Diagnostic Imaging in Psychiatric Disorders: A Closer Look at the Use of MRI in Schizophrenia

Alëna A. Balasanova, HMS III
Gillian Lieberman, MD
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Agenda

**Part I**
- What is Magnetic Resonance Imaging (MRI) and why do we use it?
- How MRI Works: A Review of Physical Principles
- Overview of Clinical Applications of MR Imaging

**Part II**
- What is Schizophrenia and how is it diagnosed?
- Review of Brain Anatomy
- MR findings in Brain Imaging of Schizophrenic Patients
- Implications of MRI findings for future research
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Part I

- What is Magnetic Resonance Imaging (MRI) and why do we use it?
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What is Magnetic Resonance Imaging (MRI) and why do we use it?

- MRI is a non-ionizing radiation imaging tool utilizing the principles of magnetism and radiofrequencies in conjunction with computer technology to create a detailed three-dimensional image of regions of interest inside of the human body.

- MR images are interpreted by highly skilled radiologists who collaborate with clinicians and researchers to:
  - Detect early signs or stages of disease
  - Diagnose disease
  - Assess treatment effects
  - Help guide surgical decision-making
  - Help guide medical management of patient care
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Part I

- What is Magnetic Resonance Imaging (MRI) and why do we use it?
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How MRI Works: A Review of Physical Principles

In order to better understand MRI technology, we must first review the key physical principles involved.

**Atoms and Spin**

- Our bodies are comprised of different kinds of tissues and cells, which are made of molecules and **atoms** of different chemical elements.
- An **atom** is the smallest component of any of these elements, and can be thought of as the tiniest particle of any tissue.
  - Each **atom** has a nucleus containing neutrons and protons, and one or more electrons bound to that nucleus. Protons have positive charge, electrons negative charge, and neutrons no charge.
  - Under normal physiologic conditions, the protons inside of the nucleus spin randomly.

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*Hydrogen* is an element that is readily abundant in the human body. Its **atoms** consist of one electron orbiting a nucleus that contains one proton and no neutrons.

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How MRI Works: A Review of Physical Principles

Understanding the Key Concept of Magnetism

**Magnetism** is a property of materials capable of attracting ferrous (iron-containing) substances and creating an external magnetic field which exerts forces on charged particles moving through that field. These materials are known as *magnets*.

**Hydrogen Proton**
- A magnet has north and south poles, which exert attractive forces on opposite poles and repulsion forces on like poles.
- The positively charged spinning proton of a hydrogen atom may be thought of as a *magnet*.

When spinning protons are exposed to a magnetic field, the forces of the field cause them to stop spinning and align parallel or anti parallel to the direction of the main magnetic field. This is the “net magnetization” effect.

How MRI Works: A Review of Physical Principles
Understanding the Key Concept of Resonance

1) When a patient is positioned in the MRI scanner, the main magnet produces a strong, stable magnetic field causing the hydrogen protons in the patient’s tissues to line up.

2) Resonance occurs when the hydrogen protons spin at a particular frequency called the Larmour frequency. **Resonance** is produced by the introduction of a specific radiofrequency (RF) pulse to the aligned protons. The protons absorb this short burst of energy, are knocked out of alignment, and begin to resonate.

3) Once the RF signal is stopped, the protons relax back to their equilibrium state within the magnetic field by releasing the absorbed energy via emission of radio signals. These signals are detected by the radiofrequency receiver coil and transmitted to a computer system for conversion into an image.

4) **Fournier transformations** are complex mathematical formulas used to synthesize radio signal data into images.

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How MRI Works: A Review of Physical Principles Relaxation Time and Weighted Images

- **Relaxation Time**: length of time for the hydrogen protons to return to equilibrium after RF pulsations
- **Weighted Imaging** refers to exploiting the inherent differences in body tissue rates of T1 and T2 relaxation to obtain images with maximal contrast of the target region of interest

**T1: Spin-Lattice Relaxation** – Recovery of Longitudinal Magnetization (parallel)

BRIGHT on T1: Fat, Blood (hemorrhage), Protein-rich Fluid, Gadolinium. White matter > Gray matter

**T2: Spin-Spin Relaxation** – Decay of Transverse Magnetization (perpendicular)

BRIGHT on T2: Fat, Fluid (e.g. CSF), Blood (hemorrhage). Gray Matter > White Matter

*Fat Suppression sequence may increase the dynamic range of the image and help differentiate bright spots

How MRI Works: A Review of Physical Principles
Clinical Correlate of Key Physical Principles

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Overview of Clinical Applications of MR Imaging

- MR is unique in its multi-planar imaging capability: axial, sagittal, and coronal images may all be obtained from the same MRI scan.

- The ability to generate images in any plane is useful for evaluating complex anatomy such as that of the brain and spinal cord.

- MRI has diagnostic capability: it allows for the diagnosis of lesions based on their known signal characteristics (e.g. white matter tract lesions in Multiple Sclerosis).

- MR is the imaging modality most sensitive for soft tissue pathology due to its ability to contrast different types of tissues (e.g. orthopedic ligament and meniscus tears otherwise unseen on plain film).

- MR capabilities are most extensive in neuroimaging: functional, diffusion-weighted, and angiography magnetic resonance scans are available today (fMRI, DWI, MRA).

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Part II

- **What is Schizophrenia and how is it diagnosed?**
- Review of Brain Anatomy
- MR findings in Brain Imaging of Schizophrenic Patients
- Implications of MRI findings for future research
What is Schizophrenia?

- Schizophrenia is a major mental disorder (Axis I) characterized by disturbances in cognition and emotional responsiveness resulting in disorganized speech, thinking and behavior.

- Complications of schizophrenia can be severe and may lead to social isolation, result in significant social dysfunction, decreased life expectancy and increased risk of suicide.

- While there is no cure for schizophrenia, it is widely believed that timely diagnosis and psychopharmacological and psychotherapeutic treatment may help reduce severity and/or progression of disease.
How is Schizophrenia Diagnosed?

The diagnosis of schizophrenia is made according to criteria set forth by the American Psychiatric Association in the DSM-IV-TR. Three criteria must be met:

1. **Presence of two or more Characteristic Symptoms for at least a 1-month period** (diagnostic requirements differ if delusions are judged to be bizarre or with certain types of hallucinations)
   - Delusions
   - Hallucinations
   - Disorganized Speech
   - Grossly Disorganized or Catatonic Behavior
   - Negative Symptoms (e.g. blunted emotional response, lack/decline of motivation, etc.)

2. **Social/Occupational Dysfunction:** marked decline in one or more major areas of functioning such as work, interpersonal relations, or self-care

3. **Duration:** continuous signs of the disturbance persist for at least six months with at least one month of active symptoms

*While MR neuroimaging is used in schizophrenia for detection of brain changes (e.g. progressive gray matter loss), it is not used for diagnostic purposes at this time*

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Review of Brain Anatomy: The Normal Brain

Review of Brain Anatomy: T1 Weighted Axial MR Image of a Normal Brain

Review of Brain Anatomy: Functional Changes in Schizophrenia

MANY BRAIN REGIONS and systems operate abnormally in schizophrenia, including those highlighted below. Imbalances in the neurotransmitter dopamine were once thought to be the prime cause of schizophrenia. But new findings suggest that impoverished signaling by the more pervasive neurotransmitter glutamate—or more specifically, by one of glutamate’s key targets on neurons (the NMDA receptor)—better explains the wide range of symptoms in this disorder.

**BASAL GANGLIA**
Involved in movement and emotions and in integrating sensory information. Abnormal functioning in schizophrenia is thought to contribute to paranoia and hallucinations. (Excessive blockade of dopamine receptors in the basal ganglia by traditional antipsychotic medicines leads to motor side effects.)

**AUDITORY SYSTEM**
Enables humans to hear and understand speech. In schizophrenia, overactivity of the speech area (called Wernicke’s area) can create auditory hallucinations—the illusion that internally generated thoughts are real voices coming from the outside.

**FRONTAL LOBE**
Critical to problem solving, insight and other high-level reasoning. Perturbations in schizophrenia lead to difficulty in planning actions and organizing thoughts.

**OCCIPITAL LOBE**
Processes information about the visual world. People with schizophrenia rarely have full-blown visual hallucinations, but disturbances in this area contribute to such difficulties as interpreting complex images, recognizing motion, and reading emotions on others’ faces.

**LIMBIC SYSTEM**
Involved in emotion. Disturbances are thought to contribute to the agitation frequently seen in schizophrenia.

**HIPPOCAMPUS**
Mediates learning and memory formation, intertwined functions that are impaired in schizophrenia.

Alfred T. Kamajian, “Schizophrenia Images and Pictures of Brains.”
Available at: http://www.schizophrenia.com/schizpictures.html. Accessed November 11, 2010
Review of Brain Anatomy:
Structural Changes in Schizophrenia

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MR findings in Brain Imaging of Schizophrenic Patients: Anatomic Changes Characteristic of Chronic Schizophrenia

- The most specific anatomic finding of brains of patients with schizophrenia as seen on MRI is the enlargement of the ventricles (particularly the lateral ventricles) as well as an increase in CSF both inside the ventricles and in other areas of the brain.

- The next slide introduces our primary patient, a 52 year old male with chronic schizophrenia. His non-contrast T1 Weighted Coronal MRI is compared to that of a 50 year old male without schizophrenia.

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In the following slide, please note:

- Increased Cerebral-Spinal Fluid (CSF) in the Left Sylvian fissure (see green arrow)
- CSF in Left temporal horn around the amygdala/hippocampus (see orange arrow)
- Enlargement of the lateral ventricles (see pink arrow)
MR findings in Brain Imaging of Schizophrenic Patients:

T1 Weighted Coronal MR Image of 50 year old male schizophrenic patient compared to normal image of 52 year old male without disease

Non-Contrast T1 Weighted Coronal MRI of Normal Control (52yo male)

Non-Contrast T1 Weighted Coronal MRI of patient with chronic schizophrenia (50yo male)

Images Courtesy of Dr. Martha Shenton, Psychiatry Neuroimaging Laboratory, Brigham and Women’s Hospital
MR findings in Brain Imaging of Schizophrenic Patients: Gray Matter Tissue Loss and Reduction in Overall Brain Volume

- Imaging studies of brains of patients with schizophrenia have demonstrated that patients suffering from chronic schizophrenia show a reduction in overall brain volume, particularly in grey matter tissue.
  - This is most evident in the superior prefrontal and temporal cortices.
  - Notably, degenerative change has also been seen in the basal ganglia, primarily in the thalamus and striatum areas.

- Studies administering repeat MRI brain scans to patients with schizophrenia have suggested that at a minimum, gray matter volume loss occurs at a rate of approximately 4% per year and may be as high as 10% in some patients.

The following series of slides introduce the non-contrast T1 Weighted MR Images of our companion patients: a 25 year old male patient with schizophrenia and a 56 year old male patient with schizophrenia.

- Images of both patients demonstrate increased CSF and increased ventricular size (pink arrows), and show decreased gray tissue brain mass (yellow arrows).
MR findings in Brain Imaging of Schizophrenic Patients:

A 25 year old male with chronic schizophrenia

(Left) Non-Contrast T1 Weighted Axial MRI of 25yo male patient with chronic schizophrenia

(Right) Non-Contrast T1 Weighted Coronal MRI of 25yo male patient with chronic schizophrenia

(Above) Non-Contrast T1 Weighted Sagittal MRI of 25yo male patient with chronic schizophrenia

Images courtesy of Alan Francis, BIDMC Department of Psychiatry
MR findings in Brain Imaging of Schizophrenic Patients

A 56 year old male with chronic schizophrenia

(Left) Non-Contrast T1 Weighted Axial MRI of 56yo male patient with schizophrenia

(Right) Non-Contrast T1 Weighted Coronal MRI of 56yo male patient with schizophrenia

(Above) Non-Contrast T1 Weighted Sagittal MRI of 56yo male patient with schizophrenia

Images courtesy of Alan Francis, BIDMC Department of Psychiatry
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Implications of MRI findings: how magnetic resonance has proved useful in past and present schizophrenia research

- At this time, it appears that MR neuroimaging is used in schizophrenia research as a tool to assess the anatomic manifestations of the psychiatric pathophysiologic processes underlying this disorder.

- Characteristic MRI findings of brain changes in schizophrenia include:
  - Enlargement of the ventricles (lateral ventricles most prominent)
  - Increased CSF in the ventricles
  - Tissue reduction in the superior and medial temporal cortices
  - Reduction in volume of the hippocampal-amygdala complex

- While structural brain imaging is non-diagnostic for schizophrenia, it has proven helpful in correlating physiologic changes to patient self-reported experiences of symptoms of the disease.
  - This is a step forward in exploring the potential neurobiological basis of schizophrenia and has provided a visual model to conceptualize how schizophrenia develops in the brain

Implications of MRI findings for future research

- MR Imaging in schizophrenia research has provided valuable insight to the degenerative processes of the brain and has allowed for better understanding of the speed with which brain tissue loss occurs, allowing for study and potential development of novel pharmacotherapeutics which may help deter the advancement of brain volume loss in these patients.

- Currently research is underway employing advanced MRI methods such as functional magnetic resonance (fMRI), diffusion weighted magnetic resonance (DWI), and most recently, whole-brain morphometric studies using high-dimensional shape transformations in the context of magnetic resonance imaging.

  - These new techniques may yield study results that provide the path for discovery of a magnetic resonance-based imaging modality that may be used as an adjunct diagnostic tool for schizophrenia sometime in the near future.
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References, continued


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