Rat Addicts

When I returned to Argonne in 1971, after my year in Atlanta, my personal research program had been pretty much on hold for all that year. I had traveled back from Morehouse several times during my time there, but those trips were primarily to fulfill a responsibility for supervising the research of a graduate student who was doing his work in my lab. This student, however, was doing his thesis research in a system that was totally unrelated to my own research interests. He was working in my laboratory because he wanted to apply some of the techniques of molecular biology to his system—the milkweed bug—and those techniques were not available in his department at the St. Louis University. Such collaborations with nearby universities were not uncommon at Argonne in those days.

During my visiting professorship at Morehouse, I was finishing up my six-year-long Argonne collaboration with embryologist Denny Smith, who had left the lab the year before I left for Atlanta. Our final research paper together was written that year. So, when I came back after that year, I was faced with some decisions concerning the direction I wanted my research to take for the future. In addition, the research environment at Argonne was beginning to change. When I arrived there in 1964, I could choose, within my field, whatever direction I wanted my research to pursue. Now, the scientific staff was beginning to be subdivided into more specified research programs. I was still able to continue some of the work Denny and I had been doing together, but I felt some pressure to look into other areas that might better fit in with the direction the laboratory was beginning to follow.

So, motivated by my experience with the Hippies in Atlanta, I decided to do some preliminary experiments on the physiology of drug addiction, to see if perhaps there might be some socially significant possibilities there. This will be the only published account of those experiments, which were interesting but never proceeded far enough to get beyond "interesting." I left the lab while they were still preliminary.

Obviously, it was not possible to do on human subjects the kinds of experiments I was proposing, so I elected to do them with rats. If you wanted to do animal experiments, Argonne was the ideal place to do them. Facilities and staffing there for maintaining research animals were almost unparalleled. A few laboratory rats were an easy addition to the population in the facility.

No credible investigator undertakes a new project without at least a faint idea of what kind of end result is hoped for. In my case, I was hoping to be able to show specific differences between addicted and non-addicted individuals in how the body deals with the drug—physiologically and anatomically. First, however, I had to see if I could make rats into addicts. This was not as simple as it might seem. The difficulty comes from the definition of "addiction." An addict is not simply an individual that is "hooked" (physiologically dependent) on the drug. That individual has to stay hooked—by personal choice. Then and only then is he/she an addict.

Withdrawal from physiological dependence on an addictive drug is associated with a multitude of unpleasant physical symptoms. It is those symptoms that drive the addict to continue use of the drug—once he/she becomes aware that the drug will eliminate those symptoms. There have been many recorded cases in which individuals had become physiologically dependent on morphine after long-term use in the medical treatment of chronic pain and yet never became addicts—simply because they never became aware that the other disagreeable symptoms they experienced when their pain went away was due to the withdrawal

of the drug. So how do you get a rat to choose to become an addict? Let's look in on the experiment and see.

The drug I chose was morphine. It was conveniently available from the veterinarians in our animal-care facility, and it's an opiate drug; a close chemical relative of heroin, which was a common street drug at the time.

Rats become physiologically dependent on morphine pretty much the same way that humans do but, obviously, the drug is not self-administered to begin with. I started off by injecting regular small doses of the drug into each of the rats, subcutaneously in the abdomen. Over a period of several weeks, the dosages were increased until it was apparent that the rats had become tolerant of a significant dose and that this dose produced evidence that the rats were "feeling no pain"—experiencing a drug-induced "high." After a week or so at that dose, they were ready for their own part in becoming addicts, because no one—human or rat—becomes an addict except by choice.

So how do you influence a rat to choose to be an addict? Actually, it's pretty straight forward. First, you stop injecting the drug and take away its water supply for two or three days. Then you restore its water, but with a maintenance dose of morphine dissolved in it. The morphine gives it a very bitter taste, but the rat drinks because it is thirsty. It is not only thirsty, but is experiencing the unpleasant symptoms of withdrawal. The morphine in the water relieves those symptoms. It has now had its first lesson in relating the bitter water with the relief of withdrawal symptoms. When that lesson has been reinforced with a repeat of the procedure, the rat is usually hooked…addicted. Then you can put two water bottles in its cage—one with pure water and the other containing morphine-water and it will choose to remain an addict by drinking just enough of the bitter water to maintain its habit.

We could then measure the amount of morphine-water that was used each day and calculate how much of the drug each rat required to remain addicted. I don't have any of the details of these results because my research notes had to stay at Argonne when I left. As I recall, most of them maintained their habit with similar amounts of daily morphine intake. There was, however, one conspicuous exception to this trend. One morning I walked into my animal room and discovered one totally spaced out rat, so bloated with water that her feet could barely touch to bottom of the cage…and her morphine water bottle was completely empty. She was still alive but she gave new meaning to the term "overdose."

Now, I had a bunch of addicted rats, and I had learned a lot, but that was just the first step in what I anticipated was going to be a lengthy research endeavor. In fact, rats addicted to morphine were not going to do me any good, because I ultimately needed to use a drug that could be labeled with a radioactive element—and that was not possible with morphine, at least not at that time. However, morphine was inexpensive and easily available, so it was ideal for the preliminary experiments in which we needed to learn how to get rats addicted. The next step was to repeat these preliminaries using methadone—a related, synthetic drug—which could be radioactively labeled. Regrettably, those experiments never came to pass, because of other obligations and, ultimately, my departure from Argonne and a career change away from laboratory research.

I have never regretted those months developing the methods for producing addicted rats. In later years, when I became involved in helping individuals learn how to interpret self-destructive behavior, those experiments proved to be a great way to teach people about the key role of personal choice in the making and maintaining of addiction.