

Deneau G, Yanagita T & Seevers M H. Self-administration of psychoactive substances by the monkey: a measure of psychological dependence. *Psychopharmacologia* 16:30-48, 1969.

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A method has been developed that permits monkeys to self-administer drug solutions, at will, through indwelling intravenous catheters. Monkeys developed psychological dependence on morphine, codeine, cocaine, d-amphetamine, pentobarbital, ethanol, and caffeine. [The *SC1*® indicates that this paper has been cited in over 425 publications.]

## Addiction in the Monkey

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Studies of drug abuse in the monkey were begun by M.H. Seevers and Tatum at the Universities of Chicago and Wisconsin in the 1930s.<sup>1</sup> They were primarily interested in the physiological phenomena of tolerance and physical dependence. At the same time, the National Research Council sponsored a collaborative effort to find a nonaddicting morphine derivative. These latter studies were conducted at the Universities of Virginia and Michigan and at the United States Public Health Service Hospital in Lexington, Kentucky. Both efforts were largely curtailed during World War II, but after the war, with the advent of methadone and meperidine, industrial laboratories began to produce many derivatives of these synthetics in the hope of finding a safer analgesic. Seevers, by then at Michigan, began to refine techniques in the monkey to determine if that species could be reliably used for preclinical studies of addictiveness to analgesics. The rhesus

monkey did prove to be suitable for studies of physical dependence to morphine-like analgesics. The question then arose as to whether the monkey would be useful for studying the psychological dependence capacity (reinforcing property) of all classes of drugs of abuse.

With the support of the Psychopharmacology Service Center, studies were begun to see if the monkey would spontaneously abuse the same drugs that people abuse. Weeks's procedure of indwelling catheterization for cardiovascular studies was adapted to the monkey. Fortunately, we had skilled shop people who helped us develop harnesses and pumps, and T. Yanagita, a postdoctoral fellow with electronic talents, developed the control circuitry.

We studied the spontaneous drug-seeking behavior of naive monkeys with each of the major classes of addicting drugs. With the exception of the hallucinogens, which did not appear to be reinforcing, chronic morphinism, cocaineism, alcoholism, and so on, in the monkey closely resembled the human condition. It was apparent that the reinforcing properties of addicting drugs could be studied in laboratory animal procedures. Others have since modified these procedures to the point that reinforcing capacity can be determined in a single day.<sup>2</sup>

It seemed that an endless series of minor technical problems had to be endured and resolved, but the excitement generated by the data produced an incomparable enthusiasm in each of us connected with the study.

[Editor's note: R.R. Griffiths and P.P. Woodson have recently reviewed<sup>3</sup> human and laboratory animal studies of caffeine-dependence, including the *Classic* paper.]

1. Seevers M H. Animal experimentation in studying addiction to the newer synthetic analgesics. *Ann. NY Acad. Sci.* 51:98-107, 1948. (Cited 5 times.)
2. Woods J H. Narcotic reinforced responding: a rapid evaluation procedure. *Drug Alcohol Dependence* 8:223-30, 1980. (Cited 15 times.)
3. Griffiths R R & Woodson P P. Caffeine physical dependence—a review of human and laboratory animal studies. *Psychopharmacology* 94:437-51, 1988.