Potential Causes of Schizophrenia

by Richard H. Hall, 1998

DA Hypothesis

The most popular explanation for the cause of schizophrenia at the neurotransmitter level is the **dopamine hypothesis**, which follows logically from the pharmacological treatment of the disorder. In it's most current form the dopamine hypothesis is that schizophrenia is due to overactivity of DA_3 and DA_4 receptors in the Mesolimbic pathway, since drugs that decrease dopamine activity in this specific pathway often alleviate the symptoms of schizophrenia. Although this theory certainly seems plausible given the dramatic effect of drugs like Clozapine, there are a number of qualifications and limitations that must be added to the theory. First, there is limited evidence, from studies of decreased schizophrenics, that they actually have more dopamine or dopamine receptors in their brain. Second, some schizophrenics are not helped by drugs that increase dopamine levels. Third, the drugs do not affect negative symptoms. At the very least the dopamine hypothesis is incomplete. The complete explanation is almost certainly more complex.

Brain Damage

The most popular theory for the causes of negative symptoms of schizophrenia is the that they are the result of some sort of structural damage in the brain. The first piece of evidence that supports this is the fact that, while positive symptoms are unique to schizophrenia, negative symptoms are similar to other neurological disorders that result from brain damage. For example, symptoms such as catatonia, the absence of a blink reflex, speech arrest, and poor visual pursuit are common symptoms for schizophrenics and for patients that suffer from brain damage. Second, autopsies of deceased schizophrenics and CT scans indicate that schizophrenics have larger ventricles than controls. Ventricles are cavities in the brain through which cerebral spinal fluid flows, so larger ventricles is an indication of tissue loss.

There is evidence that the primary locus of the damage that is most important in schizophrenia is in the prefrontal cortex. Those diagnosed with schizophrenia perform very similarly to patients with frontal lobe damage on a card sorting task. Further, brain imaging techniques indicate that schizophrenics show a characteristic low level of activity similar to those with frontal lobe damage, and in contrast to control subjects, when performing this card sorting task. This **hypofrontality** theory of schizophrenia appears diametrically opposed to the dopamine hypothesis, which is essentially a "hyperdopamine" theory. However, one potential explanation for how these two phenomena may work together relies on the concept of supersensitivity introduced in the module on *Pharmacological Treatment of Schizophrenia*. There is a pathway, rich in glutamate neurons, that runs from the prefrontal cortex to the ventral Tegmental area, which regulates the release of dopamine in the Mesolimbic pathway. This low level of glutamate activity in the frontal lobe would presumably lead to lower **basal release** of dopamine in the Mesolimbic pathway. Basal release is the spontaneous release of neurotransmitter which is constantly occurring in the nervous system, independent of any environmental stimuli. This low level of basal release would in turn cause dopamine receptors in the Mesolimbic pathway to

become supersensitive, so that they would over react to environmental stimuli. (This explanation is illustrated in Figure 1).

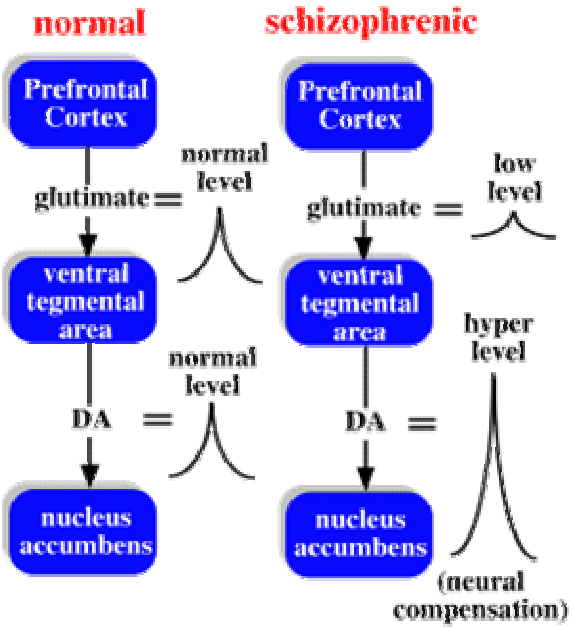

Figure 1. Neural Compensation Explanation of Hyper and Hypo Dopamine Hypotheses