Advanced neurological magnetic resonance imaging

Richard Watts
Department of Physics and Astronomy, University of Canterbury, Christchurch

In the past year we have established a research programme in magnetic resonance imaging (MRI). This has brought together a wide range of both basic and clinical scientists from different institutes, including the new Van der Veer Institute for Parkinson's and Brain Research, the University of Otago Medical School, Christchurch Hospital, and the University of Canterbury. This unique expertise allows both the development of new techniques for MRI data acquisition and analysis as well as their application to clinically important questions.

Functional magnetic resonance imaging

While the structural anatomy of the brain has been reasonably well understood for a long time, the way in which the living brain functions has been more elusive. However, correlations between neurological deficits following stroke and other brain injuries, and post-mortem findings suggested that the brain is divided into functionally distinct processing units. For example, damage to the parts of the brain identified by Broca and Wernicke were found to lead to specific deficits in the production and comprehension of language respectively. It is only in recent decades that functional neuroimaging of the living brain has become possible using techniques such as positron emission tomography (PET) and functional MRI (fMRI).

In fMRI experiments, the subject usually alternates between performing a mental task and resting (or an alternative task) while repeated images of the brain are rapidly acquired. Areas of the brain in which there are strong correlations between the performance of the task and the MRI signal time course are then identified as having been involved in that task.

When the subject starts to perform the task, neuronal activity increases in those parts of the brain required. These areas require additional energy, which is provided by an increase in the regional blood supply. This increase in blood flow leads to an increase in the blood oxygenation level (the ratio of oxyhaemoglobin to deoxyhaemoglobin), which in turn changes the magnetic properties of the blood and hence the MRI signal. It is interesting to note that it has been known for nearly 70 years that the magnetic properties of oxygenated and deoxygenated blood are different [1], but it is only in the last 15 years that this difference has been put to use with functional MRI [2].

Such fMRI studies are giving new insights into the workings of both healthy and diseased brains (for example, Fig. 1). In Christchurch there is particular interest in applying fMRI to Parkinson's disease, bipolar disorder, depression, swallowing disorders, and responses to facial expressions.

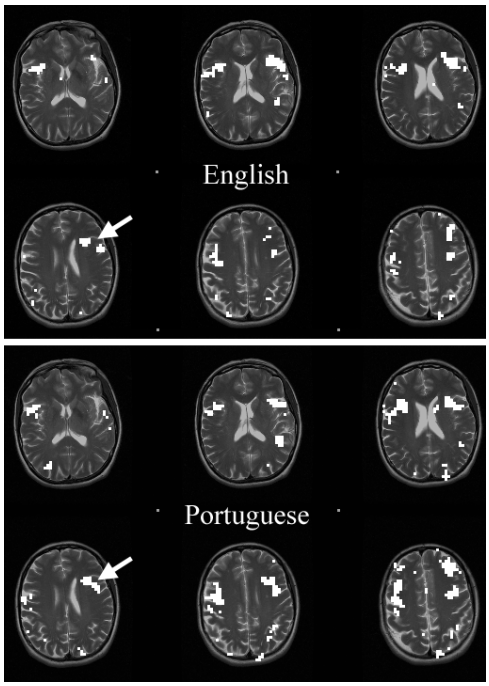

Figure 1. fMRI of a bilingual subject asked to think of words beginning with different letters of the alphabet. While broadly similar areas of the brain are involved in both languages (bright white blocks near the edge of the brain), subtle differences in the production of English and Portuguese words (arrows) are observed.

Richard Watts started his research career with a DPhil in Physics from the University of York (UK), studying the magnetic properties of thin films. This was followed by postdocs in Grenoble (France) and Sheffield (UK). In 1998 he finally saw the light and moved into Medical Physics (specifically MRI) with a post at Cornell University Medical College in New York, where he became an Assistant Professor of Physics in Radiology. In 2003 he took up his current position as a Senior Lecturer in the Department of Physics and Astronomy of the University of Canterbury.

Diffusion MRI

Diffusion is the random motion of molecules due to thermal energy. MRI can be made sensitive to both the amount of diffusion of water in the brain and its variation with direction.

The directional variation of diffusion yields unique information about the structure of the brain. Different parts of the brain are connected by bundles of axons, which form white-matter fibre tracts. These bundles of fibres with similar orientations restrict the diffusion of water, with diffusion parallel to the fibres being less restricted than perpendicular (a factor of 4 in the apparent diffusion constant is observed in the largest fibre bundles). Using MRI we can identify the direction of greatest diffusion, and hence infer the fibre orientations throughout the brain. This allows us to follow fibres from one part of the brain to another, a recent development known as white-matter tractography (Fig. 2) [3, 4]. It should be noted that while the MRI signal is made sensitive to the microscopic structure of the brain, the resolution of the images obtained is nowhere near sufficient to image individual fibres. When viewing images such as those shown in Fig. 2, each line represents a single pathway though the diffusion dataset; it does not represent a single fibre.

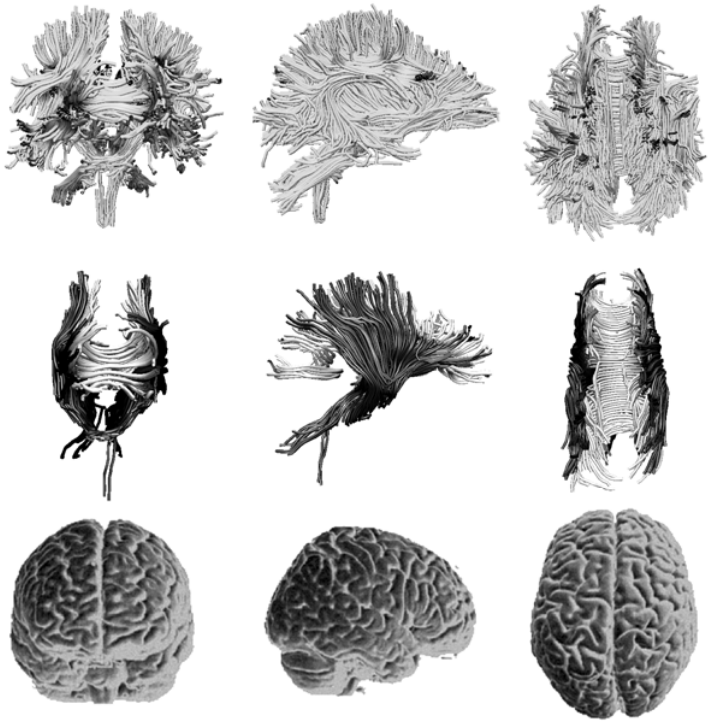

Figure 2. White-matter fibre tracking using diffusion MRI, showing (top row) fibres throughout the entire brain, and (middle row) fibres comprising the (dark) corticospinal tract and (light) corpus callosum. From left to right the images show views from the front, side and top of the brain, as indicated by the rendered brain (bottom row).

White-matter tractography follows fibre bundles from one part of the brain to another. It is the only technique that allows such in-vivo determination of connectivity. White-matter tractography is giving unique insights into the fundamental wiring of the brain, and is extending our understanding of the workings of the brain and the effects of disease.

While white-matter tractography can produce spectacular images, the main clinical utility of diffusion MRI is that accurate, quantitative measures that relate to microscopic tissue integrity can be derived. However, natural anatomical variations between subjects make quantitative comparisons difficult. One approach is to have an expert define regions of interest in each brain on the basis of his/her knowledge of brain anatomy. To avoid this subjective, labour-intensive task, we use image processing techniques to 'warp' each brain onto a standard template. This allows automatic statistical maps to be generated, highlighting areas of difference in the diffusion parameters [5]. We have applied this analysis to a study of professional boxers, and identified parts of the brain which appear to show microscopic damage long before it is visible on 'conventional' MRI scans.

We will also apply diffusion MRI to a range of clinical problems, including the assessment of mild closed head injury, Parkinson's disease, autism, multiple sclerosis, and brain development in normal, pre-term and methadone-exposed infants.

Conclusions

MRI offers amazing flexibility in the range of types of contrast that can be obtained, as well as excellent differentiation between soft tissues. We have outlined two recent developments that give contrast based on blood oxygenation and water diffusion. An important advantage of MRI over X-ray and nuclear medicine-based techniques is its safety, due to the absence of ionising radiation. This allows, for example, longitudinal studies of child development or monitoring of disease progression that would not otherwise be feasible.

The combination of functional and diffusion MRI offers the exciting prospect of understanding both the functional organisation and connectivity within the brain. fMRI allows us to identify the tasks performed by each functional unit, while diffusion MRI shows the white-matter tract connections between them.

References

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