Aging, Brain Plasticity and Diffusion MRI

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What We Will Talk About Today

• Overview of the Aging Brain

• Overview of what is Brain Plasticity?
  How to Promote Brain Plasticity?

• What is Diffusion MRI?
  What does brain tissue water diffusion tell us about
  brain tissue microarchitecture and brain plasticity?

• Diffusional Kurtosis Imaging (DKI)
  How DKI can help assess brain aging, brain plasticity
  and brain disease?
The Aging Brain

Morphological changes → volume changes
Molecular changes
Functional changes

Refs:
Hertzog et al., Psychological Science in Public Interest. 2009

Figure 4
A conceptual model of the scaffolding theory of aging and cognition (STAC).
Brain Plasticity

- Brain plasticity is an inherent property of the adult human brain.
- The brain responds to neural insults by engaging in continuous functional reorganization and functional repairs to support cognitive function.
- Cognitive and/or motor training can stimulate brain functional reorganization and repair.
- It is well accepted that cognitively active older adults, who engage in cognitive activities such as reading, playing cards, puzzles, and crosswords, or participate in targeted cognitive interventions, have a reduced risk for AD and other dementias.

The Buzz word is ...

Refs: Mattson and Magnus
www.nature.com/reviews/neuro 2006
Brain Plasticity

COGNITIVE REMEDIATION

Intervention strategies to modify deterioration in memory and other cognitive domains

- Cognitive Stimulation
  - Participation in activities which generally enhance cognitive and social functioning, using non-specific techniques such as discussion or reminiscence

- Cognitive Training
  - Provides theoretically driven strategies and skills to improve or compensate for specific cognitive functions

- Cognitive Rehabilitation
  - Focus on identifying and targeting individual areas of weakness in daily functioning, and implementing strategies to improve or compensate for these difficulties

- Internal: Incorporate mental techniques to facilitate cognitive processes – e.g. "chunking" pieces of information to assist encoding

- External: Use practical aids to compensate for weaker cognitive processes – e.g. writing information down to reduce the burden on memory processes

Figure 1: Cognitive remediation terminology

Sources: Medala and Richardson, 2006; Stazar et al., 2006; Anwanda and Louwrens, 2002;Stockwell, 2008; Clare and Woods, 2008.

Refs:
Mowszowski et al., International Psychogeriatrics. 2010
What is Diffusion MRI?

What is MRI?

Siemens 3 Tesla Whole Body MRI (head and whole body MRI)

DWI

Contrast Manipulation

PD-weighted  T₁-weighted  T₂-weighted
• Brain water >80%

• The micro-architecture of brain tissue is complex and formed by a network of different compartments (vascular, intra- and extracellular) and cell types (neurons, glial cells).

• Water diffusion in brain is influenced by micro-architectural components (e.g. intracellular organelles and macromolecules) and physical barriers (e.g. cell membranes) of the tissue.

• Therefore, it is also reasonable to assume that knowledge of the properties of water diffusion is be informative of the normal brain structure and the disease processes.
Diffusion Tensor Imaging (DTI)

- It is the current method
- Gaussian Diffusion

Gaussian vs. Non-Gaussian Diffusion

- Water diffusion is characterized (in its simplest form) by a Gaussian distribution of the displacement probability.

- The complex microstructure of tissue causes the displacement probability to deviate from a Gaussian distribution.

- Thus, the “degree” of non-Gaussianity is governed by the complexity of the tissue’s micro-architecture.

Example: water in a cell

Example: water in an axon
Diffusional Kurtosis Imaging (DKI)
Gaussian and Non-Gaussian Diffusion

Diffusion metric maps. Data acquired at 3T in ~ 5 min.
Age-Related Non-Gaussian Diffusion Patterns in the Prefrontal Brain

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Purpose: To characterize age-related MR diffusion patterns of the prefrontal brain cortex microstructure using a new method for investigating the non-Gaussian behavior of water diffusion called non-Gaussian diffusion kurtosis imaging (NGDI).

Materials and Methods: Measures of mean diffusivity (MD), fractional anisotropy (FA), and mean kurtosis (MK) were compared in the prefrontal brain cortex of 24 healthy volunteers (adolescents, young adults, and elderly) ranging in age from 13 to 86 years. A Mann-Whitney test was used to compare subject groups with respect to the diffusion measures, and linear regression was used to characterize the change in each diffusion measure as a function of age.

Results: We found significant age-related changes in the elderly adult group, with increase of MD and decrease of FA.

Conclusion: The current study demonstrates distinct age-related changes in prefrontal brain microstructure with significant age-related changes in mean kurtosis (MK) and FA. These changes suggest that diffusion kurtosis is able to characterize the age-related changes in the prefrontal brain microstructure. The brain undergoes structural and morphological changes throughout the various stages of development and aging (1-3). The prefrontal brain shows significant volume changes (4) with increases in white matter and thinning of gray matter during adolescence and early adulthood, and white and gray matter loss with aging. All of these structural changes are reported to be associated with cognitive changes (4,5,6).

Diffusion tensor imaging (DTI) has been used to demonstrate age-related microstructural changes in the prefrontal brain. During brain development, water diffusivity decreases and anisotropy increases and, during aging, water diffusivity increases and anisotropy decreases (7-14). These prior studies have mainly focused on white matter changes because DTI is sensitive to tissue anisotropy. It has long been appreciated that diffusion-weighted magnetic resonance imaging is ex-
Quantitative Diffusion (DKI) in AD
A DKI Model for White Matter

The white matter (WM) consists of two non exchanging compartments:

- Intra-axonal space (IAS)
- Extra-axonal space (EAS)

White Matter Integrity Parameters:
- Axonal water fraction (AWF) → Axonal Density
- Intra-axonal diffusivity $-D_{\text{axon}}$ → Intra-axonal injury
- Radial extra-axonal diffusivity $D_{e,\perp}$ → Myelin Density
- Axial extra-axonal diffusivity $D_{e,\parallel}$ → Axonal Density

All WMI parameters can exclusively be extracted using the DKI metrics of non-Gaussianity

DTI vs. DKI Fiber Tracking

Same dataset and seed points!
Center for Biomedical Imaging

The Medical University of South Carolina (MUSC) has recently established the Center for Biomedical Imaging (CBI). The CBI provides state-of-the-art imaging resources to support clinical and research activities, provide opportunities to advance the imaging field, disseminate new technologies and approaches to the larger community, and train and mentor young investigators interested in developing and applying biomedical imaging to clinical and research problems. The mission of the CBI is to maximize the impact of imaging at MUSC by providing leadership and infrastructure that enables the university to address local and national priorities and developing regional and national collaborations that strengthen capabilities and enhance the university’s image. The CBI also provides opportunities for basic and clinical scientists to collaborate and discover new ways to study diseases and disease processes, to develop and apply this knowledge to clinically relevant research, and to translate advances to the community. The CBI includes approximately 4500 square feet of space at 30 Bee Street, as well as approximately 9000 square feet in the new Bioengineering Building.

Space at 30 Bee Street is the main facility for human imaging research and houses a Siemens 3T TIM Trio MRI scanner equipped with integrated fMRI paradigm presentation equipment. The scanner operates with a 100% mandate for research use and is covered by a master research agreement with Siemens Medical. The site also contains an image analysis laboratory and bioengineering facility along with subject interview and changing rooms. Researchers also have access to clinical Siemens 1.5T and 3T Vero MR scanners, located within the Radiology Department in the Clinical Sciences Building. The space at the Bioengineering Building house offices, wet and dry labs, classrooms, an auditorium, a Bruker 7T/30 animal MRI system, a bioluminescence imager, and a Siemens micro PET/CT scanner. There is also an animal quarantine room within the imaging center itself dedicated to holding animals that have been imaged.

http://academicdepartments.musc.edu/cbi
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