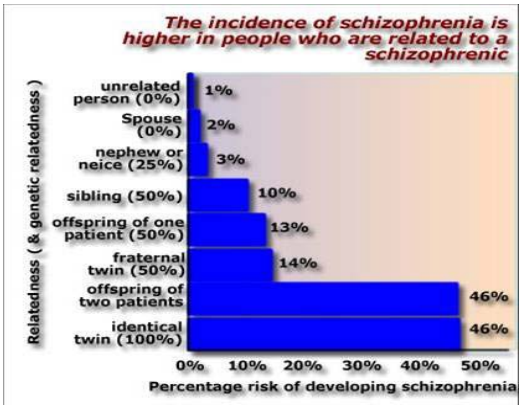
BIOLOGICAL EXPLANATIONS OF SCHIZOPHRENIA

These explanations come from the **biological approach** to abnormality. They focus on **genetics**, **brain biochemistry**, and **neurodevelopmental influences** (i.e. **brain damage**).

Genetics and schizophrenia

Schizophrenia is a disorder that tends to run in families. **Family resemblance studies** tell us that our 'lifetime chance' of developing the condition (if there is no family history of it) is around 0.2-2% (i.e. the population incidence). However, if we have *one schizophrenic parent*, the chance is around 13%, and if both parents are schizophrenic it rises to 46% (see below).



These data comes from **retrospective studies**. Unfortunately, retrospective studies depend on people's memory and/or recorded data from schools, hospitals, etc, which is not always reliable. However, **prospective studies** have confirmed this greater familial 'risk'. For example, the **Copenhagen High-Risk Study** looked at children born in 1962, who could be classified as either 'low risk' (neither biological parent was schizophrenic) or 'high risk' (one or both parent was schizophrenic).

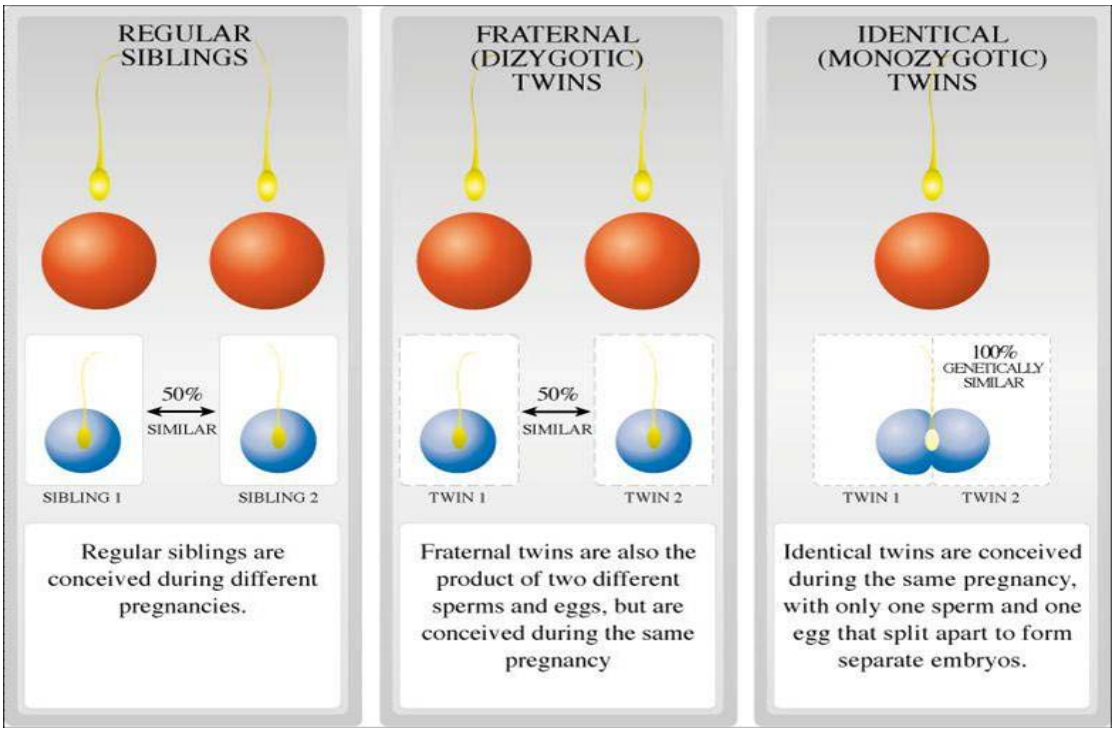
The children were 10-18 at the start of the study, and were matched on age, gender parental socioeconomic status, and residence, all of which are known to be risk factors in schizophrenia. Therefore, any difference between the 'low risk' and 'high risk' groups can probably be explained in terms of differences between their parents (i.e. whether they were schizophrenic or not).

The data indicate that the incidence of schizophrenia in the 104 'low risk' children is 1.9% (which is the same as the population incidence in Denmark). However, for the 207 'high risk' children the incidence is 16.2%. This supports the idea that genetic factors play a role in schizophrenia.

A similar study (the **New York High-Risk Project**) has reported similar findings after a 25 year follow-up. However, by way of evaluation, we should note that the main weakness of these family resemblance studies is that families tend to *share environments*, so we don't know how much genes and the environment are each contributing.

One study which has tried to control for the role of the environment is the **Israeli High-Risk Study** (1967 - onwards). This looked at the incidence of schizophrenia in children of schizophrenic parent(s) raised in their own *family environment*, and those raised in a *kibbutz*. The research shows that when the effects of the environment are controlled for, 'high-risk' children are still more likely to develop schizophrenia than 'low-risk' children.

Another methodology is the **twin study**. Monozygotic (or identical) twins (MZs) share identical genes. Therefore, if one twin develops schizophrenia, and schizophrenia is genetic, the other twin should develop the condition as well.



The key measure in twin studies is the **concordance rate (CR)**, which is defined as **the probability that a second twin will develop a disorder given that the first twin already has**. The higher the concordance rate, the more likely it is that genetic factors are involved. The lower the concordance rate, the more likely it is that environmental factors are involved. The table below shows data obtained from several studies conducted in several countries (and the concordance rate is expressed as a percentage). Note that at this point, only the data relating to MZ twins is relevant. The data relating to DZ (non-identical) twins will be dealt with later.

Study	'Narrow' concordance*		'Broad' concordance*	
	% MZs	% DZs	% MZs	% DZs
Rosanoff *et al.* (1934); USA (41 MZs, 53 DZs)	44	9	61	13
Kallmann (1946); USA (174 MZs, 296 DZs)	59	11	69	11–14
Slater (1953); England (37 MZs, 58 DZs)	65	14	65	14
Gottesman and Shields (1966); England (24 MZs, 33 DZs)	42	15	54	18
Kringlen (1968); Norway (55 MZs, 90 DZs)	25	7	38	10
Allen *et al.* (1972); USA (95 MZs, 125 DZs)	14	4	27	5
Fischer (1973); Denmark (21 MZs, 41 DZs)	24	10	48	20

* 'Narrow' based on attempt to apply a relatively strict set of criteria when diagnosing schizophrenia. 'Broad' includes 'borderline schizophrenia', 'schizoaffective psychosis', 'paranoid with schizophrenia-like features'.

The data from these seven studies (which looked at 447 MZ pairs), show that the concordance rates range from 14-65% for 'narrow range' (mean = 46%) and 27-69% for broad range (mean = 52%). For at least some researchers, these concordance rates suggest that genetic factors do play a role in schizophrenia.

However, the problem with the data above is that it comes from MZs who have been brought up in the *same environment* (especially in the womb!). So, even if the concordance rate was very high, we couldn't be sure how much of it was being caused by genes, and how much by the environment. One way around this is to look at the concordance rate for schizophrenia in identical twins that have been **separated at (or shortly after) birth**

and reared in completely different environments. Under these circumstances, **Gottesman & Shields (1982)** found a concordance rate of 58%. However, the main issue with this sort of study is that of sample size. In this kind of study, the chances of someone being an identical twin, who was separated at birth, and then went on to develop schizophrenia, is bound to be small. Gottesman and Shields' study is based on a sample size of only 12, which is hardly big enough for any firm conclusions to be drawn.

An alternative methodology which tries to control for the role of the environment involves looking at the development of schizophrenia in children of schizophrenic parents who have been **adopted and raised in a non-schizophrenic environment** (the Israeli High-Risk Study referred to previously kind of uses this methodology, but the children in that study are not adopted). One of the major studies in this area is **The Finnish Adoption Study**, which began in 1969.

All of the adopted children in this study (both 'low risk' and 'high risk') ranged in age from 5 to 7, and had been separated from their mothers before the age of 4. The incidence of schizophrenia in 'low-risk' children raised in an adoptive home is 1.1%. However, the incidence of schizophrenia in 'high-risk' children raised in an adoptive home is 10.3%, which also supports the idea that genetic factors play a role in schizophrenia.

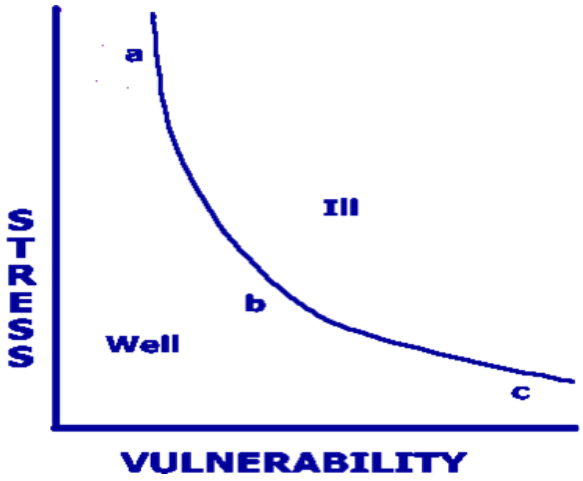
Sample size is not an issue in these studies. However, a reanalysis of the data showed that only children who were adopted into families with *poor communication* were at an increased risk of developing schizophrenia. This is important because at least some researchers see the family as playing an important role in the development of schizophrenia (see Psychological explanations of schizophrenia).

Yet another methodology is to **compare the concordance rate** in identical (MZ) and non-identical (dizygotic or DZ) twins. Any kind of twin pair (MZ or DZ) usually live in (or share) the same environment. However, whilst identical twins also share genes, non-identical twins do not. So, if genetic factors are involved, the concordance rate should be higher in MZs than DZs. If you refer back to the table on page 3, it clearly is the case that the concordance rate is consistently higher for MZ twins.
Recall that for MZ twins the average concordance rate is 46% (narrow range) and 52% (broad range). For DZ twins, the average concordance

rate is 10% (narrow range) and 13% (broad range). Thus, a person is around three times more likely to develop schizophrenia if s/he is an identical twin whose twin pair develops the condition than if s/he is a non-identical twin whose twin pair develops the condition. Again, this is taken as good evidence that genetic factors play a role in schizophrenia.

Note that in all of the above research, the concordance rate is *lower* than the theoretically expected 100%, leaving plenty of scope for environmental factors. Additionally, whilst it is generally accepted that there is a genetic influence in schizophrenia, there is no strong evidence concerning the gene or genes involved.

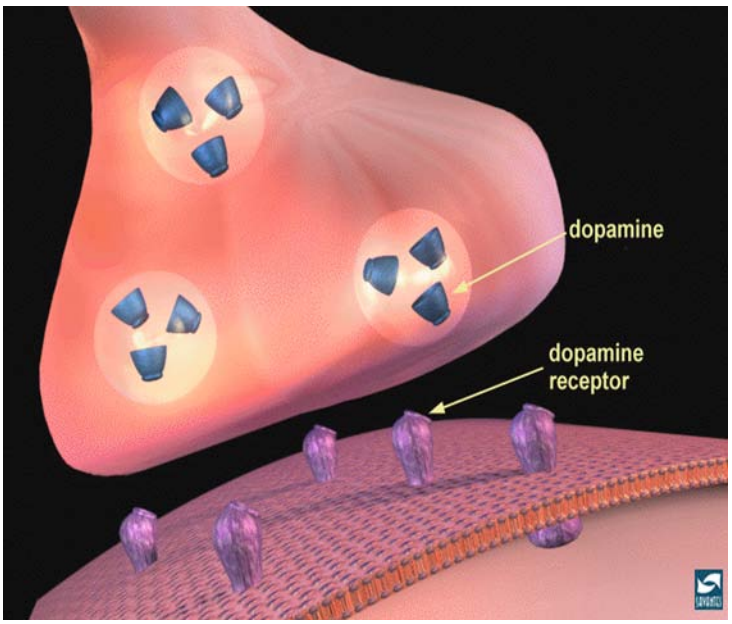
More recent research has looked at the **gene-environment interaction** in schizophrenia. The proposal here is that schizophrenia could be a result of an interaction between **genetic predisposition** and **environmental sensitivity**. This is called the **diathesis-stress model**, and proposes that all of us have some degree of biological vulnerability (*diathesis*) to schizophrenia. If environmental *stressors* (e.g. critical life events) are sufficient to 'trigger' this vulnerability, then schizophrenia occurs. If they are not, it doesn't. This can explain why schizophrenia is more likely to develop at some ages rather than others, and why some people who have a family history of schizophrenia do not develop the condition.



Brain biochemistry and schizophrenia

If genetic factors are important, they are likely to exert their influence through brain biochemistry. The clinical characteristics of schizophrenia share *some* similarities with the effects of hallucinogenic drugs. In the 1950s, studies found presence of the hallucinogen DMT in the urine of schizophrenics. It was also found that when DMT levels increase, the symptoms are more severe. This led to the **inborn-error of metabolism hypothesis**, which says that some people inherit a metabolic error that causes the body to break down naturally occurring chemicals into toxic ones, and this causes schizophrenia.

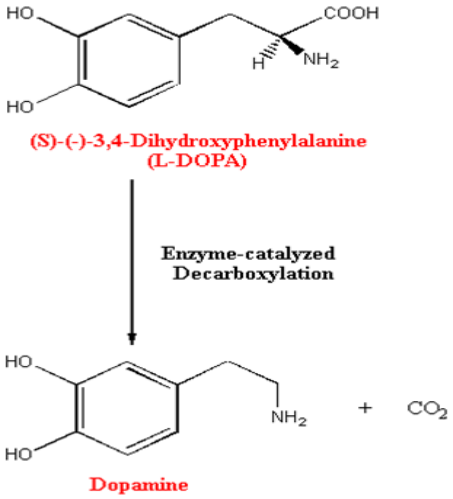
The main weakness of this hypothesis is the actual *lack* of similarity between schizophrenic symptoms and effects of hallucinogens. However, there are structural similarities between certain hallucinogenic drugs and **neurotransmitters** that are found in the brain. One of these neurotransmitters is **dopamine**.



Post-mortem studies conducted by **Iverson (1979)** indicated that dopamine is *more concentrated* in the schizophrenic brain, especially in the limbic system. According to the **dopamine theory of schizophrenia**, schizophrenia is a result of:

- Dopamine **over-production** by the brains of schizophrenics
- More dopamine being **utilised** by the brains of schizophrenics
- More dopamine **receptors** in the brains of schizophrenics

Whichever of these is true, there is a large body of evidence to support the dopamine theory of schizophrenia. For example, drugs that are used to treat schizophrenia are highly effective, and they work by blocking dopamine receptor sites. Additionally, the drug that is used to treat Parkinson's disease works by increasing dopamine levels in the brain. Parkinson's disease is a result of the under-production of dopamine in parts of the brain that need it. The drug, which is called L-DOPA, is converted to dopamine, and is highly effective in reducing the symptoms associated with Parkinson's disease. However, too much of it induces schizophrenic-like symptoms in sufferers of Parkinson's disease.



Finally, the recreational drugs **cocaine** and **amphetamine** indirectly stimulate dopamine receptors, and (a) induce a schizophrenic-like disorder or (b) exacerbate symptoms in schizophrenics.

However, we cannot accept the dopamine theory completely, because there are at least three criticisms we can make of it. First, dopamine may not be the only neurotransmitter involved. So-called atypical anti-schizophrenic drugs are also effective in treating schizophrenia, but they *seem* to work by blocking **serotonin receptors** rather than dopamine receptors.

Second, it is possible that schizophrenia may interfere with dopamine production, that is, rather than being a *cause* of schizophrenia, alterations in the amount of brain dopamine may be a *result* of schizophrenia. However, given the effect of increasing dopamine levels in sufferers of Parkinson's disease, this seems unlikely.

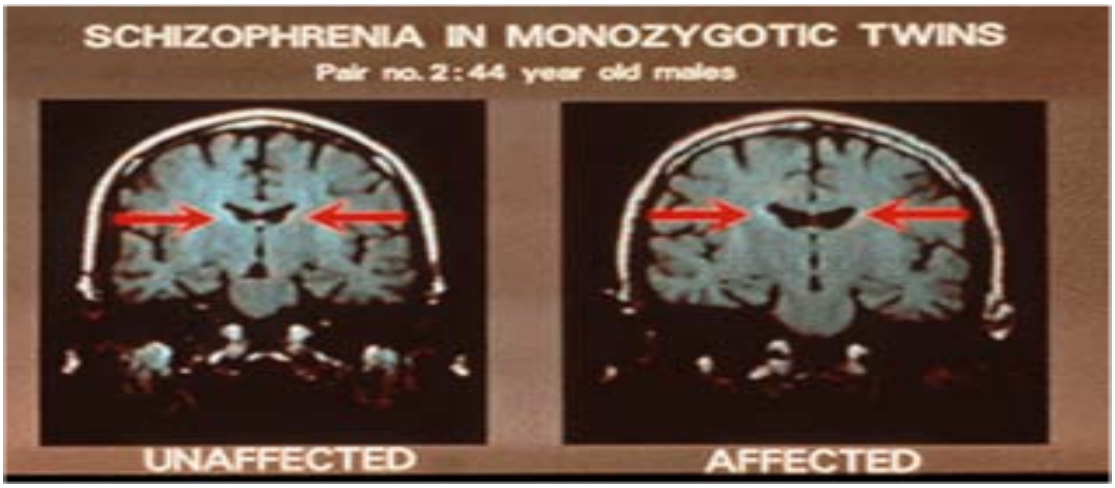
Third, although the anti-schizophrenic drugs are 'generally' very effective, they do not have a noticeable effect on at least some schizophrenics, even though they are exerting the same biochemical effect as with those schizophrenics for whom the drugs are effective.

Notwithstanding these criticisms, most psychologists accept that dopamine plays some role in the development of schizophrenia, even if that role is not entirely clear.

Neurodevelopmental influences (brain damage) and schizophrenia

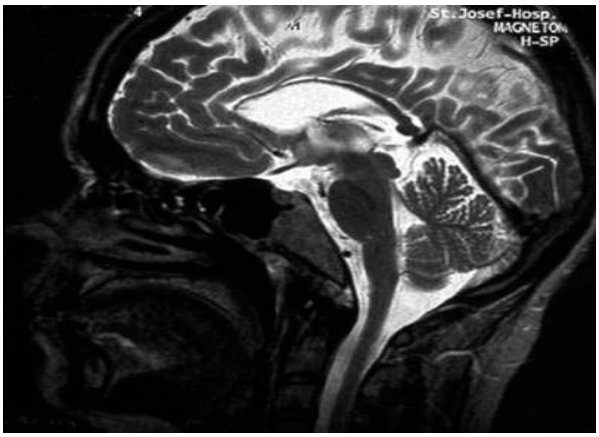
Schizophrenia is what is called a **heterogeneous condition**, that is, there are several different sub-types each of which is dominated by particular characteristics. Research conducted by **Crow (1995)** showed that anti-schizophrenic drugs were very effective in treating the more exotic symptoms (so-called **positive** or **Type 1** symptoms), but much less effective at treating symptoms like emotional disturbances and a lack of drive (**negative** or **Type 2** symptoms). This finding has led to the proposal that there might be *more than one cause of schizophrenia*: 'Type 1 schizophrenia' is probably caused by dopamine, whereas 'Type 2 schizophrenia' may be a result of **brain damage**.

MRI studies suggest several structural differences in schizophrenic brains. One of these is enlargement of brain **ventricles**, the fluid filled chambers that bathe the brain and supply it with nutrients:

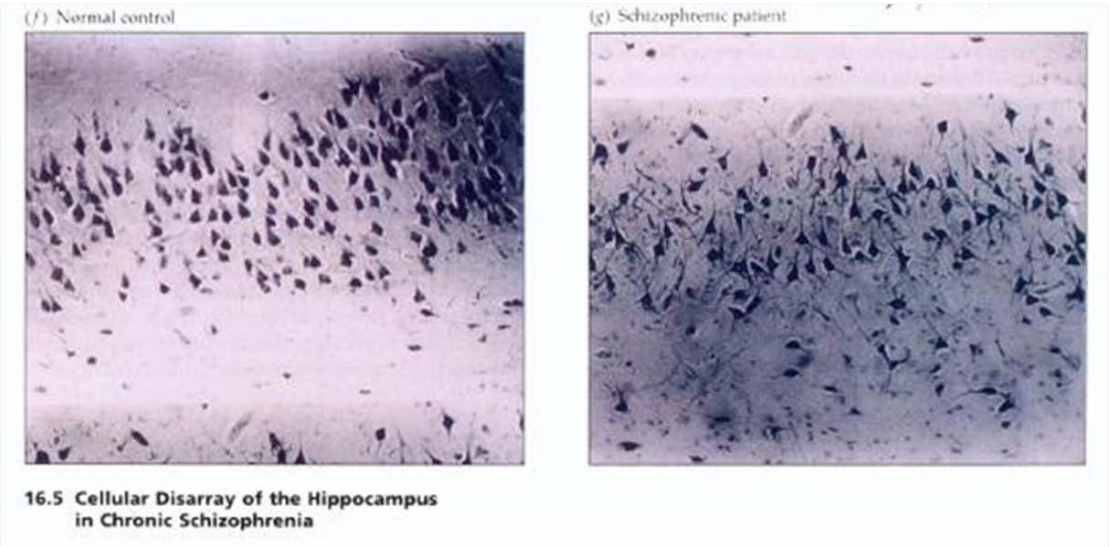


Loss of brain volume associated with schizophrenia is clearly shown by magnetic resonance imaging (MRI) scans comparing the size of ventricles (butterfly shaped, fluid-filled spaces in the midbrain) of identical twins, one of whom has schizophrenia (right). The ventricles of the twin with schizophrenia are larger.

Another structural difference concerns the **corpus callosum**. This structure ordinarily consists of around 250 million fibres that enable the left hemisphere of the brain to exchange information with the right half. In non-schizophrenics, it is uniformly dense. However, in schizophrenics, it is thinner at the front of the brain than at the back. Presumably, there are fewer connections, which means that information would be exchanged less effectively, and this could be a cause of schizophrenia:



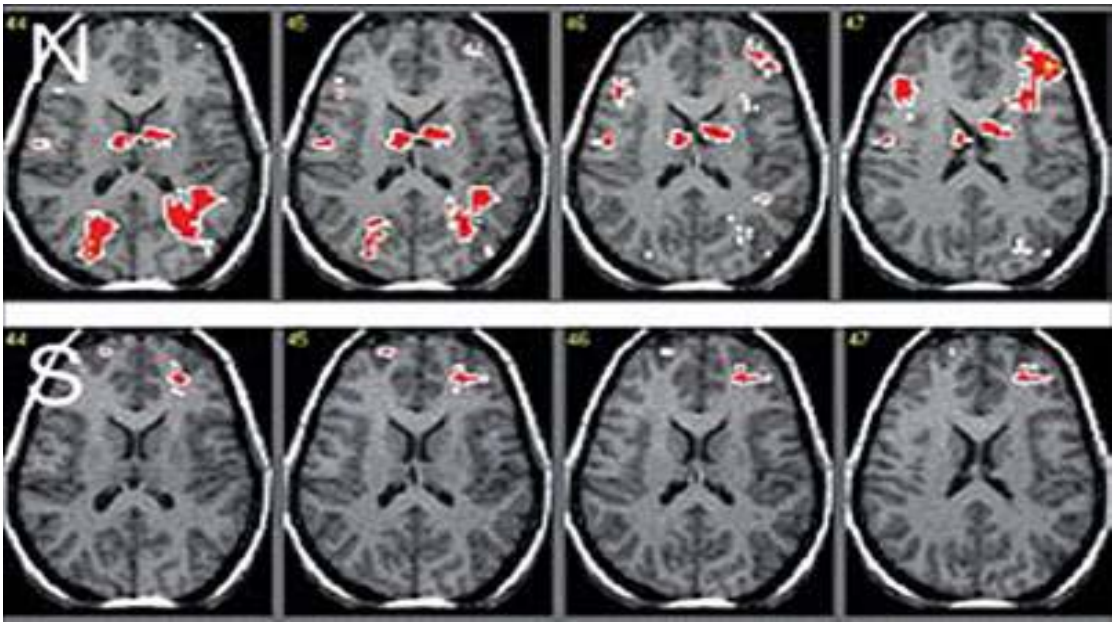
A third structural difference that has been found is in the **hippocampi**. These structures are involved in transferring our conscious experiences into long-term memory. In schizophrenics, there is considerable cellular disarray, which might cause disturbances in the way information is processed and passed into long-term memory, and these disturbances manifest themselves as schizophrenia:



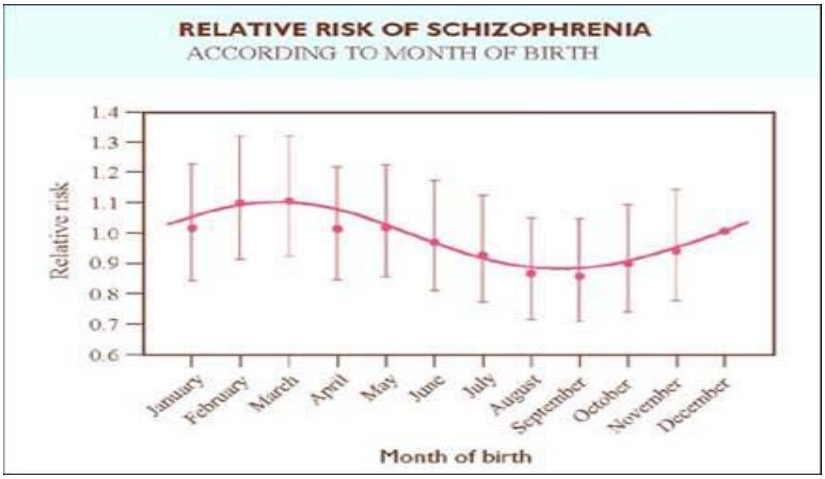
16.5 Cellular Disarray of the Hippocampus in Chronic Schizophrenia

Finally, it has also been found that there is decreased brain activity in schizophrenics (S) compared with non-schizophrenic controls (N) when people are asked to do particular tasks. The picture below is from an

fMRI study examining executive functioning (e.g. asking a person to think about how they would organise somebody's birthday party). The red areas indicate heightened cortical activity:



We should, however, note that some of the findings regarding structural differences have not always been consistent, and it has been argued that the differences could be a *result* rather than a cause of schizophrenia. That said, it has been known since the late 1920s that an overwhelmingly high proportion of people diagnosed with schizophrenia, especially in the northern hemisphere, are born in the late winter and early spring. This has been called the **season of birth effect**. Research shows that this effect has remained constant in England and Wales over the latter half of the twentieth century.

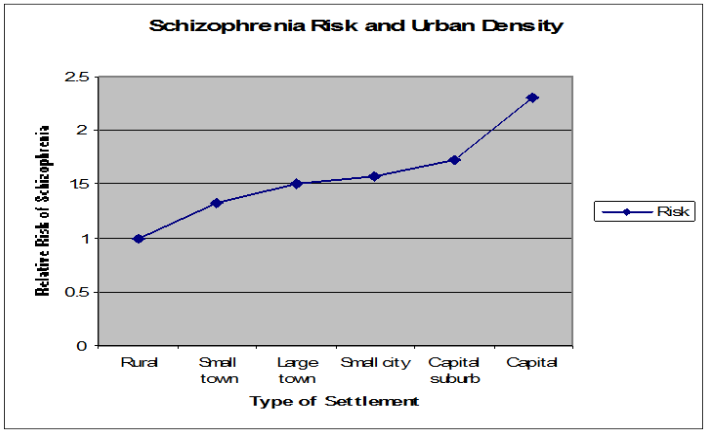


Although brain damage can occur at any time, researchers have been particularly interested in the possibility that schizophrenia may be a result of brain damage occurring pre-natally (i.e. during foetal development). One of the most widely researched possibilities is that schizophrenia is a result of pregnant mothers being infected during pregnancy with a **virus**.

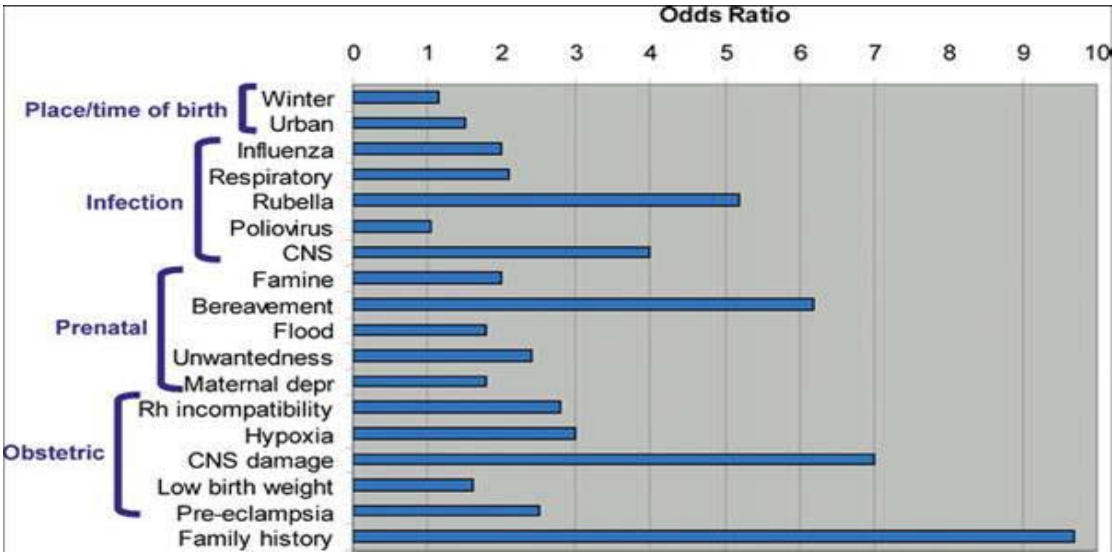
A number of maternal viral infections have been proposed. These include measles, scarlet fever, polio, diphtheria, pneumonia, and, especially, influenza A. It is believed that the 25- to 30-week foetus is most vulnerable because of the accelerated cortical growth that occurs at this time. This could explain the season of birth effect.

The viral agent is argued to enter the foetal brain and gestate until it is activated by either hormonal changes in puberty or another viral infection. Alternatively, there may be a gradual degeneration of the brain which eventually becomes so severe that the characteristics of schizophrenia emerge. This hypothesis could explain why there are structural abnormalities in the schizophrenic brain.

However, according to **Hare (1983)**, the incidence of schizophrenia increased in the nineteenth century with urbanisation, which precipitated many infectious diseases. With urbanisation came more hospitals, and in turn more detected cases of illnesses in general. So, the figures may simply reflect diagnostic statistics rather than more actual cases of schizophrenia. **Marcelis et al. (1998)** have found a high positive correlation in the Netherlands between urban birth and later development of schizophrenia. However, they prefer to explain this finding in terms of social factors (such as stress, divorce, noise, pollution and crime) rather than viral factors.



Although the 'season of birth' effect is well-established, it is not clear that it is best explained in terms of a 'maternal virus'. Indeed, there are a number of equally attractive alternative explanations for it. For example, it could simply be the case that people who are likely to produce schizophrenic offspring are more likely to try and have a baby at certain times of the year rather than other times.



The diagram displays the increased relative risk (or "odds ratio") that is associated with some of the more well-researched environmental factors (family history/genetics is included for comparison) that have been linked with schizophrenia. In this diagram, the "odds ratio" represents the relative increase in risk associated with schizophrenia, where a "1" is average. So, a child born during the winter months (January through March/April, in the Northern hemisphere) has about a 10% higher risk of schizophrenia than average. A person born in an urban environment has about a 50% (with an odds ratio of 1.5) higher risk of developing schizophrenia.