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Chemical system in brain behaves differently in cocaine addicts, UT Southwestern scientists find

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UT Southwestern Medical Center researchers have identified a chemical system in the brain that reacts differently in cocaine addicts, findings that could result in new treatment options for individuals addicted to the drug.

"We found that the amount of blood flow in areas of the brain known to be involved in the rewarding effects of cocaine and craving was different in cocaine addicts, compared with healthy subjects," said Dr. Bryon Adinoff, professor of psychiatry at UT Southwestern and lead author of a study that appeared in *Neuropsychopharmacology*. "Now we have a new target for pharmacologic intervention."

The researchers studied changes in the brain's cholinergic system, which involves the neurotransmitter acetylcholine and its receptors, or docking points, on brain cells to which the chemical attaches. Disruption of this system has been implicated in Alzheimer's disease. In animal models of addiction, the neurotransmitter has been shown to affect how hard an animal will work to get a drug, but until now, the cholinergic system's relation to addiction in humans hadn't been explored.

For this study, researchers looked at how alterations in the cholinergic system affected the limbic region in the brain of cocaine-addicted subjects. The limbic region of the brain supports functions such as emotions, behavior, learning and long-term memory. It includes brain

structures such as the hippocampus and amygdala.

Much addiction-related work has focused on other chemicals in the brain, particularly dopamine. Dopamine is associated with the "pleasure system" of the brain and is released by naturally rewarding experiences such as food, sex and the use of drugs like cocaine.

"Very few treatments affecting these other chemical systems have been effective at helping cure addiction," said Dr. Michael Devous, professor of radiology at UT Southwestern and an author of the paper. "We have discovered abnormalities in the cholinergic system of cocaine addiction that may relate more to the addictive process than the reward process."

On two different days, researchers injected two substances known to be safe in humans into 22 healthy subjects and 23 cocaine addicts who had abstained from the drug for one to six weeks. The substances - scopolamine and physostigmine - act on acetylcholine receptors. On the third day, subjects were given saline. After each injection, subjects underwent brain scans using single photon emission computed tomography (SPECT) to look at blood flow in the limbic region.

"It's a complicated system," said Dr. Adinoff, holder of the Distinguished Professorship in Drug and Alcohol Abuse Research. "The idea was to push it; it didn't matter whether the system was more active or less active, we just wanted to see if it changed."

Both scopolamine and physostigmine induced blood flow changes in limbic brain regions, but the flow patterns were different in cocaine addicts and healthy subjects.

One of the most intriguing areas affected by both substances was the tail of the hippocampus, Dr. Adinoff said. Other research has shown that this section controls environmental cues that may make someone more

likely to continue to use cocaine.

"That makes sense," Dr. Adinoff said. "It's a very specific and isolated region with lots of cholinergic receptors."

The amygdala, which is involved with cue-induced cravings, also was affected by pushing the cholinergic system.

"Both of these areas of the brain are relevant to drug cravings and reward, so perhaps we could inhibit desire for a drug by giving medication that would affect these systems," Dr. Adinoff said.

Dr. Adinoff said the next step would be to use functional magnetic resonance imaging (fMRI) to assess how the cholinergic system affects decision-making processes in addicts that heighten the risk of relapse.

Provided by UT Southwestern Medical Center

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