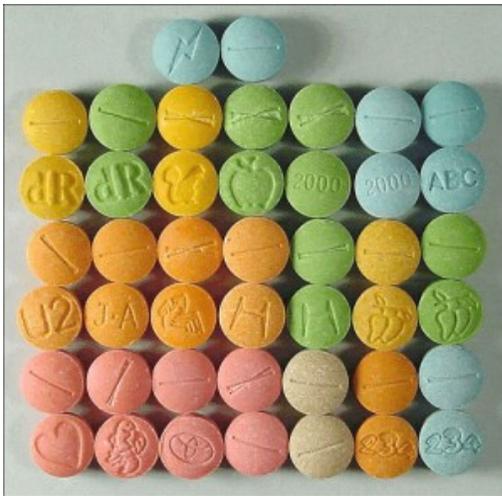


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Ecstasy and the Neurobiology of Social Behavior

Posted Rob Mitchum at 4:58 PM CT, August 25, 2009



Have you heard of 3,4-Methylenedioxymethamphetamine? Maybe its acronym MDMA? Or perhaps its more common street name, ecstasy? Though it's a drug that has been used recreationally for decades, long enough to be the inspiration for books and songs, ecstasy remains scientifically mysterious, with most of the research focusing on harmful long-term effects to users' brains. Left unanswered is a key question about ecstasy: why do people take it?

Far less research has been devoted to ecstasy's unusual effects, which include an increased sense of friendliness, empathy and sociability in users. MDMA is closely related chemically to the drugs methamphetamine and mescaline, but the psychological effects of those drugs are very different: hallucinogen and stimulant effects may be caused by ecstasy, but are not the primary desired effects people seek out by taking the drug.

Feelings of empathy and sociability are also difficult concepts to measure in animals, where most drug research is still performed for legal and ethical reasons. How do you determine whether MDMA makes a rat "friendlier" with other rats? One method, employed in a 2005 study, measured the likelihood of rats to lie next to each other, sort

of a cuddle test. Sure enough, a dose of MDMA increased the likelihood that rats who had not previously met would lie next to each other.



But the human relevance of watching rats cuddle is, suffice to say, limited. So Gillinder Bedi, Ph.D. (above, left), a post-doctoral fellow in the laboratory of University of Chicago Professor of Psychiatry and Behavioral Neuroscience, Harriet de Wit, Ph.D. (below, left) designed experiments to test the effects of ecstasy on people's subjective feelings and the way their brains process the emotions of other people. The first of two papers on the subject was published recently in the journal *Psychopharmacology*. "There is only so much you can glean about social experiences from an animal," Bedi said. "I think it is a fascinating drug in terms of its effects on social behavior and function, in particular given that these social effects appear to be a fundamental part of the reinforcing effects of the drug. So, in this way ecstasy gives us a window into a broader issue, which is how drug effects and social factors interact at a more biological level, and whether such interactions are an important part of why people use drugs." Bedi and her colleagues recruited people who had used



ecstasy in the past and gave them one of two different doses of the drug or placebo. After allowing any effects to set in, the subjects were asked how they felt – sure enough, they felt more sociable and, to a lesser degree, friendlier, replicating previous studies.

Researchers then guided the subjects to an MRI machine, where images were taken of their brains as they viewed a picture set of people making different facial expressions. Those under the influence of MDMA showed both a heightened response to happy faces and a dampened response to angry faces. A brain region called the ventral striatum, which is associated with reward processing, showed stronger activation to happy versus neutral faces in subjects given MDMA, the authors found. Conversely, when angry faces were showing, the response of the amygdala, a region involved in the processing of negative emotions was reduced, suggesting a lower sensitivity to social threat.

These changes in emotional processing may thus underlie people's greater social ease after using ecstasy and explain some of the drug's unique effects. "If you think about what processes might mediate allowing people to give up their defenses, then if they're less responsive to an angry face they might be more able to speak or more able to talk about things they would otherwise be judged by," de Wit explained.

The results, when combined with what scientists know about MDMA's effects on neurotransmitters, may also say something about the neurobiology of social behavior that isn't drug-induced. MDMA potently stimulates the release of the neurotransmitter serotonin by both increasing its release and blocking its clearance. Increasing the amount of released serotonin was already known to have emotional effects in humans - anti-depressant drugs such as Prozac (fluoxetine) and Zoloft (sertraline) are known as

selective serotonin reuptake inhibitors (SSRIs), and have some similar effects on the processing of emotional faces, without the mood effects of ecstasy. Bedi's results, then, lend further insight to serotonin's role in both emotional processing and social behavior.

An even more intriguing neurochemical connection is hinted at by Bedi's research and more directly supported by previous work on the drug. Oxytocin is a hormone and neurotransmitter that is something of a celebrity as far as brain pharmacology goes, having received widespread media coverage for encouraging monogamy and maternal behavior in rodents to inspiring trust and generosity in humans. It doesn't take a Ph.D. to sense an overlap in the effects of oxytocin and MDMA, and sure enough, researchers have recently observed increases in the blood oxytocin levels in MDMA-dosed humans – who again report feelings of, as the Dutch researchers describe it, amicability and gregariousness.

So does MDMA work by stimulating the brain's natural signal for trust and bonding? Are raver kids taking ecstasy to recreate the feelings of a female prairie vole looking to form a bond with a male? Would the effects of MDMA on people's sociability and emotional processing make it a promising therapeutic agent, as some have controversially suggested, for assisting psychotherapy or treating psychiatric conditions like post-traumatic stress disorder? A lot more research on MDMA's mechanism of action remains to be done, Bedi said, but the clues are accumulating.

“Our results don't seem to support enhanced empathy, but they do hint at deactivation of identification and responses to threat, which, in highly anxious people for instance, might allow them to engage more in the therapeutic endeavor,” Bedi said. “But one of the biggest questions regarding use in therapy, to my mind, is how to generalize from the drug experience to the off-drug time, and our results don't speak to that at all.”

See: Bedi G, Phan KL, Angstadt M, de Wit H. Effects of MDMA on sociability and neural response to social threat and social reward. *Psychopharmacology (Berl)* 207:73-83, 2009.

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