

40 - B. Genetics of Schizophrenia

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How important is the genetic contribution to schizophrenia? The relative risks for first-degree relatives / twins of probands are higher than relative risks due to any individual environmental factors. Without genetic contribution, schizophrenia cannot be explained. Risk to family members: In the attached chart 'parents' refer to one parent having schizophrenia, where the risk to the child is 13%. If both parents have schizophrenia, then the risk is 46% - close to monozygotic twin risk. The risk to a half sibling is 4%. Note that for the children and siblings of individuals with schizophrenia, the increase in risk is around 10-fold, but it is somewhat less than this in parents. This is probably 'explained by a reduction in the reproductive opportunities, drive, and possibly fertility of affected individuals' (Craddock et al. 2005).

□ Monozygotic (MZ) concordances = 41–65% □ Dizygotic (DZ) concordances = 0–28% □ Broad heritability = 80% □ The most frequent personality disorder in relatives of schizophrenia patients is schizotypal personality disorder (DSM)-nearly 15% can be diagnosed with it. □ Twin studies had shown significantly higher MZ concordance rates for schizophrenia when probands had hebephrenic or nonparanoid subtypes than paranoid subtypes.

□ Psychotic symptom dimensions consistently show only modest familial aggregation in affected sibling pairs, and rather weak and inconsistent relationships with the familial risk of psychoses. So the severity of schizophrenia is not directly associated with a family history or genetic loading.

Gene suspected in schizophrenia

Locus

NRG1 Neuregulin 8p12-p21 DTNBP1 dysbindin 6p22 G72 13q34 DAAO (interacts with G72) D amino acid oxidase 12q24 RGS4 Regulator of G protein signalling 4 1q21-22 COMT Catechol-o-methyl transferase 22q11 DISC1 Disrupted in Schizophrenia 1q42

Revision #1

Created 2026-01-04 20:03:27 UTC by Omar Ayman

Updated 2026-01-04 20:03:27 UTC by Omar Ayman