

Genetic Factors in Substance Use Disorders

Lifetime risk for alcohol abuse or dependence

Risk for abuse or dependence on drugs other than alcohol

Dependence on alcohol or other drugs probable lifetime risk

With what we know about the complicating factor of alcohol in so many major medical problems, it is wise to once again stress the need for consistent screening of substance use.

Regarding alcohol, 30% to 50% of users have more minor problems related to their use of this substance. Difficulties include driving while impaired with alcohol (whether arrested or not), missing school or work because of intoxication or a hangover, arguments with friends or family members due to intoxication or disputes about the person's drinking, and so on.

Personality Disorders

Antisocial Personality Disorder (ASPD) closely tied to the risk for subsequent alcohol and drug abuse or dependence.

- ♦ Lifetime risk for abuse or dependence on alcohol is more than 65%.
- ♦ Lifetime risk for abuse or dependence of other substances is at least 35%.

ASPD Page 645 - 649 in DSM-IV (301.7).

Characteristics of ASPD:

- ♦ high levels of impulsivity
- ♦ inability to learn from mistakes
- ♦ lack of empathy for others

Environmental Influences

ASPD initially develops independently of alcohol or drug dependence.

Psychological Theories

Psychological theories must be tested while controlling for potential psychological responses or test results that are a consequence of recent substance use, withdrawal, or the antisocial personality disorder.

Contribution of the psychological characteristics is difficult to document.

One theory suggests substance use problems are viewed as adaptations in an attempt to alleviate problems in personality development, emotional suffering, and related difficulties.

Tension reduction

- ▶ Many substances actually increase physiological measures of tension.

Other theories include:

- ▶ a self-awareness model
- ▶ self-handicapping
- ▶ an opponent process model
- ▶ transactional theories
- ▶ the use of substances to achieve feelings of powerfulness

Some theories focus on behavioral conditioning through reward or reinforcement.

- ▶ Research demonstrates that substances of abuse have psychological rewards.

Socio-Cultural Theories

The availability of substances, their cost, and society's attitudes toward these substances has an impact on use patterns.

Highly reinforcing substances (heroin, cocaine) can markedly increase the risk for problems.

Specific socio-cultural theories have arisen to attempt to explain why higher rates of some substance use disorders (e.g., alcohol dependence) are seen in some subgroups of the population, for example:

- ♦ Native Americans
- ♦ Irish Catholics
- ♦ French

but lower rates are seen in others (e.g., Jewish individuals).

Genetic Factors in Substance Use Disorders

Alcoholism provides best study group, reflected in the fact that::

- ♦ alcohol use problems have been documented for hundreds of years;
- ♦ the rate of alcohol dependence has remained relatively stable in recent decades; and
- ♦ there is a higher prevalence of alcohol abuse or dependence compared to other substance use disorders.

Approaches to studying genetic influences in alcoholism can be seen as a prototype for evaluating genetic influences in medical or psychiatric disorders in general.

Family Studies

- ♦ The risk for alcoholism is threefold to fourfold higher in close relatives of alcoholics—the closer the genetic relationship the greater the risk, and the greater number of alcoholic relatives the greater the risk.

Twin Studies (raised in same household)

- ♦ Attempt to control for the relative importance of genetic and environmental factors.
- ♦ If a disorder were related to childhood environment, then the twin of someone with that disorder should be at high risk for the same problem, no matter what type of twinship is involved.
- ♦ Of the six or so twin studies of alcoholism that have been carried out in the world, all but one show the potential importance of genetics.
 - In one study, the risk for alcoholism in the identical twin of an alcoholic is 60%, while the risk in a fraternal twin is 30%.

Adoption

- ♦ All adoption studies conducted since 1950 demonstrate a markedly increased risk for alcoholism in children of alcoholics, even when raised by non-alcoholics.
- ♦ Most of these studies show no markedly increased risk for schizophrenia, major depressive disorder, or major anxiety disorders in these children of alcoholics.

Complicating Factors

A search is underway for biological and genetically controlled factors that increase the risk of alcoholism.

Such studies are difficult because:

- ♦ There are subgroups of alcoholics that carry high levels of risk for alcoholism for different reasons.
- ♦ The genetic factors in alcoholism do not act alone.
- ♦ The mode of inheritance of alcoholism does not follow the simple genetic forms described by Mendel.
 - It does not appear to be autosomal dominant, recessive, or sex-linked.
 - Alcoholism appears to be inherited as a variety of genetic material that acts together to increase the risk (polygenic inheritance), or as a limited number of dominant genes that only occasionally express themselves.

Biological Factors

Low levels of enzyme monoamine oxidase.

- ▶ This might be one of the genetically influenced factors that interacts with other influences to produce the final alcoholism risk.

Enzymes that metabolize the substance can affect risk.

- ▶ For example, alcohol breaks down to form aldehyde dehydrogenase

People with this enzyme pattern break down alcohol to acetaldehyde, the latter substance accumulates in their blood and causes a flush to the skin, a rapid heart rate, and other characteristics.

A second important inherited biological factor that might increase the alcoholism risk.

- ▶ A brain wave pattern (a lower amplitude or smaller size of the P300 wave of the event-related potential) that might decrease their ability to recognize subtle changes in the environment.

A third possible mechanism, children of alcoholics have been demonstrated to show lower levels of intensity of response to alcohol at an early age.

- ▶ Increased risk for repeated heavy drinking in the future.

Study: Children of Alcoholics (COAs)

Reactions to alcohol in children of alcoholics might be associated with an increased future risk for alcoholism.

453 drinking (but not alcohol dependent) sons of alcoholics and controls was carried out when they were approximately 20 years of age.

- ♦ Sons of alcoholics and sons of non-alcoholics
 - family history positive (FHP)
 - family history negative (FHN)

- ♦ Two different doses of alcohol in the laboratory

Groups were almost identical on the time to peak blood alcohol concentration and the rate of disappearance of alcohol from the bloodstream.

Diminished response to alcohol was a characteristic of about 40% of the sons of alcoholics but less than 10% of the sons of non-alcoholics.

Diagnosis at Follow-up by Family History: Percentages

	<i>FFP</i> <i>n=241</i>	<i>FFN*</i> <i>n=182</i>
<i>No Diagnosis</i>	49	72
<i>Alcohol:</i>		
<i>Dependence</i>	28	12
<i>Abuse</i>	13	6
<i>Stimulant:</i>		
<i>Dependence</i>	10	4
<i>Abuse</i>	1	1
<i>Marijuana:</i>		
<i>Dependence</i>	8	4
<i>Abuse</i>	3	2
<i>Primary Affective Disorder</i>	2	6
<i>Primary Anxiety Disorder</i>	1	1

*1 person later found he was adopted and could not be classified

Summary

Many factors contribute to the decision to first take substances, to continue use of these agents, to the development of temporary problems, and to the production of abuse or dependence.

Numerous socio-cultural, psychological, and personality characteristics have been hypothesized to be related to the risk for alcoholism and other substance use disorders.

Using the alcohol use disorders as an example, there are data from family, twin, and adoption studies suggesting that alcoholism is genetically influenced.

Numerous factors have been identified as being relatively unique to individuals at high future risk for alcoholism (i.e., children of alcoholics) compared to controls.

Children of alcoholics are significantly more likely than children of controls to demonstrate low levels of response to alcohol as measured by subjective and objective findings.

- The low level of response to alcohol has been shown to relate to a very high risk for future alcoholism.

Are you screening every patient?

Suggested Literature

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