What you can learn from drunk monkeys

A remarkable NIH study says you're just as likely to become an alcoholic from a bad childhood as from bad genes

Being alone is not normal for rhesus monkeys, and being a loner means a monkey will most likely have a taste for alcohol. Likewise, innate sociability is key to understanding chronic alcoholism among humans, argues NIH researcher Dee Higley: "People become alcoholics not because they feel bad but because they have social problems."

BY MEREDITH F. SMALL

I AM STANDING IN AN ANIMAL RESEARCH lab dressed entirely in blue paper—paper shower cap, paper shirt and pants, even blue paper shoes. My face is covered with a plastic shield, and my hands are gloved. This getup is required because I am holding a newborn rhesus monkey, a tiny ball of fur with button-brown eyes and hair that sticks straight up off the top of its head. The baby wiggles around in my hands, grabs my thumbs, and makes "coo-coo" noises that are heartbreakingly endearing. I look into his eyes and think that this little guy might just be the cutest thing I've ever seen. Harder to deal with is the reality that this research monkey may become a chronic alcoholic. Even more disturbing is the idea that his future alcoholism is not rooted in bad genes alone. Instead, a contrived unhappy childhood could push him toward the bottle.

For the past 15 years, a National Institutes of Health research team led by psychologist Dee Higley has been raising rhesus monkeys to develop an animal model for chronic alcoholism. Higley has discovered that although genes matter when it comes to the risk of alcoholism, attachment to a mother and a normal early social life also have a major impact. When monkeys are removed from their mothers at birth and never allowed to bond with a parent, when they have to rely on peers rather than mom for social lessons, they often end up social zeros with a taste for booze. And if they have a genetic history that makes them vulnerable to alcohol abuse, a bad childhood will be just enough to tip the balance and turn them into chronic alcohol abusers.

The complex influences of genes and experience on alcohol consumption in monkeys places Higley smack in the middle of the debate about the etiology of human alcoholism. Is alcoholism a disease, an illness beyond our control, as we have been led to believe? Or is it a product of society, of upbringing, something we might be able to change?

ALCOHOL IS THE MOST WIDELY used and accepted psychoactive drug in the world. Alcohol abuse is devastating to individual health, and it casts a wide net of pain across families and society. The National Council on Alcoholism and Drug Dependence claims that more than 13 million American adults are alcoholics, and another 76 million have been affected by an alcoholic in the family. Drinking is also implicated in many crimes, including assault, rape, and homicide. In all, alcohol contributes to an estimated 100,000 deaths annually.

Two-thirds of the population drink, but half of all booze is consumed by only 10 percent of the people in this country. Clearly, some drinkers are prone to alcohol abuse, while others can party occasionally with restraint. So why is it that some people just can't stay on this side of the buzz?

Until Victorian times alcoholism was considered a moral issue—only the weak-willed succumbed. But when physicians introduced the idea that excess alcohol consumption might be a sickness, the disease model for alcoholism became fashionable. There was hope in this diagnosis: If alcoholism is a disease, there must be a treatment and a possible cure. The disease model led to the establishment in 1935 of Alcoholics Anonymous,

an organization founded largely on the premise that alcoholism is a progressive, biologically based illness.

Today most people believe that abusive drinking is a physical or mental condition that is biologically predestined. Based on twin and adoption studies, there indeed appears to be some genetic influence on the pattern of alcoholism. In a study published in 1998, Marc Schuckit of the University of California at San Diego found that 40 percent of college-age children of alcoholics have a low reaction to alcohol, compared with only 10 percent of the children of nonalcoholics. Presumably, the low reaction says something about the biology of these individuals, a biology they inherited from their parents. More tellingly, follow-up studies revealed that those with a low reaction were more likely to become alcoholics by age 35.

Monkeys growing up without parents around tend to consume enormous amounts of alcohol

Research also indicates there is a relationship between alcoholism and genetic deficiencies in the opioid and dopamine receptors in the brain. Kenneth Blum of the University of Texas Health Science Center and Ernest Noble of the University of California at Los Angeles reported in the 1990s that they had discovered a form of the gene for a dopamine receptor that could derail the normal pleasure pathway and push people to become addicted to alcohol, cigarettes, or food.

But not all children who grow up with the suspected genes for drinking do so, and sometimes someone with no family history of alcoholism suddenly becomes a drunk. Clearly, genes alone don't explain why some people are more at risk than others. Now some researchers have begun to suspect that alcoholism lies in social and psychological influences that mold a personality already susceptible to mind-altering substances.

DEE HIGLEY AND I ARE STROLLING by a row of outdoor cages at the National Institutes of Health Animal Care Center in Poolesville, Maryland. Higley, 48, a tall man with a buzz cut and a warm smile, looks like an academic version of Gene Hackman on a good day. In front of each cage, he asks me, "Who do you think are the chronic drinkers?" Even with 20 or so adult rhesus monkeys per cage, it's easy to see which animals have been imbibing that day. Just like the regulars at a local bar, some animals are draped across each other or lounging about alone, too blitzed to groom themselves or run about like the teetotalers. Some monkeys hungrily suck a red or green liquid that flows from a contraption on the side of the cage. Higley says both liquids are laced with an artificial sweetener, but only one is 8.5 percent alcohol. The alcohol is available five days a week for an hour a day. I'm looking at the end of happy hour.

Based on the consumption patterns of 300 animals, Higley has found that monkeys soon establish a routine. Some regularly abstain, some imbibe occasionally, and 10 to 20 percent of the animals consume at a rate that matches human alcoholism. Higley has come to the startling conclusion that how the monkeys are treated as infants can predict which will be at risk.

At the Animal Care Center, some newborn monkeys are removed from their mothers and hand reared for a month. The youngsters are then placed in a larger cage with little ones their age to form a peer group. Other babies born at the same time are allowed to stay with mom for seven months and then put with peers; they provide the normal controls for the study. At 4 years of age, the beginning of adulthood for rhesus monkeys, they're all offered a drink. "Those that grow up without parents around just consume enormous amounts of alcohol—about double what the mother-reared monkeys do," says Higley. "And they are more likely to get intoxicated on a daily basis. They also show a number of other kinds of behaviors that are characteristic of human alcoholics." In other words, they not only drink like alcoholics, they act like alcoholics.

In 1987 psychiatrist Robert Cloninger theorized that alcoholism could be traced to two different personality types that correspond to specific drinking patterns. Type I alcoholics, Cloninger suggested, are people emotionally dependent on others and afraid of risk. They typically start drinking in adulthood as social drinkers and end up addicted; drinking for them is a sedative against anxiety. In contrast, type II alcoholics begin drinking early and hard in their adolescence, seeking out alcohol as they seek out other risky situations. Unlike type I alcoholics, their drinking is not about curbing anxiety but a desire for the euphoria of a high combined with an inability to stop once they start. Type IIs typically have little impulse control. And type IIs are almost exclusively male.

Higley has found the same distinctive types of drinkers in monkey groups. Some monkeys are constantly anxious and love to drink, like human type I alcoholics. Others echo the human type II alcoholics—they are anxious, yet they like to take risks, have little impulse control, and are aggressive and antisocial. One big difference between the monkey type IIs and their human counterparts is that female rhesus monkeys are just as likely as males to be impulsive risk takers who turn to the bottle.

"I suspect culture produces the [gender] difference in humans," Higley says. "Women growing up in human society are told that drinking a lot is something that you shouldn't do." But female monkeys are free to be impulsive and drink as much as they want without being admonished to act like ladies.

Higley has also found that impulsive behavior and drinking have an enduring biological basis. Although there are probably many neurotransmitters responsible for appreciating alcohol, serotonin seems to be especially predictive in monkeys. In humans, a low level of serotonin activity is implicated in depression, obsessive-compulsive disorders, eating disorders, and suicide. "Serotonin is, in a sense, the brakes of the brain," Higley points out. "It regulates what we do with our emotions, what we do with our motivations, what we do with our behavior." Without decent serotonin activity, we lose control of our impulses.

Back at Higley's office, our paper clothes shed, Higley rocks back in his chair and offers a twist on the old joke

about two guys in a bar: "Two guys walk into a bar, one with high serotonin and one with low serotonin. They start drinking, and then in comes another guy who is aggressive and drunk. He rudely grabs a pretty girl they've been talking with. The high-serotonin male decides to walk away. The low-serotonin guy plows right in, and before long he's in the middle of a fight. The difference is in the braking, the stopping."

For the monkeys in Higley's lab, serotonin seems to have the same influence. Those with low levels of a spinal-fluid marker for serotonin activity called 5-hydroxyindoleacetic acid, or 5-HIAA, are the ones with little impulse control and the urge to drink and drink. Higley has also found the same serotonin-impulse control relationship in groups of free-ranging rhesus monkeys living on an island off the coast of South Carolina. Along with primatologist Patrick Mehlman, Higley discovered that male monkeys with lots of fight scars had low serotonin function. Over a three-year period, these males turned out to be the guys who not only started fights but also readily jumped into everyone else's conflicts, and they typically were the ones involved in fights that escalated out of control.

"When monkeys raised without their mothers reach adolescence, they are happy to drink from a bottle that is laced with a winelike solution," Dee Higley says. Some monkeys will drink until they pass out.

Like the low-serotonin males in Higley's lab, the scarred males on the island appear to be social losers. They migrated to new groups much sooner than other males and spent most of their time alone. And they also ended up dead more often. Eleven migrating males died during Higley and Mehlman's study, and 10 of those 11 came from the low-serotonin group.

The free-ranging monkeys were never exposed to alcohol, but Higley is confident that given the chance, the low-serotonin males would become classic type II alcoholics. "There is a certain impulsive quality about them," he says. "They leap from branch to branch rather than proceeding with caution, they threaten those higher in rank, with no chance of winning. They don't look at the consequences of their behavior."

The best childhood in the world won't necessarily make up for low serotonin activity

And the researchers can follow this pattern linking low serotonin and impulsive behavior over generations. "In the lab, we have a rhesus named Devil Monkey. He and his offspring tend to get in more fights, be loners in their social groups, and consume more alcohol," Higley says. Devil Monkey runs his group like a dictator and has a long history of aggression toward others. He has the lowest serotonin levels Higley has ever seen, and his offspring also have low levels.

In contrast, the members of a family headed by a congenial monkey named Redford are quite different. "All his offspring seem to be invulnerable to early negative experiences. Despite their social groups, they aren't anxious and don't get in many fights," says Higley. Members of the Redford clan tend to have normal or high levels of serotonin, and they don't drink as much.

But Higley's observations of monkeys in the lab also suggest that decent parenting can prevent some monkeys born with low levels of serotonin from being pushed toward alcohol. The key seems to be an early attachment to mom. "From attentive mothers, little monkeys get 'wait' signals, and they get discipline," says Higley. "Peer-reared monkeys don't get those stop signals; when peer groups have conflict, it's resolved by brute force. There are no mothers to regulate negotiation, so these monkeys don't know how to resolve social problems." Many of the peer-raised monkeys grow up to be drinkers.

Still, neither genes nor environment make the outcome certain. The best childhood in the world won't necessarily make up for a genetic blueprint for low serotonin activity and a history of family alcoholism. And some monkeys with the genes for adequate serotonin activity might be buffered against an abnormal childhood, but that buffer goes only so far. When a less-vulnerable, mother-raised monkey is uprooted and left alone in a cage for several days, shaking her monkey world to the core, she's much more likely to drink until she has returned to the group.

JUST LIKE HUMANS, THE MONKEYS in Higley's study are set up by their genes and then rocked by experience. All the biological influences are presumably inherited, but so far no one can point to specific genes, or a single biological process, that accurately predicts alcoholism. In fact, most researchers who believe in the disease model say that genes can explain only half the risk. If half of the vulnerability is due to family upbringing and life experience, can chronic alcoholism really be called a disease?

Psychologist Stanton Peele suggests that we may have carried that model too far. At his Web site, and in various articles and books, Peele argues that no one has conclusively shown that there is a biological basis to alcoholism or any other addiction. Instead, Peele believes that personal and social expectations torque biological tendencies to such a degree that any study seeking to identify genetic underpinnings is suspect.

Look at what people do, he suggests. Not everyone who is anxious or impulsive is a problem drinker, and many people who are hard-core alcoholics stop drinking without treatment. There is data to back up that view. In 1992 the National Institute on Alcohol Abuse and Alcoholism interviewed 4,542 adults who at some time in their lives had been alcohol dependent according to diagnostic criteria used by the American Psychiatric Association. At the time of the study, 28 percent were still heavy drinkers, but 22 percent had given up alcohol and 50 percent drank in moderation. Therefore, roughly three-quarters of these people would no longer be considered alcoholics. Interestingly, those who

were treated for alcohol abuse didn't fare any better on average than those who had no treatment.

"Natural remission is overwhelming in its importance," Peele says. "And yet it is systematically ignored by researchers." If alcoholism is a disease, how can so many people cure themselves?

Peele also points to the low rate of alcoholism and alcohol-related problems among Asians. Normally, alcohol is broken down by the enzyme alcohol dehydrogenase (ADH), which in turn produces acetaldehyde, a toxic compound that can cause high blood pressure, skin flushing, and vomiting. Most people get rid of acetaldehyde with another enzyme called aldehyde hydrogenase (ALDH2). But about 10 percent of Asians have a genetic variant of this enzyme that is inactive; as a result, they feel sick when they drink and rarely become alcoholics. Another 40 percent of the Asian population is heterozygous for this genetic variant; members of this group feel the high from alcohol faster than those with the more common form of the enzyme and tend to drink less.

Researchers have assumed that biology alone is at work here, but Peele wonders about those Asians who have the normal enzyme but also choose to drink in moderation or not at all. And he wonders why people would avoid alcohol just because it takes smaller quantities for them to feel the effects. Being biologically sensitive to alcohol has certainly not prevented other ethnic groups, such as Native Americans, from having alcohol problems.

Peele suggests that the difference may be cultural values, not biology. When cultures disdain drunkenness, those sanctions alone may be the more powerful preventative factor. "The [biological] theories can't make sense of the most obvious aspect of human addiction and self abuse—natural remission and value choices," he says. "Nonetheless, the researchers pursue them madly."

HIGLEY, OF COURSE, IS KEENLY aware of the social context of alcohol abuse. "You don't wake up with a set of genes as a new infant and end up an alcoholic," he says. "It's the interaction with the environment that's going to determine what you become."

Higley also speaks from personal experience, because alcoholism has touched his family. "My grandfather died of alcoholism," he says. "He literally froze to death in the snow in an alcoholic stupor. He died before I was even born, but there's no question that it had a tremendous impact on the family."

Watching monkeys, as well as charting his own relationship with alcohol, has convinced Higley of the curative power of family. He offers a simple explanation for why his genes did not push him down a path of alcohol abuse: "I grew up in Utah," he says, laughing. "I know nothing about alcohol. I'm a Mormon."

From *Discover,* July 2002, pp. 41-44. © 2002 by Meredith F. Small. Reprinted by permission of the author.