New Avenues of Research Explore Addiction's Disrupted and Destructive Decision Making Research Findings
Vol. 18, No. 4 (November 2003)

By Arnold Mann, NIDA NOTES Contributing Writer, and Patrick Zickler, NIDA NOTES Staff Writer [Abstract]
Volume 18, Number 4 (November 2003)

One of the hallmarks of addiction is the compulsive seeking and use of drugs, even in the face of mounting harmful consequences. Addicted individuals repeatedly make self-destructive decisions--for example, choosing immediate gratification, such as relief from craving, despite that choice's long-term negative consequences, which include loss of health, employment, and quality of life. These decisions are made in the brain's frontal region, where benefits and risks are weighed and choices are made. NIDA-supported research has begun to shed light on the underlying neurobiological mechanisms by which drugs disrupt the "thinking" regions of the frontal brain and lead to the destructive decisions that characterize addiction.

Substance Abusers Choose Short-Term Rewards Despite Mounting Losses

Researchers used a computerized card game to study substance abusers' decision making. The player above has clicked on Deck A, turning up both a $100 win and a linked $300 loss (screen captures). Besides analyzing how players changed their game strategies in response to such results, the researchers measured their level of excitement with skin sensors.

At the University of Iowa, Dr. Antoine Bechara and colleagues evaluated decision making through use of a computerized card game that involved a conflict between short- and long-term gain or loss. In an initial study, they found that a majority of substance-dependent individuals made poor decisions, choosing high immediate gratification without regard for higher future costs. A subsequent study revealed that a large subgroup of these individuals are so hypersensitive to reward--either immediate or delayed--that they make choices without regard for punishment or harm. At the University of California, San Diego, Dr. Martin Paulus and other researchers combined decision-making tasks with brain imaging and found that methamphetamine-addicted individuals displayed distinctive patterns of frontal brain activity that resulted in decision making in which habit and compulsion overrode recognition of harm associated with repeated errors.

Choosing High Reward Despite High Costs

Dr. Bechara's research grew out of the observation that many substance-dependent individuals appear to exhibit a decision-making impairment similar to that of patients who have suffered injury or disease of the brain's ventromedial (VM) prefrontal cortex. Both groups appear to make choices based on the prospects for immediate benefit rather than on future consequences--either positive or negative.

In an initial study designed to confirm the hypothesis that the VM cortex plays a role in decisions made by substance abusers, the researchers evaluated decision making in three groups of participants using a computerized version of a gambling task developed by Dr. Bechara for patients with VM cortex dysfunction. The task simulated real-life decisions involving reward, punishment, and uncertain outcomes. One group included 46 individuals (21 men, 25 women, average age 33) receiving treatment for dependence on alcohol, cocaine, or methamphetamine; the second group consisted of 10 VM patients (5 men, 5

women, average age 45); and the third group had 49 people (21 men, 28 women, average age 38) with no history of either substance abuse or VM damage.

Two-thirds of the substance-dependent individuals showed impaired performance and anticipatory responses similar to those of ventromedial patients.

Researchers assessed participants' decisions as they made selections from four sets of cards offering different monetary rewards or punishments. Two of the sets offered high immediate gains but were poor choices over the long run; continued selection from those sets of cards eventually resulted in net monetary losses. The two other sets represented good choices, offering smaller immediate reward but yielding modest winnings over the long term. The researchers also used perspiration sensors to assess participants' physiological responses during the test as they pondered their choices and were rewarded or penalized for their decisions.

Substance-dependent individuals in this study fell into two categories. One group, roughly a third, was indistinguishable from the healthy controls in their decision-making performance and their anticipatory/emotional responses to reward and punishment, or loss. Two-thirds of the substance-dependent individuals, however, showed impaired performance and anticipatory excitement similar to those of the VM patients, with continued preference for immediate high gains despite mounting long-term losses. "This supports the hypothesis that poor decision making by some substance-dependent individuals is associated with a dysfunctional VM cortex," explains Dr. Bechara.

The researchers then used a variation of the gambling task to further analyze the decision-making patterns displayed by substance abusers in the first task. This time, the researchers arranged cards into two sets. One set included some high immediate losses but long-term rewards; the other set yielded small immediate losses, even smaller immediate rewards, and long-term losses. This test was designed to determine whether hypersensitivity to reward or an inability to observe and act on patterns of results drove substance abusers' choices.

Showing High Sensitivity to Reward
Taken together, two variations of the gambling task identified three distinct subgroups among substance-dependent individuals--a subgroup with apparently normal decision-making patterns and two subgroups with impaired decision making.

For one group (36 percent), performance was indistinguishable from that of normal controls.
A second group (23 percent) made decisions that matched the pattern of patients with VM lesions to the prefrontal cortex: They made choices that favored short-term rewards, even though this strategy resulted in long-term loss.
The largest group (41 percent) appeared to make decisions that were driven primarily by a hypersensitivity to reward. They chose from decks that offered either immediate or delayed reward, irrespective of short- or long-term loss. "Their impaired behavior and choices did not seem to be tied to dysfunction in the thinking prefrontal region but to the presence or prospect of pleasure," Dr. Bechara says. This group had abnormally high physiological responses when they uncovered a high-payoff card, greater excitement when choosing from decks with larger rewards, a willingness to accept greater punishment to obtain a larger reward, and high pleasurable expectations for reward. "For them, drugs are overwhelmingly attractive; their foot is really on the accelerator," says Dr. Bechara.

"This research reveals important variations in performance among individuals with addiction and that a chronic pattern of substance abuse may be attributable to different dysfunctions in the decision-making processes," according to Dr. Steven Grant of NIDA's Division of Treatment Research and Development. "It also suggests the possibility of developing assessment tools to identify different types and degrees of drug-induced impairment or vulnerability and tailoring treatments to address specific behavioral manifestations of addiction."

Linking Disrupted Brain Activity to Impaired Decision Making
In a study that combined brain imaging and analysis of decision making, Dr. Paulus and his colleagues directly examined brain regions and functions that may underlie skewed decision making among methamphetamine-dependent individuals. The researchers found that methamphetamine dependence is associated with decisions based more on habit than on evaluation of possible success or failure. Moreover, functional magnetic resonance imaging (fMRI) showed that methamphetamine-dependent participants had different patterns of brain activity when making decisions than did those who were not dependent on the drug.

By revealing different degrees of impairment, this research may hold clues to treatment success and aid the selection of appropriate therapeutic approaches.

"The decisions they make and the brain regions involved in making decisions suggest that the responses of methamphetamine-dependent individuals are not controlled by consideration of what works over what does not," Dr. Paulus says. Dr. Paulus's study included 14 methamphetamine-dependent men (average age 41) enrolled in an inpatient treatment program. On average, they had used the stimulant for 17 years and at the time of the study had been abstinent for 25 days. The study also included 10 men and 4 women (average age 39) with no history of substance abuse or dependence.

The researchers used fMRI to monitor brain activity while participants tried to predict whether an image of a car would appear on the left or right side of a computer screen. As in Dr. Bechara's gambling task, the game was rigged: The researchers manipulated the computer so that each participant's predictions were correct exactly half the time during one round of the game, 80 percent of the time during another round, and only 20 percent during a third round. The researchers then observed the participants to see how they adjusted their prediction-making strategies when their error rates changed.

The researchers focused on a particular strategy, "win-stay/lose-shift"--that is, choosing the left or right screen again if it was correct on the last response, and choosing the other side if it was incorrect. Both groups of participants used this simple and natural strategy some of the time. However, participants with no history of methamphetamine abuse moved away from it as their error rates rose, apparently seeking an alternative approach that would yield better results. Methamphetamine abusers, in contrast, tended to stick with the win-stay/lose-shift strategy no matter how often their predictions were wrong. When analyzed statistically, their responses were related only to their most recent result, rather than their overall degree of success or failure.

"Our findings suggest that stimulant dependence is a state dominated by habit-based learning, in which a response is made irrespective of associated outcomes. Studies that investigate these patterns of response can begin to explain the mechanisms that underlie either the susceptibility to drug taking in some individuals or the consequences of repeated

drug taking. Understanding these mechanisms may ultimately lead to identifying people at risk for addiction or susceptible to relapse," Dr. Paulus says.

"In this study, the decisions made by methamphetamine abusers look to some extent like those exhibited by psychiatric patients with disorders associated with the brain's frontal regions," Dr. Grant observes. "The methamphetamine abusers don't shift strategies even when things are going wrong. It's not clear why this occurs. They appear to be unable to effectively recognize a pattern of persistent error and adjust appropriately."

Because fMRI produces real-time images of activity throughout the brain, the researchers were able to see that methamphetamine-dependent participants used different brain regions during the task; in some regions, this difference--like the differences in decisions themselves--was related to error rates. "In individuals who were not addicted to methamphetamine, frontal brain areas that are critical for decision making were more active at lower error rates, when they were successfully predicting the outcome," Dr. Paulus says. "These areas were most active in methamphetamine abusers when error rates were highest and the outcome was most unpredictable. In short, the fMRI findings and the behavioral results support a hypothesis that the subjects do not rely on the likelihood of success or failure."

"Neurochemical changes in the midbrain occur in the earliest stages of drug abuse and addiction," says Dr. Grant. "But the frontal regions, which are connected to the midbrain with intricate feedback circuits, are the site of compulsion and cognition. Disrupted function of these sites is crucial to the impaired decision making by which addiction is maintained.

"These decision-making studies don't yet tell us whether drugs act directly in the frontal region to disrupt function or whether the damage done in the midbrain reward system is transferred to the frontal cortex through altered neurochemical pathways. But at the very least, they demonstrate a widespread impact of drugs on the brain and the crucial role of the frontal cortex in maintaining addiction," Dr. Grant explains.

By revealing different degrees of impairment, this research may hold clues to treatment success and aid the selection of appropriate therapeutic approaches to help patients overcome addiction's destructive pattern of decision making.

Sources

Bechara, A., and Damasio, H. Decision-making and addiction (Part I): Impaired activation of somatic states in substance dependent individuals when pondering decisions with negative future consequences. Neuropsychologia 40(10):1675-1689, 2002.
[Abstract]

Bechara, A.; Dolan, S.; Hindes, A. Decision-making and addiction (Part II): Myopia for the future or hypersensitivity to reward? Neuropsychologia 40(10):1690-1705, 2002.
[Abstract]

Paulus, M.P., et al. Decision making by methamphetamine-dependent subjects is associated with error- rate-independent decrease in prefrontal and parietal activation. Biological Psychiatry 53(1):65-74, 2003.
[Abstract]