

Alcoholism and Addictive Behavior

Alcohol use in the United States is exceedingly common, yet half of all the alcohol drunk is consumed by only 10% of the population.⁹³ This in itself implies that some individuals drink too much. Yet consuming "too much" alcohol does not make one an alcoholic, and there is great variation from place to place, and from one era to another, in what is considered acceptable. To further complicate the picture, alcohol consumption varies between the sexes, between socioeconomic strata, and between occupations. Consequently, it is very difficult to determine what is "normal" for alcohol consumption. Yet it is often rather easy to identify someone who exceeds that normal level of consumption.

The American Psychiatric Association defines alcoholism as being of two types. The less damaging type is alcohol abuse, which is a psychological dependence on alcohol. An alcohol abuser is psychologically dependent on alcohol, he may indulge in occasional heavy alcohol consumption, and he continues to drink despite mounting evidence of occupational or social problems. The more damaging type of alcoholism is alcohol dependence, which is both physical and psychological dependence on alcohol. An alcohol-dependent person shows all of the signs of alcohol abuse, together with signs of increased alcohol tolerance and physical symptoms on withdrawal from alcohol. It has been estimated that between 10 and 31% of men in the United States are alcoholic, so prevalence of the disease is quite high.¹⁰

Virtually everyone has firsthand knowledge of alcoholism, either as the relative or close friend of an alcoholic, or as one

who suffers from the disease. It will come as no surprise to most that alcoholism is familial, and that a tendency to alcoholism severely affects some families. But whether such a family history is caused by shared genes or shared environment has been a contentious issue for a long time.

The idea that drug addiction is similar to alcoholism, and that addictive behavior in general may be hereditary, is more controversial than the idea that alcoholism is hereditary, in part because we know so much less about drug addiction. But alcoholism and drug addiction have much in common, and both types of addictive behavior can be devastating. Alcohol is believed to have been the underlying cause of death for as many as 100,000 people in the United States in 1990 alone.⁹⁴ This number is so large because alcohol is thought to contribute to 40–50% of all motor vehicle fatalities, 16–67% of all accidental deaths in the home and workplace, 60–90% of all deaths from cirrhosis of the liver, and 3–5% of all cancer deaths. By contrast, illicit drugs of all kinds, including crack and heroin, even when combined with drug-related accidental deaths, were responsible for about 20,000 deaths in the same year. Thus, from a national perspective, alcoholism is a far more serious problem than is drug abuse, since alcohol causes five times as many deaths.

Split Twin Studies of Alcoholism

The children of alcoholic parents are about five times more likely than normal to become alcoholic themselves.¹⁰ But this does not prove that alcoholism is hereditary, because children of alcoholic parents may have been brought up in an environment that encourages alcoholism. As we have seen so often before, the most reliable first approximation of the heritability of alcoholism is obtained by studying twins split at birth and raised in different environments. This was done recently, using the records of several large alcohol abuse treatment centers in Minnesota. A search through the medical records identified 599 patients who had received treatment for alcohol abuse and who

reported having a sibling of the same age. Both siblings were contacted, to determine whether they were twins and to recruit them to the study if possible. Twins were eliminated from the study if both could not be contacted, or if both were not of the same sex, since males and females may not have the same risk of alcoholism. An exhaustive effort enrolled a total of 169 same-sex twin pairs, of whom roughly half were identical, half fraternal. There were more than twice as many male twins than female twins, which is consistent with the higher incidence of alcoholism among men. But there were still a fair number of female twins enrolled, making it possible to determine whether men and women indeed do differ in their risk of alcoholism.

It was found that identical twins were at a higher risk of concordance for alcoholism than were fraternal twins, which clearly shows a role for genes.¹⁰ However, the difference between identical and fraternal twins was fairly small, suggesting a rather weak role for genes in the genesis of alcoholism. For males, identical twin concordance was 76%, while fraternal twin concordance was 61%. A computer analysis of these concordances concluded that alcoholism is only 36% heritable for men. For females, identical twin concordance was 36%, while fraternal twin concordance was 25%, implying that heritability for women is only 26%. These conclusions are consistent with the impression that alcoholism risk is greater for men than women, but the overall risk of alcoholism related to genes alone is surprisingly small.

Interestingly, it was found that, for both men and women, alcohol dependence is substantially more heritable than alcohol abuse (Table 1). From a psychiatric standpoint, alcohol dependence and alcohol abuse are easily separated from one another. Dependence tends to develop quickly in certain teenagers and young adults, whereas abuse develops slowly in middle-aged and older people. Dependent alcoholics often describe becoming dependent very soon after their first drink, whereas alcohol abusers typically were able to drink socially for many years before problems developed. Alcohol-dependent people show alcohol-seeking behavior and often have an antisocial personality type, whereas alcohol abusers tend to be anxious, especially

Table 1
Characteristics of the Two Types of Alcoholism^a

Characteristic features	Type of alcoholism	
	Abuse	Dependence
Age at onset	>25 years	< 25 years
Ability to abstain for extended periods	Common	Rare
Social drinking to overcome anxiety	Common	Rare
Guilt and fear about alcohol dependence	Common	Rare
Fighting and arrests while drunk	Rare	Common
Alcohol-related job problems	Rare	Common
Multiple drinking binges	Rare	Common
Alcohol needed to maintain function	Rare	Common
Probable cause of alcoholism	Loss of control	Alcohol-seeking
Basic personality type	Anxious	Antisocial
Heritability		
For men	38%	60%
For women	0%	42%

^aAdapted from several studies comparing alcoholism in twins.^{10,93}

in social situations, and to drink excessively because they lose control. To put it another way, alcohol dependence appears to be a manifestation of an underlying personality disorder, whereas alcohol abuse may be a way to cope with normal levels of stress. In this light, it is not surprising that familial risk is highest for early onset alcoholism, a type of dependence that almost certainly arises from a personality disorder and can develop in very young teenagers. This type of alcohol-seeking behavior is an entity quite distinct from alcohol abuse, although abusers may inherit a susceptibility to loss of control after drinking. The familial risk of alcoholism is higher for the children of severe or early onset alcoholics, so a severely affected parent is more likely to have alcoholic children than is a mildly affected parent. The fact that level of risk varies in this manner implies that alcoholism is a

multifactorial disorder, caused by several to many different genes acting somehow in concert.

The major weakness of this study is that it examined a group of people with an alcohol problem severe enough to drive them to seek treatment. Most alcoholics never seek treatment, so the twins in this study were probably more severely affected than most alcoholics. Generally speaking, those alcoholics who do seek treatment are more likely to have a range of psychiatric problems associated with their illness. The twins analyzed in this study had a higher-than-average incidence of clinical depression and anti-social personality disorder, and also tended to have an early onset of alcoholism. In addition, these twins were almost exclusively white, so that little insight could be gained into the heritability of alcoholism in other races. Finally, there may have been a problem in the mathematical model used to calculate heritability. This model assumed that the parents of an alcoholic child are each no more likely than average to be alcoholic themselves. Of course, this assumption would fail if an alcoholic chooses to have children with another alcoholic. In other words, if the mating options of an alcoholic are at all constrained by their disease, as they would likely be, then alcoholics may be more likely than normal to have children with another alcoholic. This kind of "assortative mating" can cause major problems for any mathematical modeling study of inheritance. For these several reasons, it is unclear to what extent the findings of this study can be generalized to the population at large.

In any case, the role of the environment appears to be considerably stronger than the role of the genes in addictive behavior, for men and women both. In fact, environment is almost half again as important as genes, for everything except alcohol dependence. If alcohol dependence is regarded as a kind of chemical imbalance that drives the individual to seek alcohol, it is not surprising that this is strongly genetic. Similarly, if alcohol abuse is regarded as social drinking gone malignant, it is also not surprising that this is strongly environmental. The varying importance of genes in the causation of alcoholism is

shown clearly by the fact that the heritability of alcoholism varies as a function of the age of onset of illness in male twins.⁹⁵ It was found that if the onset of problem drinking occurred at or before age 20, the heritability of alcoholism was as high as 73%, whereas problem drinking with a late age of onset was only 30% heritable. Men with an early onset of problem drinking were also more at risk for drug use, school misconduct, and precocious sexual behavior.

The environment clearly has a strong causative role in alcoholism, as confirmed by cross-fostering studies.⁹³ A cross-fostering study is one that follows children from an alcoholic familial background, who are adopted by either alcoholic or nonalcoholic parents. Any differences in the incidence of alcoholism in these children can be attributed to the environment, since all of the adopted children share a similar genetic heritage. Similarly, children from a nonalcoholic background, adopted by either alcoholic or nonalcoholic parents, are followed, to round out the picture. This kind of cross-fostering study is quite difficult to do, since adoption agencies typically try to place adopted children with families that are not affected by alcoholism. Yet even the best agencies make mistakes, and alcoholism may develop as a problem after a child has already been placed with the adoptive family. Cross-fostering studies are generally considered to be a very robust way to address heritability, since the influence of genes can be clearly separated from the influence of the environment.

Scientists working in Sweden were able to find 862 adult men, all born to single women in Stockholm between 1930 and 1949, and all of whom had been adopted at a young age by nonrelatives.⁹³ Complete information about alcohol abuse, mental illness, and medical illness was available for each of these adoptees, and for their biological and adoptive parents, because of the sophisticated public health system in Sweden. Both children and parents were classified as to whether they were alcohol-dependent or alcohol abusers, on the basis of these medical records. Alcoholics were considered to be abusers if they became alcoholic after the age of 25 and if there was no record of

Table 2
Rate of Alcoholism among Adopted Children^a

	Abuse		Dependence	
	Environmental exposure		Environmental exposure	
	No	Yes	No	Yes
Genetic exposure				
None in family	4%	4%	2%	4%
Family history	7%	12%	17%	18%

^aThe rate of alcoholism in adopted male children, coming from different genetic backgrounds and adopted into different environments. These data are from a cross-fostering study design, in which the inheritance of severe alcoholism is determined in children adopted away from their biological parents.⁹³ This study design enables scientists to separate hereditary and environmental causes of alcohol abuse or dependence.

imprisonment or criminal behavior. Alcoholics were considered to be dependent if their alcoholism began in adolescence, and if there was a record of serious criminality beginning at about the same time. Results from this study showed clearly that there is a strong component of both environmental and genetic causation in alcoholism (Table 2).

Children with no family history of alcoholism are generally at a low risk of becoming alcoholic themselves, no matter what the environment is like. Children with a family history of alcohol abuse are at a somewhat higher-than-normal risk of becoming alcohol abusers themselves, even if the adoptive family environment does not include an alcoholic. But these children are at a much higher risk of abuse in an alcoholic adoptive family. Children with a family history of alcohol dependence are at high risk of alcohol dependence, whether or not the family environment includes an alcoholic. Overall, it was found that a family history of alcohol abuse increases a child's risk of alcoholism about twofold, while a family history of alcohol dependence increases risk fivefold. On the other hand, an alcoholic family environment does not increase the risk of alcohol abuse at all in the absence of a family history. An alcoholic family environment does increase the risk of alcohol dependence about twofold, even in the absence of a family history of alcoholism, but this

finding is based on a very small number of children at risk. Overall, the effect of low social status is to increase the risk of alcohol abuse for all people. The greatest weakness of this study arises from the great strength of the adoption system in Sweden; nearly four times as many children were placed with nonalcoholic adoptive parents as were placed with alcoholic parents. Thus, relatively few children were put at risk because of an alcoholic family environment. Consequently, scientists may not have an accurate assessment of the role of environment in the causation of alcoholism.

The Sobering Story of the A1 Allele

Because alcoholism is a disease that has many manifestations and is clinically complicated, one might expect it to be fairly complicated from a genetic standpoint. Yet this expectation was completely overturned by a group of scientists who found evidence that one particular gene, called the A1 allele (or form) of the dopamine receptor, was strongly associated with alcoholism.⁹⁶ Dopamine is a chemical that acts as a messenger between neurons in the brain; the dopamine receptor is the protein that actually binds to dopamine and so receives the signal carried by this molecule. It was intuitively appealing to many scientists that the dopamine receptor be involved in addictive behavior because dopamine itself is known to be involved in some pleasure-seeking and addictive behaviors. Consequently, a gene that controls expression of the dopamine receptor would be an obvious site of mutation in alcoholics. Yet this study remains largely unreplicated to this day, even though a great deal of effort has been spent trying to confirm the findings. Several of the original scientists have backed away from the claim that the A1 allele is critical in alcoholics, and most scientists now believe that the original report was wrong. But the story of the A1 allele remains as a sobering demonstration of the difficulty involved in doing behavioral genetics.

The original data about the A1 allele of the dopamine receptor was obtained by scientists who studied preserved brain tissue from a tissue bank.⁹⁶ Tissues were obtained from 35 alcoholics and 35 nonalcoholics, all of whom had died many years previously, and who were then paired by age, sex, and race. Each of the tissues was tested for differences in expression of nine different genes. The only gene found to differ significantly between the two groups was the dopamine receptor allele known as A1. The A1 allele was present in 69% of the alcoholics, but in only 20% of the nonalcoholics. Given that the number of samples analyzed was reasonably large (70 in all), this difference was highly significant from a statistical standpoint. Although no one knew how a single protein could predispose an individual to develop a disease as complex and variable as alcoholism, the finding nevertheless implied that the dopamine receptor was somehow linked to development of alcoholism. This was very exciting, because it raised the possibility that a test could be developed to screen for alcoholism in the general population. Since 28 million Americans are the children of alcoholics, a strong linkage between alcoholism and the expression of a single gene would make it quite easy (and very lucrative) to develop a test kit to identify those most at risk of alcoholism. Initially, the only reservation about this study was that 20% of nonalcoholics also had the A1 allele; this makes a test kit less useful, since many people identified as being at risk would never actually become alcoholic. But this finding also seemed to imply that the A1 allele is not strongly linked to alcoholism, since a fair number of people with the gene never did develop the illness.

Soon after publication of the first piece of research on the A1 allele, another study was published that confirmed that the A1 allele is more common among alcoholics.³⁶ However, the newer study also suggested that the A1 allele might be involved in a range of mental illnesses, including attention deficit-hyperactivity disorder, autism, and Tourette's syndrome (Tourette's is an unusual mental illness that causes the sufferer to have uncontrollable outbursts of repetitive behavior, including verbal and

physical tics, incomprehensible speech, and violent swearing). This newer study of the A1 allele analyzed brain tissue removed at autopsy from 108 healthy individuals, and compared this to tissue from 86 alcoholics, 48 patients with attention deficit-hyperactivity disorder, 18 autistic patients, and 147 patients with Tourette's disease. The A1 allele was present in 22% of the normal individuals, but it was found in 43% of alcoholics, 46% of patients with attention deficit-hyperactivity disorder, 55% of autistic patients, and 45% of Tourette's patients. Therefore, incidence of the A1 allele was more than twice as high as normal in all four of the patient groups. This finding was significant in a statistical sense, but relatively unimpressive nonetheless, because it shows that the A1 allele is not closely linked to alcoholism. Since the A1 allele was present to the same extent in several different disease states, some of which are not at all closely related to alcoholism, the linkage specifically to alcoholism is weakened. Yet the most striking thing about the newer study was that no patient group had the very high frequency (69%) of the A1 allele found in the first study. The fact that the A1 allele is not found in most alcoholics implies that it is not the primary cause of alcoholism, although it may act to modify the expression of another gene more closely linked to alcoholism. Perhaps the A1 allele is more common among alcoholics who develop medical problems from their drinking, or perhaps the A1 allele is somehow associated with a range of different compulsive diseases including alcoholism.

More recently, the A1 allele has fallen even further from grace. A study that examined 44 alcoholics and 68 nonalcoholics was unable to find any difference in A1 allele frequency between the two groups.⁹⁷ When alcoholic subjects were more closely examined, it turned out that A1 allele frequency was unrelated to age of onset, family history, total alcohol consumption, antisocial personality, or physical ailments associated with drinking. A meta-analysis, which is a formal reanalysis of data published by other scientists, showed that there was much more difference in A1 allele frequency between different ethnic groups than there was between alcoholic and nonalcoholic subjects from a single ethnic group.⁹⁸ For example, A1 allele frequency is less than 10%

in Yemenite Jews, is about 40% in American blacks, and is about 80% in Cheyenne Indians. Yet the mean A1 allele frequency in alcoholics of all ethnicities is 42%, while the mean allele frequency in nonalcoholics is 34%. When the early data, the data that started the whole controversy, were excluded from further consideration, the mean A1 allele frequency was 36% in both alcoholics and nonalcoholics. Finally, when modern molecular biological techniques were used to examine the fine structure of the A1 allele, it was found that there was no difference between alcoholics and nonalcoholics.⁹⁹ A group of 113 alcoholics was compared to a group of 34 nonalcoholics and a group of 106 patients with schizophrenia, and it was found that there were no consistent differences in the A1 allele between any of these groups. In fact, two of the scientists who had reported the first very controversial results were also involved in this last study, thus recanting their belief in the importance of the A1 allele in alcoholism.

The sorry saga of the A1 allele is a vivid demonstration of the fact that gene linkage studies are very difficult to do properly. There is no reason to think that the original paper on the A1 allele was in any way dishonest, but it does appear to be completely wrong nonetheless. Simply because a result is consistent with expectations, and can be explained from a theoretical standpoint, does not make it correct. A new result, even if it seems to have great explanatory power, should not be accepted at face value until it has been replicated. It is incumbent on scientists to test and replicate all new findings, so that grains of truth can be found and the chaff of error discarded. Yet we must be careful not to discard or downplay what we do know about alcoholism; alcoholism is an illness for which many people inherit a genetic proclivity. While we do not know exactly which genes are responsible for this inborn proclivity, we do know that the genes exist.

Is Drug Addiction a Heritable Trait?

Drug addiction is in many ways similar to alcoholism, so there is an expectation that drug addiction will also have a

component of heritability. However, there is much less evidence for the heritability of drug addiction than for the heritability of alcoholism, simply because drug addiction has been a serious problem for much less time. A diagnosis of childhood hyperactivity disorder predisposes an adult to become an alcoholic or a drug abuser, suggesting that there may be a set of genes that generally predisposes an individual to develop addiction later in life.⁹⁵ Alcoholism and drug addiction also have in common that both are more common among individuals with antisocial personality disorder, i.e., the personality disorder that is associated with pathological disregard for the rights and feelings of others. Both alcoholism and drug addiction tend to afflict those with an inability to inhibit impulsive behavior and little inclination to consider personal risk when weighing behavioral options. There is evidence from experiments with animals that both alcoholism and drug addiction are more easily induced in animal strains that have an abnormally low level of fear or a great interest in novel stimuli¹⁰⁰; this suggests that alcohol dependence in humans might be linked to similar personality traits. There is even some thought that mapping the genes involved in addictive behavior in mice might eventually allow an extrapolation to humans, but this prospect is, at best, a long way in the future.

The expectation that drug addiction is a heritable trait is at least partially confirmed by the fact that alcoholics are often drug abusers as well. Among male twins separated at birth, at least one of whom was alcoholic, more than 40% of men met the criteria for abuse or dependence on drugs (other than alcohol or tobacco).¹⁰ These findings are consistent with those of other scientists, who found an increased rate of drug abuse among the children of alcoholics, and also among the children of parents with other psychiatric problems. For males, identical twin concordance for drug abuse was 63% and fraternal twin concordance was 44%, while for females, identical twin concordance was 22% and fraternal twin concordance was 15%. It was estimated that drug abuse or drug dependence was 31% heritable for men, but only 22% heritable for women. The higher heritability of drug addiction in men than women is consistent

with the higher heritability of alcoholism in men, although the reasons for this sex difference remain unknown. Yet overall, drug abuse is substantially less heritable than alcoholism. In fact, the heritability of drug addiction in women is so low that it is not significant in a statistical sense, so it may not even be real. It is too bad that this study was weakened by the fact that it specifically excluded addiction to tobacco, one of the most powerful and harmful drugs ever used.

The same scientists who first proposed that the A1 allele of the dopamine receptor gene is related to alcoholism recently proposed that this same gene is also related to drug addiction.¹⁰¹ These scientists reported that the A1 allele was present in 51% of cocaine users but in only 16% of drug-free control subjects. Overall, the gene was found in 44% of 504 drug abusers, while it was present in only 28% of the control individuals. Yet it is not at all clear why the frequency of the A1 allele should vary from 16 to 28% in control individuals who are presumably comparable. While these scientists claim that the new findings are evidence for the A1 allele being somehow involved in reinforcing compulsive behavior, the jury is still out on this claim. Given the recent and repeated failures to replicate the A1 allele data for alcoholism, one cannot view these recent claims with much optimism.

Genes and Addictive Behavior

The relationship between genes and addictive behavior is particularly contentious because several recent high-profile studies were found to be flawed. These studies claimed a strong linkage between alcoholism and a gene known as the A1 allele of the dopamine receptor. The fact that this linkage has now been discredited should not be seen as a failure for behavioral genetics, but rather as a measure of the overall success of science. The A1 allele was apparently a false trail that many scientists were led down, but science is inherently a self-correcting process that involves building consensus. Later, when other scientists were unable to replicate the first study of the A1 allele, these scientists

were still able to publish their contradictory findings. The result was a spirited dialogue among scientists which has not yet been completed. Basically, the putative identification of the A1 allele was never seen as the end of the story; it was just the beginning of another chapter in the story.

From split twin studies, there is legitimate reason to think that genes play a role in addictive behavior, whether or not we have yet identified the particular genes involved. The split twin study summarized here involved 169 same-sex twin pairs; certainly it would have been more compelling if more twin pairs had been involved in this study, but 169 is a very respectable sample size. In short, there can be no question that alcoholism, and probably drug addiction as well, has a hereditary component. The only argument is about the relative magnitude of the hereditary component, compared to the undeniable environmental component in addictive behavior.

Crime and Violence

Crime and violence are facts of life for many Americans; in 1990 alone, 19 million crimes were committed, and nearly a third of them involved violence.¹⁰² The most common form of violent crime is assault, the attack of one person on another. Aggravated assault, which involves a weapon or causes serious but nonfatal injury, accounted for roughly 30% of all violent crimes, while simple assault accounted for another 50% of violent crimes. By comparison, forcible rape and murder are rare; rape accounts for about 2% of violent crimes, while violent crime results in the death of the victim in 0.4% of cases. Yet, in 1990, 23,000 people were murdered; the fact that these deaths represent less than 1% of the violent crimes in the United States shows the magnitude of the problem. The rate of violent crime in the United States far exceeds that of any other industrialized nation. Among 16 such nations surveyed in 1988, the United States had the highest rate of murder, the highest rate of assault, and the highest rate of sexual assault.

Those most at risk of suffering from violent crime are racial or ethnic minorities; blacks were 41% and Hispanics 32% more likely than whites to be victimized.¹⁰² The rate of death by homicide among blacks is about 5 times higher than among whites, and the death rate among young black males specifically is 20 times higher than among older white females. In many ways, the victimizers resemble the victims; perpetrators of violent crime are overwhelmingly male (89% of those arrested) and blacks are 6 times more likely than whites to be arrested for