Specialty area: Schizophrenia

Speaker Name: Vincent Magnotta (vincent-magnotta@uiowa.edu)

Highlights

- MR methods exist to study brain anatomy, function, and metabolism. Knowing the best methods to apply to study these complex psychiatric disorders and address the hypotheses proposed will enhance our understanding of their neurobiology
- Ability to translate imaging findings to interpretation based on physics, chemistry, etc.
- Equally as complex as image acquisition are analysis approaches. Often type of acquired images will dictate analysis strategies.

Talk Title: Schizophrenia: What the Physicist Can Add

Target Audience

- Psychiatrists with an interest in the study of schizophrenia or other psychiatric disorders
- MR Physicists/Engineers/Image Processing interested in tackling the most complex organ in the body
- Basic scientists interested in translating findings from the bench to bedside.

Outcome/Objectives

1. Have a basic understanding of MR techniques that can be used to study the brain and their relative strengths and weaknesses
2. Understand how to form multidisciplinary teams to advance the understanding of schizophrenia
3. Learn how to translate findings from “bench to bedside” or “bedside to bench” to better interpret imaging findings. In addition, understand the basic strengths/weaknesses of each scale

Purpose

Schizophrenia is a major psychiatric disorder with significant morbidity, greatly needs better therapies, and new imaging methods are needed to better understand the neurobiology of this disease. There are many conflicting neuroimaging studies in schizophrenia suggesting that despite the severity of the disease relatively “subtle” changes occur in the brain and/or we need improved classification of the illness. Improved imaging techniques are needed to study brain changes and this may suggest that metabolic changes may cause a cascade of events that lead to abnormal development/pruning, function, and connectivity.

Methods

Anatomical Imaging

- Started with 2D CT and MR imaging (increased ventricular size)
- 3D Gradient Echo Imaging (CP Coil)
    - Resolution: 1x1x1.5mm, Time: ~10 minutes
    - Gross volumes
    - Tissue classification and gross anatomical volumes – Talairach based ROIs
    - Automated segmentation
    - Surface Generation and cortical parcellation
- Improved 3D Gradient-echo imaging
    - Parallel Imaging and higher density receiver arrays
    - Move from 1.5T to 3T
    - Resolution: 0.8-1.0mm isotropic; Time: ~5minutes
    - New sequences:
        - Multi-echo FLASH
        - Multi-echo MP-RAGE
        - MP-2RAGE
- 3D Variable Flip Angle sequences (CUBE, SPACE)
    - 3D T1, T2, or FLAIR images
    - Resolution: 0.8-1.0mm isotropic, Time: 5-8 minutes
    - Supports FLAIR
- Improved reliability and delineation of anatomical structures such as the hippocampus

Functional Imaging

- Blood Oxygen Level Dependence (BOLD) is the primary tool
    - Task based fMRI
        - Block design
        - Event related design
        - Naturalistic fMRI- during hallucinations, watching a movie/video clip, more natural paradigms
    - Resting state fMRI
        - Study functional brain connectivity
        - Many analysis techniques
            - Seed voxel
            - ICA
            - ALF
            - Graph theory
    - Recent Improvements: Multi-band acquisitions, SNR of multi-channel coils on the cerebral cortex
- Alternate functional imaging approaches
    - Blood flow measurements – ASL
    - Blood volume techniques: VASO
    - Measurements of electrical signals: Magnetic source
    - Metabolic sensitive techniques

Quantitative MR Imaging

- Several quantitative parameters can be mapped
  - T1
  - T2
  - T1rho – Chemical exchange rate
  - Diffusion – measurement of water motion and direction
  - MTR – White matter myelination
  - QSM - measurement of magnetic susceptibility
  - Others
- Probe tissue properties that have a physical meaning
- Typically slow
  - New compressed sensing techniques may accelerate these acquisitions
  - Limited spatial coverage

Metabolic Imaging

- ^{1}H MRS (STEAM, PRESS)
  - Metabolites of interest: NAA, Choline, Creatine, lactate, myo inositol, glutamate, glutamine
- ^{31}P MRS
  - Metabolites of interest: αATP, βATP, γATP, phosphocreatine, phosphomonoester, phosphodiester, inorganic phosphate, pH
- Chemical Exchange Techniques
  - CEST
  - APT
  - T1rho
- Hyperpolarized ^{13}C
  - Bicarbonate
  - Glucose
  - Pyruvate
- Novel Contrast agents (animal models only)
- Functional metabolic imaging
  - EPSI
  - PEPSI
  - CEST
  - T1rho

Study Design

- During study design you must understand the most appropriate imaging techniques to address the specific aims of the study
- Time is money and what are ways to reduce acquisition time, improve resolution or sensitivity of the techniques.
- Translate findings from humans to mouse models or vice-versa.
  - Small animal imaging provides this opportunity

    - Determine optimal model for conducting experiment (human, animal, phantoms)
- Define the scale of the study
    - Reliability of the experimental techniques
    - SNR and estimates of sample size
- Oversee data acquisition
    - Define imaging protocol
    - Identify image artifacts
    - Quality assurance program
    - Handle scanner "upgrades"
- Identify image analysis approaches
- Help to provide interpretation of results based on the physics

Results

- Major findings to date using MR imaging
    - Anatomical Changes
        - Reduced intracranial volume
        - Increased ventricular volume
        - Regional volumes: hippocampus and amygdala
        - Cortical thinning
        - Reduced white matter connectivity using diffusion scalars
    - Functional Changes
        - Low information processing found to be relatively intact with integration of stimuli impaired
        - Impaired emotional processing in amygdala
        - Impaired learning in frontotemporal circuits
    - Metabolic changes
        - Decreased NAA
        - Elevated glutamatergic indices in frontal cortex and basal ganglia
        - Elevated Glx in hippocampus

Discussion

- What are the gaps in the literature
    - Impact of metabolic changes on brain function
    - Need to improve temporal resolution of metabolic imaging techniques
    - Identify impact of anatomical changes on functional changes
    - Which comes first: metabolic, function, or anatomical changes
    - How do we handle impact of medication on the results
- How we share and merge data across many imaging studies using a variety of imaging protocols
    - How do we describe experiments, analysis approaches, such that data could be merged
    - How do we define patient symptoms, medication, cognition and uses these as covariates in the analysis

Conclusion

- Much has been done and we have learned a lot about schizophrenia
- However we have just scratched the surface.
- Great opportunities exist to more fully understand the disease, evaluate treatments, or provide guidance for the development of new therapies
- MR phycists are needed to advance our imaging techniques to address these important questions

References

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