Injections Temporarily Turn Slacker Monkeys Into Model Workers

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Laboratory monkeys that started out as careless procrastinators became super-efficient workers after injections into their brains that suppressed a gene linked to their ability to anticipate a reward.

The monkeys, which had been taught a computer game that rewarded them with drops of water and juice, lost their slacker ways and worked faster while making fewer errors.

Government researchers used a new technique to temporarily block a gene, known as D2, that normally produces receptors for the brain chemical dopamine—a component in the perception of pleasure and satisfaction.

Terrence Sejnowski, a neurobiologist at the Salk Institute for Biological Studies in La Jolla, called the experiment a "tour de force" for opening a new way of modulating brain chemistry. "The ability to block a specific type of receptor in a specific part of the brain could allow a new generation of therapeutics with fewer side effects," he said.

The results, reported Tuesday in the Proceedings of the National Academy of Sciences, could also shed light on mental illnesses that involve motivation, such as obsessive compulsive disorder and mania.

It turns out that the work ethic of rhesus monkeys resembles that of many humans.

"If the reward is not immediate, you procrastinate," said Barry Richmond, a neurologist who led the study at the National Institute of Mental Health.

The task at hand was a computer game in which a monkey, perched in a plexiglass cage in front of a computer monitor, would release a lever each time a red dot on the screen turned green. Only quick responses counted.

The number of successes needed for a reward varied—one, two or three. A gray bar on the monitor told the seven monkeys in the experiment of their progress, brightening as a drink became imminent.

Before their genetic treatment, the monkeys in the test dawdled when the
gray bar was dim. Only when it glowed did they become conscientious.

All that changed after a snippet of DNA known as an "anti-sense expression vector" was injected into a part of the brain known as the rhinal cortex. The vector suppressed the expression of the D2 gene for several weeks, hampering the ability of the rhinal cortex to detect dopamine.

The monkeys no longer understood the meaning of the gray bars. As a result, their interest never waned. They worked their levers like obsessed gamblers, never knowing when the jackpot would be delivered. They stopped only after their thirst was quenched.

To the researchers, the results made sense.

Dopamine is related to the reward pathways in the brain. The rhinal cortex is a part of the brain where meaning is attached to recognized objects. The hardworking monkeys acted as if their rhinal cortexes had been removed.

But don't expect any gene-suppressing injections for chatty office workers or inattentive students.

"Perhaps they would look like manic people all the time," Richmond said.

The research could help in understanding the neural circuitry in people who have any of a variety of disorders.

Schizophrenia and Parkinson's disease are related to dopamine pathways.

Other illnesses are linked to some fault in the reward circuitry of the brain. Manic people work even when the rewards are insignificant. In depression, no amount of work seems worth the reward. In obsessive compulsive disorder, the rewards never seem to register. Drug abusers risk danger for their reward.

The research also advances the use of the vector technique, which had been used before in mice but never in primates.

Because it can be used to target specific genes in specific parts of the brain, the technique could become a valuable tool in brain research, said Mortimer Mishkin, an NIH neuroscientist who was not part of the study.

"And it's temporary, which is a huge advantage, because you can look both before and after," he said.

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