



Advances in MR Imaging and the Questions They Answer

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Magnetic resonance imaging (MRI) provides many windows into the physiology of the brain, providing sensitive measures to follow nutrition interventions. Three particularly promising techniques are discussed: magnetic resonance spectroscopy (MRS), diffusion tensor imaging (DTI), and magnetic resonance elastography (MRE). These techniques allow us to monitor changes in brain metabolism, neuronal connectivity, and tissue structure.

MRS

Nuclei with different chemical environments give off signals at different frequencies during an MRI experiment. In a normal MRI structural scan, the protons in water far outnumber other protons and the image mostly reflects water density, along with relaxation effects specific to different tissue compositions. However, with MRS, data acquisition occurs with water signal suppressed and a readout over time is obtained that is sensitive to these varying frequencies. With standard proton MRS, several metabolites are available that have sufficient concentration to be detected and quantified using their characteristic signatures in the frequency spectrum. These include N-acetylaspartate (NAA), glutamate, glutamine, creatine (Cr), choline (Cho), myo-inositol, along with a few others, depending on the experimental setup.¹

MRS is sensitive to the functional state of the tissue, often demonstrating predictive power for future development trajectories or for future pathological deteriorations. In one study, infants were scanned at term with MRS, and the results indicated that cerebellar NAA/Cho ratio predicted performance on a cognitive test that was performed at 24 months.² In a study at the other end of the age-scale, Erickson and colleagues found that NAA levels declined with age in older adults, but that fitness compensated for the aging effect.³ The researchers further found that NAA mediated the relationship between fitness and working memory performance.

During the long history of MRS, several nutrition studies have been conducted, demonstrating that MRS is sensitive to both acute and long-term dietary interventions. For example, Babb and colleagues performed a study in which healthy adults ingested Cho-containing compounds at a rate equivalent to 50 mg/kg.⁴ Over the 3 hours of MRS scanning that followed the ingestion, Babb

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et al found 6% increases in the Cho/Cr ratio and 3% increases in the Cho/NAA ratio (Fig 1). Over a longer term, Lyoo and colleagues had subjects ingest Cr monohydrate over the course of 2 weeks.⁵ MRS of an axial slice of the brain demonstrated increases in brain Cr at scans after both 1 week and 2 weeks.

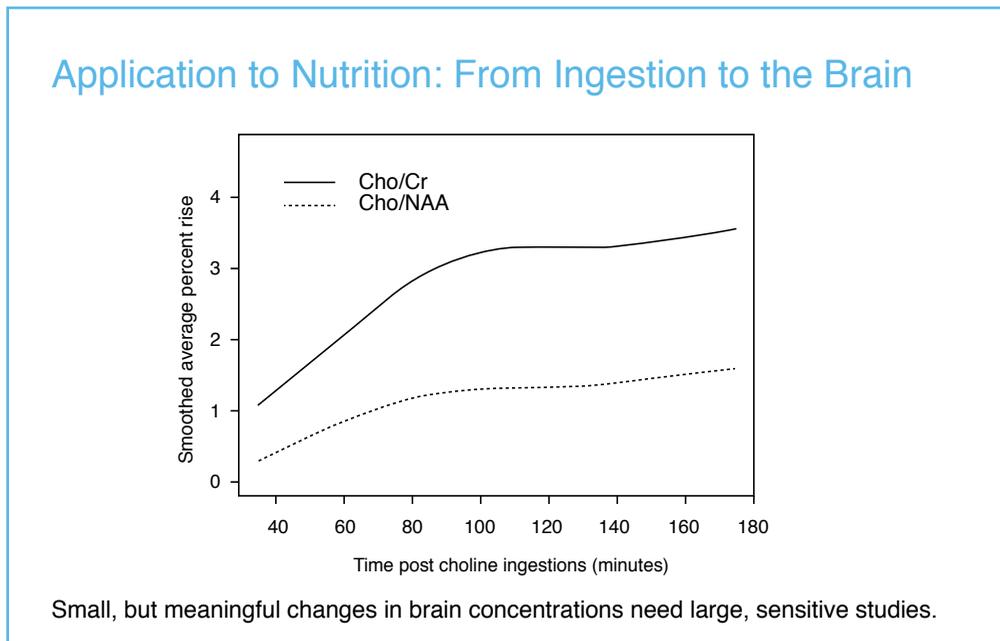


Fig 1. Effects of choline ingestion on the brain.⁴ Subjects given equivalent of 50 mg/kg free Cho ingested orally. Magnetic resonance spectroscopy obtained 30 minutes to 3 hours post-ingestion. Six percent increase in Cho/Cr and three percent increase in Cho/NAA at peak.

Cho=choline, Cr=creatine, NAA=N-acetylaspartate

Source: Babb SM et al. Oral choline increases choline metabolites in human brain. *Psychiatry Res.* 2004 Jan 15;130:1-9. Reprinted by permission of Elsevier.

Current applications of MRS are limited by low signal-to-noise and low spatial resolution for resolving distributions of metabolites. Since specific regions of the brain often are associated directly with specific behavioral deficits, these limitations likely reduce the ability of MRS to detect functionally relevant changes. Several technologies hold great promise for increasing the spatial resolution of MRS to interrogate specific brain regions for functionally relevant measures of metabolism. These include advanced acquisition trajectories,⁶ multinuclear acquisitions taking advantage of other magnetic resonance-active nuclei, and denoising techniques based on prior spatial and temporal information.^{7,8}



DTI

DTI acquisitions with MRI sensitize the image acquisition to small movements of diffusing water. With many barriers to water diffusion in a cell, including the cell membrane and myelin layers, the water diffusion in white matter is not isotropic. By examining this anisotropy, characteristics of neuron and myelin integrity can be examined.

Non-invasive measures of white matter integrity using DTI have seen increasing use in studies of age-related declines in cognitive behaviors.⁹⁻¹¹ These DTI measures have been verified in animal models showing that the diffusion properties in a neural fiber bundle give important information about the integrity and the myelination of brain fiber pathways.^{12,13}

Although DTI measures very small displacements of water, it does so with a large volume averaging to summarize this information at the level of an imaging pixel. Sensitivity to fine structures of white matter is inhibited by large voxel sizes, requiring more complex acquisitions to estimate multiple axonal fiber types within a voxel. Our bioengineering group at the University of Illinois has developed high spatial resolution DTI acquisitions to try to resolve fine-scale structures to enable leveraging of simple models of the diffusion process (Fig 2).¹⁴

High Spatial Resolution DTI

- Average diffusion properties within an imaging voxel—reduce partial volume effect
- Heterogeneity within a voxel: multiple fibers variation in direction, small lesions
- Precision depending on spatial resolution/ diffusion encoding scheme

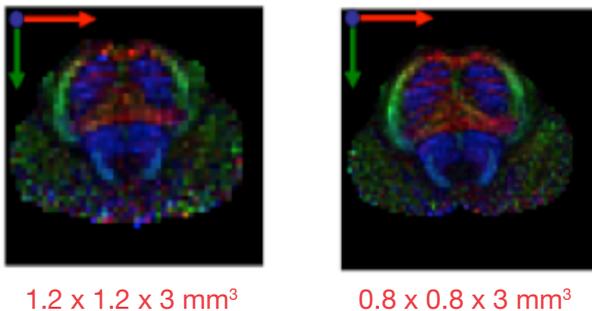


Fig 2. Some features of high spatial resolution diffusion tensor imaging (DTI).¹⁴

Source: Karampinos DC et al. High-resolution diffusion tensor imaging of the human pons with a reduced field-of-view, multishot, variable-density, spiral acquisition at 3 T. *Magn Reson Med.* 2009 Oct;62(4):1007-1016. Reprinted by permission of John Wiley and Sons.

MRE

The mechanical properties of biological tissues have been shown to vary greatly throughout tissues and in disease states. The shear modulus of brain tissue, in particular, varies significantly between and within white matter structures in the brain.^{15,16} Recently, it was demonstrated through the use of MRE that the shear modulus of brain tissue decreases in neurodegenerative disease such as Alzheimer's¹⁷ and normal pressure hydrocephalus.¹⁸

MRE uses slight mechanical actuation to induce small displacements in tissues.¹⁹ The propagation of these displacements can be used to infer the mechanical stiffness of tissues, along with other mechanical properties. MRE of the brain requires high spatial resolution and high sensitivity to delineate wavelength effects in fine neural structures. We have developed techniques to enable localized MRE of white matter structures in the brain.²⁰ These developments will enable future studies of the impact of nutrition and brain chemistry on the structural integrity of specific brain areas.



Conclusion

MRI provides many windows into the physiology of neural structures. MRS can be used to examine localized brain chemistry and metabolism, DTI to assess white matter axonal connectivity and integrity of the membranes and myelin, and MRE to provide information on the overall structural integrity of brain tissue. This multiparametric space allows for specific physiological questions to be asked with respect to the impact of a nutrition intervention on the brain.

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