

Report on the Evidence Supporting a Biological Basis for Schizophrenia

Schizophrenia has a lifetime prevalence of approximately 1% of the population. The disorder tends to be chronic, with the typical pattern being a life-long history of acute psychotic episodes superimposed upon chronically poor psychosocial adjustment. However, as we shall see below, important differences exist between sub-groups of patients with schizophrenia. These differences are seen in terms of clinical presentation, treatment responses, and course of illness. It may well be that schizophrenia is not a single disorder, but rather that it represents a final common **syndrome** of behaviours, and findings about mental status, with multiple possible causes. Understanding these differences will be critical for the MEDICAL care of persons with schizophrenia; they imply that a "blanket" approach to persons with schizophrenia is inappropriate and potentially harmful. Each individual with schizophrenia will require a full assessment; care will need to be provided by persons trained in understanding the unique biological and psychological framework that makes up that individual. A brief review of the evidence for a biological basis of schizophrenia follows.

1. Genetic Evidence

There is strong and consistent evidence supporting a genetic basis for schizophrenia. The risk for developing schizophrenia in the general population is 1%. The risk for relatives of an affected person are as follows:

- non-twin sibling: 8%
- child of a parent with schizophrenia: 12%
- fraternal twin: 12%
- child of two parents with schizophrenia: 40%
- identical twin: 47%

In no genetic illness do both identical twins always suffer the disease. When identical twins are raised by adoptive parents, their risk remains the same. Furthermore, the more severe the schizophrenia, the more likely that both twins will get the disorder. In summary, the evidence suggests that the genetic influence outweighs the influence of the environment.

2. Biological Evidence

The dopamine hypothesis of schizophrenia states that there is over activity in the dopamine systems in schizophrenia. The hypothesis grew out of the finding that all effective anti-psychotic medications block dopamine brain receptors, and that their potency is correlated to the strength of binding to dopamine type 2 (called D2) receptors in the brain. Other observations have given support to this hypothesis. the administration of drugs which increase dopamine activity exacerbates psychotic symptoms in some persons with schizophrenia. Post mortem neurotransmitter studies have reported increased numbers of D2 receptors in critical portions of the brain -- areas such as the basal ganglia and the limbic system. However, not all studies have been consistent with these findings. Furthermore, it is clear that anti-psychotic medications are effective in treating psychosis of any origin, suggesting that elevated dopamine activity may not be specific to schizophrenia. And finally, studying the brains of deceased persons with schizophrenia is fraught with problems, not the least of which is the fact that prior

treatment with anti-psychotic medication can, in and of itself, increase dopamine receptor levels. The new technology of Positron Emission Tomography (PET) holds much promise for the study of dopamine receptors in the brains of live, unmedicated persons. The main implication for the dopamine hypothesis today continues to be the firm finding of reduced frequency, duration, and severity of psychotic episodes in persons treated with anti-psychotic medication.

3. Structural Brain Imaging Evidence

Computed tomography (CT) studies have provided evidence of enlarged **ventricles** and enlarged **cortical sulci** in large proportions of persons with schizophrenia. These findings suggest a decrease in brain volume. In those patients who have these findings, the enlargement of ventricles and sulci is evident at the onset of illness, and does not progress over the course of the illness. Enlargement of the ventricles may be more common in males. Ventricular enlargement correlates with larger numbers of hospitalizations. A complimentary finding has been reported by some, but not all, authors. They have found that skull volume is reduced by 3-5% in persons with schizophrenia. Since brain growth drives skull growth, these findings suggest that the process causing schizophrenia takes place prior to the completion of brain growth (approximately age 18).

Magnetic Resonance Imaging (MRI) studies have been better able to examine small areas of the brain, and to detect differences in gray versus white matter. MRI studies to date have focused primarily on the temporal lobes -- most such studies have been consistent in finding loss of temporal lobe volume and loss of temporal lobe gray matter volume. A single study examining the entire brain showed that gray matter, but not white matter, was reduced in all cortical areas examined for in the brains of persons with schizophrenia. Another important finding with MRI has been an absence of the degeneration of the brain seen in degenerative diseases six months into the illness. This strongly suggests that the process leading to schizophrenia is a developmental error occurring prior to birth, rather than a degenerative or destructive process.

4. Neuropathological Evidence

Most neuropathological studies have been consistent in finding abnormalities in the brains of deceased persons with schizophrenia. The areas usually involved include the limbic forebrain, (especially the amygdala and the hippocampus), and the basal ganglia (including the caudate, nucleus accumbens, and olfactory tubercle).

5. Functional Anatomic Studies

Positron Emission Tomography (PET) studies are in their infancy. This technology allows the researcher to observe the brain's function in living subjects. It now appears that actively psychotic, unmedicated persons with schizophrenia show an over-activation of the frontal lobes, while chronic, non-psychotic medicated patients are "hypo-frontal". When given a cognitive challenge (which utilizes the frontal lobes), schizophrenic persons did poorly on the test, and failed to activate their frontal lobes on PET. Differences in temporal lobe laterality, and a decrease in parietal lobe activation, have also been observed. A very robust finding has shown that anti-psychotic medication administration "turns on" the basal ganglia.

6. Cognitive Studies

Studies have demonstrated a large proportion of persons with schizophrenia have profound **cognitive deficits**. These include difficulties with higher-order attention; insight, judgment, abstractional abilities, comprehension and retention of complex verbal and non-verbal material, and recognition and production of non-verbal affects (e.g. the reading of emotional expression on a face, the production of emotional sounds/nuances when speaking). The pattern of deficits is often unique to an individual, although patterns across sub-groups of persons with schizophrenia are seen. These findings have especially important implications for care-givers working with persons with schizophrenia. For example, when deciding upon treatment options, persons with schizophrenia may not be able to attend to lengthy discussion. They will often lack the insight to make decisions in their own best interests, especially when the issues are complex. For example, medication refusal is common, and may reflect difficulties in judgment and insight. An untrained advisor may "misread" a facial expression given by the person with schizophrenia as meaning understanding or consent. If handled inappropriately, excessively verbal interactions may increase the schizophrenic person's confusion, and hence level of distress, and may thus exacerbate a psychosis. All of these examples are intended to illustrate that care-givers at all levels (including physicians, nursing staff, allied health disciplines and advocacy workers) require a tremendous amount of knowledge and experience when working with this very challenging population.

Summary

The evidence reviewed strongly suggests a biological basis for schizophrenia. However, it is likely that the "disorder" is instead a "syndrome" with multiple possible **etiologies** and outcomes. An understanding of, and experience with, the complex brain and behaviour relationships seen in persons meeting the diagnostic criteria for schizophrenia, is crucial for care-givers at all levels.

Glossary of Terms

1. **cognitive deficit:** difficulty thinking or working things out
2. **cortical sulci:** the name given to the "valleys" between the "ridges" in the cortex of the brain
3. **etiologies:** causes
4. **prevalence:** frequency of occurrence
5. **syndrome:** set of symptoms
6. **ventricle:** the name given to the four hollow parts of the brain

*Written by Robert van Reekum, M.D. F.R.C.P.(C) and J.M. Cleghorn, M.D. F.R.C.P.
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