Hope for treating relapse to methamphetamine abuse

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A new study at the U.S. Department of Energy's (DOE) Brookhaven National Laboratory suggests that vigabatrin (a.k.a. gamma vinyl-GABA, or GVG) blocks drug-seeking behavior in animals previously trained to associate methamphetamine with a particular environment. Specifically, animals pre-treated with vigabatrin lost interest in spending time in a location where they had previously been given methamphetamine. The results will appear in the February 2009 issue of *Synapse*, now available online.

"Reinstatement of drug-seeking behavior after an extended period of abstinence is the number-one cause of drug-addiction relapse," said Brookhaven neuroanatomist Stephen Dewey, who led the research team. "This animal study suggests that vigabatrin could potentially prevent human methamphetamine addicts from relapsing."

According to the National Institute on Drug Abuse, methamphetamine is a very addictive stimulant that is quickly becoming an American public health epidemic. There is currently no effective treatment for methamphetamine addiction.

Vigabatrin is a pharmaceutical agent first tested as a possible treatment for a variety of addictions in animal studies led by Dewey at Brookhaven Lab (http://www.bnl.gov/CTN/GVG/). It is the only drug that has been shown to block any behavior associated with methamphetamine use, and is currently being tested by Catalyst Pharmaceutical Partners (http://www.catalystpharma.com/) for safety and efficacy against

cocaine and methamphetamine addiction in humans in Phase II clinical trials across the U.S.

"In human drug abusers, many things can cause relapse — exposure or access to drugs, environmental cues that trigger thoughts of the drug, or stress," said Dewey. "If vigabatrin can prevent relapse, it could have a huge impact by helping drug abusers regain control over their lives."

In the current study, rats were first put through a series of conditioning tests that taught them to expect methamphetamine in one chamber of a three-chamber apparatus and saline solution in another chamber. The researchers then allowed the rats to roam freely among the three chambers. If the rats spent the majority of their time in the chamber where they had been given methamphetamine, the scientists knew they had established a "conditioned place preference."

Once this preference was established, the researchers extinguished it by giving the rats saline injections in both chambers, again allowing the animals to have free access to all chambers until the rats had no preference for the previously methamphetamine-associated chamber for at least six consecutive days.

Once extinguished, however, it is possible for a conditioned preference to be reinstated — just as it is possible for a recovered drug addict to relapse. To reinstate the place preference in this experiment, Brookhaven scientists injected the rats with methamphetamine in the neutral chamber. Immediately, rats went to the chamber where they had received methamphetamine and remained there for the duration of the exposure period.

Then, once the reinstatement of a preference was clearly demonstrated, the researchers tested the effectiveness of vigabatrin at blocking it. They pre-treated animals with vigabatrin two-and-a-half hours before giving

them another priming dose of methamphetamine followed by free access to all three chambers. When pre-treated with vigabatrin, the rats no longer showed any preference for one chamber over another.

Dewey's group is now conducting studies to examine whether GVG will also block an environmental cue previously shown to produce relapse to drug-seeking behavior.

"These studies have wide implications for addressing the number-one cause of relapse to drug seeking behavior. If we can successfully block drug-induced reinstatement, then our ability to block environmental cue-induced relapse is significantly enhanced," Dewey said.

Source: Brookhaven National Laboratory