#103780 ALCOHOLISM

A number sign (#) is used with this entry because of the demonstrated role of multiple genes in determining the genetic susceptibility that is supported by family, twin, and other studies.

The tendency for drinking patterns of children to resemble those of their parents has been recognized since antiquity, e.g., in the observations of Plato and Aristotle (Warner and Rosett, 1975). Alcoholism is probably a multifactorial, genetically influenced disorder (Goodwin, 1976). The genetic influence is indicated by studies showing that (1) there is a 25 to 50% lifetime risk for alcoholism in sons and brothers of severely alcoholic men; (2) alcohol preference can be selectively bred for in experimental animals; (3) there is a 55% or higher concordance rate in monozygotic twins with only a 28% rate for like-sex dizygotic twins; and (4) half-brothers with different fathers and adopted sons of alcoholic men show a rate of alcoholism more like that of the biologic father than that of the foster father. A possible biochemical basis is a metabolic difference such that those prone to alcoholism have higher levels of a metabolite giving pleasurable effects or those not prone to alcoholism have higher levels of a metabolite giving unpleasant effects. Schuckit and Rayses (1979) found that, after a moderate dose of alcohol, blood acetaldehyde levels were elevated more in young men with alcoholic parents or sibs than in controls.

A certain degree of organ specificity in the pathologic effects of alcohol is observed. For example, patients have cardiomyopathy, cirrhosis, or pancreatitis but rarely more than one of these. A genetic basis of organ specificity is evident in Wernicke-Korsakoff syndrome (277730) and pancreatitis from type V hyperlipidemia (238400).

Cloninger (1987) identified 2 separate heritable types of alcoholism. Type 1 alcohol abuse had its usual onset after the age of 25 years and was characterized by severe psychological dependence and guilt. It occurred in both men and women and required both genetic and environmental factors to become manifest. By contrast, type 2 alcohol abuse had its onset before the age of 25; persons with this type of alcoholism were characterized by their inability to abstain from alcohol and by frequent aggressive and antisocial behavior. Type 2 alcoholism was rarely found in women and was much more heritable. Abnormalities in platelet monoamine oxidase activity were found only in type 2 alcoholics (Von Knorring et al., 1985). See comments by Omenn (1988).

Crabb (1990) reviewed biologic markers for increased risk of alcoholism. Aston and Hill (1990) performed complex segregation analysis of 35 multigenerational families ascertained through a pair of male alcoholics. They concluded that liability to alcoholism is, in part, controlled by a major effect with or without additional multifactorial effects. However, mendelian transmission of this major effect was rejected, as was the hypothesis that the major effect is due to a single major locus.

The candidate gene approach was used by Blum et al. (1990) and by Bolos et al. (1990) to investigate a possible relationship of the dopamine D2 receptor (DRD2; 126450) to alcoholism. Although Blum et al. (1990) suggested an association between a particular allele at the DRD2 locus, Bolos et al. (1990) could not confirm this. In family studies, Bolos et al. (1990) excluded linkage between alcoholism and the DRD2 locus.

In connection with a collection of 11 research reports on the genetics of alcohol-related traits, Buck (1998) gave a brief review on recent progress toward the identification of genes related to risk for alcoholism.
Catechol-O-methyltransferase (COMT; 116790) is an enzyme that has a crucial role in the metabolism of dopamine. Lachman et al. (1996) suggested that a common functional genetic polymorphism in the COMT gene, which results in 3- to 4-fold difference in COMT enzyme activity, may contribute to the etiology of mental disorders such as bipolar disorder and alcoholism. Since ethanol-induced euphoria is associated with the rapid release of dopamine in limbic areas, it was considered conceivable that subjects who inherited the allele encoding the low activity COMT variant would have a relatively low dopamine inactivation rate, and therefore would be more vulnerable to the development of ethanol dependence. In 2 Finnish populations of type 1 (late-onset) alcoholics, Tiibonen et al. (1999) found a markedly higher frequency of the low activity allele (L). They estimated that the population etiologic (attributable) fraction for the LL genotype in alcoholism was as high as 13.3%.

Kauhanen et al. (2000) and Lappalainen et al. (2002) found an association between susceptibility to alcoholism and a leu7-to-pro polymorphism in the neuropeptide Y (NPY) gene; see 162640.0001.

Event-related brain potentials (ERPs) are recordings of neuroelectric activity, usually in response to some task, made from electrodes on the scalp. ERPs are altered in patients with a variety of psychiatric disorders and in members of their families, compared with the general population. Alcoholic subjects have a reduction of amplitude of the P3 component, a positive peak approximately 300-600 ms after a stimulus, that remains after long periods of abstinence from alcohol (Porjesz and Begleiter, 1985). A similar reduction in P3 amplitude is also seen in young alcohol-naive sons of alcoholic probands (Begleiter et al., 1984). Almasy et al. (2001) presented results of a genomewide linkage screen for amplitude of the N4 and P3 components of the ERP, measured at 19 scalp locations in response to a semantic priming task for 604 individuals in 100 pedigrees ascertained as part of a collaborative study on the genetics of alcoholism. N4 and P3 amplitudes in response to 3 semantic stimuli showed significant heritabilities, the highest being 0.54. Both N4 and P3 amplitudes showed significant genetic correlations across stimulus type at a given lead and across leads within a stimulus, indicating shared genetic influences among the traits. N4 amplitudes showed suggestive evidence of linkage in several chromosomal regions, and P3 amplitudes showed significant evidence of linkage to chromosome 5 and suggestive evidence of linkage to chromosome 4.

Liang et al. (2003) demonstrated that in alcohol-preferring and -nonpreferring rats, a polymorphism in the alpha-synuclein gene (SNCA; 163890) maps to the same location as a QTL for alcohol preference.

SEE ALSO

Propping et al. (1981)

REFERENCES

PubMed ID : 11102287

PubMed ID : 2339688
3. Begleiter, H.; Porjesz, B.; Bihari, B.; Kissin, B.:
   PubMed ID: [6474187](https://www.ncbi.nlm.nih.gov/pubmed/6474187)

   PubMed ID: [1969501](https://www.ncbi.nlm.nih.gov/pubmed/1969501)


6. Buck, K. J.:
   **Recent progress toward the identification of genes related to risk for alcoholism.** Mammalian Genome 9: 927-928, 1998.
   PubMed ID: [9880654](https://www.ncbi.nlm.nih.gov/pubmed/9880654)

7. Cloninger, C. R.:

8. Crabb, D. W.:
   PubMed ID: [2298906](https://www.ncbi.nlm.nih.gov/pubmed/2298906)

9. Goodwin, D.:


11. Lachman, H. M.; Papolos, D. F.; Saito, T.; Yu, Y. M.; Szumlanski, C. L.; Weinshilboum, R. M.:
    PubMed ID: [8807664](https://www.ncbi.nlm.nih.gov/pubmed/8807664)

   PubMed ID : 12665621

14. Omenn, G. S. :
   PubMed ID : 3189329

15. Porjesz, B.; Begleiter, H. :

16. Propping, P.; Kruger, J.; Mark, N. :
   PubMed ID : 10819022

17. Schuckit, M. A.; Rayses, V. :
   PubMed ID : 758678


   PubMed ID : 4036659

20. Warner, R. H.; Rosett, H. L. :

CONTRIBUTORS

Victor A. McKusick - updated : 6/10/2003
Victor A. McKusick - updated : 1/24/2001
Victor A. McKusick - updated : 8/4/1999
Victor A. McKusick - updated : 2/26/1999

CREATION DATE
