PRESS RELEASE

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Cocaine Addiction: Phase-Specific Biology and Treatment?

New findings from a study in Biological Psychiatry

Philadelphia, PA, June 30, 2014 – Current pharmacotherapies for addiction follow the dictum "one size fits all". Medications are prescribed in the same way for all patients, regardless of whether they have just started experimenting with a drug or have an established drug habit. Even more troubling, there are no FDA-approved pharmacotherapies for some addictions, such as compulsive cocaine use.

Perhaps testing drugs in ways that focus on particular phases of addiction or particular clinical features of addiction, such as a patient's level of impulsivity, might advance the development of drug treatments for cocaine addiction.

Addiction is characterized by a transition from strategic drug-seeking (i.e., where a decision is made to try a drug to generate a desired effect) to habitual drug-seeking (i.e., where the behavior is triggered by the availability of drugs, particularly in contexts associated with drug use). Habitual drug use is less dependent than strategic use on whether the person actually enjoys the effects of the drug or whether there are negative subjective effects or problems associated with taking the substance.

The transition from strategic to habitual drug-seeking is associated with changes in the brain, where dopamine systems are involved in shifting the representation of drug-taking in the striatum region of the brain from the lower (ventral) part of the striatum, implicated in reward, to the higher (dorsolateral) striatum, implicated in habits.

Researchers now have identified the stages of this process that are sensitive to blockade of dopamine receptors, potential therapeutic targets, and the important role that impulsivity plays in this process. They report their results in the current issue of *Biological Psychiatry*.

They administered a dopamine receptor-blocking drug, α-flupenthixol, directly into the dorsolateral striatum of rats at different phases of addiction. They found that the rats transitioned from insensitivity to sensitivity to the drug's inhibitory effects on cocaine-seeking, but that this transition was also influenced by the inherent impulsivity of the rats.

Early in the addiction process, all rodents were insensitive to the drug's effects, but it did suppress drug-seeking in animals with long-standing cocaine self-administration. They also found that highly impulsive animals made the transition from drug insensitivity to sensitivity more slowly than animals with low levels of impulsivity.

"The results of this study are important because they show that although both impulsive and non-impulsive rats developed cocaine-seeking habits, this was delayed in high impulsive rats," said first author Dr. Jennifer Murray, from University of Cambridge.

These data suggest that impulsivity does not simply promote compulsivity through the facilitation of habits, but rather that these are interacting independent processes.

Murray added, "It is suggested that vulnerability to addiction conferred by impulsivity is less influenced by the propensity to develop drug-seeking habits and more by the inability of an individual to regain control over these habits that are rigidly and maladaptively established in the brain."

"The notion that particular brain mechanisms are engaged only at particular phases of the addiction process strikes me as an important insight that has yet to be harnessed in developing new medications for addiction treatment," said Dr. John Krystal, Editor of *Biological Psychiatry*. "This study

highlights that dopamine receptor blockers might play a role, but only at particular phases of the addiction process."

The article is "Increased Impulsivity Retards the Transition to Dorsolateral Striatal Dopamine Control of Cocaine Seeking" by Jennifer E. Murray, Ruth Dilleen, Yann Pelloux, Daina Economidou, Jeffrey W. Dalley, David Belin, and Barry J. Everitt (doi: 10.1016/j.biopsych.2013.09.011). The article appears in *Biological Psychiatry*, Volume 76, Issue 1 (July 1, 2014), published by Elsevier.

Notes for editors
Full text of the article is available to credentialed journalists upon request; contact Rhiannon Bugno at +1 214 648 0880 or Biol.Psych@utsouthwestern.edu. Journalists wishing to interview the authors may contact Dr. Jennifer Murray at +44 (0) 1223 765285 or jem98@cam.ac.uk.

The authors' affiliations, and disclosures of financial and conflicts of interests are available in the article.

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