SOUTHWESTERN NEWS

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UT SOUTHWESTERN SCIENTIST EXPLORES CAFFEINE-SIGNALING ACTIVITY IN BRAIN FUNCTION

DALLAS – Aug. 29, 2002 – Every morning millions of Americans reach for the world's most popular drug to help them start their day.

"That drug is caffeine," said Dr. James Bibb, assistant professor of psychiatry at UT Southwestern Medical Center at Dallas. Bibb is one of the authors of a new report explaining how caffeine exerts its stimulatory effect by altering the biochemistry of the brain. The findings appear in an August issue of *Nature*.

"Caffeine is the most frequently self-administered drug in recreational use worldwide today," Bibb said. "And yet we know little about how caffeine works in the brain, whether with the kick from a double espresso or small jolts from tea or cola. We do know it is rewarding, can enhance cognition and performance, and induce dependence at the same time."

Bibb said most people would never consider that the effects of their morning coffee would have any similarities to those of cocaine, long known to be a powerful and dangerous recreational drug. But research is showing that the two stimulants similarly alter a specific signaling activity within the brain.

The researchers involved in the *Nature* paper used genetically altered mice lacking DARPP-32, a protein known to play a role in drug addiction, to explore questions about caffeine's stimulant effects. Normal mice given a 7.5 milligram/kilogram dose of caffeine showed a dramatic increase in long-range (locomotion) and short-range (motility) movements for as long as 100 minutes. This amount of caffeine is the equivalent of about three cups of coffee for a person weighing 160 pounds. When scientists gave the mice lacking DARPP-32 the same dose, it had little effect. Only by doubling the dose to 15 mg/kg were researchers able to overcome the knockout effect of gene deletion.

Bibb said these results were similar to those of his previous studies that explored the same biochemical pathways activated by cocaine.

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Bibb explained that it has been known for some time that caffeine owes much of its stimulant action to its ability to block receptors, such as those for adenosine, in the brain. Adenosine, one of the four building blocks of DNA and an important signaling molecule in the brain, forms the backbone of the energy-storage molecule ATP. ATP helps maintain equilibrium, or balance, between its energy use and electrical activity throughout the cells, sending signals along specific brain pathways.

Bibb is a former Rockefeller University scientist who is continuing his research at UT Southwestern on the processes in the brain that control addiction and other neurological and psychiatric disorders. Much of his research involves identifying processes that regulate brain biochemistry and determining how these are triggered by specific drugs of abuse or neuropsychiatric diseases. Some of his early findings on these biochemical pathways and how cocaine affects them have appeared in two earlier reports in *Nature.*

Bibb said insights into the mechanisms of both cocaine and caffeine on the brain have led him to investigate the processes in the brain that control sleep. He is currently working on new sleep studies with other scientists, including Dr. Robert Greene, vice chairman of psychiatry for VA services at UT Southwestern.

"We find that in the brain many processes are related, and it is well-known that caffeine can induce insomnia and that adenosine can induce sleep. By studying sleep we may also learn more about drug addiction and other disorders," Bibb said.

The caffeine research was conducted by scientists at Rockefeller University in New York City; the Karolinska Institute in Stockholm, Sweden; and the "Mario Negri" Institute for Pharmacological Research in Milan, Italy.

The study was funded by the Swedish Research Council, the National Institute of Mental Health and the National Institute on Drug Abuse.

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