

The NMR revolution in brain imaging

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Nuclear magnetic resonance (NMR) technology is accelerating a revolution in medical and scientific neuroimaging that began in the 1970s with the introduction of powerful new x ray methods—computed tomography, positron emission tomography, and single photon emission computed tomography. Refinement of these technologies continues as applications for which they are uniquely well suited are defined.

Summary points

Magnetic resonance imaging has become the premier imaging technique in medicine

It is the first well known member of a large array of NMR techniques

Several newer NMR techniques have medical and scientific potential

Such techniques are minimally invasive

Their power and versatility are unprecedented

They can make medical care more cost effective

Most clinicians are familiar with magnetic resonance imaging, which has recently become the most generally useful imaging modality for medical diagnosis.¹ But conventional magnetic resonance imaging is only the first of an array of methods that will eventually comprise the NMR diagnostic armamentarium. We use the generic term “nuclear magnetic resonance” to emphasise the versatility of the technology. New NMR methods are in various stages of implementation and, combined with conventional magnetic resonance imaging, they are on the verge of changing medical practice so extensively that to describe the process as a revolution may ultimately seem conservative.

NMR technology differs fundamentally from x ray methods. It uses the magnetic properties of atomic nuclei that occur naturally in the body; mostly hydrogen (¹H) in water and other molecules, although several other nuclei, including phosphorus (³¹P), carbon (¹³C), lithium (⁷Li), sodium (²³Na), nitrogen (¹⁵N), and oxygen (¹⁷O), are in regular use for medical research, and diagnostic applications are on the horizon.²

As measurements are made by synchronising atomic nuclear signals already present in tissue, NMR methods are among the least invasive diagnostic techniques available.³ At the cost of adding a minor degree of invasiveness, drugs that enhance contrast by altering the magnetic properties of tissues improve diagnostic utility. Because it can distinguish among signals from several biochemical molecules NMR technology has inherent chemical specificity. Such features make NMR methods the richest source of information about living tissue available from any imaging technology.

Diffusion and perfusion NMR imaging

New NMR techniques with important consequences for daily medical practice include diffusion weighted imaging and magnetic resonance angiography in ischaemic stroke⁴⁻⁵; figure 1 shows the advantage of these over conventional magnetic reso-

nance imaging for detection of early ischaemic stroke. When such a lesion is present, diffusion weighted imaging shows it clearly, and magnetic resonance angiography can often show the occluded artery without use of catheters, injected contrast agents, or ionising radiation.

The lesion in figure 1 is barely detectable by conventional magnetic resonance imaging. x Ray computed tomography would not have shown it at all, being characteristically negative in ischaemic stroke for many hours after the lesion is evident on conventional magnetic resonance imaging. When only x ray computed tomography is available time critical treatment decisions must be made either in the absence of precise information about the lesion or at the expense of invasive and costly x ray angiography. The advantages of diffusion weighted imaging and magnetic resonance angiography for diagnosis of early stroke are so great that much recent literature suggests that NMR methods will soon largely replace x ray computed tomography in the management of this condition.⁶⁻⁹

In addition to imaging of large cerebral arteries and veins by magnetic resonance angiography, NMR perfusion imaging can measure blood flow through capillary beds.^{4,10} The state of brain perfusion associated with ischaemic and other lesions can be investigated. Both magnetic resonance angiography and perfusion imaging can be done without contrast enhancing agents, but contrast agents used for NMR imaging (for example, gadolinium chelates) cause allergic reactions less frequently than those used for x ray studies, and use of them increases anatomical resolution and sensitivity to several disease processes.

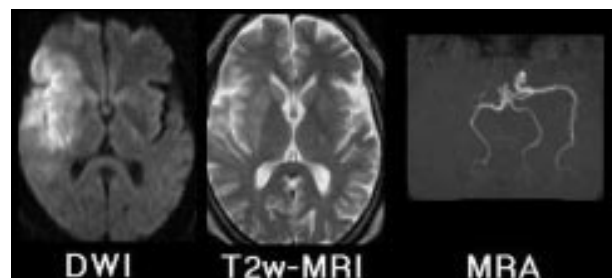


Fig 1 Magnetic resonance images 9.5 hours after onset of clinical stroke syndrome. Diffusion weighted imaging (DWI) shows hyperintense signal from physiologically damaged tissue surrounding right sylvian fissure—conventional T2 weighted imaging shows only subtle changes in same region. Magnetic resonance angiography (MRA) shows flow void in right internal carotid and middle cerebral arteries

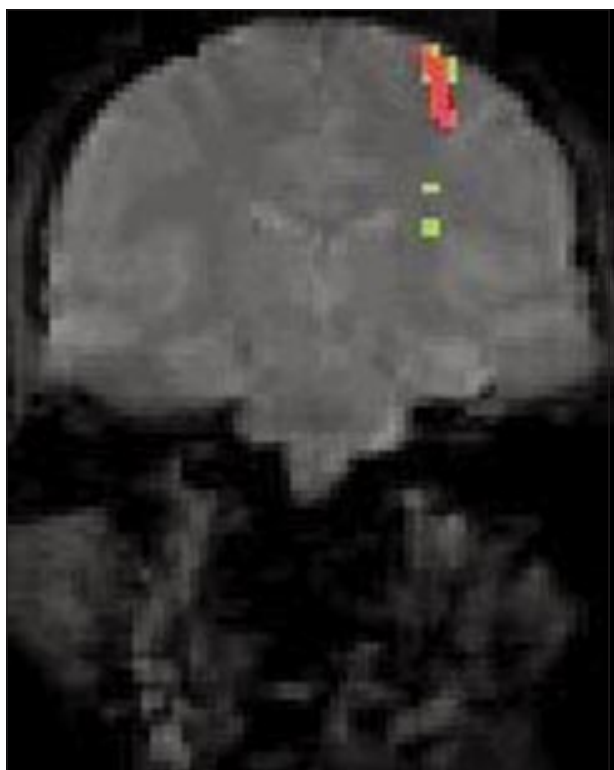


Fig 2 Functional magnetic resonance image of normal subject performing finger movements (conventional coronal magnetic resonance image in grey). Coloured regions identify tissue in which blood flow increases to meet extra metabolic requirements of task

Functional magnetic resonance imaging

Functional magnetic resonance imaging can detect changes in blood oxygenation caused by increased metabolism of activated parts of the brain (fig 2).¹¹ This has become a powerful tool for cognitive neuroscience research and brain activity mapping to preserve critical functions in patients needing neurosurgery.¹²⁻¹³

Functional magnetic resonance imaging can be used to study any motor, sensory, or cognitive task that a patient can perform while in a scanner. Since functional magnetic resonance imaging requires no catheterisation or injection of contrast agent, observations can be repeated easily. It can be combined with contrasted studies for specific purposes, such as determination of the anatomical relation between a tumour mass and a brain region serving some key function. Functional magnetic resonance imaging is a powerful tool for studying the relation between brain and behaviour and how this is affected by disease.

Magnetisation transfer imaging

Magnetisation transfer imaging detects changes in the properties of water protons and some other magnetic nuclei as they move from one physical state or chemical configuration to another. The technique can be used to probe protein-water interaction and the rates of some key chemical reactions that are catalysed by enzymes. Its most productive medical application has been in the study of brain white matter disease, notably multiple sclerosis, where it shows lesions and aspects of pathophysiology opaque to other NMR methods and to x ray computed tomography.¹⁴⁻¹⁷

Magnetic resonance spectroscopy

Magnetic resonance spectroscopy detects magnetic nuclei other than water protons.¹⁸ Lactate, some amino acids, and several other small metabolites in the brain can be measured in living tissue by detection of signals from their hydrogen nuclei.

Magnetic resonance spectroscopy of ³¹P detects several small metabolites that contain phosphorus—ATP, phosphocreatine, and inorganic phosphate among them. Magnetic resonance spectroscopy for the detection of metabolites containing ¹³C, ¹⁵N, and ¹⁷O is becoming the premier technology for measurement of metabolic rates in living tissue. Brain pH can be measured by its effects on pH sensitive ³¹P and ¹H signals.¹⁹

Magnetic resonance spectroscopy is unique among measurement technologies in the range of chemically specific studies that it can make on living undisturbed tissue—for example, analysis of antiepileptic drug effects on brain metabolism,²⁰⁻²¹ demonstration of low γ -aminobutyric acid concentrations in the brains of patients with alcoholism and hepatic encephalopathy,²² and detection of chemical abnormalities in the white matter of patients with multiple sclerosis before changes can be seen on magnetic resonance images.²³

Spectroscopic imaging

Spectroscopic imaging is an extension of magnetic resonance spectroscopy, which allows mapping of the distribution of specific compounds in the living brain. The technique is complex, but it is so powerful a way of studying normal and diseased brain chemistry that numerous laboratories are working to make it generally available. It has already been used to study several disease states including epilepsy,²⁴ panic attacks,²⁵ and brain tumours (fig 3).²⁶

All the NMR techniques discussed above are feasible in humans with appropriately equipped NMR instruments only a little different from thousands of medical imaging scanners already in regular use worldwide. The combination of power, versatility, and non-invasiveness presented by these methods has no historical parallel. Only comparisons with all of microscopic technology from Leeuwenhoek's optical instrument in the 17th century to modern scanning tunnelling electron microscopes, or molecular biology, give an idea of the scale on which NMR technology is unfolding.

Owing to the brain's comparative immobility, NMR measurements are more advanced there than elsewhere in the body. As motion artefacts in thoracic and abdominal viscera are brought under control by methods that acquire images quickly the full range of NMR methods in use by neurologists and neurosurgeons will become available to a wider range of physicians—a movement already under way in cardiology.²⁷⁻²⁸

NMR methods have their own limitations, which must be taken into account. As with x ray computed tomography they are not, and will never be, bedside procedures. Patients undergoing them must be free of magnetic implants and instruments. Even non-magnetic metallic implants may degrade image quality near the implant and diminish the test's diagnostic value. Some

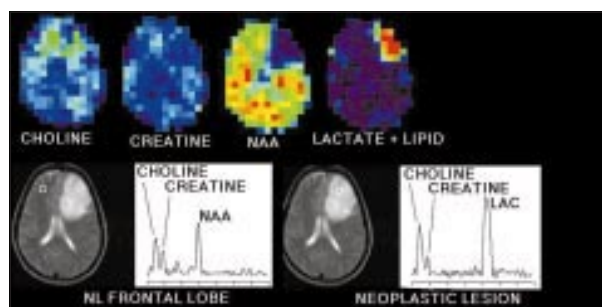


Fig 3 (Top) Spectroscopic image of patient with glioblastoma multiforme. Colour images display topographical distribution of intensities of NMR signals from several cerebral metabolites including total choline, total creatine, N-acetylaspartate, lactate, and lipid. (Bottom) Tissue section examined displayed by conventional magnetic resonance imaging. Metabolite signals can be displayed as spectra from volumes (white squares) referenced to magnetic resonance image (graphs). Compared with right frontal lobe, neoplastic tissue in left frontal lobe shows increased choline, lactate, and lipid signals but decreased N-acetylaspartate signals

patients are unable to tolerate the confines of a scanner or to keep still; sedative and anti-anxiety drugs can be helpful in such cases. Traditional routines of medical practice will need modification to take advantage of the opportunities offered by NMR technology; in particular closer consultation between referring and imaging physicians will be necessary to choose which of many possible measurements are most important for each patient.

But some limitations are more apparent than real. Many physicians may have heard that magnetic resonance imaging is too expensive for routine diagnostic use. We believe the opposite will prove to be true. In terms of technical maturity and familiarity to the medical profession NMR technology is today about where x ray computed tomography was 20 years ago—when it too was considered overly expensive—but the former is far more powerful. As NMR methods achieve technical and operational maturity over the next decade we predict that their power, versatility, and non-invasiveness will pay back their implementation costs many times over, by earlier and more accurate diagnosis leading to more effective treatment of diseases, fewer errors, and fewer admissions to hospital.

Important as those practical gains will be if our expectations are accurate, they are not the end of the story. Beyond them lie the benefits of reduced patient distress from onerous procedures and especially the time that more efficient diagnosis can recover for unhurried conversation between physician and patient.

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