

Module 6: Substance Abuse Disorders with Emphasis on Genetics

Duration: 90 minutes

Goal:

- ♦ To provide a description and discussion of genetic factors that increase the risk for substance abuse or dependence.

Objectives:

Following this module the participant will be able to:

- ♦ Describe the roles of personality, psychological, and socio-cultural factors as they affect substance abuse and dependence.
- ♦ Describe the importance of genetic factors in substance abuse disorders.

Teaching Activities:

Introduction	10 minutes
Roles of Personality factors	15 minutes
Role of Psychological factors	15 minutes
Role of Socio-cultural factors	15 minutes
Genetic factors	30 minutes
Summary	5 minutes

Teaching Format:

This training is designed to be delivered primarily in a classroom / didactic lecture format. The design will incorporate a method which presents accepted data for presentation in a medical school environment. Information will be presented by the instructor for facilitated discussion of some concepts.

Suggested Literature

Blane, H. T., & Leonard, K. E. (Eds.). (1987). Psychological theories of drinking and alcoholism. New York: Guildford Press.

Brehm, N., Khantzian, E. J., & Dodes, L. M. (1993). Recent developments in alcoholism: Psychodynamic approaches. Recent Developments in Alcoholism, 11, 453-471.

Lowinson, J. H., Ruiz, E., & Millam, R. B. (Eds.). (1992). Substance abuse: A comprehensive textbook (2nd ed., pp. 39-1037). Baltimore, MD: Williams and Wilkins.

Schuckit, M. A. (1994). A clinical model of genetic influences in alcohol dependence. Journal of Studies of Alcohol, 55, 5-17.

Schuckit, M. A. (1994). Low level of response to alcohol as a predictor of future alcoholism. American Journal of Psychiatry, 151, 184-189.

Schuckit, M. A. (1995). Drug and alcohol abuse: A clinical guide to diagnosis and treatment (4th ed.). New York: Plenum.

Schuckit, M. A., & Gold E. O. (1988). A simultaneous evaluation of multiple markers of ethanol/placebo challenges in sons of alcoholics and controls. Archives of General Psychiatry, 45, 211-216.

Schuckit, M. A., & Hesselbrock, V. (1995). Alcohol dependence and anxiety disorders: What is the relationship? American Journal of Psychiatry, 151, 1723-1734..

Schuckit M. S., & Smith, T. L. (1996). An 8-year follow-up of 450 sons of alcoholic and control subjects. Archives of General Psychiatry, 53, 202-210.

Teaching Outline

Module 6. Substance Abuse Disorders with Emphasis on Genetics

Note to Instructors:

Before starting to teach you may want to review the goals and objectives of this module.

I. Introduction

Provide the following information.

- A. Any discussion of the etiology of substance use disorders must distinguish between factors that impact on initial use, those related to continued use, issues relevant to the development of temporary problems, and causes of abuse or dependence.
- B. Social factors, attitudes towards substances, and their availability (e.g., cost and the number of outlets that sell the substance) all contribute to an individual's decision to initially use a substance.
- C. The nature of the substance, society's rules, and characteristics of the individual all contribute to continued use.
- D. Biological factors also play a role. For example, someone who has a tendency for severe nausea when taking opiates is less likely to continue use of that substance.

Ask the following series of questions to determine the participants' level of awareness of the magnitude of the substance abuse problem.

Instructor can determine whether to give the answers as the questions are presented or to wait until after all the questions are asked and then present the answers on the OHD/Slide 6.1.

- ♦ What is the percentage risk for the development of alcohol abuse or dependence for males in the U.S.?
- ♦ What is the percentage risk for the development of alcohol abuse or dependence for females in the U.S.?
- ♦ What percentage of the general population will develop a dependence or abuse pattern with drugs other than alcohol?

OHD/Slide 6.1 on screen.

Refer to HO6.1.

- E. The lifetime risk for alcohol abuse or dependence is:
- ◆ approximately 15% in men
 - ◆ 5% to 8% in women
- F. The risk for abuse or dependence on drugs other than alcohol approaches 6% or so in the general population.
- G. Dependence on alcohol or other drugs has a probable lifetime risk:
- ◆ approximately 10% for men
 - ◆ approximately 5% for women
- H. 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.
- I. Regarding alcohol, 30% to 50% of users have more minor problems related to their use of this substance. These 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.
- J. The causes of temporary problems still reflect those that impact on the initial use, but now it is likely that some biological and personality forces contribute as well.

Emphasize the next question.

- ◆ Are you screening every patient?

This can be rhetorical but is open for input.

The instructor can refer to module 3 of this series for information about screening technique.

If the instructor does not choose to expand on the topic, continue on to the next section.

II. The Roles Of Personality, Psychological, And Socio-Cultural Factors In Substance Abuse And Dependence.

OHD/Slide 6.2 on screen.

Refer to HO6.2.

A. Personality Disorders

1. At least one major Axis II disorder, the antisocial personality disorder (ASPD), is closely tied to the risk for subsequent alcohol and drug abuse or dependence.
2. Among individuals with ASPD the lifetime risk for abuse or dependence on alcohol is more than 65%, while the lifetime risk for abuse or dependence of other substances is at least 35%.
3. The antisocial personality disorder can be clearly defined using reliable criteria as listed in DSM-IV.

The instructor may want to expand upon the DSM-IV criteria.

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

4. The characteristics of individuals with ASPD include:
 - ♦ high levels of impulsivity
 - ♦ an inability to learn from mistakes
 - ♦ lack of empathy for others
5. In a heavy-drinking or drug-using society, these characteristics are likely to predispose an individual to develop problems with substances and to continue use despite even severe consequences.
6. ASPD appears to develop initially independently of alcohol or drug dependence (i.e., the first stage of ASPD conduct disorder is seen long before substance use problems develop) and ASPD predicts a worse prognosis once substance use disorders develop.
7. So, at least one personality disorder, itself likely to be genetically influenced, impacts on the risk for alcoholism and drug dependence.

8. Most other personality disorders as defined by DSM-IV do not have the same quality of data regarding their contribution to an enhanced risk for subsequent substance use disorders.
9. Although there does appear to be a relationship between the borderline personality disorder and the future risk for substance use disorders more study of this connection is required.

B. Psychological Theories

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Refer to HO6.3.

1. In addition to the personality disorders, a number of psychological theories have been developed regarding a predisposition toward substance use disorders.
2. These 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.
3. The definitive contribution of the psychological characteristics to actual substance use problems is difficult to document.
4. One set of theories focuses on psychodynamic issues.
5. One theory suggests substance use problems are viewed as adaptations in an attempt to alleviate problems in personality development, emotional suffering, and related difficulties.

The instructor might choose to expand upon these theories using the reference by Brehm et al., (1993) but no definitive relationships with substance use disorders have been established.

6. The potential importance of the ability of substances to reduce levels of tension (and to serve as a reward) has also been researched.
7. Many substances actually increase physiological measures of tension, and almost all increase symptoms of tension when taken in high doses or on a long-term basis.

8. Other psychological theories include a self-awareness model, self-handicapping, an opponent process model, transactional theories, the use of substances to achieve feelings of powerfulness, etc.

The instructor may choose to expand here, again no definitive data have been developed.

9. Some important theories focus on behavioral conditioning through reward or reinforcement.
10. Most research demonstrates that substances of abuse can serve as psychological rewards, either through the effects they produce during intoxication or by the alleviation of withdrawal.
11. People are likely to repeat actions they find rewarding.
12. This reward theory crosses over to some important biological hypotheses.
13. A specific brain area rich in the neurochemical dopamine exists in the ventral tegmental area of the brain and might serve as a partial pathway for drug reinforcement as well as other pleasurable experiences.
14. Once again, the role of these mechanisms is of theoretical importance, but a definitive relationship to actual substance use disorders is difficult to establish.

Emphasize the next question and repeat if necessary.

- ♦ Are you screening every patient?

Ask if there are any questions at this time.

If the participants are ready, proceed with the following information.

C. Socio-cultural Theories

Start this section by asking the participants the following question.

- ♦ Can you tell me what some socio-cultural factors or theories might be?

Allow the participants time to respond

OHD/Slide 6.4 on screen.

Refer to HO6.4.

1. There are also a number of socio-cultural theories that have been developed.
2. The availability of substances, their cost, and society's attitudes toward these substances has an impact on use patterns.
3. For highly reinforcing drugs, such as heroin and cocaine, use can markedly increase the risk for problems in most individuals.
4. Thus, epidemics of use of these substances have been reported in the context of greater levels of drug purity or lower costs in various locales.
5. Here problems can be a fairly direct consequence of use.
6. For the highly reinforcing substances and for those with less dramatic effects, 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
 - ♦ Frenchbut lower rates are seen in others (e.g., Jewish individuals).
7. Such theories often focus on whether alcohol is used as part of religious ceremonies, the attitudes towards alcohol and drunkenness in the home, etc.
8. However, no generalizable theories have been shown to actually relate to the risk for substance use disorders.
9. For instance, the same influences that are felt to help protect some groups (e.g., use of alcohol in religious ceremonies in the Italians and in Jews), are present in some groups with high rates of alcoholism (e.g., the French).
10. It is important to place psychological, personality, and socio-cultural theories into perspective:
 - ♦ Most clinicians and researchers recognize the potential importance of these factors.
 - ♦ Careful research in this area is most difficult to carry out. Results are frequently affected by pre-existing major disorders (e.g., ASPD), test scores or observations may result from recent substance use patterns as opposed to contributing to the initial substance use or problems, and results in one population have been difficult to replicate in another.

- ▶ While the major focus of this module is on the biological and genetic spheres, this is more a reflection of the quality of the data currently available than a definitive conclusion about the relative importance of the different types of mechanisms potentially operating here.
- ▶ It is important to remember that the final risk for a substance use disorder is likely to result from a combination of socio-cultural, personality, psychological, and biological factors.

This concludes the section on socio-cultural theories.

Ask participants if they have any questions.

After allowing a few minutes for questions move on to the next section.

III. The Importance Of Genetic Factors In Substance Use Disorders

Provide the following information.

1. The best data on the role of genetic influences in substance use disorders are available regarding alcohol abuse or dependence.
2. This reflects 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.
3. This combination allows for studies of multiple generations which have been exposed to substantial risk for problems with the drug should a predisposition exist.
4. Approaches to studying genetic influences in alcoholism can be seen as a prototype for evaluating genetic influences in medical or psychiatric disorders in general.

OHD/Slide 6.5 on screen.

Refer to HO6.5.

5. The first type of support for genetic influences in alcoholism comes from family studies.
6. 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.
7. On the other hand, the risks for most other psychiatric disorders are not markedly increased in the family members of alcohol dependent individuals who themselves don't have other major psychiatric disorders.
8. Family studies do not prove a genetic contribution because characteristics can run in families for genetic or environmental reasons.
9. Twin studies attempt to control for the relative importance of genetic and environmental factors.
 - ♦ Members of twin pairs raised in the same household share the same childhood environment.
 - ♦ 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.
 - ♦ Identical twins share 100% of their genes while fraternal twins share only 50% of their genetic material.
 - ♦ Therefore, if a disorder such as alcoholism were genetically influenced, then the identical twin of an alcoholic should be at a higher risk than a fraternal twin.
 - ♦ 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%.

Instructor note: These data also demonstrate that environment must be important or the risk would be 100% in identical twins of alcoholics.

10. The third major type of genetics study looks at the outcome in children of alcoholics when the offspring were adopted out early in life and raised without knowledge of their biological parents' problems.
 - ♦ All adoption studies conducted since 1950 demonstrate a markedly increased risk for alcoholism in children of alcoholics, even when raised by non-alcoholics.
 - ♦ The adoption studies also demonstrate that being raised in the home of an alcoholic does not increase the risk for alcoholism among children of alcoholics above that predicted just by having an alcoholic biological parent.
 - ♦ Most of these studies show no markedly increased risk for schizophrenia, major depressive disorder, or major anxiety disorders in these children of alcoholics.

Instructor note: The reference by Schuckit and Smith (1996) and Schuckit (1994) may be useful for this piece.

OHD/Slide 6.6 on screen.

Refer to HO6.6.

11. A search is now underway for biological and genetically controlled factors that actually 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 (e.g., those with and without ASPD).
 - ♦ The genetic factors in alcoholism do not act alone.
 - There is an interaction between genetic and environmental influences, as exemplified by the lack of 100% risk for alcoholism in the identical twins of alcoholic individuals.
 - ♦ The mode of inheritance of alcoholism does not follow the simple genetic forms described by Mendels.
 - It does not appear to be autosomal dominant, recessive, or sex-linked.

The instructor may wish to expand upon this.

- Alcoholism appears to be inherited as a variety of genetic material that act together to increase the risk (polygenic inheritance), or as a limited number of dominant genes that only occasionally express themselves (e.g., a dominant mode of inheritance with incomplete penetrance).

Ask participants the following question.

- ♦ Do you know any potentially inherited biological factors for increasing the risk of alcoholism?

Allow participants sufficient time to respond to the question.

OHD/Slide 6.7 on screen.

Refer to HO6.7.

12. A number of potentially inherited biological factors have been evaluated as possible mechanisms for increasing the alcoholism risk.
13. Low levels of activity of the enzyme monoamine oxidase, even in the absence of the antisocial personality disorder, might make an individual more impulsive and therefore more likely to begin using substances and continue use even in the face of adverse consequences. However, the data are not definitive and results might reflect temporary effects of smoking.
 - ♦ This might be one of the genetically influenced factors that interacts with other influences to produce the final alcoholism risk.
14. Enzymes that metabolize the substance can affect risk.
 - ♦ Alcohol for example, aldehyde dehydrogenase forms that are less active at lower blood acetaldehyde levels are observed in about half of Chinese, Japanese, Korean, and related Asian individuals.
 - ♦ When 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.
 - ♦ People with this flush are less likely to drink heavily and less likely to develop alcoholism. There is a second possibly important inherited biological factor that might increase the alcoholism risk.

- ♦ Alcoholics and their children have been demonstrated to have evidence of 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.
 - ♦ This characteristic could make it more difficult for alcoholics and children of alcoholics to decide on any given occasion when it is time to stop drinking.
15. In a third possible mechanism, children of alcoholics have been demonstrated to show lower levels of intensity of response to alcohol at an early age (i.e., they can “hold their liquor well”).
- ♦ This might increase the risk for repeated heavy drinking in the future, since individuals with this characteristic might require more alcohol than individuals lacking this characteristic to achieve intoxication or the desired effect.
 - ♦ That, in turn, might increase the risk for developing alcohol-related life problems and being diagnosed as an alcoholic. It is these data that will be used as an example of how to study biological factors in alcoholism.

OHD/Slide 6.8 on screen.

Refer to HO6.8.

16. Reactions to alcohol in children of alcoholics might be associated with an increased future risk for alcoholism.
17. An evaluation of 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 with a family history positive (FHP) and family history negative (FHN) individuals) were challenged with two different doses of alcohol in the laboratory.
 - ♦ The two groups were almost identical on the time to peak blood alcohol concentration and the rate of disappearance of alcohol from the bloodstream.
 - ♦ The two groups had been carefully matched on their usual quantity and frequency of alcohol intake, as well as on their demographic profiles.

18. Despite the similar past drinking histories and similarity in rates of disappearance of alcohol, the children of alcoholics were more likely to show low levels of response to the alcohol.
19. A 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.

OHD/Slide 6.9 on screen.

Refer to HO6.9.

20. On an average of eight to ten years following the initial evaluation, all 453 men were located and 450 were interviewed.
21. An evaluation of the history of each subject since initial testing was developed through structured interviews with both the subject and his spouse (or close friend).
22. This demonstrates the eight-to ten-year course for the development of alcohol or other substance use disorders or psychiatric syndromes.
23. It can be seen that the FHP (children of alcoholics) group had a markedly elevated risk for alcohol abuse or dependence, demonstrated only a slightly increased risk (nonsignificant) for dependence on drugs other than alcohol, and showed no increased risk for major psychiatric disorders.
24. For the 424 men on whom full data are available, the 132 individuals who subsequently developed alcoholism had significantly lower levels of reaction to alcohol than the 292 men who did not go on to develop alcoholism.
25. Additional studies of animals and human twins have demonstrated that the intensity of reaction to alcohol does appear to be genetically influenced.
26. One factor that might interact with environment to increase or decrease the chances of developing a very heavy drinking pattern with a subsequent high risk for being diagnosed with alcohol abuse or dependence is the level of response to alcohol.
27. These data demonstrate an approach to studying genetic factors in alcoholism, and emphasize the importance of both genetics and environment.

IV. Summary

Refer to HO6.10.

1. 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.
 - ♦ It is likely that different factors account for the different levels of an individuals' possible relationship with substances (i.e., initial use at one end, and dependence at the other).
2. Numerous socio-cultural, psychological, and personality characteristics have been hypothesized to be related to the risk for alcoholism and other substance use disorders.
 - ♦ It is likely that a combination of these influences interacts with a person's higher or lower biological level of predisposition toward substance dependence.
 - ♦ It is easier to study the biological aspects than the socio-cultural, personality, or psychological attributes.
3. Using the alcohol use disorders as an example, there are data from family, twin, and adoption studies suggesting that alcoholism is genetically influenced.
4. As is likely to be true for all of the substance use disorders, the type of genetic contribution is complex and difficult to study.
5. 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.
6. Used as an example of a way of thinking about such risk factors, data were presented regarding the low level of responsivity to alcohol as a potential risk factor for alcoholism.
 - ♦ 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.
7. These data can have implications for prevention and perhaps early treatment.

The instructor may expand upon this.