

Researchers identify key step in cocaine-induced heart enlargement, sudden death

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Cocaine, in concentrations commonly sold on the street, causes the abnormal buildup of primitive proteins in heart muscle – a process causing heart enlargement that can ultimately lead to sudden death, report researchers at the University of South Florida College of Medicine and James A. Haley Veterans' Hospital.

The study was published in the July 2006 issue of the *Journal of Cardiovascular Pharmacology*.

"This finding is important because cocaine-related deaths most commonly occur in young people between the ages of 18 and 29, many of whom are totally unaware of the drug's toxic effects," said Robert Henning, MD, professor of medicine at the USF College of Medicine at the Haley VA Hospital.

Using heart muscle cells from adult rats, Dr. Henning and his colleagues found that cocaine activates the enzyme calmodulin kinase II (CaMK), which increases calcium within the heart muscle cells. The increase in calcium appears to be a key step in prompting the accumulation of primitive fetal proteins not normally found in adult heart muscle cells – a process that causes the muscles cells, and eventually the heart, to enlarge. It also triggers irregular heart rhythms that can cause sudden death.

The researchers also demonstrated that the CaMK inhibitors Nifedipine and KN-62 appear to limit the accumulation of abnormal proteins in heart muscle, suggesting they may be a useful therapy for cardiac

hypertrophy, or enlarged heart.

The USF researchers' findings may also have wider implications for other forms of heart enlargement caused by chronic disease. "The biomolecular pathway that we've identified likely also plays an important role in heart hypertrophy due to hypertension, heart attacks and heart failure," Dr. Henning said.

In cardiac hypertrophy, or enlarged heart, the heart's main pumping chamber becomes abnormally large as a result of an increased workload. In time, fibers of the heart muscle thicken and become less able to relax, reducing the heart's capacity to meet the body's demands for normal blood circulation.

Approximately 5 million Americans use cocaine on a regular basis. Cardiac hypertrophy may affect as many as 47 percent of chronic cocaine users with normal blood pressure, Dr. Henning said.

Source: University of South Florida Health

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