# A Junkie Model for Parkinson's Disease

The misfortune of a 23-year-old junkie has provided new hope for sufferers of Parkinson's disease, a brain disorder that causes uncontrollable tremors and interferes with voluntary muscular movements. Through a careless error in his basement laboratory, a long-time drug user stumbled upon a compound that in effect creates parkinsonism, and government scientists have now used that chemical to develop an animal model to study the causes and treatment of the disorder. The accompanying bad news, the researchers say, is that there may be an epidemic of Parkinson's disease in the making, as more and more basement chemists get a head start in developing the shaking palsy.

The recent discovery actually had its origins in 1977, when a man was admitted to the clinic of the National Institute of Mental Health in Bethesda, Md.; rigid and unable to swallow, he was diagnosed as a catatonic schizophrenic and treated with anti-psychotic drugs and electroshock — unsuccessfully. When he was finally treated with levodopa (a standard treatment for parkinsonism), he improved dramatically.

According to Irwin J. Kopin, an NIMH neuroscientist involved in the case, the patient had a nine-year history of drug abuse — particularly opiate abuse — and, having recently studied organic chemistry in college, he had begun manufacturing his own drugs — in particular a drug similar to but 40 times as active as Demerol. After taking this drug for several months, however, he began taking shortcuts in synthesizing the compound, and as a result he was producing drugs that were slight variants of the synthetic opiate. After using a sloppy batch for four to five days, he developed the symptoms of Parkinson's disease, which persisted for three months before his arrival at NIMH.

According to Kopin, the man was treated successfully with the anti-Parkinson drugs L-dopa and then bromocriptine (he abused the L-dopa) for 18 months, but whenever the treatment was discontinued the symptoms of parkinsonism reappeared. The man finally killed himself, and an autopsy revealed cell death in the brain's substantia nigra, a major dopamine pathway that is damaged in naturally occurring Parkinson's disease.

Kopin and his colleagues described the case in PSYCHIATRY RESEARCH in 1979, which is where it would have ended had it not been for a recent incident in northern California. Six heroin addicts were hospitalized with severe parkinsonism, which a team of Stanford University scientists traced to a batch of China White heroin that had been sold on the streets during the summer of 1982. As reported in the Feb. 25 SCIENCE, these patients also responded well to L-dopa treatment and, as with the Maryland case, there appears to be no sign of remission six months after the symptoms appeared.

Photos: NIMH

*Monkey with induced Parkinson's disease is hunched over and rigid prior to receiving L-dopa treatment (left). After receiving L-dopa, the monkey straightens and moves normally about the cage in a laboratory at the National Institute of Mental Health.*

When narcotics agents finally traced the heroin to a home laboratory in the Bay Area, they found a drug called MPTP, a toxic by-product of MPPP, a synthetic opiate. The California scientists, aware of the NIMH case report, sent the drug to NIMH chemist Sanford P. Markey, who confirmed that it was the same drug the original patient had inadvertently manufactured. The NIMH scientists immediately began using the compound in animal experiments and this week announced that they had succeeded in creating a model of Parkinson's disease in monkeys.

According to Richard Burns, another of the government scientists, the parkinsonian monkeys (who have received a single dose of MPTP) show the muscular rigidity and palsy typical of human parkinsonism; they have brain lesions precisely where they would be expected; and they respond dramatically to L-dopa. Parkinson's disease is caused at least in part by destruction of dopamine-producing cells in the substantia nigra, which depletes the supply of that neurotransmitter; but the human disorder is related to changes in other neurotransmitter systems as well, so the monkey model will allow scientists to isolate the symptoms of parkinsonism that are related specifically to dopamine deficiency. (Burns asks that anyone suspecting they may have taken MPPP contact him at 301-496-1891.)

Scientists will also be able to use the new model to study the so-called "on-off reaction," which confounds the treatment of parkinsonism. For unclear reasons, patients treated with L-dopa for a long time tend to become very sensitive to its effects; they go through wide swings in their ability to control movement, from complete rigidity at one extreme to involuntary movements on the other. If this phenomenon can be created in the monkeys, Kopin says, it may be possible to see what is going on in the brain and ultimately to design more precise treatments. The NIMH team is already using radioactively labeled MPTP to observe the drug's course of action in the brain.

One characteristic of the drug's action is of particular concern: a single dose appears to cause irreversible brain damage, and although the deterioration continues even after the drug is discontinued, the outward symptoms of the brain damage are delayed in their appearance. The practical effect of this is that, 20 years from now, there may be an epidemic of parkinsonism among drug users — and presumably even former drug users. Dopamine depletion occurs naturally with aging, Kopin says, and Parkinson's disease is generally seen in the elderly. "There are probably a lot of people out there who have taken a single dose of the drug and have not developed the disease," Kopin told SCIENCE NEWS. "But they have a head start."

*—W. Herbert*