MENTAL ILLNESS AND INHERITED PREDISPOSITION—schizophrenia and bipolar disorder

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FACT SHEET

58

Important points
- Conditions included under the ‘umbrella’ term of mental illness are schizophrenia and bipolar disorder (manic depression)
- The genetic basis is an inherited predisposition to develop the condition

The schizophrenias
- The chance that anyone in the population will develop schizophrenia is about 1% (ie. 1 chance in 100)
- Where there is a family history, risks for family members of developing schizophrenia increase with the number of affected relatives and their degree of relatedness
- Symptoms include psychotic episodes; there may also be disorganisation of thoughts and feelings and social withdrawal
- It is likely that several different genes are involved, perhaps causing susceptibility to different forms of schizophrenia. Several genes have been identified to date
- The environmental factors that trigger the condition remain unknown but may include pregnancy complications and problems during delivery, recreational drug use such as cannabis and methamphetamine (also called speed or ice)

Bipolar disorder
- Formerly called manic depression, it is a disorder of mood and is characterised by major mood swings: generally fluctuating from ‘high mood’ (mania) to ‘low mood’ (depression)
- The chance that anyone in the population will develop bipolar disorder is about 2-3% (ie. 2-3 chances in 100)
- Where there is a family history, risks for family members of developing bipolar disorder increase with the number of affected relatives and their degree of relatedness
- There are several forms of bipolar disorder characterised by the severity of the depression and/or mania. Several different genes are thought to be associated with bipolar disorder in different families
- The environmental factors that trigger the condition are still largely unidentified
- Predictive genetic testing is not available to determine if a family member is at risk of developing schizophrenia or bipolar disorder
- Currently risks for developing the condition are based on data collected on many families.

A number of conditions that affect the way a person thinks, feels and acts are grouped under the ‘umbrella’ label of mental illness. Most mental illnesses can be treated.

The conditions include:
- Depression
- Anxiety
- Personality disorders
- Schizophrenia
- Bipolar disorder (manic depression)

The chance that anyone in the population will develop a form of mental illness such as schizophrenia and bipolar disorder during a lifetime is:
- 1 or 2 in 100 (1% - 2%)
- The same regardless of socioeconomic level, occupation, ethnicity, culture and intelligence
- Higher than the general population risk where there is a family history of these mental illnesses

Recent research has highlighted the genetic basis of some forms of schizophrenia and manic depression.

This Fact Sheet deals only with the genetic basis of these two forms of mental illness.

The schizophrenias
Just as the term mental illness is an ‘umbrella’ for a number of different conditions, the term ‘schizophrenias’ is used because there is likely to be a number of different conditions under this ‘umbrella’.

There is a wide variety of symptoms and not all people diagnosed with the condition always exhibit all the symptoms which usually first appear in late adolescence or early adult life.

Symptoms always include a psychotic episode(s) that include losing touch with reality, hallucinations, delusions, and paranoia. They may also include disorganisation of thoughts and feelings and social withdrawal.

Clues to the genetic basis of schizophrenia

Many studies have demonstrated that schizophrenia can run in families.

The evidence that heredity plays a role in the development of some forms of schizophrenia has come from studying identical twins and other family situations.

- If an identical twin (monozygotic twin) develops schizophrenia, then the chance that the other twin will also develop it is 1 chance in 2 (ie. 50%)(see Table 58.1)
- This genetic involvement has been confirmed by studying identical twins who were raised separately (therefore not sharing the same environment) as well as studying adopted children of mothers with schizophrenia
- Risks for family members of developing schizophrenia increase with the number of affected relatives and their degree of relatedness (see Table 58.1)

Inherited predisposition and schizophrenia

Our genes, that are part of chromosomes, provide the information for our bodies to grow and develop, and to work properly throughout our life (see Genetics Fact Sheet 1). When the information in the genes is changed in some way, the information sent to the cells may be different.

Inherited predisposition means that a person has inherited from a parent one or more gene copies containing variations in the information that do not cause a problem directly.
Environmental factors

Twin studies show that genes are not the only factor influencing the development of schizophrenia.

- Where one twin of a non-identical twin pair ( dizygotic twins; fraternal twins) develops schizophrenia, there is only about a 15% chance or 15 chances in 100 that the other twin will also develop the condition.
- While this is higher than for the general population who have about 1 chance in 100 (1%) of developing the condition (see Table 58.1), it suggests that environmental factors are involved and interact with a genetic susceptibility.

The environmental factors are still largely unidentified but research suggests that they may include pregnancy complications and problems during delivery and recreational drug use such as cannabis and methamphetamine (also called speed or ice).

Bipolar disorder

Bipolar disorder, which used to be referred to as manic depression, is a disorder of mood and is characterised by major mood swings.

- A person with the condition will experience periods of intense activity (termed mania) and other periods of feelings of hopelessness (termed depression).
- The mood swings appear to occur spontaneously, without any obvious external cause. The pattern of ‘highs’ and ‘lows’ can occur repeatedly with little or no breaks between each episode or may occur periodically between long periods when the person shows no symptoms. There are several forms of bipolar disorder including:
  - **Bipolar disorder type 1** (classical form of the condition) in which affected individuals develop extreme forms of mania, lose touch with reality, often become psychotic and have delusions and hallucinations. This condition is quite severe and often leads to hospitalisation.
  - **Bipolar disorder type 2** is characterised by a milder form of mania (termed hypomania). While the individual with this condition can have periods of extreme excitability, have excessive energy, often lose their inhibitions and have impaired judgment, they do not experience hallucinations nor do they become psychotic.

There are not such major differences in the symptoms of depression between the two types of the condition but it is important to note that it is estimated that about 10% of people with the disorder do not experience the depression and just express the mania.

As for schizophrenia, many studies have shown that bipolar disorder can run in families.

Clues to the genetic basis of bipolar disorder

The evidence that heredity plays a role in the development of some forms of bipolar disorder has come from studying identical twins and other family situations.

- If an identical twin develops bipolar disorder, then the chance that the other twin will also develop it is 40%-70% or approximately a 1 chance in 2 (see Table 58.1).
- This genetic involvement has been confirmed by studying identical twins who were raised separately (therefore not sharing the same environment) as well as studying adopted children of mothers with schizophrenia.

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**Table 58.1:** Approximate familial risks in schizophrenia and bipolar disorder for close blood relatives of an affected person (not related by marriage). [Second degree relatives: aunts, uncles, nephews, nieces or grandparents]

<table>
<thead>
<tr>
<th>Affected relative</th>
<th>Risk for developing the condition (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Schizophrenia</td>
</tr>
<tr>
<td>No close relative (general population risk)</td>
<td>1</td>
</tr>
<tr>
<td>Identical twin (monozygotic)</td>
<td>40-50</td>
</tr>
<tr>
<td>Both parents</td>
<td>45</td>
</tr>
<tr>
<td>Brother/sister and one parent</td>
<td>15</td>
</tr>
<tr>
<td>Parent</td>
<td>13</td>
</tr>
<tr>
<td>Non-identical twin (dizygotic)</td>
<td>10</td>
</tr>
<tr>
<td>Brother/sister</td>
<td>9</td>
</tr>
<tr>
<td>Second-degree relative</td>
<td>3</td>
</tr>
<tr>
<td>First cousin</td>
<td>1-2</td>
</tr>
</tbody>
</table>

Abnormal chromosome regions

### Chromosome 1

- **1p:** hypocomplex (resulting in hypofunction of a gene involved in brain development) is associated with some forms of bipolar disorder.

### Chromosome 6

- **6p:** abnormalities are associated with some forms of bipolar disorder.

### Chromosome 13

- **13q:** abnormalities are associated with some forms of bipolar disorder.

### Chromosome 22

- **22q:** the gene designated as G72, located on the long arm of chromosome 22, is associated with some forms of bipolar disorder.

It appears that there is also an increased risk for having a child affected by schizophrenia at some time in their life if their father was aged over 50 when they were born.

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Genes, inherited predisposition and bipolar disorder

The genetic contribution is likely to interact with other factors such as environmental influences to trigger the condition.

Genes

The evidence for the exact role of genetics in bipolar disorder is still accumulating. Genes thought to be associated with bipolar disorder in different families are located on several different chromosomes.

- A gene called Fat, located on chromosome 4, which has an important role in the brain. People with a variation in this gene appear to be at twice the risk of developing bipolar disorder, though it is not yet clear exactly why.
- Variations in a gene called Slynar, located on chromosome 12, which is also active in the brain but of unknown function.
- Variations in a gene located on the long (q) arm of chromosome 18 (18q) have also been linked to bipolar disorder type 2.

Environmental factors

Heredity is not the only factor influencing the development of bipolar disorder.

- Where one twin of a non-identical twin pair (fraternal twins) develops bipolar disorder, there is only about a 20% chance or 20 chances in 100 that the other twin will also develop the condition.

- While this is higher than for anyone in the general population who has about 2-3 chances in 100 of developing the condition (see Table 58.1), it suggests that other environmental factors are involved, and interact with a genetic predisposition.

These environmental factors however, are still largely unidentified.

Is predictive genetic testing possible to determine if a family member is at risk of developing schizophrenia or bipolar disorder?

Genetic testing is not available.

It will still be some years before it is possible to translate these findings into being able to predict who in a family is at increased risk for developing these forms of mental illness, when one or more family members have the condition.

Currently risks for developing the condition are based on data collected on many families (see Table 58.1).

Genetic counselling can assist in providing current information about the genetic basis of the condition to the family so that risks for the condition in other family members can be estimated correctly (see Genetics Fact Sheet 3).

Other Genetics Fact Sheets referred to in this Fact Sheet: 1, 3, 11

Information in this Fact Sheet is sourced from:


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