

# **The Validity of Substance Dependence: Biological and Clinical Evidence**

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Debate has raged for decades about the question of whether alcohol dependence and other substance dependences are or are not diseases. This unproductive discourse has tended to ignore the basic definition of what constitutes a disease. By definition, a disease involves an impairment of the normal state of the living animal or any of its components due to genetic, pathogenic, or environmental factors or any combination of thesees.<sup>1</sup> Logically a disease, or disorder, should be identifiable by a unique constellation of symptoms. Indisputably, alcohol can be considered an environmental agent.

A brief review of the recent literature and accumulating data will present the case that alcohol dependence as defined by the DSM-IV/DSM-IV-TR<sup>2,3</sup> meets the criteria of involving genetic factors and presents as a unique constellation of symptoms. Dependences concerning other substances such as cocaine also appear to involve genetic predispositions, and as for alcohol, dependence for a given substance typically presents clear and distinct syndromes. This would support the distinction of dependence from abuse and the criteria that a diagnosis of dependence should supersede a diagnosis of abuse.

The issue of dependences being unique clinical disorders from abuse is more than a semantic exercise—it has relevance to clinical practices. The extent to which dependent individuals have different biological and/or psychological reactions to a given substance should influence the type and extent of treatment required as compared to those who are misusers, or abusers. Likewise the goals of treatment and the long-term prognosis may differ for the dependent as compared to the abuser.

## **Genetics and Biology**

The Collaborative Study on the Genetics of Alcoholism has identified five chromosomes that may cause one to be predisposed to developing alcohol dependence.<sup>4,5,6</sup> These findings are consistent with the expectation that multiple genes influence risk for alcohol dependence in addition to previously identified gene alleles such as those for ADH (alcohol dehydrogenase)

related to risk for dependence.<sup>7</sup> An intriguing study of Japanese men has found that ALDH (aldehyde dehydrogenase) alleles, related to facial flushing, are related to drinking behavior, but the ADH alleles are related to level of alcohol intake among non-flushers.<sup>8</sup> Taken together, the genetic and biological studies point to variable susceptibility for not only alcohol dependence, but also to genetic influences on the behaviors that may predispose one to become dependent.

The importance of genetic factors on the development of dependence for other substances is also being explored. Twin studies suggest that heritabilities for cocaine dependence among women may be 0.65 as indicated by the concordance rates for MZ (monozygotic) and DZ (dizygotic) twins. The concordance rates for cocaine dependence for MZ and DZ twins were 35% vs. 0% while use concordance rates were 54% and 42% respectively.<sup>9</sup> A large study of males is consistent with substance-specific heritability and shows that individuals with alcohol dependence prior to developing stimulant dependence had the most severe clinical patterns.<sup>10</sup>

Other studies further illustrate possible predispositions to dependence and relapse. For example, alcohol dependent individuals have greater sensitivity to painful stimulation, but alcohol appears to have a normalizing effect on pain and discomfort for them.<sup>11</sup> Animal studies have indicated that certain dopamine receptors have a time-dependent influence on relapse to cocaine and heroin seeking.<sup>12</sup>

Even with the overwhelming evidence that alcohol dependence and probably other substance dependence has a genetic and biological component, one must keep in mind several facts. First, just because a condition has a genetic or biological component, does not mean that it is not treatable. Second, behavioral interventions are critical to proper management and normalizing functioning for a variety of chronic conditions such as hypertension, diabetes, and asthma. Finally, if dependence is to be properly recognized and treated, diagnostic approaches must utilize behavioral measures because no adequate or practical biological diagnostic procedures exist.

### **Clinical Differentiation of Dependence From Abuse, or Misuse**

The literature and the data to be presented here indicate that dependence can be differentiated from abuse or misuse. This is of practical importance in the identification and proper treatment of both dependence and abuse. Dependence may be considered the more serious

and chronic condition while abuse typically is less serious and is more likely to resolve with or without treatment.

Studies using different assessment instruments with different populations find that dependence emerges as distinct from abuse, or misuse. Comprehensive studies of alcohol have demonstrated convincing evidence for a clear distinction between dependence and abuse.<sup>13</sup> The distinction extends to prognosis in that dependent individuals are less likely to be trouble free during a five-year period.<sup>14</sup> Other studies also have found that prognosis is linked to baseline severity for substances such as cocaine.<sup>15</sup> Previous studies using the SUDDS-IV structured interview<sup>16</sup> and similar instruments have shown dependence to emerge as distinct from abuse for a variety of substances.<sup>17</sup>

The following discussion draws upon a sample of 4,892 individuals who are Minnesota state prison inmates. The sample includes 547 women and 4,338 men between 18 and 65 years of age. Just over half (51%) are Caucasian; 31% are African-American; 9% are Native Americans; and 6% are Hispanics. The remainder are of Asian or mixed ethnicity. Fifty-five percent of the inmates were dependent on at least one substance, and an additional 20% met abuse criteria. Of the total sample, 32% are dependent on only one substance, and 23% are dependent on two or more substances.

Since a dependence diagnosis for a given substance supercedes the abuse diagnosis, the use of abuse will refer only to those who do not also meet dependence criteria. However, as will be seen, the vast majority of dependent individuals would qualify for the abuse criteria as well.

Alcohol dependence is the most prevalent diagnostic category with 31% of the cases, followed by marijuana dependence with 19%. The prevalence rates for cocaine and other stimulants are equal at 12%, and heroin dependence is only 3% in this population. Abuse prevalence rates for all substances are lower than for the respective rate of dependence. Abuse diagnosis prevalences are 16%, 12%, 4%, 3%, and under 1% for alcohol, marijuana, cocaine, other stimulants, and heroin respectively.

As can be seen in the table, not only is abuse less prevalent than dependence for each substance in this population of inmates not seeking treatment, but also the symptom profiles with respect to DSM-IV criteria differ dramatically as illustrated by the number of positive abuse criteria. For all substances, the majority of each abuse diagnostic group is positive for only one

of the four criteria, and fewer than 5% are positive for all four. In contrast, about 80% of the cases in the typical dependence group are positive for three or more of the abuse criteria. The only exception is marijuana where 55% of dependent cases are positive for three or more criteria.

By definition, the abuse cases cannot be positive for more than two of the dependence criteria, but again, the typical abuse case either reports no dependence indications or at most one. The typical dependent case for any given substance typically endorses at least five of the seven dependence criteria. Again, the marijuana dependence group appears to have the lowest indications of severity while the heroine dependence group appears to manifest the greatest level of severity as indicated by the number of positive dependence criteria. Alcohol, cocaine, and other stimulants present relatively similar prevalences for the number of positive dependence criteria.

The prevalences of dependence vary among some of the ethnic and gender subgroups, but for those who met criteria for dependence, Caucasian females were the only subgroup showing significantly greater severity levels than their male counterparts within a given ethnic group. In other words, once the DSM-IV threshold of dependence is met, the typical individuals in the gender by ethnic subgroups tend to present similar severity profiles.

The dependence vs. abuse distinction may extend to at least that portion of adolescents who have sufficient use histories to develop positive DSM-IV criteria for the disorders. A sample of 251 adolescents in community and juvenile justice treatment facilities were interviewed with the PADDI (Practical Adolescent Dual Diagnostic Interview).<sup>18</sup> The typical adolescent in this sample was between 15 and 17 years of age. Of the 203 cases who met criteria for substance dependence, 88% were positive on five or more of the seven dependence criteria. The clinical profiles of these youngsters was comparable to that found in the adults.

## **Summary**

The accumulating genetic and biological evidence suggests that alcohol and other substance dependences have a number of biological underpinnings. In addition, careful examination of the events and behaviors that define dependence and abuse according to DSM-IV criteria reveals that for most individuals, dependence can be clearly distinguished from abuse, or misuse. Outcome studies provide evidence that the prognoses for abuse and dependence differ, thus

adding further weight to the argument that clinical practice should distinguish between dependence and abuse in treatment planning and establishing therapeutic goals.

### Comparison of Diagnostic Criteria Prevalences for Dependent and Abuse Cases

Number of Positive Dependence Criteria	Alcohol		Marijuana		Cocaine		Stimulants		Heroin	
	Dependent N = 1496	Abuse. N = 766	Dependent N = 592	Abuse. N = 914	Dependent N = 609	Abuse. N = 185	Dependent N = 586	Abuse. N = 129	Dependent N = 127	Abuse. N = 25
None	--	41%	--	32%	--	44%	--	39%	--	20%
1	--	30%	--	33%	--	29%	--	33%	--	48%
2	--	29%	--	35%	--	27%	--	28%	--	32%
3	15%	--	20%	--	9%	--	11%	--	4%	--
4	14%	--	21%	--	11%	--	13%	--	9%	--
5	16%	--	20%	--	15%	--	15%	--	10%	--
6	18%	--	18%	--	25%	--	20%	--	18%	--
7	37%	--	21%	--	40%	--	41%	--	59%	--
Number of Positive Abuse Criteria										
None	2%	--	3%	--	2%	--	1%	--	1%	--
1	7%	39%	14%	55%	5%	62%	5%	61%	6%	64%
2	14%	36%	28%	33%	15%	28%	14%	23%	13%	20%
3	31%	21%	32%	10%	37%	10%	28%	16%	35%	12%
4	45%	4%	23%	2%	41%	<1%	52%	0%	45%	4%

## REFERENCES

- <sup>1</sup> Webster's Third New International Dictionary of the English Language Unabridged. (1981). Springfield, MA: G. & C. Merriam Company.
- <sup>2</sup> American Psychiatric Association, 1994. *Diagnostic and Statistical Manual of Mental Disorders (4<sup>th</sup> ed.)*. Washington, DC: Author.
- <sup>3</sup> American Psychiatric Association, 2000. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision*. Washington, DC: Author.
- <sup>4</sup> Nurnberger, J. I., Foroud, T., Flury, L., Su, J., Meyer, E. T., Hu, K., Crowe, R., Edenberg, H., Goate, A., Bierut, L., Reich, T., Schuckit, M., & Reich, W. Evidence for a locus on chromosome 1 that influences vulnerability to alcoholism and affective disorder. *American Journal of Psychiatry*, 158(5), 718-724.
- <sup>5</sup> Foroud, T., Edenberg, H. J., Goate, A., Rice, J., Flury, L., Koller, D. L., Bierut, L. J., Conneally, P. M., Nurnberger, J. I., Bucholz, K. K., Li, T. K., Hesselbrock, V., Crowe, R., Schuckit, M., Porjesz, B., Begleiter, H., & Reich, T. (2000). Alcoholism susceptibility loci: confirmation studies in a replicate sample and further mapping. *Alcohol: Clinical and Experimental Research*, 24(7), 933-845.
- <sup>6</sup> Foroud, T., Bucholz, K. K., Edenberg, H. J., Goate, A., Neuman, R. J., Porjesz, B., Koller, D. L., Rice, J., Reich, T., Bierut, L. J., Cloninger, C. R., Nurnberger, J. I., Li, T. K., Conneally, P. M., Tischfield, J. A., Crowe, R., Hesselbrock, V., Schuckit, M., & Begleiter, H. (1998). Linkage of an alcoholism-related severity phenotype to chromosome 16. *Alcohol: Clinical and Experimental Research*, 22(9), 2035-2042.
- <sup>7</sup> Whitfield, J. B., Zhu, G., Duffy, D. L., Birley, A. J., Madden, P. A., Heath, A. C., & Martin, N. G. (2001). Variation in alcohol pharmacokinetics as a risk factor for alcohol dependence. *Alcohol: Clinical and Experimental Research*, 25(9), 1257-1263.
- <sup>8</sup> Tanaka, F., Shiratori, Y., Yokosuka, O., Imazeki, F., Tsukada, Y., & Omata, M. (1997). Polymorphism of alcohol-metabolizing genes affects drinking behavior and alcoholic liver disease in Japanese men. *Alcohol: Clinical and Experimental Research*, 21(4), 596-601.
- <sup>9</sup> Kendler, K. S. & Prescott, C. A. (1998). Cocaine use, abuse and dependence in a population-based sample of female twins. *British Journal of Psychiatry*, 173, 345-350.
- <sup>10</sup> Raimo, E. B., Smith, T. L., Danko, G. P., Bucholz, K. K., & Schuckit, M. A. (2000). Clinical characteristics and family histories of alcoholics with stimulant dependence. *Journal of Studies on Alcohol*, 61(5), 728-735.
- <sup>11</sup> Stewart, S. H., Finn, P. R., & Pihl, R. O. (1995). A dose-response study of the effects of alcohol on the perceptions of pain and discomfort due to electric shock in men at high familial-genetic risk for alcoholism. *Psychopharmacology*, 119(3), 261-267.
- <sup>12</sup> De Vries, T. J., Schoffelmeer, A. N., Binnekade, R., Raaso, H., & Vanderschuren, L. J. (2002). Relapse to cocaine- and heroin-seeking behavior mediated by dopamine D2 receptors is time-dependent and associated with behavioral sensitization. *Neuropsychopharmacology*, 26(1), 18-26.
- <sup>13</sup> Hasin, D., Van Rossem, R., McCloud, S., & Endicott, J., 1997. Alcohol dependence and abuse diagnoses: Validity in community sample heavy drinkers. *Alcoholism: Clinical and Experimental Research*, 21, 213-219.
- <sup>14</sup> Schuckit, M. A., Smith, T. L., Danko, G. P., Bucholz, K. K., Reich, T., & Bierut, L., 2001. Five-year clinical course associated with DSM-IV alcohol abuse or dependence in a large group of men and women. *American Journal of Psychiatry*, 158(7):1084-1090.
- <sup>15</sup> Simpson, D. D., Joe, G. W., & Broome, K. M. (2002). A national 5-year follow-up of treatment outcomes for cocaine dependence. *Archives of General Psychiatry*, 59(6), 538-544.
- <sup>16</sup> Hoffmann, N. G. & Harrison, P. A. (1995). *SUDDS-IV: Substance Use Disorder Diagnostic Schedule-IV*. Smithfield, RI: Evince Clinical Assessments.
- <sup>17</sup> Hoffmann, N. G., DeHart, S. S., Campbell, T. C., in press. Dependence: Whether a disorder or a disease; it is not a "concept." *Journal of Chemical Dependency Treatment*.
- <sup>18</sup> Estroff, T. W. & Hoffmann, N. G. (2000). *PADDI: Practical Adolescent Dual Diagnosis Interview*. Smithfield, RI: Evince Clinical Assessments.