
EDITORIAL

From Prozac to Ecstasy: The Implication of New Evidence for Drug-Induced Brain Damage

Our society looks upon psychiatric drugs with such naïve trust that it raises the moral, societal and “therapeutic” status of an illegal drug when it can be compared to a psychiatric drug. Thus Matthew Klam’s personal account in the January 21, 2001 *New York Times Magazine* praised the amphetamine Ecstasy as a “whooper of an antidepressant” that is better than Prozac®. Although illegal in the United States and elsewhere, Ecstasy or MDMA (methylenedioxymethamphetamine) has been used extensively since the 1980s as a “recreational” drug. It is known to cause degeneration of serotonin nerve cells and axons in rats (Ricuarte, Byran, Strauss, Seiden, & Schuster, 1985).

In defense of MDMA, Klam criticized the U.S. government for funding and publicizing research that documents the brain-damaging effect of MDMA. He pointed out that “Prozac-style antidepressants produce some morphological [structural] abnormalities in the serotonin nerve network of rats that resemble changes seen with Ecstasy taken in high levels. Yet few people advocate the banning of Prozac.”

Klam is right that U.S. government health agencies are eager to show that illegal drugs cause brain damage but are reluctant to inform the public that selective serotonin reuptake inhibitor (SSRI) antidepressants have similar damaging effects. He is also right that the kind of research used to justify a ban on MDMA could also be used to justify a ban on the SSRI antidepressants. In some research studies, the MDMA and SSRIs are shown to produce nearly identical morphological changes in the brain (see below). However, Klam arrives at the wrong conclusion. His observations should have raised his concern about both MDMA and the SSRIs. Instead, taking the lead from the cultural overvaluation of antidepressant drugs, he makes even more outlandish and dangerous claims for MDMA.

Unfortunately, Klam’s views are given credence by their publication in the *New York Times*. The appearance of this personal, undocumented story in a prestigious international newspaper indicates the extent of our cultural acceptance of illegal and legal drugs for mood alteration. The unbridled enthusiasm for a stimulant agent is darkly reminiscent of Freud’s ecstatic enthusiasm for

cocaine that ended in addiction (Byck, 1974). Closer to home, it is also reminiscent of the LSD fad of the 1960s which left many people with permanent cognitive dysfunction.

MOUNTING EVIDENCE OF SSRI-INDUCED BRAIN DAMAGE AND DYSFUNCTION

Meanwhile, evidence is mounting that all drugs that stimulate serotonergic neurotransmission can cause lasting anatomical abnormalities. A recent study by Kalia, O'Callaghan, Miller, and Kramer (2000) found morphological abnormalities in serotonergic neurons in rats after the administration of four days of high doses of MDMA, fluoxetine (Prozac®) and sertraline (Zoloft®), as well as fenfluramine. After reviewing the literature, the authors concluded: "Collectively, these results lend support to the concept that all compounds acting on brain serotonin systems . . . could produce similar effects on the morphology of cerebral serotonin systems" (p. 92). Wegerer and colleagues (1999) found "persistently increased density of serotonin transporters in the frontal cortex of rats treated with fluoxetine during early juvenile life" (p. 1). The young rats were exposed to Prozac for only two weeks, but the changes lasted for at least 90 days into the adulthood of the rats. These long-lasting changes took place in the most highly developed portion of the brain—the frontal lobes. The authors warned that administering SSRI antidepressants to children and youth during the greatest periods of brain plasticity might result in lasting brain dysfunction.

A study by Norrholm and Ouimet (2000) demonstrated that single doses of fluoxetine and fluvoxamine (Luvox®), as well as desipramine, caused abnormal growth in brain cells in the temporal lobe in young rats. The changes remained at the last examination three weeks after treatment. The authors concluded: "These results show that acute antidepressant treatment can impact dendritic length and spine density, and raise the possibility that chronic fluoxetine treatment arrests spinal development into young adulthood" (p. 205). Malberg, Eisch, Nestler, and Duman (2000) found that fluoxetine given to adult rats for two to four weeks stimulated proliferation of brain cells in the temporal lobe. They considered it potentially "therapeutic"; however, the changes are obviously pathological. Freo, Ori, Dam, Merico, and Pizzolato (2000) documented marked reductions in glucose metabolism in multiple regions of the rat brain, including the frontal cortex, limbic system, and the basal ganglia, after two weeks of treatment with fluoxetine. They felt that this widespread effect might account for the supposedly broad range of therapeutic effects of fluoxetine. However, these changes constitute widespread suppression of metabolic activity, and this is far more likely to account for the broad range of adverse effects caused by the drug.

Gilbert and associates (2000) found that paroxetine (Paxil®) decreased the thalamic volume in pediatric patients diagnosed with obsessive-compulsive disorder. The authors suggested that the effect is therapeutic, but once again the results are obviously pathological.

Western society is all too willing to turn to drugs, illegal or legal, for the solutions to life's problems. Western science and medicine is too eager to overlook serious and potentially permanent adverse effects of antidepressants or to

justify them as potentially therapeutic. Instead of seeking drug alternatives we need to find individually satisfying approaches to living principled, creative, loving, and courageous lives (Breggin & Breggin, 1994). The choice is not between drugs and psychotherapy, but between drugs and all of the many psychological, social, and spiritual approaches that human beings have available to overcome depression and to live inspired lives.

REFERENCES

- Breggin, P., & Breggin, G. (1994). *Talking back to Prozac*. New York: St. Martin's Press.
- Byck, R. (Ed.). (1974). *Cocaine papers by Sigmund Freud*. New York: New American Library.
- Freo, U., Ori, C., Dam, M., Merico, A., & Pizzolato, G. (2000). Effects of acute and chronic treatment with fluoxetine on regional glucose cerebral metabolism in rats: Implications for clinical therapies. *Brain Research, 854*, 35-41.
- Gilbert, A., Moore, G., Keshavan, M., Paulson, L., Narula, V., Mac Master, P., Stewart, C., & Rosenberg, D. (2000). Decreased thalamic volumes of pediatric patients with obsessive-compulsive disorder who are taking paroxetine. *Archives of General Psychiatry, 57*, 449-456.
- Kalia, M., O'Callaghan, J., Miller, D., & Kramer, M. (2000). Comparative study of fluoxetine, sibutramine, sertraline and dexfenfluramine on the morphology of serotonergic nerve terminals using serotonin immunohistochemistry. *Brain Research, 858*, 92-105.
- Klam, M. (2001, January 21). Experiencing Ecstasy. *New York Times Magazine*, pp. 38 ff.
- Malberg, J., Eisch, A., Nestler, E., & Duman, R. (2000). Chronic antidepressant treatment increases neurogenesis in adult rat hippocampus. *Journal of Neuroscience, 20*, 1-7.
- Norrholm, S., & Ouimet, C. (2000). Chronic fluoxetine administration to juvenile rats prevents age-associated dendritic proliferation in hippocampus. *Brain Research, 883*, 205-215.
- Ricuarte, G., Byran, G., Strauss, L., Seiden, L., & Schuster, C. (1985). Hallucinogenic amphetamine selectively destroys brain serotonin nerve terminals. *Science, 229*, 986-988.
- Wegerer, W. V., Moll, G., Bagli, M., Rothenberger, A., Ruther, E., & Huether, G. (1999). Persistently increased density of serotonin transporters in the frontal cortex of rats treated with fluoxetine during early juvenile life. *Journal of Child and Adolescent Psychopharmacology, 9*, 13-24.

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