The dopamine hypothesis suggests that dopamine over-activity causes schizophrenia. Dopamine over-activity could happen in one of the following ways:

* + Too much dopamine
	+ Too much dopamine and not enough norepinephrine
	+ Over activity of dopamine receptors

**Too much dopamine?**

During the 1970s a popular theory was that an excess of the neurotransmitter dopamine caused schizophrenia. This was based on observations that an overdose of amphetamine causes schizophrenia like symptoms in normal participants (e.g., Snyder et al., 1974) and when given to schizophrenic patients, amphetamines tend to exaggerate their symptoms (Snyder et al., 1974). Amphetamines enhance the synaptic activity of dopamine (Snyder, 1976).

**Too much dopamine and not enough norepinephrine?**

Wise & Stein (1973) proposed that a lack of the enzyme that converts dopamine to norepinephrine causes schizophrenia. This results in too much dopamine and not enough norepinephrine. This is a plausible theory because norepinephrine is involved in the brain's reward system; so low levels of norepinephrine in the reward centres of the hypothalamus may lead to a malfunctioning of the reinforcement system, which could account for symptoms of anhedonia. Anhedonia is the inability to feel pleasure from activities  or events that normally cause pleasure.

More evidence in support of this model comes from findings that catecholamines, such as dopamine and norepinephrine, modulate certain cognitive functions (Foote et al., 1975). For example, Foote et al., (1975) found that application of norepinephrine to the cells in the auditory cortex of squirrel monkeys increased the rate of firing of stimulus specific cells (neurons that are firing in response to a real sound) relative to background cell activity. This could account for the auditory hallucinations experienced by those with schizophrenia as they may be failing to discriminate between external stimuli and the background activity of their brain.

A problem with the norepinephrine-under-activity/dopamine-over-activity theory, however, is that the antipsychotic medication clozapine works by blocking norepinephrine receptors, i.e. reducing the activity of norepinephrine. If a deficit of norepinephrine were a factor in schizophrenia it would be expected that clozapine would make the symptoms worse, not better.

 **Overactivity of dopamine receptors?**

An alternative theory suggests that it is the over-activity of a particular type of dopamine receptor (D2) rather than too much dopamine that leads to schizophrenia. The reasoning behind this theory is that:

* + Phenothiazines which are used to treat schizophrenia block dopamine receptors (Iverson, 1975)
	+ A number of different dopamine receptors have been found. These have been labelled D1 – D5 (Kebabian & Calne, 1972)
	+ The effectiveness of the phenothiazines is highly correlated to the extent to which they bind to D2 receptors
	+ The extent to which they bind to other dopamine receptors is not correlated (Peroutka & Snyder, 1980).

It may be, therefore, that the D2 receptors in the brains of schizophrenia patients are over-active. If it was too much dopamine that was responsible for schizophrenia then other receptors would be affected. This is supported by studies that show that there is no more dopamine in the brains of schizophrenics than normal participants.

Moreover, researchers have found a larger than usual number of dopamine receptors in the autopsied brains of schizophrenics. While this could be due to the use of antipsychotic medication, Strange (1992) has found increased dopamine receptors in the autopsied brains of schizophrenics who have never taken antipsychotic medication.

This theory, however, is weakened by the fact that clozapine does not bind very strongly to D2 receptors, yet is highly effective as a treatment for schizophrenia. Clozapine binds to half of the D1 receptors and half the D2 receptors. It also has a high affinity for blocking serotonin receptors, as well as norepinephrine, histamine and D4 receptors (Mackay, 1994). This suggests that schizophrenia may involve multiple neurotransmitter abnormalities.