


FUNCTIONAL MRI (FMRI)

BY

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Introduction

- ▶ Functional MR imaging (fMRI) is a rapid MR imaging technique that acquires images of the brain during activity or stimulus and at rest.
- ▶ Scanning procedures and restrictions are generally similar to clinical MR.
- ▶ Most fMRI studies use changes in BOLD contrast, although other measures exist.
- ▶ Functional MRI creates a series of images that capture blood oxygen levels in parts of the brain that are responsible for movement, perception, and cognition.

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- ▶ fMRI is becoming the diagnostic method of choice for learning how a normal, diseased or injured brain is working, as well as for assessing the potential risks of surgery or other invasive treatments of the brain.
 - ▶ Detects the changes in blood oxygenation and flow that occur in response to neural activity
 - ▶ If the MRI experiment is done while a mental task is given to a subject, a so-called functional magnetic resonance image (fMRI) is generated. fMRI is used to map different sensor, motor and cognitive functions to specific regions in the brain.

History of fMRI NMR

- ▶ nuclear magnetic resonance
- ▶ Felix Bloch and Edward Purcell
- ▶ 1946: atomic nuclei absorb and re-emit radio frequency energy
- ▶ 1952: Nobel prize in physics MRI
- ▶ 1973: Lauterbur suggests NMR could be used to form images
- ▶ 1977: clinical MRI scanner patented
- ▶ 1977: Mansfield proposes echo-planar imaging (EPI) to acquire images faster
fMRI
- ▶ 1990: Ogawa observes BOLD effect with T_2^* blood vessels became more visible
as blood oxygen decreased
- ▶ 1991: Belliveau observes first functional images using a contrast agent
- ▶ 1992: Ogawa & Kwong publish first functional images using BOLD signal

Advantages & Disadvantages

- ▶ • **Pros:**
- ▶ Can see activation in addition to high res brain structures
- ▶ Scanners can be fitted to present stimuli
- ▶ Higher spatial and temporal resolution than PET
- ▶ Minimal invasive
- ▶ • **Cons:**
- ▶ Cannot trace neurotransmission like PET
- ▶ Blood flow is, again, only an indirect correlate of brain activity

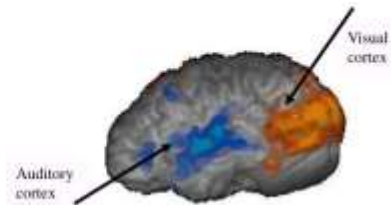
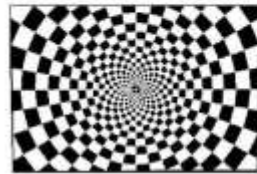
Why is fMRI Used?

- ▶ Examine the anatomy of the brain
- ▶ Determine precisely which part of the brain is handling critical functions such as thought, speech, movement and sensation, which is called brain mapping
- ▶ Help assess the effects of stroke, trauma or degenerative disease (such as Alzheimer's) on brain functions
- ▶ Monitor the growth and function of brain tumors .
- ▶ Guide the planning of surgery, radiation therapy, or other surgical treatments for the brain

PROCEDURE

- ▶ a series of baseline images are taken of the brain region of interest when the subject is at rest, as A
- ▶ the subject performs a task
- ▶ a second series of images is taken, as A'
- ▶ the first set of images is subtracted from the second, as $B=A'-A$
- ▶ the areas that are most visible in the resulting image, B, are presumed to have been activated by the task

One example



- A healthy subject was asked to listen to sentences being spoken while watching a screen with a flashing checkerboard presented. The sentences started and stopped at slightly different times than the flashing picture was turned on and off.
- On the basis of the differences in timing activation in the brain, the areas responsible for hearing (in the middle of the brain in grey) and vision (in the back of the brain in white) could be localized by fMRI (Image courtesy of Dr. S. Smith from www.fmrib.ox.ac.uk).

Medical Significance of fMRI

- ▶ Different tasks activate different parts of the brain
- ▶ When listening to music, a specialized area in the auditory cortex along the sides of the brain shows an increased signal
- ▶ The locations vary for different cases and individuals.

a diagnostic method

- ▶ learning how a normal, diseased or injured brain is working
- ▶ assessing the potential risks of surgery or other invasive treatment of the brain.
- ▶ planning brain surgery -- monitor normal brain function as well as any disturbed brain function.
- ▶ While research is still ongoing, it appears that fMRI can also help assess the effects of stroke, trauma or degenerative disease (such as Alzheimer's) on brain function

fMRI?

- ▶ It aims to determine the neurobiological correlation of behavior by identifying the brain regions (or “functioning modules”) that become “active” during the performance of specific tasks in vivo.
- ▶ It extends traditional anatomical imaging to functional imaging.
- ▶ observe both the structures and which structures participate in specific functions
- ▶ improving our understanding of a variety of brain pathologies.
- ▶ such as the addictive behaviours of gambling or drug abuse, are without structural brain changes.

the principle:

- ▶ when a brain region is being used, arterial oxygenated blood will redistribute and increase to this area.

Functional Resolution

- ▶ The ability of a measurement technique to identify the relation between underlying neuronal activity and a cognitive or behavioural phenomenon.
- ▶ Functional resolution is limited both by the intrinsic properties of our brain measure and by our ability to manipulate the experimental design to allow variation in the phenomenon of interest.

How to measure neural activity?

- ▶ The physiology of neural activity involves many complex processes.
- ▶ MR has the capability to measure parameters related to several neural physiological functions, including:
 - ▶ changes in phosphorus metabolism and metabolic byproducts
 - ▶ blood flow
 - ▶ blood volume
 - ▶ blood oxygenation Capillary beds within the cortex

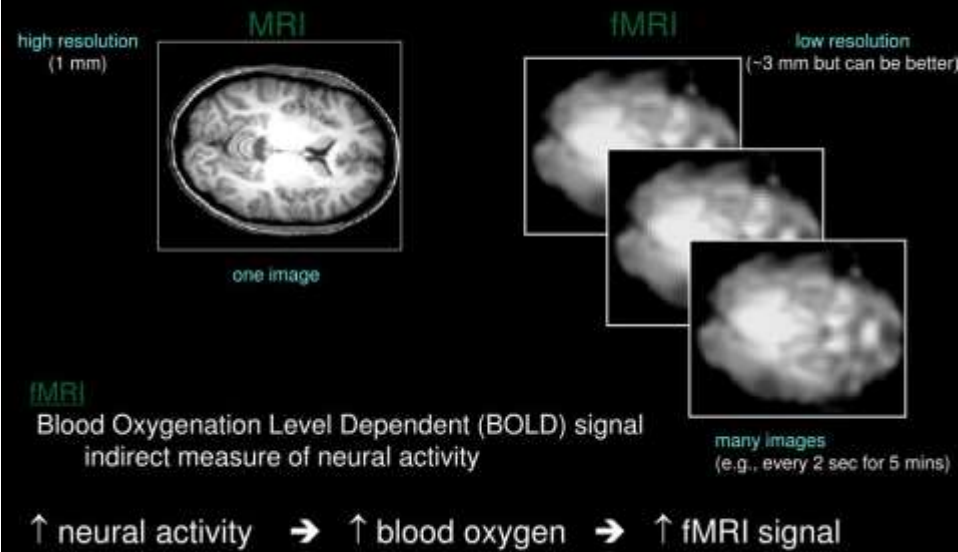
Type of functional MRI:

- ▶ **BOLD fMRI**
- ▶ Measures blood oxygenation, i.e., regional differences in oxygenated blood

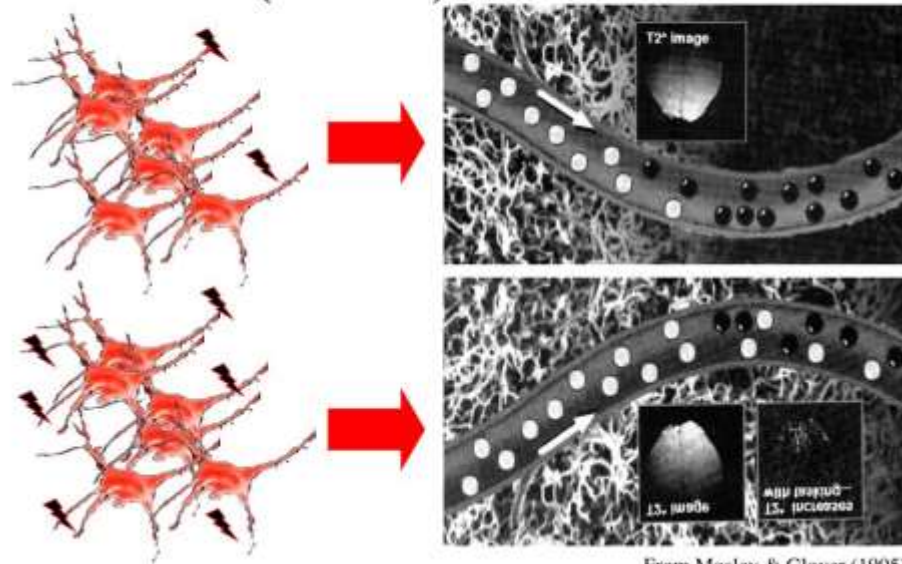
BOLD fMRI

- ▶ Blood Oxygen Level Dependent Contrast
- ▶ Based on:
 - ▶ (1) different magnetic properties of deoxy- and oxyhemoglobin
 - ▶ (2) coupling of oxygenated blood flow and neuronal activity
- ▶ High spatial and temporal resolution
- ▶ 3-6 second delay in hemodynamic response ---limits optimal temporal resolution.
- ▶ Compares images taken during active and rest states within a single session

MRI vs. fMRI



Blood Oxygenation Level Dependent (BOLD) Contrast



From Mosley & Glover (1995)

Magnetic properties of deoxy- and oxyhaemoglobin

- ▶ Deoxyhaemoglobin is paramagnetic .
- ▶ The presence of deoxyhaemoglobin in vessel causes a **susceptibility** difference between the vessel and its surrounding tissue.
- ▶ Then causes dephasing of MR proton signal
- ▶ Leading to a reduction in the value of $T2^*$, which causes a darkening of the image

- ▶ oxyhaemoglobin is diamagnetic.

Susceptibility artifacts

- ▶ The magnetic susceptibility of a material
- ▶ a measure of how much magnetization is produced within it when it is placed in a magnetic field.
- ▶ Susceptibility differences between tissues can lead to signal loss in MR scans, especially in EPI scans.
- ▶ The susceptibility difference between deoxygenated and oxygenated blood is the basis of the BOLD effect used to detect fMRI signals.

HDR (Hemodynamics Response)

- ▶ the time courses of the changes in blood flow, blood volume and blood oxygenation that occur in the brain in response to brain activity.
- ▶ In the brain, neuronal activity is thought to cause a local increase in blood flow (CBF), which leads to an increase in blood oxygenation and blood volume (CBV).
- ▶ Upon activation, oxygen is extracted by the cells, increasing the level of deoxyhaemoglobin in the blood. And it is compensated for by an increase in blood flow in the vicinity of the active cells, leading to a net increase in oxyhaemoglobin.
- ▶ Signal changes

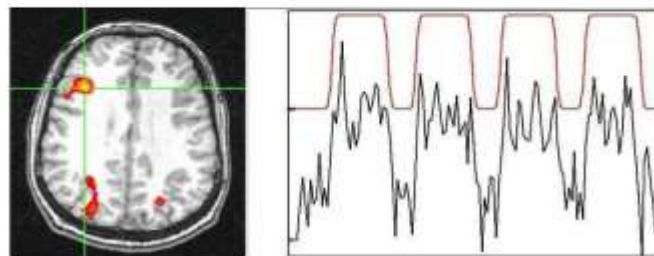
T2*-weighted imaging

- ▶ T2*-weighted images are performed which take advantage of the different magnetic properties of deoxy- and oxyhaemoglobin.
- ▶ Because of the magnetic properties of the deoxyhaemoglobin molecule which causes rapid dephasing, T2* signal is retained longer in a region when it has more oxygenated blood compared to when there is less oxygenated blood.
- ▶ Thus, an area with more oxygenated blood will show up more intense on T2*-weighted images compared to when there is less oxygenated blood around.

Evolution of BOLD Response



* Example



A typical BOLD time course with 4 "active" states and 4 "resting" states.

- With prior knowledge of the activation timing, we can perform a statistical test on the data to determine which areas of the brain are active, then overlay this statistical map (shown in color) on a high resolution MR image so that one can visualize the functional information in relation to relevant anatomical landmarks.
- There are a wide variety of different software packages that facilitate processing, analysis and display of fMRI data in addition to many different stimulus delivery packages: <http://www.fmri-world.de/> The choice of each depends largely on the onsite resources and the specific application.

Potential Clinical Applications

- ▶ fMRI, while used primarily as a research tool, does have clinical applications that span a broad range of disease processes and medical fields including:
 - ▶ Epilepsy
 - ▶ Schizophrenia
 - ▶ Diabetes
 - ▶ Overactive Bladder
 - ▶ Parkinson's Disease
 - ▶ Depression

Epilepsy

- ▶ Epilepsy is a neurological disorder of the brain that affects nearly 3 million people living in the United States.
- ▶ Seizures are the outcome of abnormal electrical activity in the brain. There are many types of seizures, and their signs and symptoms depend on the part of the brain affected.
- ▶ The benefits of fMRI in epilepsy surgery include the reduced need for the services of a complex medical and surgical team, reduced patient exposure to invasive diagnostic testing, reduced medical and surgical complications and reduced medical costs.

Schizophrenia

- ▶ Schizophrenia, considered the most chronic, disabling and expensive mental illness,
- ▶ Functional MRI studies are helping researchers connect the clinical signs and symptoms associated with schizophrenia, such as deficits in working memory and language function, thought disorder and impaired social cognition, with decreased brain activity.
- ▶ fMRI is also a source of physical clinical evidence that can help the clinician make a diagnosis, develop and monitor treatment and offer a prognosis.
- ▶ Functional MRI studies eventually may help clinicians evaluate the efficacy of medical interventions.

Diabetes

- ▶ a disease characterized by the inability to maintain normal blood glucose levels.
- ▶ recent research using fMRI shows that, under certain circumstances, having type 1 diabetes can affect cognition.
- ▶ Furthermore, there is an association between early onset (childhood) diabetes and the development of mild brain atrophy, lower non-verbal intellectual ability, and slower psychomotor speed in adulthood.
- ▶ Potential Clinical Applications Overactive

Bladder

- ▶ Urinary urgency, or overactive bladder, is a common condition that affects more than 17 million people in the United States.
- ▶ Physicians currently treat this condition using behavior modification to re-establish normal brain-bladder communication and medication to suppress detrusor muscle contractions.
- ▶ fMRI studies have revealed the potential for drug treatment strategies.
- ▶ Functional MRI research findings eventually could lead to therapeutic approaches directed at specific areas of the brain rather than the bladder.

Parkinson's Disease

- ▶ Parkinson disease (PD), a progressively degenerative neurologic illness,
- ▶ Functional MRI studies are revealing new information about the effects of PD on the brain and behavior.
- ▶ Functional MRI helps us better understand how PD disrupts spontaneous movements by showing how people learn and perform automated or "built-in" motions such as accurate typing.
- ▶ More importantly, fMRI studies show that specialized training regimens help patients with PD learn how to use other parts of their brain in efforts to re-establish fluid movement.

Depression

- ▶ Depression, one of the most common psychiatric illnesses in the world, affects nearly 19 million people in the United States.
- ▶ Functional MRI studies are helping researchers decipher the relationship between depression and brain activity and develop evidence-based medical care strategies.
- ▶ fMRI studies also could help clinicians predict which patients will benefit from cognitive behavioural therapy (CBT) that helps them stop ruminating over negative information.



THANK YOU FOR PAYING ATTENTION