SOUTHWESTERN NEWS

Media Contact: Amy Shields
214-648-3404
amy.shields@utsouthwestern.edu

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UT SOUTHWESTERN RESEARCHERS INDENTIFY MECHANISM BY WHICH COCAINE ELEVATES BLOOD PRESSURE

DALLAS – March 5, 2002 – Researchers at UT Southwestern Medical Center at Dallas have identified the underlying mechanism by which cocaine triggers hypertensive crisis, the most severe form of high blood pressure and one of the most common cocaine-related, cardiovascular emergencies in the United States.

The findings, reported in today's issue of *Circulation*, may lead to the development of new treatment strategies for cocaine-induced blood pressure elevation and related complications including stroke and acute myocardial infarction.

"The underlying mechanism of the blood-pressure-raising effect of cocaine use in humans has not been well studied," said Dr. Wanpen Vongpatanasin, senior author of the study and assistant professor of internal medicine. "Most of us believe that cocaine increases blood pressure mainly by preventing clearance or reuptake of noradrenaline from blood vessels into the nerve endings and the excess levels of noradrenaline cause blood vessels to constrict. However, we found that this mechanism plays a very small role in humans. Instead, cocaine increases blood pressure by stimulation of the heart to cause rapid heartbeat and increased cardiac output. This elevation in blood pressure, if severe or persistent, can lead to damage of multiple vital organs such as the heart, brain and kidney."

Approximately 25 million Americans have tried cocaine, and the drug is the most frequent cause of drug-related deaths reported by medical examiners. In 1999, cocaine use was cited in 30 percent of all drug-related emergency department visits and cocaine is the most commonly used illicit drug among people seeking care in hospital emergency departments or drug treatment centers.

"The textbook explanation of cocaine-related elevated blood pressure is based on evidence from previous studies in rats and mice," said Dr. Meryem Tuncel, lead author of the study and a postdoctoral fellow in hypertension. "However, anesthesia used to sedate these

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animals interferes with the effects of cocaine on the central nervous system, and it is very difficult to show that even a large dose of cocaine can increase blood pressure in animals. Therefore, we suspected that the results would be different in humans."

The investigators administered a small, medically approved dose of cocaine nose drops to 15 healthy cocaine-naive study participants. To directly measure the drug's effect on blood vessels without influencing the brain or heart, the researchers administered two different doses of cocaine into the artery of the forearm and measured blood pressure, forearm blood flow and forearm venous noradrenaline concentration in the same study participants on two different days.

Microelectrodes, which are similar to acupuncture needles, were used to record sympathetic nerve activity during administration of the cocaine nose drops.

The researchers found that when cocaine is given directly into the artery in the upper arm, it causes blood vessels to constrict as shown in previous animal studies.

"However, when cocaine is given through the nose, it causes dilation, rather than constriction of the blood vessels," Vongpatanasin said.

"Blood pressure is determined by two factors, vascular tone and cardiac output. If intranasal cocaine increases blood pressure and the blood vessels dilate instead of constrict, the cardiac output must increase.

"Now that we know the mechanisms involved in how cocaine elevates blood pressure, I think we should refocus our strategy to use medications that will affect sympathetic stimulation of the heart rather than medications that have effects only on blood vessels."

Other researchers who contributed to the study were Dr. Ronald Victor, chief of hypertension; Drs. Paul Fadel and Zhongyun Wang, postdoctoral researchers in internal medicine; and Debbie Arbique, a senior registered nurse in internal medicine.

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