Module:
Techniques in Neuroscience

Week 1
Understanding the brain:
Who we study, how and why?

Topic 1
The living brain
- Part 1 of 3

Dr Vincent Giampietro
Senior Lecturer, Department of Neuroimaging, King's College London

Slide 3:

My name is Vincent Giampietro, and I'm a lecturer in the Department of Neuroimaging at King's College, London. I have a background in computer science and biomedical engineering, and my research focuses on developing novel analysis methods, particularly in the field of fMRI, which is functional magnetic resonance imaging. With my colleagues, we're currently exploring the possibility of using neuroimaging as a treatment option for when you use a real-time fMRI neurofeedback.

Slide 4:

This session will give you an introduction to the world of neuroimaging, which will, of course, not be an exhaustive review of the field but rather a gentle introduction to the main methodologies.

Neuroimaging can be roughly split between structural and functional neuroimaging and in the first part, you will discover the co-evolution of these two domains, from the pre-neuroimaging days to today's technologies. The second part will focus on functional neuroimaging and you will discover the most commonly used techniques and how they differ. Finally, in the last part we will look in more details at fMRI - functional magnetic resonance imaging - which is the current technique of choice for mapping the brain in action.

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This section, we contrast the evolution of structural and functional neuroimaging, arguing that these two subdomains evolved in parallel. As their name suggests, structural imaging is focused on studying brain anatomy, while functional imaging investigates the living, dynamic brain.

Slide 7:

The brain has always fascinated. Seen as a secondary organ in Aristotelian times, it then became considered to be the 'siege of the mind' in the 2nd century, thanks to the Greek physician Galen. The Renaissance so revived interest in accurate neuroanatomy, and works such as the study of brain physiology from Leonardo da Vinci, shown here, do certainly represent an early form of structural brain imaging.

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Lesion studies that study functional deficits after brain damage have been an invaluable tool to further understanding of the relationship between brain and behaviour; one of the main drawbacks being, of course, that it was only after the patient's death that a precise location of the lesion could be obtained.

One of the most famous cases illustrated here is that of Phineas Gage, a railroad worker who survived having a metal rod go through his left frontal lobe. This triggers changes in his personality and behaviour.

Slide 9:

Angelo Mosso was a 19th century Italian physiologist whose work has recently been rediscovered. He's hailed as one of the pioneers of functional brain imaging for his work linking cerebral blood flow and cognition. He observed, even measured, brain pulsations in the fontanelles of newborns, and in the exposed brain of patients with skull defects via the apparatus which is depicted here in this slide.

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In addition to recording brain pulsations, Angelo also attempted to measure brain activity by weighing the brain with a balance of his fabrication. His idea was that increased blood flow to the brain linked to cognitive functions will tilt the balance, but it isn't clear if this technique worked at all. But, it certainly bears resemblance to functional magnetic resonance imaging that requires a participant to lie still in an MRI scanner whilst being head-strapped and instructed not to move.

Slide 11:

X-rays were first used to image the human body by Wilhelm Rontgen, a German physicist who had discovered them and produced a famous picture of his wife's hand, who is then claimed to have declared, 'I have seen my death'. The second photo depicts an early X-ray set up called a Crookes tube from the late 1800s that shows both men unaware of radiation risks and therefore unprotected.

Slide 12:

Soon after the inventions, X-rays started to get used for medical diagnostics, but it soon became apparent that imaging the brain in this way was far from ideal, in part due to the lack of X-ray contrast within a scale.

Ventriculography and pneumoencephalography were derived techniques invented by Walter Dandy, a US neurosurgeon in 1919 to address this issue by generating contrast for removing ventricular CSF through a hole in the skull and replacing it with air for the former while doing the same for lumbar puncture for the latter. These procedures were risky and triggered significant side effects, including death. But, they were amazingly still in use until the 1970s before being replaced by more modern imaging modalities such as CT scanning.

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Measuring brain function in real time was rendered possible in the early 20th century through the invention of electroencephalography, EEG. The first human recording, shown here- the top line is the EEG recording, and the bottom line is a 10-hertz timing signal. So, this first human recording was obtained in 1924 by Hans Berger, a German psychiatrist and physiologist, and for the first time, depicted the electrical activity of the brain through brainwaves. Early milestones of EEG history include the first measure of epileptic spikes only 10 years after this graph was produced, and the characterisation of the several stages of sleep in 1953.

Slide 14:

Early EEG set-ups were - not surprisingly - pretty cumbersome and certainly not as portable as their 21st-century equivalent that you can now even find in games. The main use for EEG in a clinic is to detect and characterise epileptic seizures. Combined with functional MRI, EEG is used not only to locate the focus of a seizure but also the whole network of brain regions involved.

Slide 15:

We have to credit Sir Godfrey Hounsfield, an English electrical engineer, for the first commercial CT scanner in 1967. It was installed in London at the Atkinson Morley's Hospital in Wimbledon. The photo on the left depicts one of the first CT scans ever taken and the other photo on the right shows an early version of the scanner itself. 'CT' stands for computed tomography and it is also known as X-ray CT or computerised axial tomography, CAT scan. The idea behind CT is to combine X-rays from many directions to reconstruct the volume of interest in slices.

Slide 16:

The most invasive of the neuroimaging technologies presented here is certainly positron emission tomography, PET. PET is a nuclear medicine technique that involves tagging an active molecule of a short-lived radioactive tracer that is then injected in the body. Tissue tracer concentration and location can then be computed by detecting the gamma rays emitted as a byproduct of the decay of the radioactive tracer. Picture A shows the increase of PET image quality over 30 years. The radioactive tracers decay quickly, they are said to have a short half-life, and thus need to be produced onsite in a cyclotron, like the one you can see in the other picture, making PET the most expensive neuroimaging technique by far.

Slide 17:

The best technology we currently have to image the structure of the brain is certainly magnetic resonance imaging, MRI. A versatile tool, MRI can be used to study brain structure in different ways, from high resolution anatomical scanning, as pictured here, to looking at microstructural changes with diffusion tensor imaging - DTI - and then mapping white matter tracks in the brain. MRI scanners are ubiquitous and in addition to their clinical possibilities, they are the workhorse of today's neuroimaging research. With little software/hardware modification, any modern clinical MRI scanner can also be used for research.

Slide 18:

Functional magnetic resonance imaging, fMRI, has been without doubt the method of choice to study brain function since it came about in the mid-90s. It constitutes a powerful way to measure dynamic changes every couple of seconds in the whole brain during experimental tasks, task-based fMRI, or at rest - this is called resting state fMRI. It is extremely common these days to open a newspaper and to stumble upon colourful representations of brain activity superimposed on high-resolution structural MRI scans. This has led to a technique being labelled a 'modern day phrenology' in its quest for finding the discrete location of specific brain functions. The reality is, of course, a lot more complicated, with cognitive function not only associated to networks of regions in the brain, but also to the way the network nodes are structurally and functionally connected.

Slide 19:

MRI scanners are versatile tools enabling clinicians and researchers to acquire drastically different images. For example, the image on the left illustrates the typical volumetric scan that clinicians use for diagnostic, while the image on the right is from an fMRI experiment with reactivations in yellow superimposed. The difference in the image quality is due to varying spatial and temporal resolution. A 3D structural image of the brain takes minutes to acquire, so this is a low temporal resolution, but this leads to a great amount of details, so it's a high spatial resolution. Conversely, for fMRI, it's all about dynamic imaging. So, we only take seconds to scan the brain, so it's a high temporal resolution, but this leads to a poor amount of details in the images, so it's a low spatial resolution. A typical hour of scanning consists of acquiring several structural scans and a handful of fMRI tasks, enabling researchers to look at their problems from different angles. This is called multimodal imaging, which also extends to other technologies, such as combined EEG and fMRI.