Rats:

* cont'd from pg.2

(NIDA) agrees with Crystal and is looking to increase their portfolio of studies of comparative cognition. NIDA funded Crystal's research on the effects of drugs on rats' information processing. In particular, he investigated the role of canabanoids, the neurotransmitters in the brain most directly affected by marijuana, on the experience of time in collaboration with Ken Maxwell and IBR Fellow Andrea Hohmann. His results indicated that rats' sustained attention to time was altered by exposure to marijuana. Crystal relates these findings to humans' subjective descriptions of a slowing of time perception after smoking pot. He insists that there is more to be learned from animals about the role of cognitive processes in drug abuse. He offers a short list of topics for which animal models could be relevant, including the physiological craving for substances, drug-seeking behavior and users' memories of previous experiences with drugs.

A dominant issue in animal research is finding ways to minimize the numbers of animals used as research subjects. In order to address this concern, Crystal makes all of his raw data available for re-analysis on his website. "There is a recent interest in making government-funded data available to as many researchers as possible," he explains. "With public data archives, you can do secondary analyses of data or combine data sets instead of repeating experiments. This is good for training, because graduate students can use existing data sets before conducting new experiments. And it ensures that you are using the smallest number of animals possible, which addresses concerns about the ethics of animal research." You can visit Crystal's archives by going to www.uga.edu/animal-cognition-lab/

How Will We Apply Genetics?

* cont'd from pg.1

seven per cent of the subjects said that they would be "very suspicious" of the safety of a drug targeted for African Americans and 40 per cent felt "very suspicious" of the effectiveness of such a drug. Condit suggests that these suspicions could increase patients' distrust in the health care profession in general and in their particular provider, specifically.

Condit concludes that the lack of reliability with which people describe their heritage, in combination with the uncertainty regarding the safety and effectiveness of the drugs themselves, calls the usefulness of the whole idea of race-specific medicines into question. However, she finds that her research gets little attention in the field of pharmacogenomics. "Geneticists don't want to be bothered," she says. "They don't consider problems created by language to be scientific. At the same time, because they are a part of our culture, the proposed link between race and biology is firmly in their heads. They are not predisposed to see it as something they have to account for in their work." She pauses, and then adds, "And it's not an easy problem to solve."

Gamblers:

* cont'd from pg.3

risks in an attempt to win back his debts. The DSM-IV also notes that pathological gamblers may display distortions in thinking, such as denial, superstitions, overconfidence or a sense of power and control.

Goodie's research is potentially relevant to therapists looking for strategies to help these gamblers stop their pattern of repetitive, unsuccessful risk-taking. "What might be going on with these people," he suggests, "is that they feel like they have some control, even if they know the losing probabilities. They have a system – it may be their lucky socks, a pattern of numbers, or whatever – that gives them the false perception that they can change those probabilities." In other words, they take greater risks because they weight the probabilities in their own favor, based on the degree of control that they mistakenly perceive themselves to have over the likely outcome. This misperception is a cognitive distortion in need of correction.

According to Goodie, the way to do this is not to educate the gambler about the probabilities and the outcomes. The gambler knows the odds are against him, and he recognizes that the stakes are high. The key to changing the pathological gambler's risk-taking behavior is to alter his perception of control. He must be shown, very convincingly, that he has no ability to change his probability of success. "Lottery probabilities can't be changed," Goodie insists. "They are one in 100 million no matter what you do."

The Institute for Behavioral Research
The University of Georgia
111 Barrow Hall
Athens, Georgia 30602

■ Fall 2004

THE INDEPENDENT VARIABLE

Institute for Behavioral Research of the University of Georgia

How Will We Apply Genetics?

Celeste Condit's Research Provides Questions and Answers.

When people talk, Celeste Condit, Research Professor in Speech Communication, listens closely. For the last eight years, she's been studying the ways in which people communicate about genetics, and in the course of those studies she began listening particularly closely to conversations about race. What she heard – at conferences and in debates within the literature – was talk about pharmacogenomics, the tailoring of medication to a person's distinct genetic profile. These talks quickly developed into a discussion about how to use race as a prescriptive marker.

In other words, researchers are interested in developing drugs that would be race-specific. For example, one drug would be prescribed to a White hypertension patient while a different one would be prescribed to an African-American. The reasoning behind this idea is that genetic variability in patterns of disease suggests that genetically specific treatments may be useful. Different people respond to different medicines in different ways. Researchers would like to be able to identify the people who would likely be helped -- or harmed -- by certain drugs more than others. Although genetic testing could provide that information, it would be very expensive to test each patient before writing a prescription. As a shortcut and a moneysaver, race is being proposed as a proxy for individual genetic profiling.

"I was unsure what African Americans would think about that," Condit says. "On the one hand, they might think it was good. Instead of taking a drug that was, by default, designed for Whites, they could get one designed for them. On the other hand, there is still a lot of suspicion based on the history of the Tuskegee project. And some people might see genetic testing as a violation of their privacy."

She applied for a grant to study the attitudes of a diverse group of people about race and genes, using messages about race-based prescription as the focus of inquiry. What she discovered could not be considered good news for the proponents of pharmacogenomics. To begin with, Condit's subjects could not reliably identify themselves as belonging to a discrete racial category. They were uncertain about their backgrounds. In fact, almost forty per cent of them did not know the race of all four of their biological grandparents. Nine per cent didn't know the geographic origin of both of their parents.

These surprising results highlight a significant problem. As it is commonly used, race is a nonspecific term. Socially designated racial categories are based on perceived differences in any number of characteristics – physical appearance, linguistics, nationality, regionality and continental origin. These categories are cultural and political, and they change over time. They are sloppy and slippery, and they mean very little on the genetic level.

Condit believes it will be difficult for doctors to match patients to racial profiles indicating who should get what drug. "Let's say you have a dark-skinned, curly-haired, Spanish-speaking male patient," she proposes. "What if he identifies himself as a Hispanic American rather than as an African-American? Which race-specific drug would you give him: the one for African Americans or the one for Whites? How will he react to the label you give him, and will he accept that drug?"

Celeste Condit, Ph.D.

"Scientists need a technical vocabulary for describing human genetic variation," she continues. "But they can't use lay racial categorizations. That language is too vague. It's not clinically specific enough to match up to the fragmented, variable pattern of underlying genetic diversity. Clinical tools require a high level of specific precision, and race doesn't meet that standard."

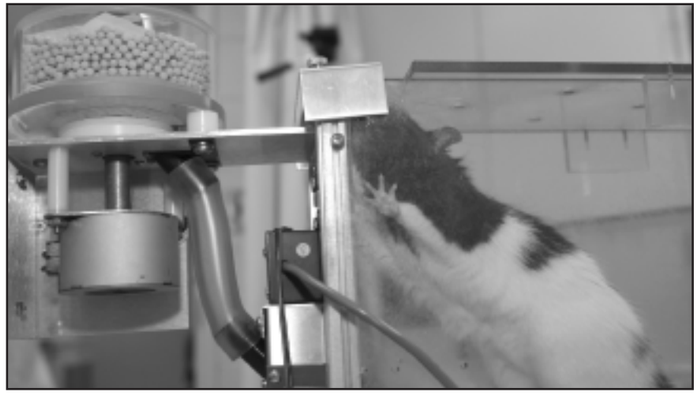
She explains that for all other animals, scientists have a quantitative definition of the amount of variation necessary to classify races. But humans don't display that level of genetic variability. By the strictest definition, racial differences between humans only account for .001 per cent of the genetic variation. According to Condit, we shouldn't even use the language of race in biological discussions.

In addition to pointing out the unreliability of racial distinctions and classifications, Condit's research indicates that patients would be suspicious of being matched to a drug prescription on the basis of race. They also question the safety and effectiveness of race-specific drugs. Forty-

* Continued on page 4

How Do You Ask A Rat What He Ate for Breakfast:

Jonathon Crystal's Research on Animal Memory Inspires Debate



Evidence of Episodic Memory

Psychologists have been preoccupied with how the mind operates since William James published The Principles of Psychology in 1890. In a computer-automated rat lab on floor of the Psychology building, Jonathon Crystal, IBR Fellow and Associate Professor in Psychology, is developing new techniques to address some old questions. His work in comparative cognition is controversial to those who insist that animals are not capable of complex cognitive processes. Others consider his research innovative, with potential applications to some devastating human problems, such as drug addiction and dementia.

Crystal is particularly interested in how we keep track of time. Short interval timing is the perception of time in the short run, such as the dawning awareness that we have been waiting too long for a bus. It is measured in seconds or minutes. However, jet lag, our difficulty adjusting to time changes when we travel long distances, is related to the body's circadian rhythms, a cyclical timing process which is measured in hours or days. Crystal believes that developing information processing theories of how animals keep track of time will provide insight into the same processes in humans.

"For one thing," he explains, "the animal model has the advantage of offering the opportunity for genetic manipulation." As an example, he describes a behavioral genetics project related to time perception that he is working on. Using mutant mice that have been bred and tested by the National Institutes of Health to have unusually short or unusually long circadian rhythms, Crystal is looking at differences in short interval timing that appear to be based on the genetic alterations in the mice's circadian rhythms.

According to Crystal, this cutting-edge methodology is one advantage of studying cognitive processes in animals. "Not only is it possible to look at the effects of genetic alterations on animals' cognitive processing," he says, "but we can study the effects of neuroanatomical and pharmacological manipulations as well. In this way, we're able to do some basic science about memory that could never be done with humans. And the results could eventually translate into therapies for human diseases like Alzheimer's."

But what types of memory processing are animals really capable of? This is a question that inspires debate in the field of comparative cognition. In the past, researchers have limited their animal studies to simple memory processes, like increases over time in passive forgetting. However, Crystal and Stephanie Babb, a graduate student in the Department of Psychology, have developed an elaborate series of experiments to demonstrate that rats are capable of episodic memory, the ability to recollect the what, when and where of a specific past event.

"The primary avenue to explore episodic memory in humans is to ask them, for example, 'What did you eat for breakfast?'" Crystal explains. "Of course, this is not possible with animals. So, we identify objective operating characteristics of cognitive mechanisms." Crystal's lab is outfitted with computer-automated mazes where data is automatically recorded when rats break photo beams at various locations in the runways and feeding troughs. In this way, he can document their memory for particular food experiences ("what") at different locations in the maze ("where") following differing time intervals ("when").

In a recent study, rats were trained to preferentially return to a specific location in the maze where chocolate – rather than regular rat food -- was available, but only after a long – rather than a short – time interval. Then the animals received a taste-aversion treatment in which chocolate was paired with lithium chloride. Following this treatment, the rats made fewer revisits to the chocolate location than in previous testing. It is Crystal's conclusion that the rats could not have reduced their rate of revisits to the chocolate location without knowledge of what, when, and where -- three necessary components of episodic memory.

Some researchers still disagree that rat memory is the same as human memory, but these disagreements are now based on data rather than personal belief systems. "For a long time," Crystal recalls, "memory researchers would say, 'Animals wouldn't be capable of this," but they hadn't conducted experiments with animals or read the animal literature. What's most productive about our approach to animal cognition is that it's empirical."

The National Institute on Drug Abuse

* cont'd on pg. 4

Goodie Studies Gamblers' Pathological Risk-Taking Behavior

Adam Goodie, Ph.D.

Let's say a person offers you a bet on a simple coin toss. If it comes up heads, you win $100; if it comes up tails, you lose the same amount. Would you take the bet? Chances are good, says Adam Goodie, IBR Fellow and Assistant Professor in the Department of Psychology, that you would not. Goodie has learned that even though people know that they have a 50/50 chance of winning, the possibility of losing feels greater that it really is. "Most people most of the time are risk averse," he says. "They will not bet $100 on a coin flip because they give less than 50 per cent weight to the probability that they will win and more than 50 per cent weight to the possibility of losing."

Goodie studies decision-making processes that underlie risk-taking behavior. "There are two pillars of all approaches to risk and uncertainty," he explains. "The magnitude of various possible outcomes and their probabilities. For example, when we play the lottery, hitting the jackpot would be an extremely positive outcome, but we don't get our hopes up too much because we know the probability is so low." His work focuses on the ways in which people's decisions deviate from probability theory, particularly in the case of pathological gamblers.

Five years ago while teaching a graduate seminar, Goodie became curious about a disconnect in the literature. "We were talking about overconfidence," he recalls. "And the literature shows that most people are overconfident. That is, they are more confident than accurate in their knowledge about events." He was struck by the seeming contradiction between these findings and most people's risk averse behavior. The confidence literature had not been integrated with the risk-taking literature. As a result, there was no good theoretical explanation of the possible connection between confidence, or people's perceptions of their ability to control their outcomes, and decision-making.

"The risk-taking literature was all about probability and its relationship to decision-making," he explains. "Betting on a random event, like a coin toss, can be objectively described and quantified; and it's easy to study because we can be sure of the probabilities." But Goodie had become curious about how perceptions of control over an event might influence risk-taking behavior. "The decision-making literature was missing the non-random component," he says. "It didn't apply to events in which we perceive that we have some control."

With a $440,000 four-year RO1 grant from NIMH that started this past July, Goodie is now developing quantitative methods for modeling the impact of control on risk attitude. He has chosen betting tasks on which the odds of winning can be controlled to some degree by the person placing the bet. For example, a person has some notion about whether his knowledge of college football is extensive or accurate enough to allow him to bet successfully on the outcome of a particular game. And if he wanted to increase his chances of winning, he could study the stats. By asking UGA research subjects about particular SEC football match-ups (such as "Which team will win? What is the probability that you are right? Would you take the bet?") Goodie can measure the impact of control, separate from probability and magnitude of outcome, on risk-taking decisions. A person who believes that he can alter the probabilities (by increasing his familiarity with the SEC rankings, in this case) may be more likely to take the risk.

With consulting assistance from Ken Winters of the University of Minnesota and Daniel Hall, Associate Professor of Statistics at UGA, Goodie plans to study the impact of these factors on the risk-taking decisions of pathological gamblers. According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), the empirically-based psychiatric classification system, pathological gambling is characterized by persistent, maladaptive gambling behavior that damages the gambler's personal, family and work life. Frequently, the gambler develops a long-term pattern of "chasing" losses by repeatedly making larger bets at greater

* Continued on page 4

Institute for Behavioral Research
1785
The University of Georgia
THE Independent Variable
Steven Beach, Ph.D., Director
Karen Smith, Ph.D., Writer

Your comments and questions are welcome. Please direct them in writing to:

IBR • The University of Georgia
111 Barrow Hall
Athens, GA 30602
Phone: 706-542-1806
Email: sbeach@egon.psy.uga.edu
Website: www.ibr.uga.edu