Module:
Techniques in Neuroscience

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

Topic 1
The living brain
– Part 3 of 3

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Slide 3:

This section provides an introduction to the most commonly used functional neuroimaging technique, functional magnetic resonance imaging - fMRI.

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The MRI scanners used for research mostly come in two strengths: 1.5 Tesla and 3 Tesla. The magnetic field of a 1.5 Tesla scanner is 30,000 times stronger than the earth's magnetic field. The magnetic field is generated by a super conductive magnet that is always on, and that requires cooling by liquid helium. Before entering the MRI room, participants and staff need to ensure that they are MR-compatible, which means that they do not carry or have any metal in their body. Participants and patients of the Institute of Psychiatry, Psychology and Neuroscience are thoroughly checked by qualified NHS radiographers before every session.

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It is pretty hard to appreciate what the strength of a magnet 30,000 times stronger than the earth's magnetic field corresponds to. This magnetic field is actually roughly equivalent to the one used in junkyards to lift cars. So, when you have an MRI scan, it's like if you were standing underneath one of these for about an hour - hopefully, without all that junk.

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Functional MRI is not a quantitative technique, in that it doesn't provide absolute measurement of brain activity. Rather, it's a contrast technique that works by comparing local magnetic perturbations associated to different

experimental conditions. Put simply, fMRI is based on the principle of cognitive subtraction, in which different experimental conditions would be associated to different cognitive states that have been statistically contrasted to find out which parts of the brain respond to what is different between your conditions. For example, this animated gif shows two stimuli that are contrasting: texture patterns versus object shapes. It's shown here that the lateral occipital cortex preferentially activates to object shapes compared to texture patterns, while early visual cortex shows the opposite effect.

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Here, you can see a video demonstration of what it feels like to have an fMRI scan. The objects that you measure, the brain in this case, has to be in the centre of the MRI scanner, so subjects only enter the scanner up to the belt, usually - this is what you can see on the left panel. The video on the right shows a typical task to be undertaken whilst in the scanner. This is a trail task, consisting in following of the joystick the numbers and letters in a specific pattern- for example, in order, in reverse order, skipping one etc - and the sound that you can hear is that of a typical fMRI scan. It is usually so loud, akin to standing next to a jack hammer in the street, that subjects wear both ear plugs and headphones.

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So, what is fMRI measuring? Well, fMRI is based on the BOLD effect, but is linked to different magnetic properties of oxy- and deoxyhaemoglobin. So, oxyhaemoglobin as I mentioned before, is diamagnetic so it's barely magnetic, and deoxyhaemoglobin is paramagnetic so it's magnetic. You can see in the picture here that when placed in a magnetic field, oxyhaemoglobin - so oxygenated blood - doesn't impact the magnetic field whereas deoxyhaemoglobin, which is magnetic, has an impact on the local magnetic field.

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So, deoxyhaemoglobin has an impact on the local magnetic field, and we make it so that the brightness in an fMRI image is directly linked to the level of local magnetic perturbation. And the more magnetic perturbation there is somewhere in the brain, the darker the image will become. So, the less magnetic perturbation there is, the brighter the image will be.

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Let's go through the whole process. Suppose you have a local increase in brain activity. For example, you have a subject lying in the MRI scanner in the dark, and suddenly, you see some visual flashes. So, what is at the visual cortex? So, a local increase in brain activity is going to trigger initially, use of the local pool of oxygen. There's always blood floating around, there's always oxygenated blood floating around. So, in the first hundreds of milliseconds after stimulation, the brain is using the oxygen which is around, which means that initially, in the parts of the brain which are suddenly more active, because they are being stimulated, there is more deoxyhaemoglobin than at rest because we are using the oxygen. More deoxyhaemoglobin, which means more magnetic perturbation than at rest, which means that the images get darker than at rest. So, in the parts of the brain which are being activated, which required more blood, the images get darker initially for the first couple hundred of milliseconds. This is what we call the initial dip in the BOLD signal. This is happening so fast, but we don't usually see it because fMRI is a slower technique. We measure, we take the brain snapshots every couple of seconds, and so we're measuring those slower processes, and these slower processes are due to the fact that after stimulation, after a couple hundred milliseconds, suddenly the brain realises it needs to send oxygen in these parts of the brain which are being activated. So, there is a large increase in regional oxygen delivery, much larger

than is needed, where the brain overcompensates, if you want. So, suddenly local area is flooded by oxyhaemoglobin. There is actually less, so it's paradoxically- even if one part of the brain is working more than before, there is actually less deoxyhaemoglobin there because the local area is flooded by oxyhaemoglobin. Because there is less deoxyhaemoglobin when at rest, there is less magnetic perturbation when at rest, which means there'll be these parts of the brain which are being activated, a couple of seconds later, the image becomes brighter. This is, of course, an oversimplification for the purpose of this session. If you want to know more, just go on YouTube, there's a lot of animations and films explaining the BOLD effect in much more details.

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So, what do we do when we have the data? Well, fMRI data analysis is a complex statistical process that can be simplified as follows. Preprocessing the data: so, when we first get the raw data from the scanner, but before we have to do any analysis we have to preprocess the data. This is to increase the signal to noise ratio, which means to remove the effects, for example, of head movement, cardiac pulsations, respiration, to smooth the data, etc, etc. After this, once we've preprocessed the data, single subject (single subject level) analysis computes where brain activity is in the subject's own brain, in relations to the given experimental model. So, this is done usually using something called a general linear modelling (general linear model, GLM). After that, once we've got the analysis in the subject's own brain, we normalise everybody's brain - because everybody, all the subjects will have different head size, different shape, everybody's tilted differently in the scanner. So, we normalise everybody's brain onto a brain template, and then this enables us to do group level statistics in order to compare and contrast brain activity between individuals; for example, between patients and controls. So, we move from the raw data, to cleaning up the data, if you want preprocessing; after this, we do single subject analysis and then we do group level analysis.

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Most fMRI papers include at least the following: some maps - some blob maps, as we call them- showing where, for example, differences in brain activity are, having been statistically significantly detected; then you will find some result tables giving precise information on the brain region of interest, for example, coordinates in standard space, effect size, p values, cluster sizes, anatomical labels; and you often also get illustrative plots, showing the direction of the detected changes.

In this paper here from the Institute of Psychiatry, Psychology & Neuroscience, it's interesting to note the authors have simply overlaid quite old, thick fMRI data on a high resolution structural scan, without attempting to further process the image to make it look nicer. This is why the fMRI response in this paper looks really blocky, rather than really well-defined and following the anatomy, but this is the real data. If you remember earlier in this session, I was talking the differences between temporal and structural resolution of anatomical versus functional MRI scans, and this is what we see here.

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Saying that, it is common practice to present fMRI results on 3D brains, especially for posters or presentations. But, in scientific publications, brain slices are the most informative.

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So, what do we study at the IoPPN? Well, the IoPPN was one of the first places in the world where fMRI was done, and we've been scanning since 1995. At any time, we have between 70 and 80 research projects going on, and

this is done on four clinical human MRI scanners, which are scanning six days a week from 8:00 AM to 7:00 PM. We have also two pre-clinical MRI scanners, which are a smaller version of the scanner for animal scanning. These are scanning seven days a week. We have one running and a second one coming online really soon. So, we must have scanned - on the human side - I guess these days about 100,000 participants doing experiments.

So, the question really shouldn't be 'What do we study at the IoPPN?', but 'What have we not studied at the IoPPN?'