanation for how the bee behavior might arise, Dr. Sejnowski said. When the dopamine neuron encounters an empty flower, it throws the bee brain into an unhappy state. The bee, in fact, cannot stand hitting so many empties. It would rather play it safe and get more numerous, smaller rewards -- or no rewards at all -- by sticking to the yellow flowers. A paper describing this work was published on Feb. 1 in the journal Nature.

This model is also consistent with what is known about human behavior and the human brain, Dr. Sejnowski said. "Your dopamine system is sitting there, making guesses about the future," Dr. Sejnowski said. "Given the state I'm in now, is it likely I'll be rewarded in the future?"

Here is how Dr. Sejnowski theorizes that the system works. Sensory information flows into the brain from the outside world and from internal representations. What you see, touch, feel, smell, taste, hear and imagine all combine to produce sensory states. These change from moment to moment.

The brain also contains memories and prior experiences about these states. Some are good; you want more. Others are to be avoided.

Both representations -- what is happening now and what you know about it from past experience -- are funneled to the dopamine system, Dr. Sejnowski said. Then a simple rule is followed. The dopamine system compares the brain's expectation of reward (gee, this was pretty good the last time I experienced it) with what is actually happening at the moment.

If the reward is higher than predicted, dopamine is sent to many parts of the brain, giving a green light to action to get more rewards. If the reward is less than predicted, the dopamine signal is not broadcast and other systems involving avoidance are activated. In both instances, action does not take place until the dopamine system has evaluated the sensory state you are in and detected an error in your prediction about it, Dr. Sejnowski said.

Dopamine cells have no intelligence, Dr. Sejnowski said. They just increase or decrease their firing rates in response to errors in predictions about the world around you. The researchers described this model on March 1 in The Journal of Neuroscience.

Both these papers involve theoretical arguments and computer models. Recent experiments carried out by Dr. Wolfram Schultz and his colleagues at University of Fribourg in Switzerland have shown that dopamine cells in monkeys do indeed behave in just the way theorized. Electrodes were placed in monkey dopamine cells and the animals were given squirts of apple juice paired with a flashing yellow light. At first, the dopamine cells would fire when the animals got the juice or saw the light, since the reward was not expected.

But when they were no longer surprised by the reward, their dopamine cells no longer fired, Dr. Schultz said. Dopamine cells only fire when the prediction is wrong, he said. And they only fire when the stimulus carries a reward.

Dr. Montague supervised an experiment by his graduate student, David Egelman, to test 40 people in an experiment similar to the one done on bees.

People sit in front of a computer screen with two buttons, labeled A and B. Whenever they press one of the buttons, a vertical bar appears on the screen, Dr. Montague said. It represents one dollar. If the whole bar is colored, it means they earn a dollar. If 60 percent of the bar is colored, they earn 60 cents. If 30 percent is colored, they get 30 cents and so forth.

The task is to push either button and to maximize the amount of money you earn over 250 trials, Dr. Montague said. You can take as long as you want and you can scribble notes on strategies you want to try.

But, like the blue and yellow flowers shown to the bee, the game is rigged. Button A gives smaller rewards, but more of them. Button B gives much larger rewards, but they occur infrequently.

Most people behaved just like the bees, Dr. Montague said. They might start by choosing A, which would give them a good return for several tries. But then A might fall to ten cents or five cents. Their dopamine systems could not tolerate this, he said, so they would switch to button B. But B, as rigged, gives many more low than high payoffs, so the player would quickly switch back to A, he said.

Those who keep switching earn far less than those who have more patience in exploring the potential payoffs in button B, Dr. Montague said. Only two players, both physicists, followed the riskier and more optimal strategy of sticking with B, he said.

This is one reason most people lose money in Las Vegas, Dr. Montague said. Their dopamine system, operating moment to moment in predicting rewards, goes berserk when they are losing and they switch strategies too often. Another reason, of course, is that the odds in every game of chance are in favor of the house, so inevitably, dopamine or no, the overall flow of money in casinos is in, not out. No system of neurotransmitters would allow most people to win at slot machines, for instance. The odds are in the machines themselves, not in the mind.
