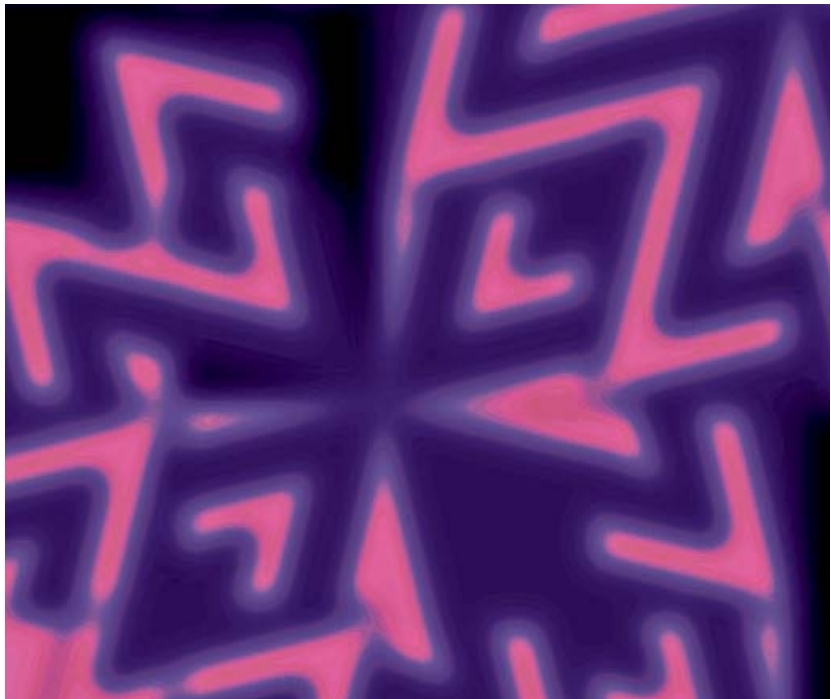


Fast Facts



Fast Facts: Schizophrenia

Shôn W Lewis and Robert W Buchanan
Third edition





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Declaration of Independence

This book is as balanced and as practical as we can make it.
Ideas for improvement are always welcome:
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Fast Facts: Schizophrenia

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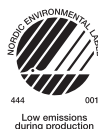
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Glossary of abbreviations

AMPA: α -amino-3-hydroxy-5-methyl-4-isoxazole propionic acid; a glutamatergic neurotransmitter

BOLD imaging: blood-oxygen-level-dependent imaging; magnetic resonance imaging that uses the natural paramagnetic properties of hemoglobin as it deoxygenates to produce an image of regional cerebral blood flow

CBT: cognitive-behavioral therapy

CPZE: chlorpromazine equivalent; the approximate dose equivalent to 100 mg of chlorpromazine (relative potency)

CSF: cerebrospinal fluid

CT: computed tomography

DTI: diffusion tensor imaging; a type of magnetic resonance imaging that allows visualization of white matter tracts

DUP: duration of untreated psychosis

DZ: dizygotic (of two fertilized eggs); dizygotic twins are non-identical

EPS: extrapyramidal side effects, e.g. akinesia, dystonia, akathisia and tremor

fMR: functional magnetic resonance; a means of imaging based on the same principles as BOLD imaging that can measure tiny metabolic changes in active areas of the brain

GPI: general paresis of the insane

MRI: magnetic resonance imaging

MZ: monozygotic (of one fertilized egg); monozygotic twins are identical

NMDA: N-methyl-D-aspartate

NMS: neuroleptic malignant syndrome; characterized by muscle rigidity, autonomic instability, fever and changes in mental status

PEG: pneumoencephalography; an old imaging technique based on the X-ray contrast of air injected into the lumbar subarachnoid space, bone and brain tissue

PET: positron emission tomography; a functional imaging technique used to measure glucose metabolism, regional cerebral blood flow or receptor occupancy

Potency: the quantity of a drug needed to have an effect

rCBF: regional cerebral blood flow

SPECT: single-photon emission computed tomography; functional imaging similar to, but less versatile than, PET

STG: superior temporal gyrus

TD: tardive dyskinesia; a major adverse effect associated with all conventional antipsychotics characterized by abnormal, involuntary movements; primarily affects the muscles of the tongue and face

VCFS: velocardiofacial syndrome; a genetic disorder characterized by palate and facial abnormalities, heart defects and various psychiatric symptoms

Introduction

Schizophrenia is a strange and often devastating disorder that starts in early life and can lead to lifelong disability. It is one of the major public health challenges.

Recent advances in research have given tantalizing insights as to the causes of schizophrenia, in particular the role of specific genes and psychosocial factors. How much do genes matter? Are psychological and social factors important? What about the effects of street drugs?

In this third edition of *Fast Facts: Schizophrenia* we cover what is new and promising in the understanding of risk factors, and cognitive and brain deficits. We also review new drug and non-drug treatment strategies, and consider the prospects these hold for better clinical and social outcomes.

Preclassical and classical descriptions

The earliest descriptions of symptoms associated with the diagnosis of schizophrenia date back to preclassical cultures. Such symptoms were then considered to be the manifestations of supernatural forces invading the individual, often as punishment for immoral behavior.

In ancient Greece and Rome, the focus for studying and understanding mental illnesses moved towards a naturalistic standpoint. Early Greek physicians described delusions of grandeur, paranoia and deterioration in cognitive functions and personality. These behaviors were attributed generally to disturbances among the associations of the four bodily humors: blood, yellow bile, black bile and phlegm.

Medieval times

In medieval times, particularly in Western societies, there was a return to the preclassical moralistic or superstitious perspectives on psychotic behavior. The classical models of illness were largely kept alive by Arab physicians, who practiced medicine according to the ideas of Hippocrates, Aristotle and Galen. These classical conceptualizations of psychosis went unchanged until the Renaissance.

The Renaissance

In Western cultures, the Renaissance led to a reemergence of interest in classical thought, with a reawakening of the conceptualization of mental illnesses, including psychoses, as naturalistic disorders. The first European psychiatric hospitals were established during this period. The 17th and 18th centuries saw an explosion of information about the workings of the body, which led to a more rational and scientific approach to diseases and the study of the mind. Organic etiologies of mental illness were adopted, and the initial descriptions and classifications of these disorders were attempted.

19th century

In the first part of the 19th century, the foundations for the modern concept of schizophrenia were established (Table 1.1). An early diagnostic system emerged and various mental illnesses were described, including epilepsy, melancholia, mania and the dementing psychotic

TABLE 1.1

Major landmarks in the development of the concept of schizophrenia

Haslam J, 1809	Published a treatise on a type of insanity that occurs in the young
Esquirol JED, 1838	Described the prognosis and long-term course of different forms of insanity
Morel BA, 1860	Described 'démence précoce' (dementia praecox), a progressive deterioration evolving quickly in young persons
Kahlbaum KL, 1863	Described a form of insanity characterized by abnormal posturing: 'catatonia'
Hecker E, 1871	Described a form of insanity characterized by onset in puberty, evolution through successive affective states, ultimately resulting in states of psychological weakness and mental deficiency: 'hebephrenia'
Kraepelin E, 1898–9	Grouped together as a single illness dementia praecox and the formerly separate entities hebephrenia, catatonia and paranoid psychosis. Distinguished dementia praecox from manic–depressive illness on the basis of disease course and long-term outcome
Bleuler E, 1911	Recognized that patients with dementia praecox did not always deteriorate, coined the term schizophrenia and described fundamental symptoms
Kasanin J, 1933	Introduced the concept of schizoaffective disorder
Langfeldt G, 1939	Introduced the concept of schizophreniform disorder
Schneider K, 1946 (translated 1959)	Proposed the existence of pathognomonic, or first-rank, symptoms

The biggest single clue we have about the cause of schizophrenia is that it often runs in families. Although this observation was made first in the opening years of the 20th century, until relatively recently it was disputed whether or not this family clustering was truly a genetic effect.

Classic studies

The most straightforward studies in population genetics are family studies. Usually, a series of schizophrenic individuals, known as probands or index cases, is selected and rates of schizophrenia are assessed in their biological families. These rates are compared with rates in the families of control probands, usually healthy volunteers. To express the results as rates, the number of affected relatives is divided by the total number and is age-corrected for relatives who either are too young to have the disorder or are not yet through the age range at highest risk.

The risk of schizophrenia in relatives depends first on how close the relative is to the proband (Figure 4.1). Spouses are at slightly increased risk because of assortative mating (i.e. selection of similar partners). The diagnostic system used affects the risk to relatives, as it does prevalence, and fewer relatives will be diagnosed with DSM-IV schizophrenia than with ICD-10 schizophrenia. Recent studies have shown an unexpected effect of sex. Relatives of female probands have higher rates of schizophrenia than relatives of male probands.

Family studies can never give conclusive proof of genetic effects, as familiarity could be due to a shared environmental factor. Nevertheless, family studies have shown that if there is a genetic effect, it does not follow a recognized Mendelian pattern of autosomal dominance, such as in Huntington's disease, or recessiveness, such as in cystic fibrosis.

Studies in twins and adopted children

Studies in twins involve probands with schizophrenia who are either identical (monozygotic: MZ) or non-identical (dizygotic: DZ).

Concordance rates in the two types of twins are compared by looking

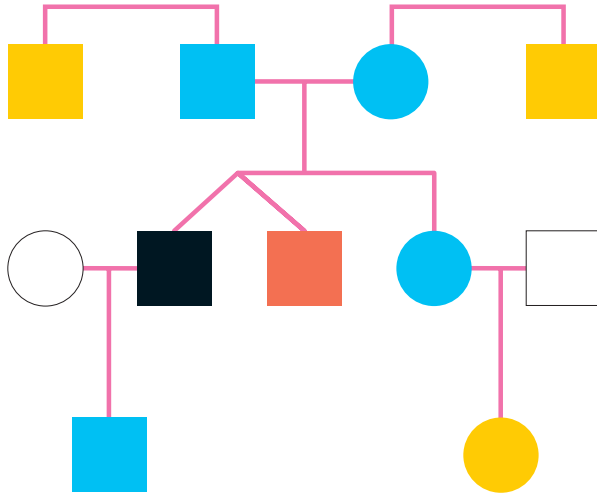


Figure 4.1 A genogram showing risk of schizophrenia in relatives. Proband (black); an identical twin (red) shares 100% of genes, risk 45%; a first-degree relative (blue) shares 50% of genes, risk 10%; a second-degree relative (yellow) shares 25% of genes, risk 3%.

at the rate at which co-twins also have schizophrenia. MZ twins share 100% of their genes and DZ twins share about 50%. The consensus from population-based studies is that concordance rates are about 45% for MZ co-twins compared with 15% for DZ co-twins. The fact that concordance is less than 100% in MZ twins suggests that non-genetic, environmental factors are also involved. However, the offspring of the unaffected MZ co-twins in discordant pairs also appear to be at increased risk of schizophrenia, suggesting that the co-twins still carry a genetic predisposition for the disease.

Adoption studies offer the most watertight evidence for genetic effects, as family environment is taken out of the equation. There are two types of study: follow-up and follow-back. Both methods have shown that it is biological parentage rather than adoptive parentage that predisposes to schizophrenia.

Follow-up studies trace the biological children of schizophrenic mothers, who were adopted into normal families at birth, and compare