Neuroimaging for Diagnosis of Psychiatric Disorders

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Abstract: Recent advances in computer technology have allowed detailed investigation of brain structures. While psychiatric disorders have been diagnosed on the basis of clinical symptomatology, the results are relatively ambiguous compared to the diagnostic procedures for physical disorders, since no objective methods of examination have been available on which to base the diagnosis. Recent studies have shown that quantitative and qualitative evaluation of MRI images has allowed us to find structural brain abnormalities in various brain regions, including the lateral ventricles, temporal lobe, and frontal lobe, to be identified in schizophrenia, and the abnormalities have been demonstrated in first episode as well as in chronic patients. Progressive volume reduction has also been reported in the lateral ventricles and superior temporal gyrus in follow-up studies. In addition structural abnormalities have been revealed in hippocampus and anterior cingulate cortex of patients with affective disorders. The concept of classical functional psychoses, such as schizophrenia and affective disorders, may change in the near future.

Key words: Schizophrenia; Affective disorder; Neuroimaging; MRI

Introduction

The diagnosis of psychiatric disorders, e.g., schizophrenia, affective disorders, and anxiety disorders, has generally been based on patients’ mental and/or psychological state as determined by clinical interviews with patients and their families, but this diagnostic process is more ambiguous than for physical diseases that are confirmed by blood tests and/or imaging tests. The implications of psychiatric disorders might change if tools were available to diagnose them more objectively.

Recently, technological advances have improved neuroimaging techniques so that they now allow analysis of the structure and function of the human brain. These techniques have played important roles in understanding the pathology of psychiatric disorders and include MRI (magnetic resonance imaging) and CT
(computed tomography), which enable observation of the structure and morphology of the brain, and PET (positron emission tomography) and SPECT (single photon emission computed tomography), which enable visualization of brain function.

Although PET has become more common as a result of recent advances in technology, it is still invasive and costly for general clinical assessments because of the need for radioactive material. More recently, a new MRI method, functional MRI, has been developed to measure blood flow, which is a reflection of neuronal activation of the brain. Functional MRI is also expected to serve as a new clinical tool, because it is noninvasive and can be performed with a standard MR system, although additional studies are required due to the complex imaging analyses. Electroencephalography (EEG) has often been used to evaluate brain function in epilepsy, encephalitis, cerebrovascular disorders, and brain injury, but no specific EEG abnormalities have been identified in psychiatric disorders, including schizophrenia and affective disorder.

MRI and CT have contributed to the diagnosis of psychiatric disorders associated with organic brain lesions, i.e., neurodegenerative disorders including Alzheimer's disease, multiple infarctions, encephalitis, and brain injury. However, MRI or CT cannot be applied to the diagnosis of schizophrenia or affective disorders, which are so-called endogenous psychoses, although it might be possible to use the images as a new diagnostic tool in the near future. This paper reviews recent findings in regard to structural abnormalities in schizophrenia and affective disorders, and brain imaging perspectives are also discussed.

Abnormalities Revealed by Structural Brain Imaging in Schizophrenia

1. Qualitative imaging studies

Schizophrenia is a chronic brain disorder with a 1% prevalence in the population. Its onset occurs in adolescence, and it is very costly to society economically. Recent studies have shown that qualitative evaluation of MRI images allows identification of structural brain abnormalities of certain degrees in schizophrenia. Mild or more severe cortical brain atrophy has been found in 57% of schizophrenia patients by MRI, and the odds of cortical atrophy were 11.7 times higher in patients with schizophrenia compared to normal subjects of the same age. Schizophrenic patients who did not respond to treatment had a 2.8 times higher incidence of cortical atrophy compared to those who responded, and cortical atrophy or ventricle enlargement was detected in 40–60% of patients with schizophrenia as opposed to 5% of normal subjects. These findings suggest that brain abnormalities can be identified by qualitative analysis, although continuous, thin (at thickest 3 mm) MR slices are required to assess structural change in the brain qualitatively.

2. Quantitative Imaging Studies

This section summarizes the results of quantitative analyses of MRI and CT data. Enlargement of the lateral ventricles and reduction of temporal and frontal lobes have often been reported in schizophrenia. Brain structure has been noninvasively investigated since CT was invented 30 years ago, and the first CT study to demonstrate ventricle enlargement in patients with schizophrenia was reported in 1976. MR acquisition techniques have subsequently advanced to the point where detailed spatial resolution, up to 1 mm, is now possible.

(1) Lateral ventricles

Lateral ventricle enlargement has been reported in 70% of the studies on schizophrenia conducted over the past ten years. Although enlargement of the lateral ventricles is not specific to schizophrenia, this suggests that structural abnormalities are based on neurodevelopmental disturbances in schizophrenia, since ventricular abnormalities have been found in other brain disorders with neurodevelopmental deficits. However, the ventricle enlargement may have resulted from brain atrophy of
the gray matter and white matter. Clinically, the enlargement of the lateral ventricles was closely correlated with duration of illness and poor outcome.2) Temporal lobe MRI has enabled identification of the boundary between the gray and white matter, which was never clearly seen on CT images. This advantage of MRI yielded more information on structural changes in the brain. The gray matter consists of several layers of neurons, while the white matter consists of bundles of their fibers, making it important to measure the two structures separately, because they have different functions.

Changes in the temporal and frontal lobes have been extensively reported in schizophrenia, although total cortical volume reduction has also been reported. The temporal lobe plays a role in processing auditory information from the ears, and the temporal lobe in the dominant hemisphere plays a central role in language in humans. Manifestations of hallucinations and delusions are assumed to be associated with language function, and for these reasons, a temporal lobe abnormality has been suspected in schizophrenia.

Decreases in volume were found in 60% of studies that measured the whole temporal lobe in schizophrenia,1) and marked gray matter volume reduction has been found in the superior temporal gyrus (STG, Fig. 1). The surface of the STG is anatomically divided into two structures: Heschl's gyrus and the planum temporale (PT). Heschl's gyrus plays a role in primary/secondary auditory information processing, while the PT is associated with language function in the dominant hemisphere. The severity of clinical assessment scores for hallucinations has been found to be associated with volume reduction of the STG.4) An abnormality of the posterior STG was also found to be significantly correlated with scores for disorganized thought in patients with schizophrenia.5)

Deficits or reversals of normal asymmetry have also been reported in left and right brain structures in schizophrenia. As an example, the PT in the STG is larger in the dominant hemisphere (left>right for normal right-handed person) than on the other side (Fig. 2), but recent studies have suggested loss or even reversal (left<right) of the asymmetry of the PT.
Parcellation studies of frontal lobe are important, since individual lobes in the frontal area have different functions. The prefrontal lobe is the critical site for working memory (Fig. 3), and correlation studies with clinical symptoms have suggested that volume reduction in the prefrontal cortex is associated with negative symptoms, i.e., affective flattening, alogia, or avolition.

(4) Structural brain abnormalities in first episode patients

It remained unclear when the structural abnormalities occur in relation to and the onset of symptoms, whether the abnormalities change over time or change after treatment. Many MRI studies have been carried out, mostly in chronic schizophrenia, because the patients are relatively easy to recruit and are maintained in a stable psychiatric state. However, the abnormalities in the chronic patients may be influenced by long-term medication with neuroleptics and anticholinergic drugs, institutionalization, and the patients’ unique life style, making it important to investigate first episode patients.
Recent studies have revealed that the gray matter volume of the left posterior STG is significantly reduced in the first episode schizophrenia compared to age-matched normal controls and patients with affective disorder, and left hippocampal volume has also been found to be smaller in the first episode of schizophrenia compared to normal controls, but not in affective disorder. The results of the search for abnormalities in first episode studies have been inconsistent in the prefrontal lobe, compared to the temporal lobe. Our recent findings have suggested bilateral volume reduction in the prefrontal gray matter in the first episode of schizophrenia relative to normal controls and affective disorders.

(5) Structural changes in follow-up studies

One of the possible advantages of first episode studies that they allow is follow up to detect possible changes over time and the effect of treatment on structural abnormalities. Although small numbers of follow-up studies have been reported, our preliminary investigation suggested that 90% of patients with schizophrenia showed 11% gray matter volume reduction in the left STG when MR measurements were made 1.5 years apart. These findings suggested that the structural abnormalities in the chronic stage may be present in the early stage of the illness and progressively change in some regions over time, although the effect of medication cannot be ruled out, since most of the subjects were treated with neuroleptics even in the first episode stage. In addition, progressive enlargement has also been reported in the lateral ventricles in schizophrenia. Although it is important to check changes of progressive enlargement, follow-up studies are extremely difficult to complete in a single institution. Rapid technological advances also impede follow-up studies because of the inequality of acquisition images between recordings.

Abnormalities Detected by Structural Brain Imaging in Affective Disorders

Affective disorders are generally classified into bipolar disorder, with cycles of depressive
and manic states, and major depression alone, with a depressive state. The prevalence of major depression has increased (3–5%) in many countries. Significant volume reduction in the hippocampus and anterior subgenual cingulate cortex and high intensity of the white matter have been reported in affective disorders although the evidence of structural abnormalities has not been as great as in schizophrenia (Fig. 4). The cingulate cortex plays an important role in emotion and will, which are associated with depressive symptoms.

PET studies have also revealed hypofunction in the anterior subgenual cingulate cortex in chronic recurrent depression, and volume reduction has been reported in this region in patients with a family history of depression, but not in patients without a family history. Unlike schizophrenia, however, there have been few reports of volume reduction in the frontal or temporal lobe in affective disorders. This suggests that structural abnormalities of the frontal and temporal cortex might be specific to schizophrenia.

**Conclusion**

Recently, technology for processing and storing large amounts of neuroimaging data has greatly advanced, and it may be possible to identify the size of individual brain regions soon after MR acquisition in physicians’ offices in the near future. The concept of classical functional psychosis, such as schizophrenia and affective disorders, may change in the near future.

**REFERENCES**


3) Gur, R.E., Turetsky, B.I., Bilker, W.B. and Gur, R.C.: Reduced gray matter volume in schizophrenia. *Arch Gen Psychiatry* 1999; 56(10):


