



## **Watching the Brain at Work: Functional MRI for Children with Epilepsy**

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Advances in brain imaging have provided unprecedented opportunities to enhance understanding of the functional organization of the brain. At BC Children's Hospital, advanced techniques of non-invasive brain imaging have been integrated into the care of children with epilepsy, as the focus of active, ongoing research involving international collaboration.

A brief overview of the basic principles and applications of functional MRI to pediatric epilepsy will help put these advances in context.

Magnetic resonance imaging (MRI) technology is an extremely fruitful, rapidly evolving technology for clinical neurosciences. MRI enables visualization of fine details of the structure of the brain and the connections among brain regions.

A very specialized MRI technique, known as functional MRI, enables observation of the brain at work. This can even be demonstrated in real time, while a person is engaged in an activity within the MRI scanner. Recording of brain activation during specific tasks permits creation of useful maps of brain organization in a specific individual.

Such brain maps are particularly important in the pre-surgical assessment of children who are candidates for epilepsy surgery. The goal of such surgery is generally to remove or disconnect discrete areas of the brain that cause seizures, while avoiding injury to areas of the brain that control important functions.

To understand how functional MRI works, it is important to review a few basic principles about how MR images are created, how the brain works when it is activated, and how brain activation affects MR images to make functional MRI possible:

An MRI scanner obtains exquisitely detailed images of the structure of the brain based upon the response of brain tissue to a very strong magnetic field.

A typical MRI scanner produces a magnetic field thousands of times more powerful than a typical refrigerator magnet.

While a person lies inside an MRI scanner, the nuclei of certain atoms, especially hydrogen, are temporarily influenced by the magnetic field.

The MRI system transmits radio frequency pulses through a specialized head coil, which alters the alignment of these nuclei (protons).

Signals are then released from the tissue, depending upon the chemical properties of the tissue.

The signals are received by the MRI scanner, and processed by computers to make images of the brain. Some tissues may appear very bright, while other tissues, of different chemical composition, may appear very dark, depending upon how the scan is set up.

By fine-tuning the scan parameters, tissue structures and characteristics can be determined with great precision.

The end result is a map of the anatomy, or structure, of the brain.

The next step is to capture information about how the brain is working. To understand how the brain works, it is important to understand that the brain's 100 billion nerve cells or neurons are organized into intricate networks which transmit information using chemical and electrical signals.

Networks in various areas of the brain are optimized for specific functions, such as vision, hearing, language and motor control. In the visual system, for example, signals coming from the eyes travel to a relay center in the brain called the thalamus, and then from there are transmitted to the brain's primary vision centers at the very back of the brain, in the occipital lobes.

When visual signals from the eyes reach the vision centers in the brain, chemical signaling molecules known as neurotransmitters are released. These molecules stimulate or "activate" the nerve cells in the vision centers.

When the visual areas become "activated", extra fuel is needed for the extra work that is done. The fuel required--blood sugar, or glucose--is obtained from blood vessels, together with oxygen. When an area of the brain is activated, we observe an increase in the consumption of glucose. As the blood vessels open up to deliver more fuel, they also provide extra oxygen to the tissues, giving them a brighter red color.

To understand the mechanism of functional MRI, it is crucial to know that the oxygen content of the blood not only affects the color of the blood, it also affects the MRI signal.

The reasons for this are as follows:

Oxygen is carried in the blood by red blood cells, which contain an oxygen-carrying protein called hemoglobin.

Hemoglobin contains iron, which affects the magnetic field of the MRI scanner.

When oxygen is bound to hemoglobin, it reduces the effect of the iron on the magnetic field.

Whenever an area of the brain becomes "activated", the blood oxygen content of the tissue rises. Whenever the oxygen content rises, the MRI signal rises.

Even a brief flash of light to the eyes will cause the MRI signal to rise to a peak over three to five seconds, and then to fall gradually back to baseline levels over about 15 to 30 seconds.

This effect, known as the Blood Oxygen Level Dependent (BOLD) effect, is the basis of most functional MRI procedures performed for clinical purposes.

To map out functional areas of the brain, it is necessary to record a series of images of the brain while a person is engaged in a task, and to look for areas of the brain in which changes in MRI signal are time-locked to the particular task.

For each task, this generally requires imaging the entire brain every few seconds for several minutes. With the availability of high-speed computers, it is possible to analyze the information and locate areas of brain activity within moments of completion of a task. This has significant benefits over previous methods, because it is much less invasive.

Thus, functional MRI procedures reduce the need for procedures such as open brain surgery for electrical mapping of brain function (craniotomy with electrocorticography), and for injection of sedatives into carotid arteries on the left and right side to test for the language-dominant cerebral hemisphere (angiography with sodium amobarbital injection, also known as the Wada test).

In preparation for brain surgery, functional MRI is of value in locating areas involved in motor control of the hands and in areas involved in language function.

Functional MRI procedures can be applied to children with customized procedures. Over the past decade, we have developed expertise in pediatric brain mapping with functional MRI through research and clinical experience in the Children's Brain Mapping Centre at BC Children's Hospital.

The biggest challenges are overcoming anxiety and restlessness. It is difficult to perform functional MRI if someone cannot cooperate. It is challenging to analyze functional MRI data if there is significant head motion. Thus, it is important for children to lie as still as possible.

It is also important to adapt tasks so that they are appropriate for children of various ages. To optimize results with children, we use a custom-built MRI simulator, giving us the ability to rehearse procedures the children to reduce apprehension and to ensure that they understand how to perform tasks correctly.

We are usually able to scan cooperative children aged eight years and older without difficulty, but we have successfully scanned children as young as five years of age.

Refinement of protocols and techniques for functional MRI is a very active area of research internationally. BC Children's Hospital is part of an international research consortium involving pediatric epilepsy surgery centers in North America, Australia, and the UK.

The goals of this research are to utilize functional MRI to evaluate organization of language function in children who are candidates for epilepsy surgery, and to measure subsequent language outcomes.

By sharing methodology and pooling information from many sites, enhanced understanding of the impact of seizure disorders upon the organization of language in the brain will be achieved.

I hope that this brief introduction to functional MRI will help readers understand why functional MRI is an important new technique. At BC Children's Hospital, we will continue to develop additional resources for further research in brain mapping and functional MRI.

These will have direct application to many children in British Columbia who live with epilepsy. Future advances in brain mapping and MRI methods will help keep BC Children's Hospital at the forefront of pediatric epilepsy care.

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