Can Structural Neuroimaging be Used to Define Phenotypes and Course of Schizophrenia?

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KEYWORDS

• Structural neuroimaging • Functional magnetic resonance imaging
• Single-photon emission computed tomography • Psychiatric diagnosis
• Psychiatric prognosis • Schizophrenia • Psychosis

KEY POINTS

- To date there is no compelling evidence that structural neuroimaging measures taken in first-episode patients predict the course and outcome of schizophrenia.
- There is evidence suggesting that neuorimaging phenotypes can be associated with outcome in schizophrenia based on progressive brain changes. The preponderance of evidence appears to support an association between progressive changes in specific brain regions and poor outcome.
- Much research to date has focused on structural magnetic resonance imaging; however, many other imaging measures could be used, such as event-related brain potentials.
- Nonstructural imaging studies have found evidence that dopamine levels measured with single-photon emission computed tomography at baseline in first-episode patients predicts poor outcome.

INTRODUCTION

There is a wide variety of neuroimaging techniques that hold great promise for understanding neuropsychiatric disorders. Theoretically it is possible that neuroimaging techniques could be used to aid psychiatric diagnosis. At the same time, it is also possible that neuroimaging techniques could be used for prognosis, to predict treatment response, and to better understand the heterogeneity of disorders. This review examines research that has attempted to use structural neuroimaging measures to understand the course and outcome of schizophrenia.

A review published 5 years ago[1] attempted to answer the question of whether any brain-imaging measure predicted outcome and course in schizophrenia. Based on

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research conducted up to that time, the answer to that question was a clear "no," because there were no neuroimaging phenotypes with enough research support to justify their use in making predictions for individual patients in clinical practice. Five years later, the answer to the question of whether neuroimaging measures can be used to predict outcome and course in schizophrenia remains negative. Overall, previous research has yet to find compelling evidence that an initial neuroimaging scan at any time in the illness predicts future outcome.

By contrast, there is fair evidence that the degree of brain changes, as measured in serial brain scans over time, correlates with poor outcome in schizophrenia. Although it is unclear whether this method could be used to predict clinical outcome, such evidence does suggest that neuroimaging phenotypes can be related to the course of the disorder. In particular, in schizophrenia there may be one or more phenotypes involving deleterious progressive brain changes over time that are related to poor outcome of the disorder.

This article reviews the status of research that has attempted to use structural neuroimaging measures as predictors or correlates of the course of schizophrenia. The authors first discuss some of the various ways that neuroimaging measures have been used to understand the course of schizophrenia. For instance, although there are many types of brain-imaging techniques, only a subset have been frequently used in researching the course of schizophrenia. Next, a focused review evaluates the evidence for whether particular brain measures can be used to understand the course of schizophrenia. Finally, recommendations are made regarding future research on using neuroimaging measures to predict the course of schizophrenia.

OVERVIEW OF PREVIOUS RESEARCH

It is possible that a neuroimaging measure related to outcome at one phase of the disorder may or may not be related to outcome at another phase of the disorder. Previous research has attempted to use neuroimaging to predict outcomes in several different phases of schizophrenia. For example, some studies have attempted to predict which individuals considered at ultra-high risk for psychosis develop a psychotic disorder or more specifically develop schizophrenia. Other studies have attempted to use neuroimaging to predict the long-term outcome in people experiencing their first episode of psychosis with schizophrenia. Others have used neuroimaging to predict outcome in chronic patients, or have examined whether changes in brain imaging over time are correlated cross-sectionally with outcome in the disorder.

In reviewing studies that have attempted to predict outcome of the disorder, the overwhelming majority have focused on structural neuroimaging involving magnetic resonance imaging (MRI) or computed tomography. It has been rare for studies to have used magnetic resonance spectroscopy (MRS), neurotransmitter receptor binding, functional MRI (fMRI), or other types of imaging techniques. More commonly, these other methods have examined cross-sectional relationships between neuroimaging and measures of symptoms or levels of functional impairment. Therefore, the main focus of this review involves structural imaging, although some evidence for other imaging modalities is also briefly reviewed.

Most studies also have tended to focus on a particular set of brain regions or neural measures (eg, total volume of gray matter). The most common has been lateral ventricle size, followed by total gray matter or whole brain size. Regarding particular brain regions, the most commonly reported have been the frontal and temporal cortices and the hippocampus. When structure has been examined it has usually included its entirety, as opposed to more specific subareas of the structure (or for