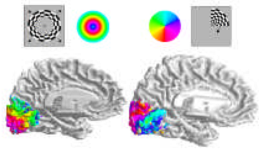
fMRI and visual brain function



Dr Elaine Anderson
UCL Institute of Ophthalmology

Brief history of brain imaging

- 1895 – First human X-ray image
- 1950 – First human PET scan - uses traces of radioactive material (carbon, nitrogen, fluorine or oxygen) to map neural activity - increased radioactivity associated with increased utilization of oxygen and glucose, signalling increased neural activity.
- 1977 – First human MRI scan
- 1991 – First fMRI paper published

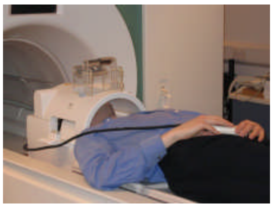
In 1992 only 4 published articles using fMRI

Today 'fMRI' search returns over 32,000 peer-reviewed articles

Non-invasive and has excellent spatial resolution

MRI scanner

Adapted for fMRI of the visual system



Participants view images on a projector screen, situated within the MRI scanner, via a mirror system mounted on the head coil

Brief overview of MRI

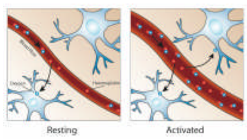
- The MRI scanner houses a very large super-cooled electro-magnet
- Research magnets typically have a strength of 3Tesla: ~ 50,000x the earth's magnetic field
- Each of the hydrogen atoms in each of the molecules of water in our body is a tiny magnetic dipole (+ve proton nucleus and a single orbiting –ve electron)
- Normally these atomic nuclei are randomly oriented, but when placed within a very strong magnetic field, they become aligned with the direction of the magnetic field
- A short pulse of radio frequency (RF) energy perturbs these tiny magnets from their preferred alignment, and as they subsequently return to their original position they emit small amounts of energy that are large enough to measure
- Different brain tissues have different amounts of water, and hence produce different intensities of signal that can be used to differentiate between them

How does fMRI work?

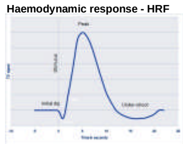
- fMRI measures changes in blood oxygenation that occur in response to a neural event
- Oxyhaemoglobin (HbO_2) is diamagnetic (weakly magnetic), but deoxyhaemoglobin (HbR) is paramagnetic (strong magnetic moment)
- Red blood cells containing **deoxyhaemoglobin** cause distortion to the magnetic field and **lower the MR signal** compared to fully oxygenated blood
- Since blood oxygenation varies depending on the level of neuronal activity, these differences can be used to detect brain activity
- This form of MRI is referred to as 'blood oxygenation level dependent', or **BOLD** imaging
- It is this BOLD signal that is reported in fMRI studies

The BOLD signal

- One might intuitively expect the oxygenation of blood to decrease with neural activity, however it is not that simple….
- The initial decrease in blood oxygenation that occurs immediately after neural activity (known as the initial dip), is thought to act as a trigger for nearby blood vessels to dilate. This results in an insurge of oxygenated blood to the area



Haemodynamic response - HRF



- However, the increase in blood volume over compensates for the increased demand in oxygen which results in blood oxygenation increasing following neural activity, instead of decreasing
- Hence, the concentration of deoxyhaemoglobin decreases, and causes the BOLD signal to elevate.

How does the BOLD signal relate to neural activity?

- A high-resolution neuroimaging 'voxel' has ~50,000 neurons
- Neural activity is modelled by the HRF which peaks at around 4-6 seconds post stimulus onset
- So what is the BOLD signal really telling us about neural activity?

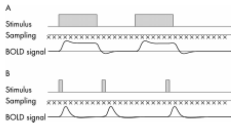
Logothetis and colleagues (2001), simultaneously recorded single and multi-unit spiking activity, as well as local field potentials (LFPs) and BOLD contrast in monkeys, and showed that the BOLD signal correlated best with local field potentials (LFPs) rather than the spiking activity

However similar research in humans - on epileptic patients with implanted electrodes - found equally good correlations between spikes and BOLD as between LFPs and BOLD (Mukamel et al. 2005)

Thus, it remains debated whether the BOLD signal reflects input to neurons (as reflected in the LFPs), or the output from neurons (reflected by their spiking activity)

Experimental Design

- **Block Design** - a stimulus is repeatedly presented for a block period of time (usually 16 or 32sec), followed by a period of 'rest' in which the haemodynamic response is allowed to return to a resting baseline. Brain activity is averaged across all trials within the block.



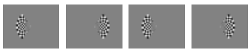
For both designs, brain images are acquired throughout the stimulus and rest periods, typically every 3-5secs

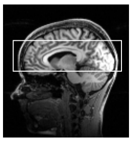
- **Event-Related Design** - measures brain activity in response in an individual trial, or 'event. But need many trial repeats to get good SNR.
- **fMRI Adaptation** - used to isolate and reduce the responses of specific neural populations. An initial stimulus is presented that is presumed to adapt the population of neurons sensitive to that stimulus (e.g.orientation). A second stimulus is then presented that is either identical or different from the initial adapting stimulus.

adapt  identical   different

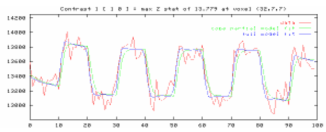
A brain area that has selectivity for the manipulated dimension (orientation), will exhibit a larger BOLD signal to the 'different stimulus' compared to the 'identical stimulus' - because the new stimulus is thought to be accessing a separate, unadapted, neural population.

Activation maps





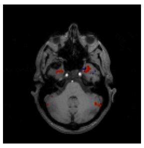
Multi-slice acquisition
~30 slices at 2mm slice thickness
~ 3 sec to acquire all 20 slices



Model the time series

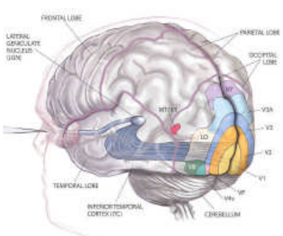
- Activation maps represent the 'activity' in each unit of the brain (voxel)
- 'Activity' is defined by how closely the time-course of the BOLD signal matches that of the visual stimulus.
- Those voxels that show tight correspondance with the stimulus are given a high activation score, voxels showing no correlation are given a low or zero score and those showing the opposite correlation (i.e. deactivations) are given a negative score.

Activation map



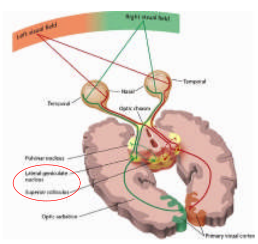
movie clip

Functionally localising the cortical visual areas V1-V3



Visual areas

~20% of cortex



Sub-cortical as well as cortical areas

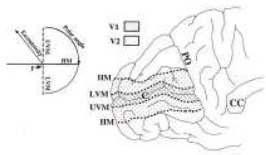
- Each cortical hemisphere represents the contralateral hemi-field of space
- Visual space is left/right and up/down inverted when mapped onto V1

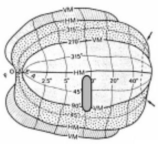
Each of the cortical visual areas V1 to V8 have been identified based on the fact that they contain a preserved representation of visual space – referred to as a 'cortical visual field map'.

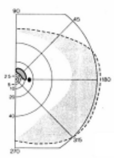
Eccentricity Map

V1: Smooth progression of representation from central visual field to peripheral field moving anteriorly along calcarine sulcus.

Note cortical magnification







Polar angle

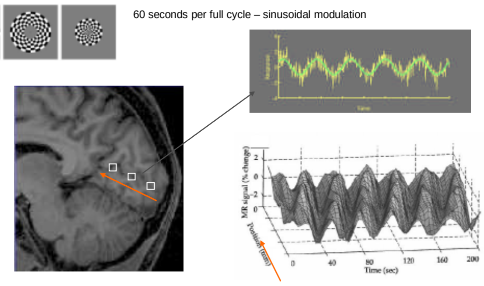
V1: Horizontal meridian represented along the calcarine sulcus. Smooth progression of hemifield representation from horizontal to lower vertical meridian above the calcarine sulcus (dorsal V1), and to upper vertical meridian below the calcarine sulcus (ventral V1).

Because the visual field is fixed with respect to the retina, and shifts with eye position, cortical visual field maps are also called **'retinotopic maps'**.

Eccentricity Map

Expanding ring stimulus

60 seconds per full cycle – sinusoidal modulation



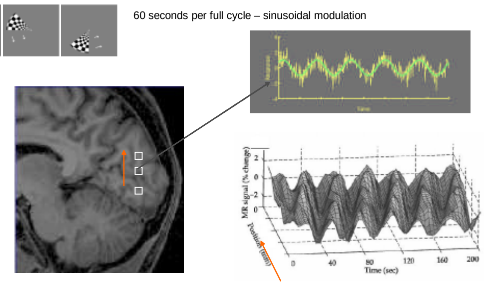
Use time series of fMRI data to look for neural activity that modulates at this frequency

Calculate the phase at which each cortical location modulates at this frequency

Polar Angle

Rotating Wedge stimulus

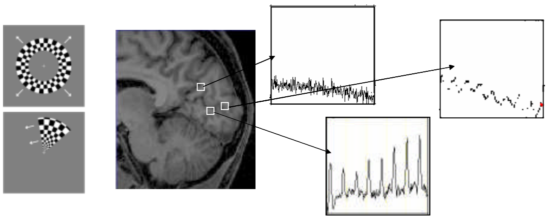
60 seconds per full cycle – sinusoidal modulation



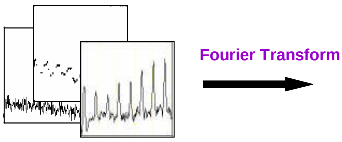
Use time series of fMRI data to look for neural activity that modulates at this frequency

Calculate the phase at which each cortical location modulates at this frequency

Fourier Analysis

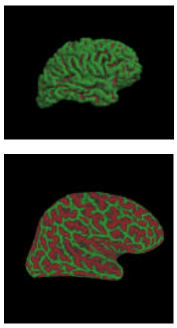


Complex data
(amplitude, phase)



Fourier analysis of the fMRI time series at stimulus frequency --> amplitude, phase
Amplitude - strength of retinotopy
Phase - spatial location
Results plotted on cortical surface

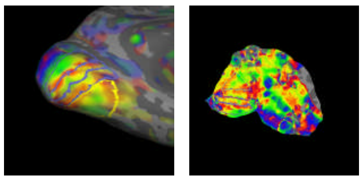
Visualising phase-encoded data



movie clip

Inflated surface of left hemisphere

Flat map of left occipital cortex



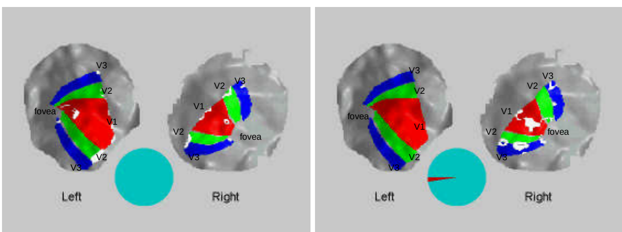
Polar Map

Polar Map

same brain, same data, different view

Travelling wave of cortical activity

Flat maps of occipital cortex

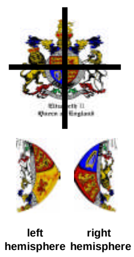


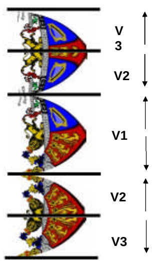
Expanding ring stimulus

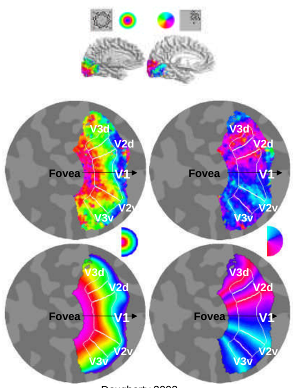
Rotating wedge stimulus

movie clip

Defining the borders between visual areas





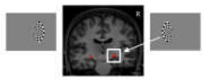


- V1/V2 meet at the vertical border
- V2/V3 meet at the horizontal border

Dougherty 2003

Functionally localising the sub-cortical visual areas

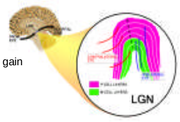
LGN

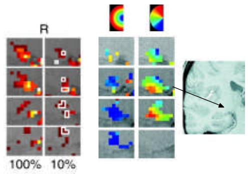


High field (3T+), high resolution imaging (1.5x1.5x1.5mm voxels)
Checkerboard stimuli scaled for cortical magnification, 100% contrast, ~4-8Hz
Block design, ~30sec R hemifield, ~30sec rest, ~30sec L hemifield, ~30sec rest

Compare R field stimulation>rest to isolate L LGN
Compare L field stimulation>rest to isolate R LGN

6 layered structure, each receiving input from the contra- or ipsi- lateral eye
4 dorsal pavocellular layers – sustained discharge, sensitive to colour, low contrast gain
2 ventral magnocellular layers – transient discharge, sensitive to luminance, high contrast gain
Due to small size and limitations of fMRI only crude visual responses can be measured



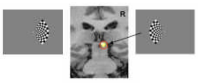


Retinotopic maps have been measured

Magno-cellular layers identified using low-contrast Vs high-contrast checkerboards. M cells exhibit significant response to the 10% stimulus AND contrast saturation.

Schneider et al. 2004

Superior Colliculus



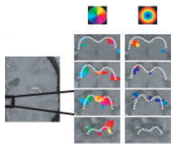
R field stimulation>rest to isolate L SC
L field stimulation>rest to isolate R SC

About 20% of retinal ganglion cells project to the SC in the retinotectal (or Koniocellular) pathway.

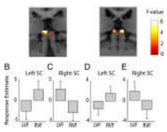
Difficult to scan due to it's small size and location in the upper brain stem - encircled by prominent blood vessels – making it susceptible to physiological noise.

High-field, high-resolution imaging, and algorithms to correct for cardiac-induced brain stem motion.

Crude retinotopic map has been achieved for phase angle only
Weak modulation to stimulus contrast
Stronger response in SC to moving stimuli than in LGN



Schneider & Kastner 2005



fMRI has confirmed in humans the naso-temporal asymmetry in sensory input that exists in monkeys (preference for temporal field stimulation).

Sylvester 2007

Why do we want to measure visual field maps?

1. There are no anatomical landmarks that can be used to delineate the different visual areas.
2. **Different visual regions are specialised for different perceptual functions, characterising the responses within a specific visual field map is essential for understanding cortical organisation of visual functions, and for understanding the implications of localised lesions.**
3. Much of our knowledge about the human brain has been derived from non-human primates, but differences between human and non-human primates make direct measurements essential.
4. Quantitative measurements of visual field maps can be used for detailed analyses of visual system pathologies, e.g. for tracking changes in cortical organisation following retinal or cortical injury (plasticity).
5. When making conclusions about visual responses within an individual on separate occasions, or between individuals within a group, it is essential to know that the same functional area is being compared. Anatomical markers alone are not reliable due to individual variability in anatomy.

Characterising responses within retinotopically defined areas

Consistency of characteristics within V1-V3

V1-V3 share a foveal confluence and their eccentricity maps run in register

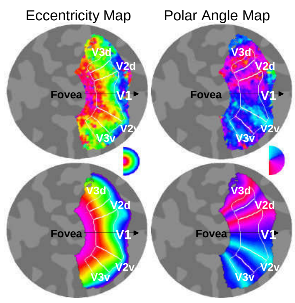
Consistency across individuals / laboratories on the way visual space is represented within V1–V3

V1 – orientation, spatial frequency, colour coding, motion sensitive

V2 – more complex pattern analysis, illusory contours

V3 – colour selective, global motion

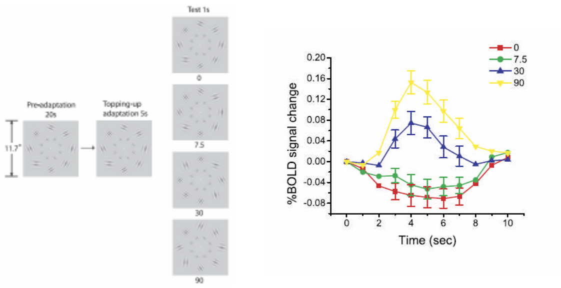
A lesion to these areas usually results in a general loss of visual function within the corresponding area of visual field



Dougherty 2003

Orientation Selectivity

- fMRI adaptation experiment
  fMRI signal in V1, V2, V3 & V4 was proportional to the angle between the adapting and test stimulus

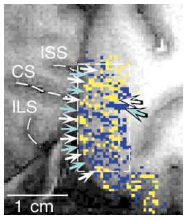


F. Fang et al 2005

Ocular dominance and orientation columns

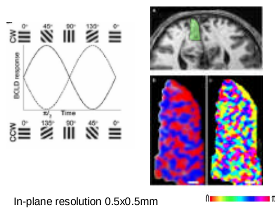
- Ocular dominance and orientation columns in human V1

Ocular dominance – 4T
Yellow = stimulation to left eye
blue = stimulation to right eye



In-plane resolution 0.47x0.47mm

Orientation Columns – 7T
Color spectrum represents the phase of the fMRI time series
Orientation pin wheels crossed ODC borders
Greater number of column devoted to representing 90deg



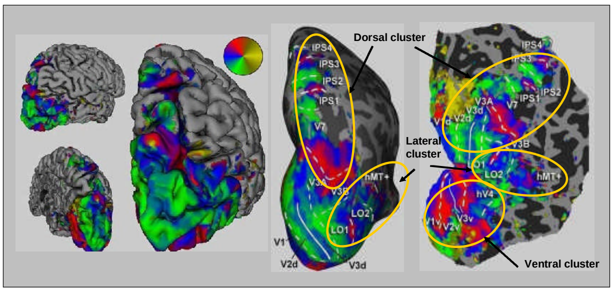
In-plane resolution 0.5x0.5mm

K. Cheng, 2001

E. Yacoub, 2008

Beyond V1-V3 – many more visual field maps identified

Grouped by common perceptual functions



Field map clusters

- **Dorsal cluster - V3A, V3B, V6, V7, IPS1-4**

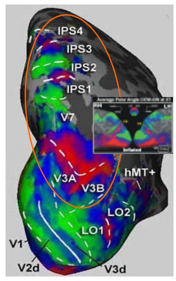
- Several small maps extending into the posterior parietal cortex
- Preferentially represent peripheral visual field, therefore need wide angle field mapping stimuli (>20deg)
- Preferentially respond to motion, motion-boundaries, depth, spatial orienting and eye-movements
- Modulate with attention
- Damage to this area results in deficits in motion perception & spatial attention

• V3A/V3B
General agreement that V3A exists but inconsistency in whether V3B exists
V3B has also been called KO by some groups
Each thought to represent the whole contralateral hemifield
Sensitive to visual motion, motion-boundaries and motion-boundary orientation

• V6 (medial motion area)
Lies in the dorsal most part of the parieto-occipital sulcus
Represents an entire contralateral hemifield
Sensitive to coherantly moving fields of dots – flow fields

• V7
Represents a hemifield of contralateral space
Renamed as IPS-0 by Swisher et al 2007 as it better describes it's anatomical position

• IPS 1/2/3/4
Identified using a variety of eye movement and attentional tasks
IPS 3 is thought to be the homologue of the putative LIP in macaque.



see Wandell review 2007

Field map clusters

- **Lateral cluster – 'Object-Selective' lateral occipital complex (LOC)**

- Heterogenous region with many course maps reported, highly convoluted cortical surface makes it difficult to study
- Large receptive fields, over-represent the central field
- Involved in object and face perception

• LO1 and LO2

Two adjacent full hemifield maps of contralateral space

Both LO1 and LO2 prefer objects to faces

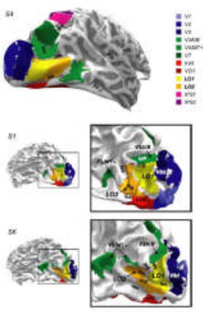
Both respond poorly to V5 motion localiser

Both areas respond more to motion boundaries than transparent motion

Processing hierarchy from LO1 to LO2

LO2 shows a greater response to complex objects than LO1

Only LO1 shows orientation selectivity



Transparent motion - random dots moved in one of two opposite directions resulting in a percept of two transparent surfaces moving across one another

Kinetic boundary – gratings of random dots moving parallel to the orientation of the stripe but alternating in direction between adjacent stripes

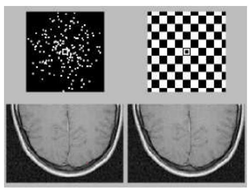
Larsson & Heeger 2006

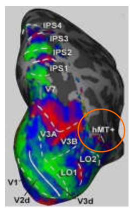
V5

V5 is highly motion sensitive and best localised using a motion localiser stimulus: blocks of moving random dots are compared to blocks of stationary random dots.

Sensitive to speed and direction of motion

movie clip





Note that both stimuli excite early visual areas, but only the moving dot stimulus excites lateral regions - believed to in the area homologous to MT and MST in the Macaque. We call this area V5 or hMT in humans.

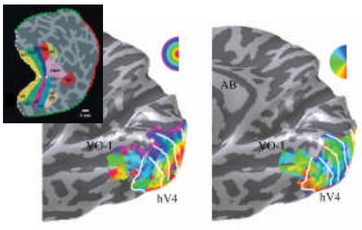
It's small size and the variability in position across individuals has made this area difficult to map. Multiple small maps are likely to exist in this region

Boynton: www.snl-b.salk.edu/boynton

Field map clusters

Ventral cluster – hV4, V8 ?, VO-1, VO-2

Subject of intense debate
More complex coding of objects and colour
Multiple colour-selective areas along the ventral surface (not just hV4)
Preferentially respond during object recognition tasks including faces, objects, text, coloured patterns
Large receptive fields, emphasise central visual field
Damage to this area can result in face blindness, colour dysfunction or alexia (inability to read text)



see Wandell review 2007

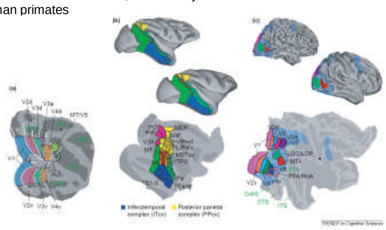
V4
- Shares a parallel (but shorter) eccentricity representation with V1-V3
- Extent of field represented is controversial, but appears to exceed a quarter field
- Thought to be involved in colour and form perception, but again this is controversial
- Given the name hV4 to distinguish it from the macaque V4 to which it has little homology

V8
- Another controversial area, identified by Hadjikhani et al 1998, but thought to overlap with what others call hV4

VO-1, VO-2
- Two further field maps have been described

Comparison with non-human primates

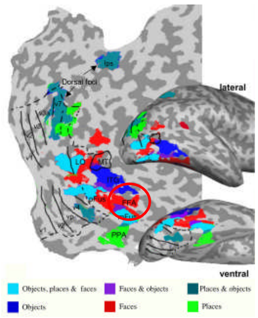
- For V1, V2 , V3, V3A and V5/MT there is generally good direct homology
- Beyond V3 there is limited consensus, in particular no dorsal region to V4 found in humans
- This may be because in humans we use visual field maps and functional localisers to define areas, rather than using characteristics related to architecture, connectivity and function that are used for defining visual areas in non-human primates



Orban 2004

monkey (a,b) and human (c)

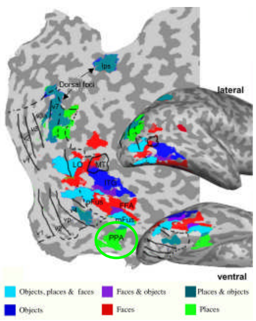
Beyond Retinotopic Cortex



Ventral occipitotemporal cortex contains subregions responding selectively:

➢ To faces vs other object types:
fusiform face area - FFA
(*Puce at al., 1996, Kanwisher et al., 1997)*

from Grill-Spector & Malach, 2003



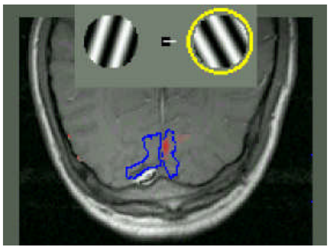
Ventral occipitotemporal cortex contains subregions responding selectively:

➢ To places vs other object types:
parahippocampal place area - PPA
(*Epstein & Kanwisher, 1999)*

from Grill-Spector & Malach, 2003

Effect of attention on fMRI activity

Effect of spatial attention on V1 activity



movie clip

Subjects were asked to alternate their attention to the stimulus in their left or right visual field and perform a speed discrimination task.

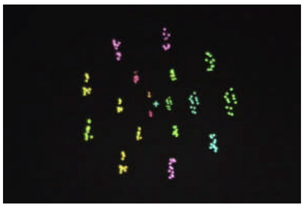
Only the focus of attention varied, and not the visual stimulus or task difficulty.

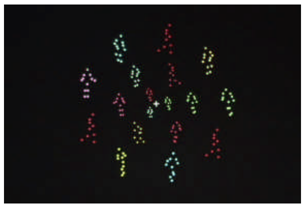
Note that activity modulates with attention to the contralateral visual field.

www.snl-b.salk.edu/boynton

Effects of Attention on Retinotopy

movie clip



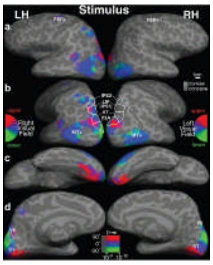


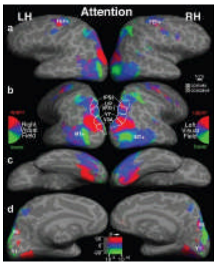
Rotating wedge stimulus with central fixation task

Rotating wedge stimulus with attention task

From Saygin & Sereno 2008, Cerebral Cortex, 18, 2158-2168

Effects of Attention on Retinotopy





movie clip

From Saygin & Sereno 2008, Cerebral Cortex, 18, 2158-2168

Attentional effects on sub-cortical responses

Attentional modulation has generally been considered a cortical mechanism. However, using fMRI attentional modulations have been observed both in the LGN and SC of humans.

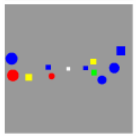
Task – covertly attend to one arm of the rotating stimulus and perform a detection task, whilst maintaining central fixation.

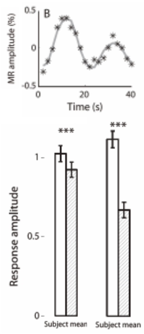
BOLD signals recorded from the LGN and SC were significantly enhanced by attention

The attentional effect greater the SC than the LGN

For the LGN the response was greater in the M layers than the P layers.

The effect was comparable for both stimulus types.





Adapted from Schneider & Kastner 2009

Summary

- fMRI - new technique, non-invasive, good spatial resolution
- BOLD signal – concentration of oxygenated blood varies with neural activity
- Activation maps represent how well the BOLD signal matches the time course of the stimulus
- Most important physical property of a visual image is it's spatial arrangement
- The spatial representation of an image is preserved in retinotopic maps throughout visual cortex, as well as sub-cortical areas
- V1-V8 identified using visual field mapping
- Field map clusters:
  - Dorsal cluster – motion, motion boundaries, depth, spatial attention
  - Lateral cluster – object processing and motion
  - Ventral cluster – colour-selective, objects, faces
- Attention enhances BOLD responses in cortical as well as sub-cortical regions

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