Brain Damage from Benzodiazepines: The Troubling Facts, Risks, and History of Minor Tranquilizers

Researchers have long-known that benzodiazepines can cause brain damage

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Last week, Britain's Independent newspaper published a bombshell for psychiatry and medicine: the country's Medical Research Council had sat on warnings voiced 30 years earlier that benzodiazepines such as Valium and Xanax can cause brain damage. As 11.5 million prescriptions for these drugs were issued in 2008 in Britain alone, my post on the revelation focused on the consequences of the cover-up for the millions of people affected.

Given the feedback I received from numerous recovering patients in Britain and the States attesting to their profound difficulties quitting such medication, as well as their continued impairment from the drugs many years later, I want to retrace the drugs' controversial history, to help explain why the suppression of evidence about their side effects is deservedly national news in Britain, and why it should be here in the States, too.

Concern about the adverse effects of this group of drugs dates to the 1970s, when vast numbers of people began taking them for stress and anxiety. Once the most-popular minor tranquilizers in Britain, the U.S., and much of Europe, benzodiazepines ("benzos" for short) include such household names as Valium, Xanax, Librium, Ativan, and Klonopin.

Between 2002 and 2007, the number of U.S. prescriptions for them grew from 69 million to 83 million. Their popularity trailed off in the 1980s and '90s, when Prozac, Zoloft, Paxil and other SSRI antidepressants outsold them as "blockbuster" drugs—so-named because their annual revenues surpassed $1 billion. But benzos actually made a comeback earlier this decade, due in part to the highly successful marketing of Xanax for more than just Panic Disorder.

With SSRIs represented in the 1980s and '90s as well-tolerated and non-addictive, as distinct from the extensive, well-documented side effects of benzodiazepines (including pronounced behavioral abnormalities and a serious risk of addiction), the resurgence of prescriptions for benzos in the early 2000s is not only striking, but a serious concern.

Back in 1975, when benzodiazepines were widely touted as a wonder drug for anything from chronic anxiety to mild stress, 103 million prescriptions were issued for them in the U.S. in that year alone. The following year, David Knott, a physician at the University of Tennessee, voiced strong concern about short-term memory loss among such patients, warning: "I am very convinced that Valium, Librium and other drugs of that class cause damage to the brain. I have seen damage to the cerebral cortex that I believe is due to the use of these drugs, and I am beginning to wonder if the damage is permanent" (qtd. in Whitaker 137).

Two years later in Britain, Malcolm Lader, an expert on benzos at London's Institute of Psychiatry, called them "the opium of the masses" because of Britain's very high prescribing rates, a pattern that correlates with Europe and the States. In Britain, a country with a population now barely exceeding 61 million, a staggering 32 million prescriptions for the drugs were written in the early 1980s.

"We knew from the start," Lader explained on the he 2002 Discovery Channel documentary In Pills We Trust, "that patients taking markedly increased doses could get dependent. But [we] thought only addictive personalities could become dependent and that true addiction was unusual. We got that wrong. What we didn't know, but know now, is that even people taking therapeutic doses can become dependent."

In the States, too, Lader spoke and wrote consistently about his concerns over long-term use of benzos. As Ray Nimmo, editor and owner of www.benzo.org.uk, pointed out to me, author Vernon Coleman noted in his 1990 book Life without Tranquilizers: "At a conference at the National Institute of Health in Washington, USA, in 1982, a British Professor of Psychopharmacology, Malcolm Lader, reported that brain scans done on a small group of patients who had been taking diazepam for a number of years had produced evidence suggesting that their brains had been damaged. Although warning that his preliminary findings needed more research, Lader pointed out that the work he had done suggested that the brains of regular benzodiazepine takers were damaged and shrunken when compared to the brains of people who had not taken benzodiazepines."

Then the controversy truly ignited. In 1989, one of Lader's colleagues, renowned anxiety specialist Isaac Marks, published in the Archives of General Psychiatry a critique of then-recent reports about Xanax and its "efficacy" in treating panic disorder (his quotation marks). Marks, with ten other eminent colleagues from comparable research institutes in France, Germany, England, Spain, Portugal, Brazil, and the States, drew yet more attention to "serious adverse effects" of the drug that only "become apparent later," he asserted—long after most clinical trials had wrapped up. He also wrote of worrying signs of brain atrophy among long-term benzodiazepine users, including "cerebral ventricular enlargement" (Marks 669).

Marks cited, among his references, Lader's 1984 essay in Psychological Medicine, "Computed Axial Brain Tomography in Long-Term Benzodiazepine Users," which stated: "Definite abnormalities were reported by the radiologist in 3 [of 20] patients . . . who had taken benzodiazepines long-term. The abnormalities comprise ventricular enlargement, widening of sulci, Sylvian and interhemispheric fissures" (Lader 205, 203).

Although Lader and two other colleagues added that "the clinical significance of the findings is unclear," they nonetheless observed: "The benzodiazepine users, as a group, had larger ventricle/brain ratios than the controls . . . About half of the patients' scans had positive 'cortical scores' as compared with only a quarter of controls. This is surprising, in view of the relatively young ages of most of our patients" (Lader 205).

In 1983, Robert Whitaker adds in his 2010 book Anatomy of an Epidemic: Magic Bullets, Psychiatric Drugs, and the Astonishing Rise of Mental Illness in America, "the World Health Organization noted a 'striking deterioration in personal care and social interactions' in long-term benzodiazepine users" (138). More recently in 2007, he continues, "French researchers surveyed 4,425 long-term benzodiazepine users and found that 75 percent were 'markedly ill to extremely ill . . . a great majority of the patients had significant symptomatology, in particular major depressive episodes and generalized anxiety disorder, often with marked severity and disability" (Whitaker 137).

Marks's 1989 critique of Xanax focused on two studies that Upjohn Pharmaceuticals (maker of the drug) had funded in the 1980s. Led by Cornell Medical psychiatrist (and later chief of the Federal mental health agency) Gerald Klerman, the studies—also published in the Archives of General Psychiatry—minimized or completely ignored the longer-term side effects that affected more than half the patients involved. The side effects included not only signs of sedation, but also ataxia [uncoordinated movement, owing to neurological dysfunction], and fatigue. Marks conceded, "The cerebral ventricular

enlargement reported in patients with anxiety/panic disorders who were long-term benzodiazepine users could be due to the disorder or to other factors rather than to the drugs, but wisdom advises caution" (Marks 669).

When I interviewed Marks in November 2005 for my book Shyness: How Normal Behavior Became a Sickness, on the creation of social phobia/anxiety disorder and the way that Paxil was marketed as its best pharmaceutical remedy, he told me about a Boston-based conference that Upjohn also had funded on Panic Disorder. At the conference, Upjohn's CEO got up and literally declared, in his opening remarks: "Look, there are three reasons why Upjohn is here taking an interest in these new diagnoses. The first is money. The second is money. And the third is money." "They were quite upfront about it," Marks marveled to me, "and they were exceedingly successful at it for the first six years" (qtd. Shyness 74).

Marks' and Klerman's dispute in Archives of General Psychiatry soon moved to and escalated in the pages of the British Journal of Psychiatry. Indeed, it became something of a transatlantic showdown, with Marks strongly implying, in the words of commentator David Healy, that "any apparent efficacy of alprazolam [Xanax] resulted more from statistical manipulation on the part of Klerman and colleagues than from a genuine efficacy of alprazolam" (Healy 196). Healy adds that Marks put some of the ensuing "hostility" down "to the fact that, by 1990, a growing number of American psychiatrists were only reimbursed for treatment if that treatment involved prescribing" (197).

Still, a sharp uptick in reported problems from Xanax and other benzos in several countries finally obliged the American Psychiatric Association Task Force in 1990 to produce a table listing withdrawal symptoms from the drugs in three separate categories: "Very Frequent, Common but Less Frequent, and Uncommon." "Very Frequent withdrawal symptoms included ‘anxiety,' ‘agitation,' and ‘irritability,' notes Peter Breggin; "Common but Less Frequent withdrawal reactions included ‘depression' and Uncommon withdrawal reactions included ‘psychosis,' ‘confusion,' ‘paranoid delusions,' and ‘hallucinations.' Noteworthy," he continues, "are the large numbers of citations used to confirm the findings listed in the table. The task force also confirmed that these withdrawal symptoms "may persist up to several weeks (occasionally for months)."

In the early 1990s, too, Upjohn finally admitted: “Certain adverse clinical events, some life-threatening, are a direct consequence of physical dependence to Xanax. These include a spectrum of withdrawal symptoms; the most important is seizure . . . studies of patients with panic disorder showed a higher rate of rebound and withdrawal symptoms with Xanax.... Other symptoms, such as anxiety and insomnia, were frequently reported during discontinuation."

"The ability of patients to completely discontinue therapy with Xanax after long-term therapy has not been reliably determined," the drug maker continued. “Withdrawal reactions may occur when dosage reduction occurs for any reason . . . withdrawal symptoms including seizures have been reported after only brief therapy with Xanax at doses within the recommended range for the treatment of anxiety. . . . Death has been reported in association with overdoses in association with overdoses of alprazolam by itself."

Where does that leave us, roughly a decade later? From Australia to Nepal and Britain to the United States, benzos are recognized as fueling powerful cravings among drug addicts. That's less surprising, perhaps, when one hears that Professor Lader declared, in a 1999 interview on BBC Radio 4, "It is more difficult to withdraw people from benzodiazepines than it is from heroin. It just seems that the dependency is so ingrained and the withdrawal symptoms you get are so intolerable that people have a great deal of problem coming off. The other aspect is that with heroin, usually the withdrawal is over within a week or so. With benzodiazepines, a proportion of patients go on to long term withdrawal and they have very unpleasant symptoms for month after month, and I get letters from people saying you can go on for two years or more. Some of the tranquillizer groups can document people who still have symptoms ten years after stopping."

According to Britain's All-Party Parliamentary Group for Involuntary Tranquilliser Addiction, which has strong support among politicians, prescribing statistics in the UK point to "the estimate of 1.5 million involuntary addicts" to the drugs in that country alone, given that in 2008 "11.5 million prescriptions for benzodiazepines" were written in Britain, and roughly ten percent of benzo users become addicted to the drugs.

Given this troubling, well-documented history, responsibility dictates that I end on a strong note of caution. Patients who are concerned about the drugs' adverse effects should NOT terminate their treatment abruptly, but should instead taper their dose carefully and very gradually, over a course of several months, to ensure their own safety. Professor Heather Ashton, a British psychiatrist who runs a renowned clinic on benzo withdrawal, supplies important safety information about recommended tapering here.

In light of this medical nightmare afflicting so many patients in so many countries, the fact that the British Medical Research Council, the nation's funders of medical research, sat on key information attesting to the drugs' risks thirty years ago is not just unethical, but nothing short of scandalous.

Important Update Since Publication:
Nina Lakhani, "Check on Benzodiazepine-Use Must Be Done, Say MPs.” *The Independent (December 5, 2010).*

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