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Research shows cocaine changes proteins and brain function

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In the first large-scale analysis of proteins in the brains of individuals addicted to cocaine, researchers have uncovered novel proteins and mechanisms that may one day lead to new treatment options to fight addiction.

The results, reported in the current issue of *Molecular Psychiatry*, released on-line today, show differences in the amounts of 50 proteins and point to profound changes in brain function related to long-term cocaine use, said Scott E. Hemby, Ph.D., of Wake Forest University of Medicine.

The researcher used technology so advanced it was like looking for differences in brain tissue with "floodlights" rather than a "flashlight," he said. Hemby and his colleagues analyzed thousands of proteins from brain tissue obtained from individuals who died of cocaine overdose and compared these "protein profiles" with individuals who died of non-drug related causes.

"The findings provide new insights into the long-term effects and damage that cocaine has on the human brain and will help guide future animal studies to further delineate the biochemical changes that comprise the addicted brain," said Hemby, associate professor of physiology and pharmacology.

The researchers compared the proteome (the entire complement of proteins expressed at a given time) between the two groups by separating

all of the proteins and then using high-throughput mass spectrometry which allowed the accurate identifcation of thousands of proteins simultaneously, Hemby said.

The unbiased nature of the technology enables the determination of novel proteins and pathway involved in disease. Using post-mortem brain tissue samples from the Brain Endowment Bank at the University of Miami, the investigators analyzed protein expression in the nucleus accumbens, a part of the brain involved in the addictive effects of drugs, in 10 cocaine-overdose victims and 10 drug-free individuals.

Analysis of thousands of proteins revealed differences between the two groups in the amounts of approximately 50 proteins, most of which correspond to changes in the ability of the brain cells to strenghten their connections and communicate with one another.

Understanding the coordinated involvement of multiple proteins in cocaine abuse provides insight into the molecular basis of the disease and offers new targets for pharmaco-therapeutic intervention for drug-abuse-related disorders, he said.

"These studies are an important and significant step to further our understanding of the vast and long-term consequences of cocaine use and may provide insights into novel targets for medication development," Hemby said.

Source: Wake Forest University Baptist Medical Center

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