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In the 11 years since Godfrey Hounsfield developed the first computed tomography scanner (for which he shared the 1979 Nobel Prize in Physiology and Medicine), the CT scan has undergone generations of technical improvements and has had a major influence on neurological diagnosis.

In psychiatry, the CT scan has been used to investigate structural brain abnormalities in schizophrenic patients in the attempt to determine the underlying pathophysiology of the disease and to link structural changes to behavior.

Major morphological abnormalities documented in schizophrenic patients are ventricular enlargement, cortical atrophy, atrophy of the anterior cerebellar vermis (the area between left and right cerebellum), reduced tissue density, and unusual cerebral asymmetries. Ventricular and cortical atrophy have received the greatest attention.

Among the first to use the CT scan to compare schizophrenic patients to age-matched controls were Johnstone and associates (1976), who found significantly enlarged ventricles in severely disabled, institutionalized patients. These findings have been confirmed and broadened by research teams at St. Elizabeths Hospital in Washington, D.C., the University of Iowa, the Nebraska Psychiatric Institute, and others.

At TRIMS, quantitative measures of the CT scans of young schizophrenic patients are being investigated by us in collaboration with Dr. Marcos Calderon of the Houston Imaging Center. The project involves relationships between CT scan measurements, neuropsychological performance, cerebral blood flow, response to neuroleptic medications, and blood chemistries. In our initial sample, 64 percent of the patients had abnormal CT scans, cortical atrophy in the left and right frontal-parietal regions being most prominent.

### **May be reversible**

Neither cortical nor ventricular abnormalities are necessarily irreversible. Reversibility has been demonstrated after termination of long-term cortico-

steroid use, after treatment of patients for anorexia nervosa and Cushing's disease, and in alcoholics who became abstinent.

Etiologies have been widely debated. Age and type of treatment seem not to be related to structural abnormalities in schizophrenic patients, but the studies suggest that these abnormalities may play a role in the illness itself. A related issue is whether the structural defects arose during the course of the illness, or predate its onset and contribute to its course.

### **May predate illness**

The Weinberger group's data (1979, 1980a and b), and the lack of correlations with length of illness, indicate strongly that ventricular enlargement in some schizophrenic patients may predate the onset of illness. This belief is strengthened by the fact that patients in the Weinberger et al. studies were acutely ill patients experiencing the first episode of their illness.

The functional importance of structural abnormalities in schizophrenic patients is unclear, but several correlations have surfaced. Compared to schizophrenic patients without structural defects, those exhibiting CT abnormalities tend to be more impaired by an unremitting illness, were poorly adjusted before they became ill, had different human leukocyte antigen profiles, were more likely to have neuropsychological impairments, and did not respond as well to neuroleptic drugs.

This latter finding does not suggest that schizophrenic patients who have enlarged ventricles cannot respond to treatment with neuroleptics.

It should be emphasized, however, that structural abnormalities, as typified by ventricular enlargement or cortical atrophy, are not specific to schizophrenia: these findings occur in a host of neurological disorders and the normally aging brain.

Yet the studies suggest that there is a subgroup of schizophrenic patients who have structural brain abnormalities.

# TRIMS Therapy Notes

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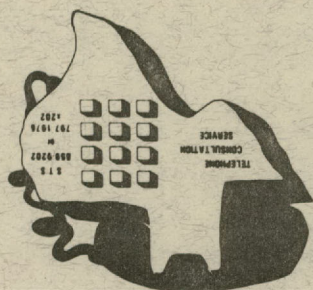
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## *Structural abnormalities in schizophrenia*

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The findings support the idea that schizophrenia, rather than being one disease, probably consists of several subgroupings.

Perhaps the greatest contribution of the computed tomography studies is their capacity to improve research design, allowing the grouping of schizophrenic patients into what may be more biologically homogeneous categories. This may help to clear up confusion, reduce discrepancies in results, and facilitate research in the etiology of schizophrenia and treatment of schizophrenic patients.

—John W. Largen Jr., Ph.D.  
Robert C. Smith, M.D., Ph.D.

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