

HRF and BOLD Basics: Introduction to fMRI and fNIRS

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University of South Carolina

PSYC 888– Affective (Cognitive) Neuroscience

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Record



Overview

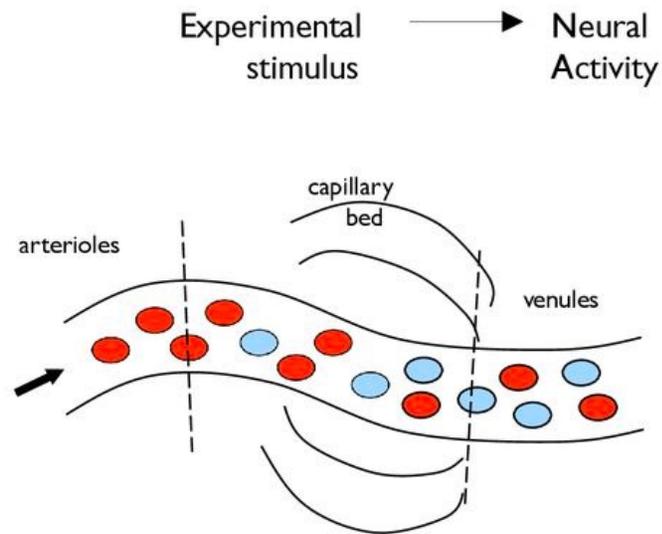
- Course updates
 - Short essay open: due 2/27
 - Hemodynamic response function (HRF) → Blood oxygenation level dependent (BOLD)
 - fMRI
 - fNIRS
- 

Words of caution about HRF/BOLD signal

- We are measuring blood flow not neural activity
- We map broad regions of brain activity – not specific neurons
 - ~100K neurons in 1 MRI voxel (3D version of the 2D “pixel”)
- Be cautious of overinterpretation of results
 - Temporal specificity is poor
- We’re tethered to the current technology

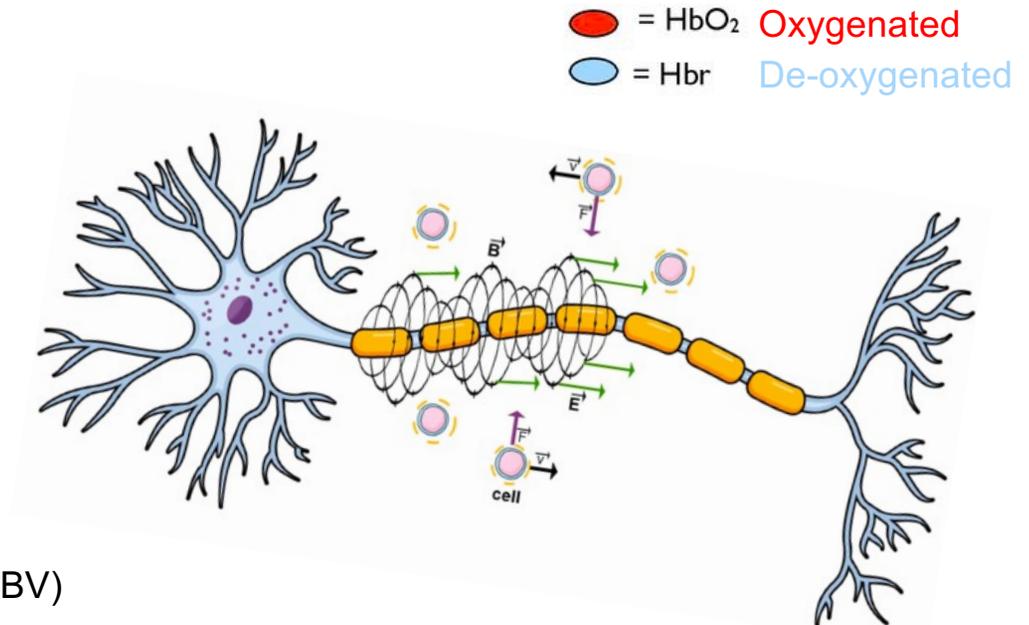


Hemodynamic response function (HRF)

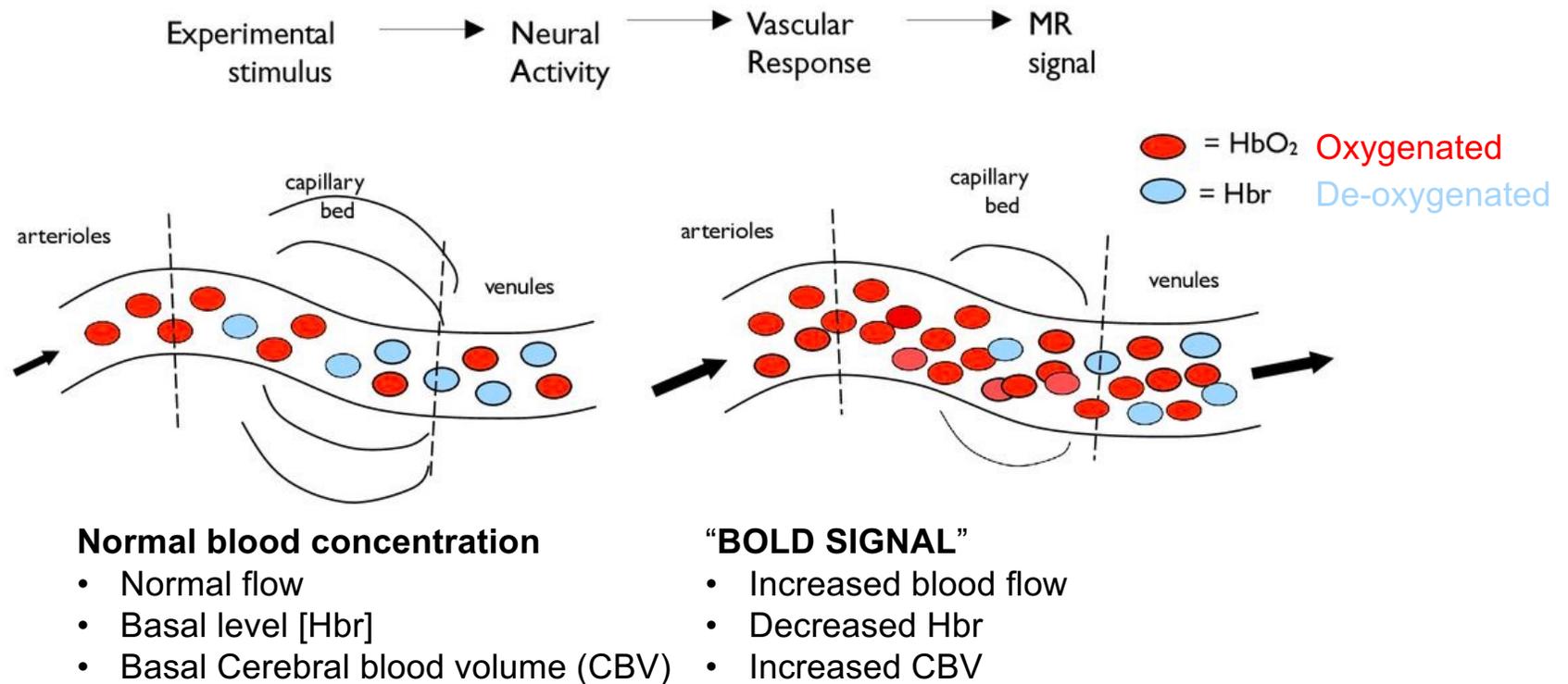


Normal blood concentration

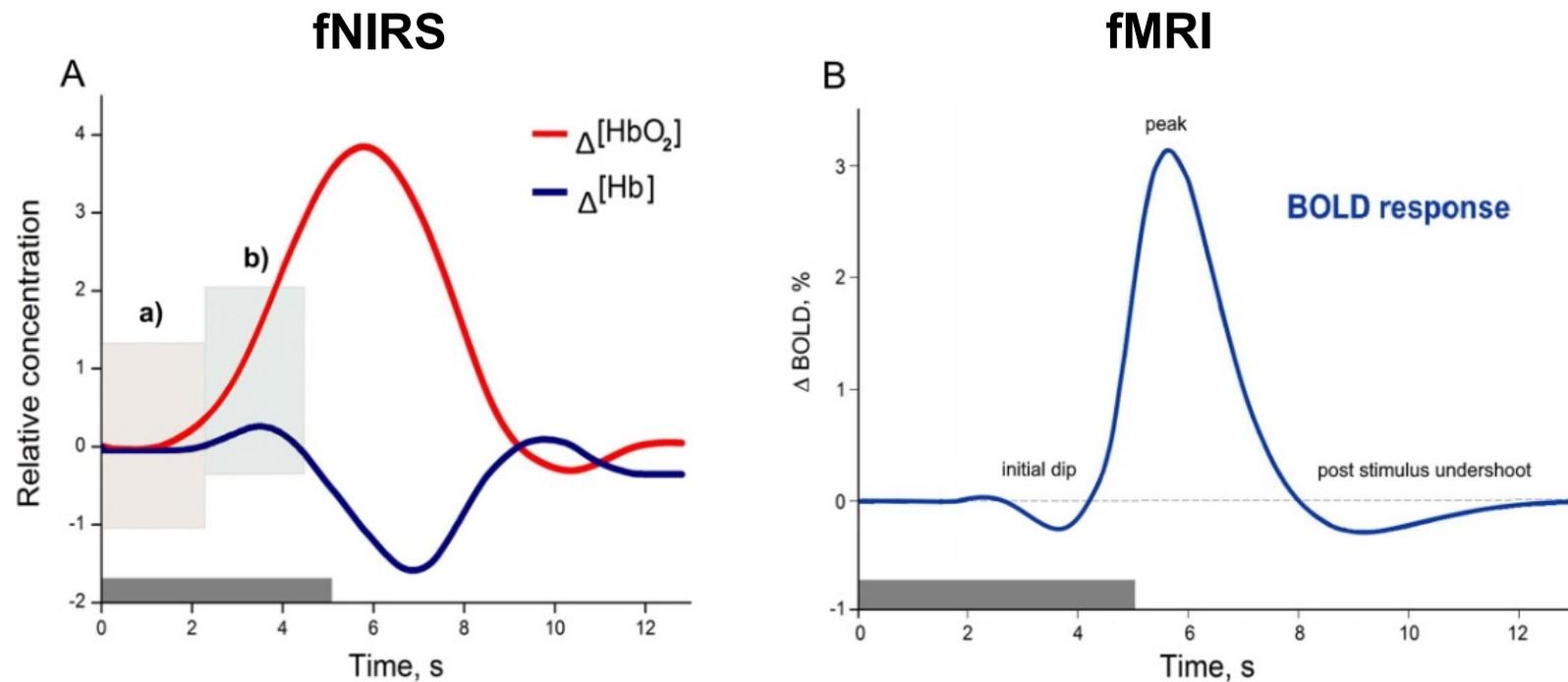
- Normal flow
- Basal level [Hbr]
- Basal Cerebral blood volume (CBV)



Hemodynamic response function (HRF)

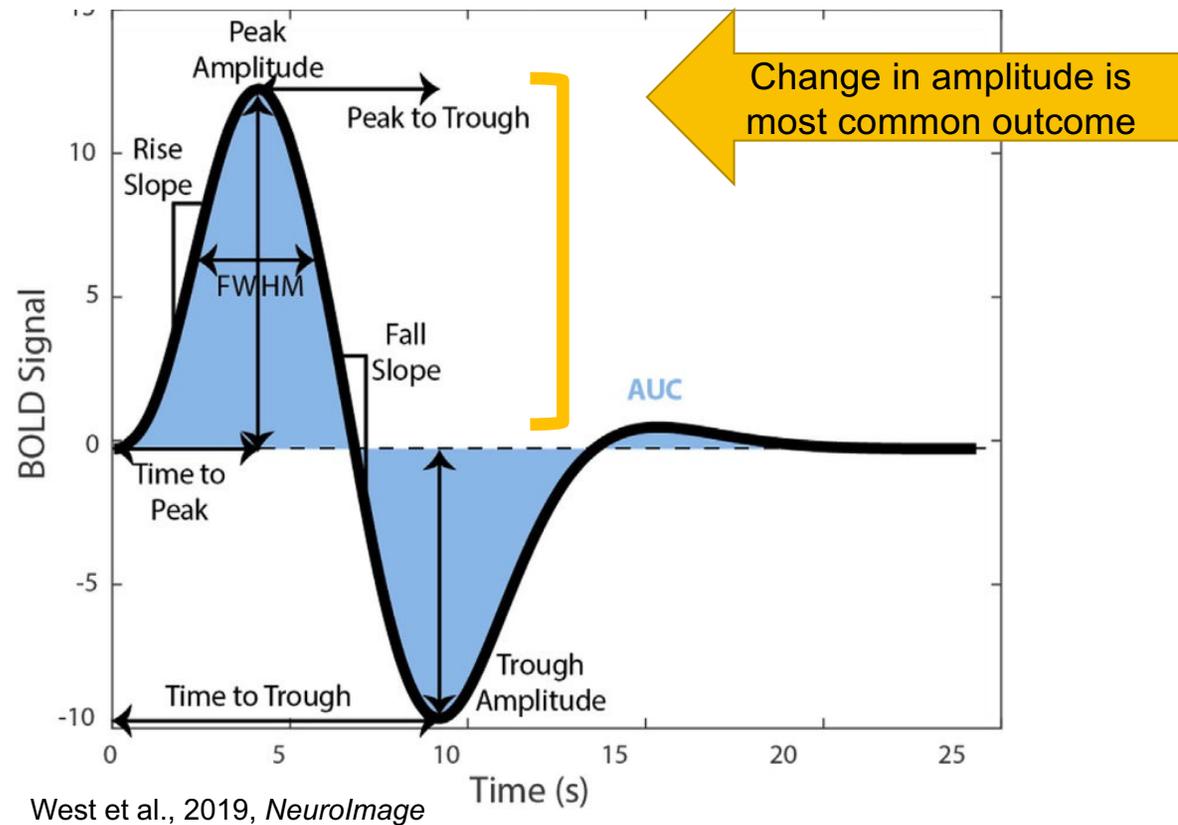


Hemodynamic response function (HRF)



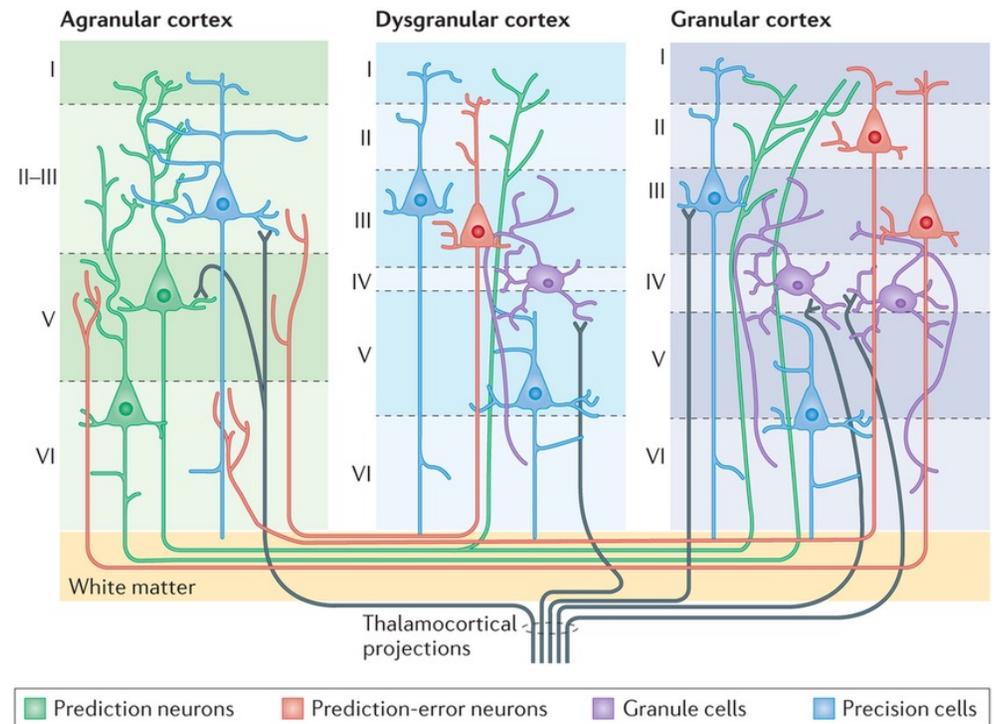
Cincuit, 2019, *Brain and Cognition*

Hemodynamic response function (HRF)



Issues for affective neuroscience experiments?

- **HRF is slow**
 - ~10-12 seconds
- **Reliant on organized microcolumns of neurons**
 - “Wired together, fired together”
 - Yet, many emo/aff regions are granular
 - Insula, thalamus
 - Cerebellum

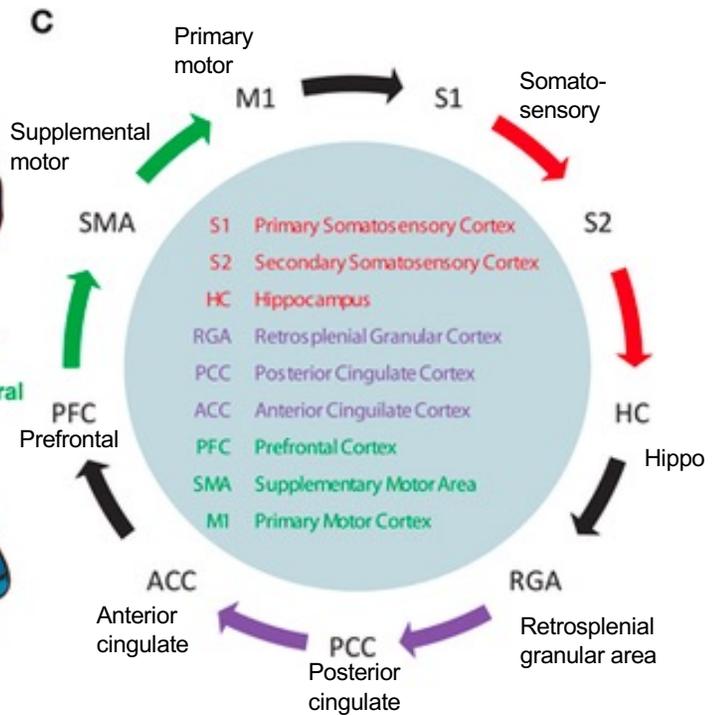
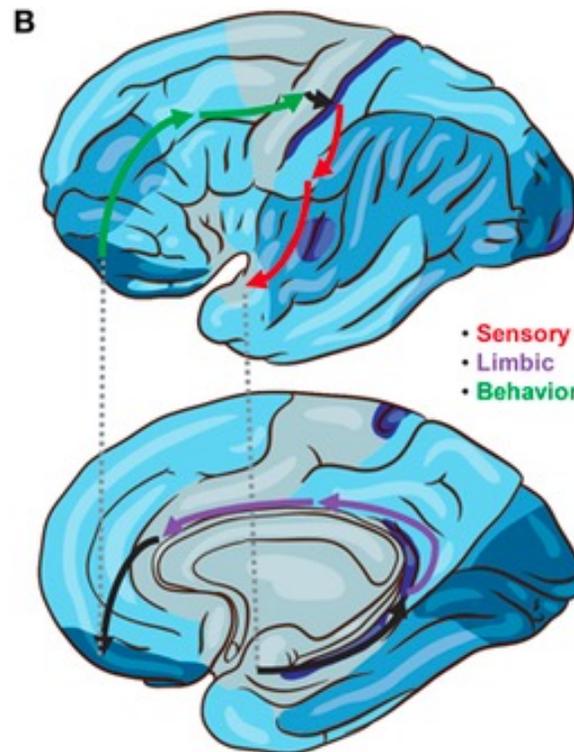
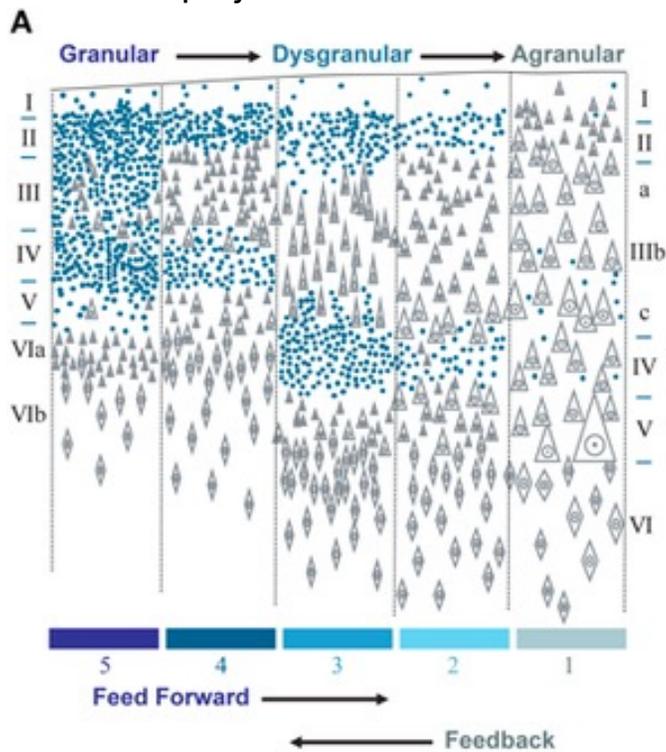


Barnett & Simmons, 2015

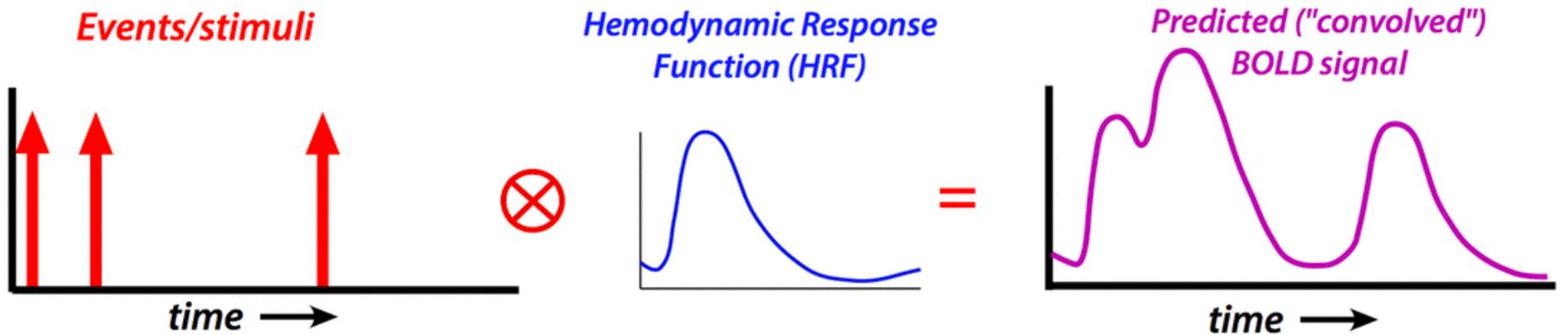
Nature Reviews | **Neuroscience**

Issues for affective neuroscience experiments?

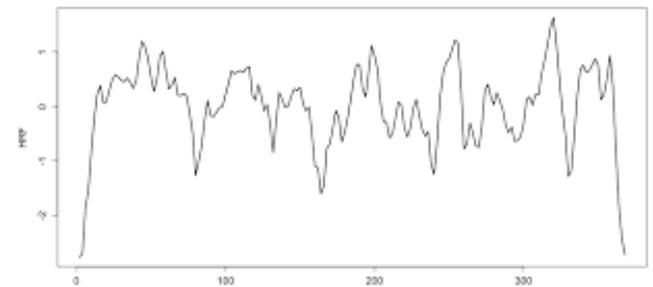
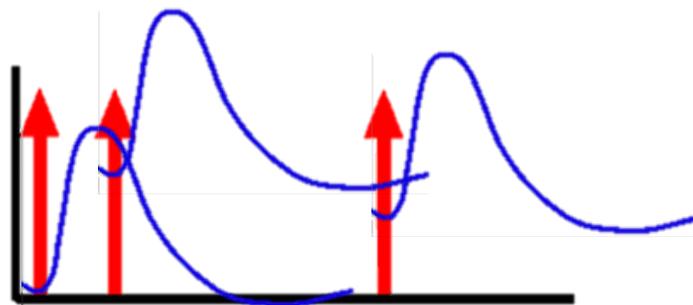
Cytoarchitectonics of bidirectional neocortical projections



HRF \rightarrow BOLD

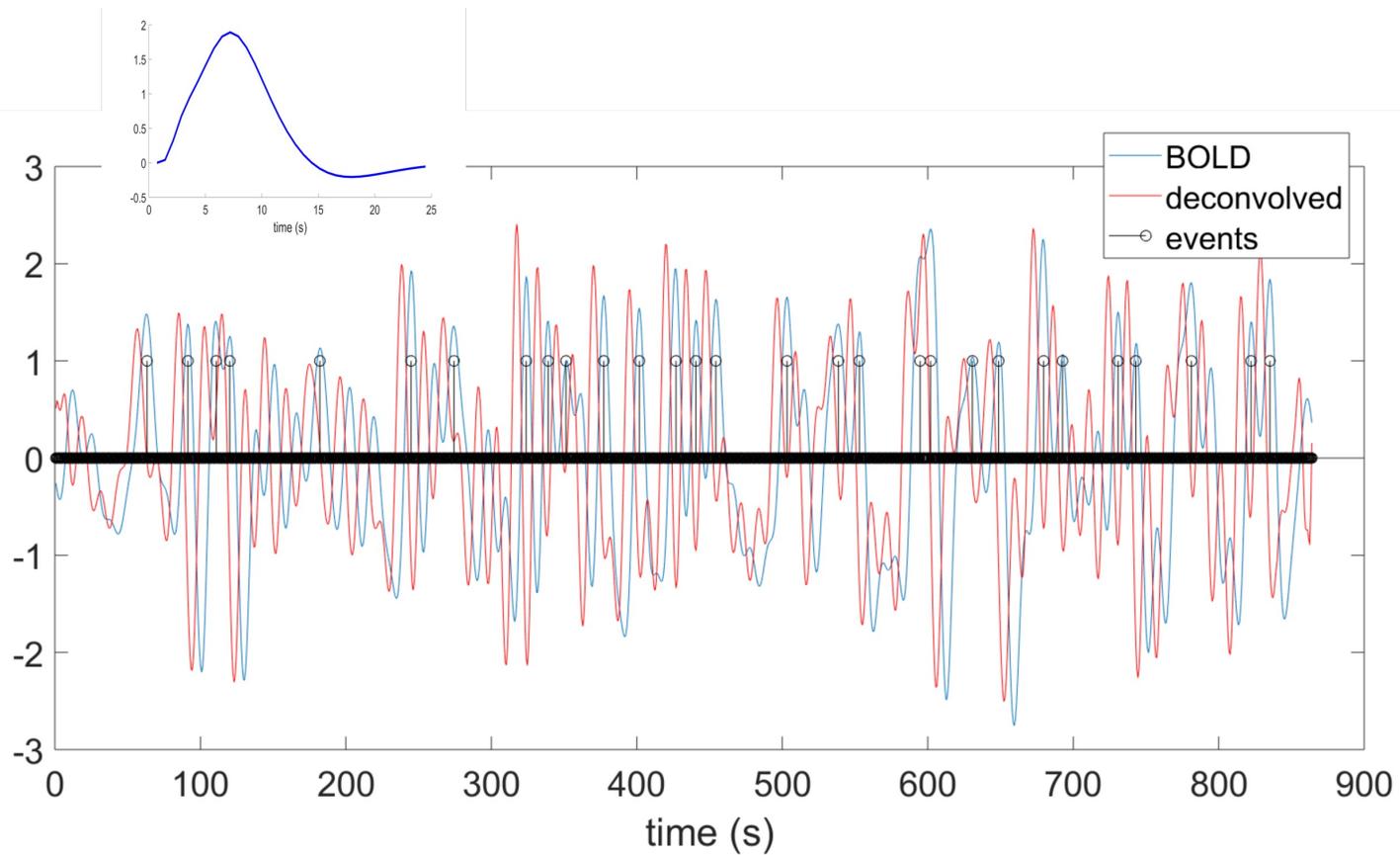


<http://mri-q.com/glm-advanced.html>



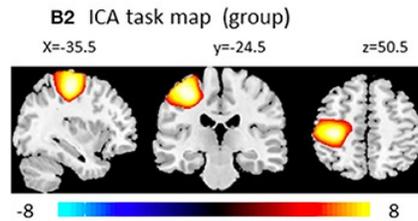
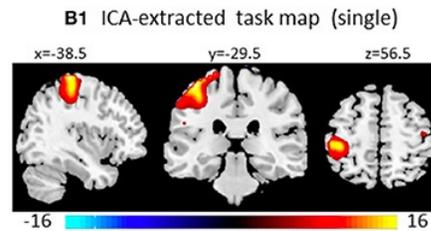
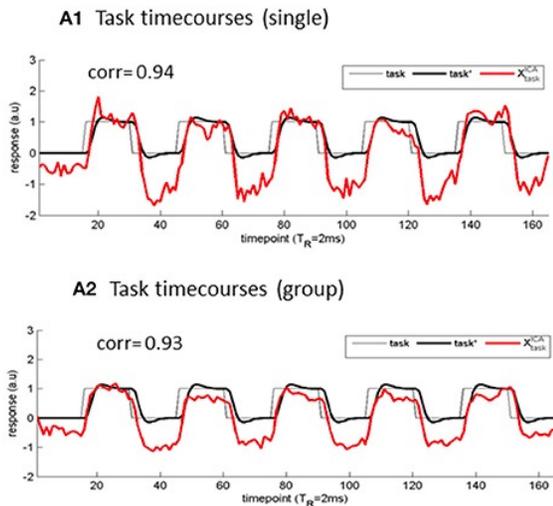
Raw times series

HRF \rightarrow BOLD

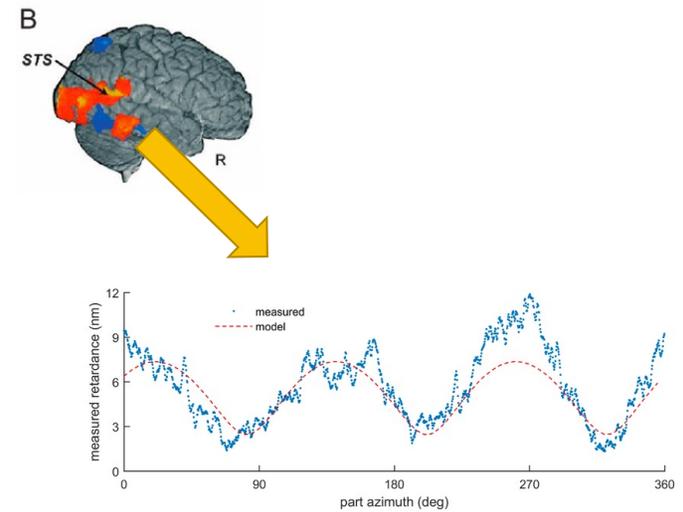


Voxel (area) selection for BOLD

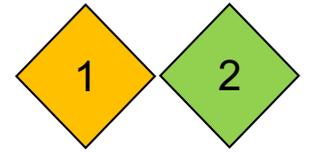
Whole brain tests



Draw structural *a priori* regions

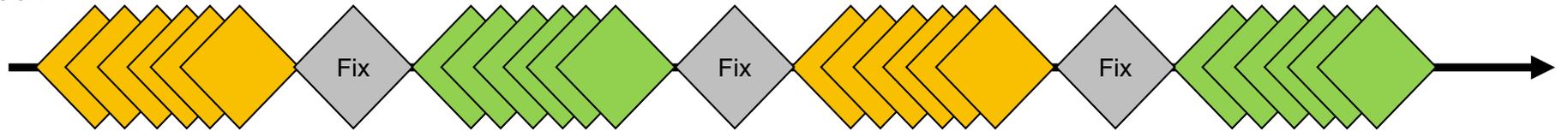


fMRI Experimental designs

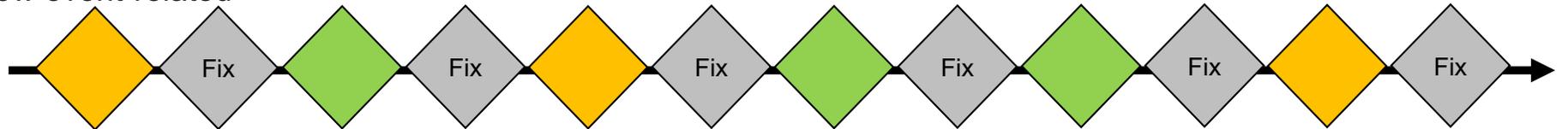


Conditions

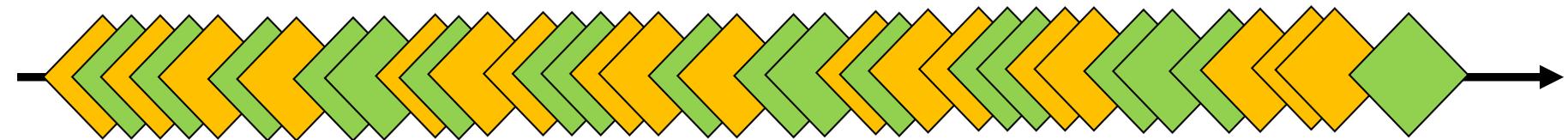
Block



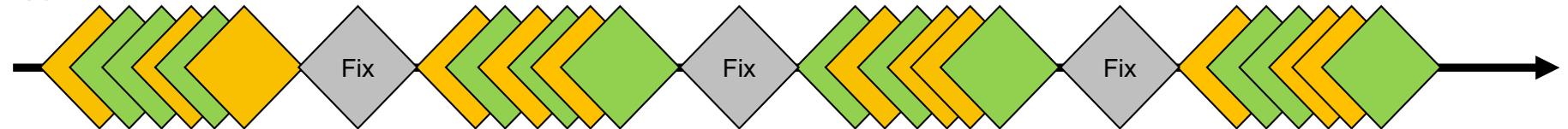
Slow event-related



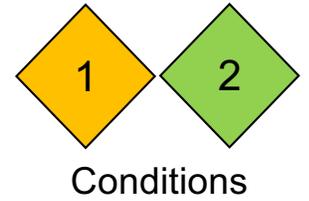
Rapid jittered event-related



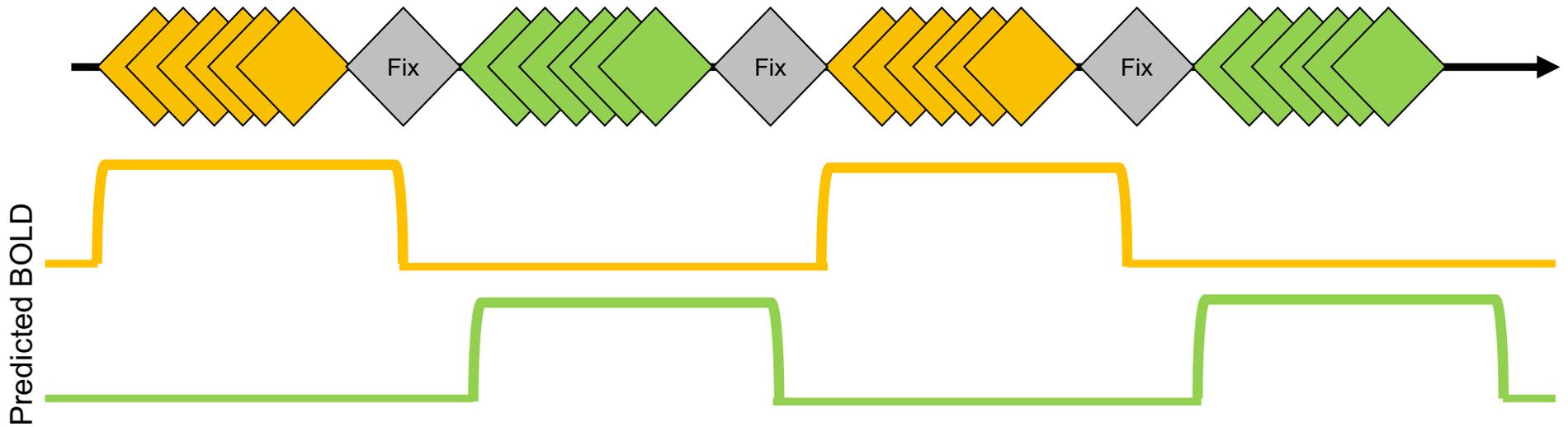
Mixed



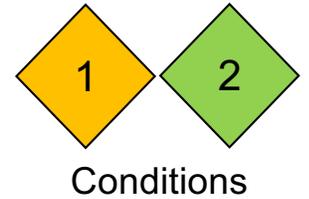
fMRI Experimental designs



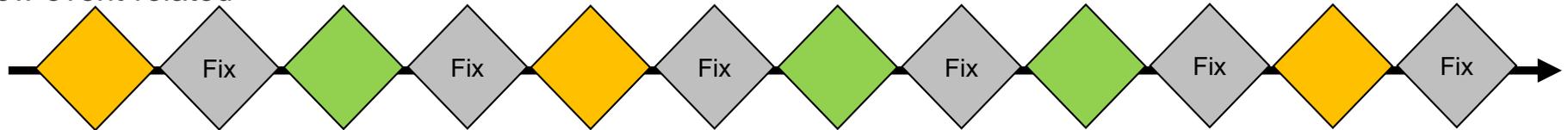
Block



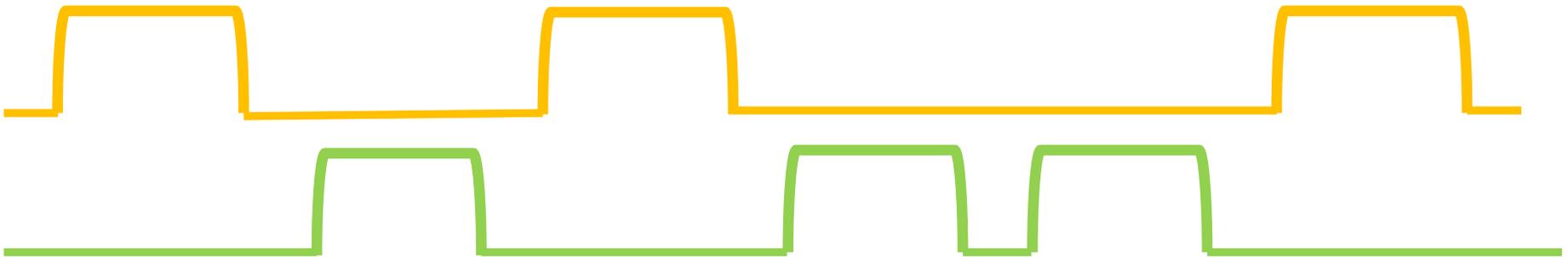
fMRI Experimental designs



Slow event-related



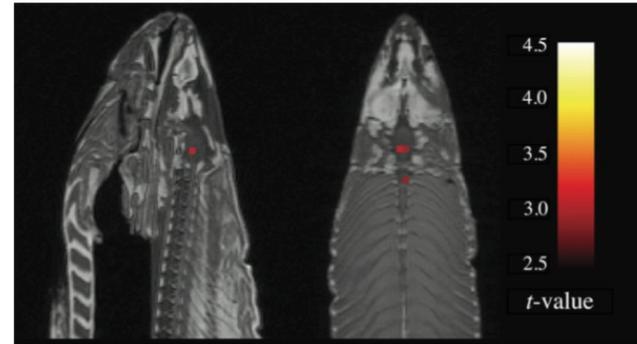
Predicted BOLD



Reading fMRI papers: Multiple comparisons

Statistical considerations: **MUST** correct for multiple comparisons

- Even Bonferroni may be too liberal
 - Assumes independent data, yet adjacent voxels are related
 - Processing data involves smoothing procedures
- Better options: random field theory, small volume correction, false discovery rate, peak and/or cluster thresholds (Poldrack, Mumford & Nichols, 2011)



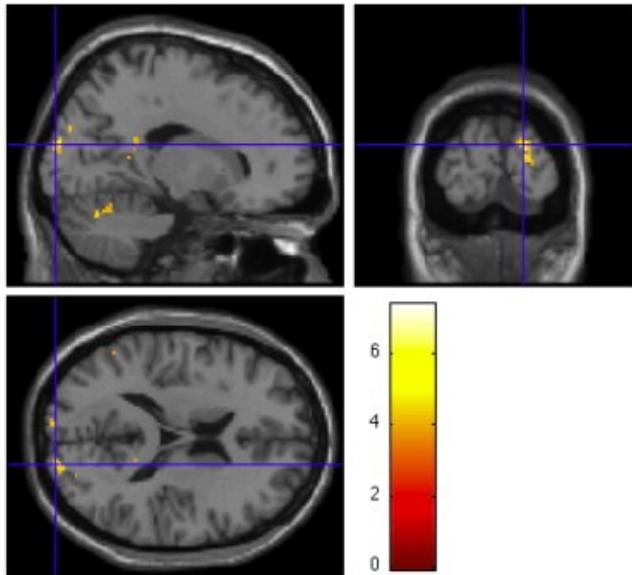
Taken from Bennett et al. (2009), uncorrected ($p = 0.001$)

Reading fMRI papers: Circularity



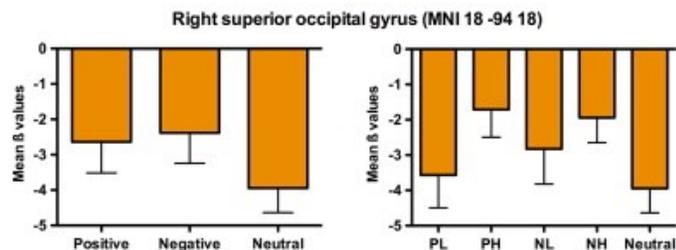
Be wary of papers that state that ROI is based upon the functional analysis

Reading fMRI papers: Imager's Fallacy



- Condition A BOLD signal significantly different than chance
- Condition B BOLD signal significantly different than chance
- Condition A > Condition B

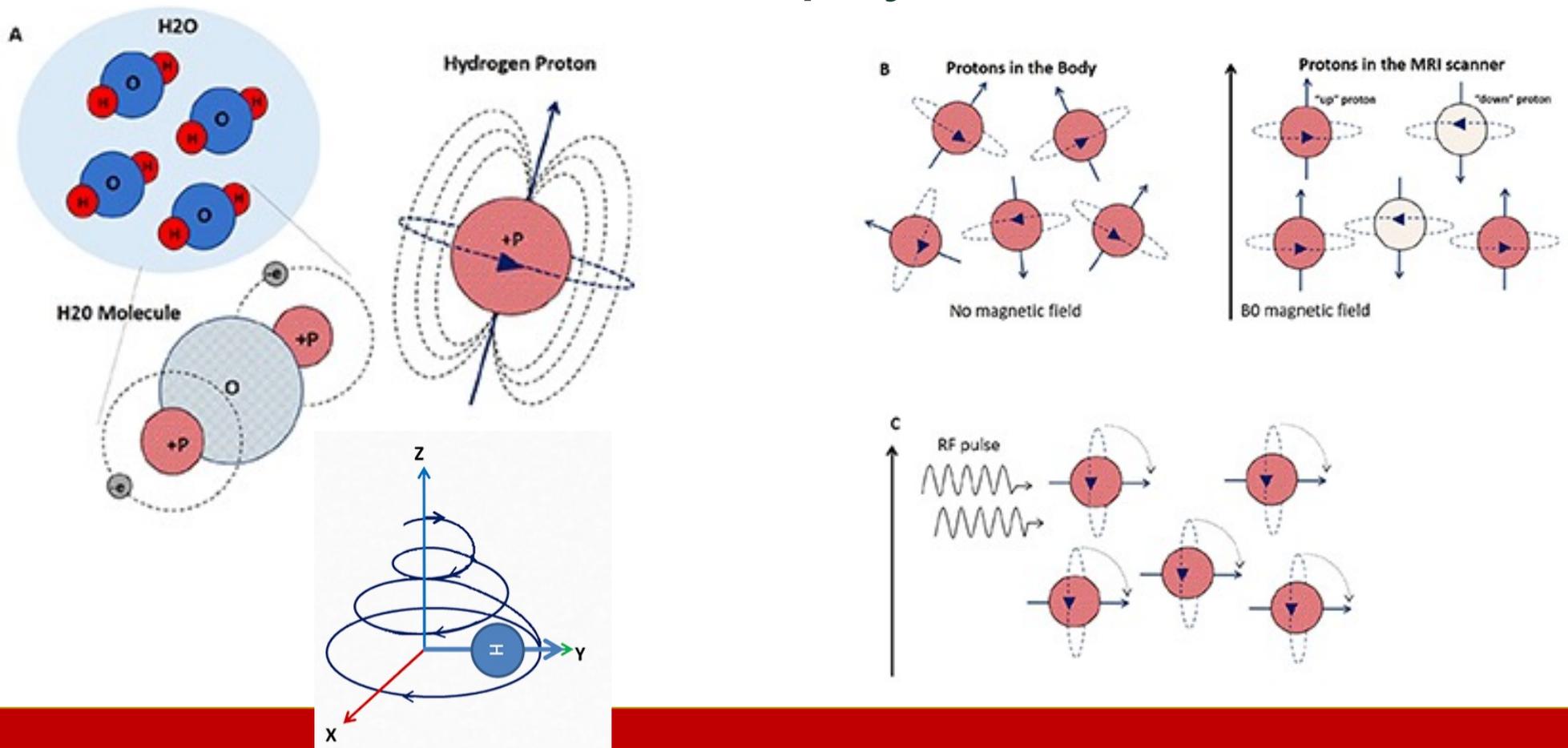
This does not mean that Condition A is “more significant than Condition B”



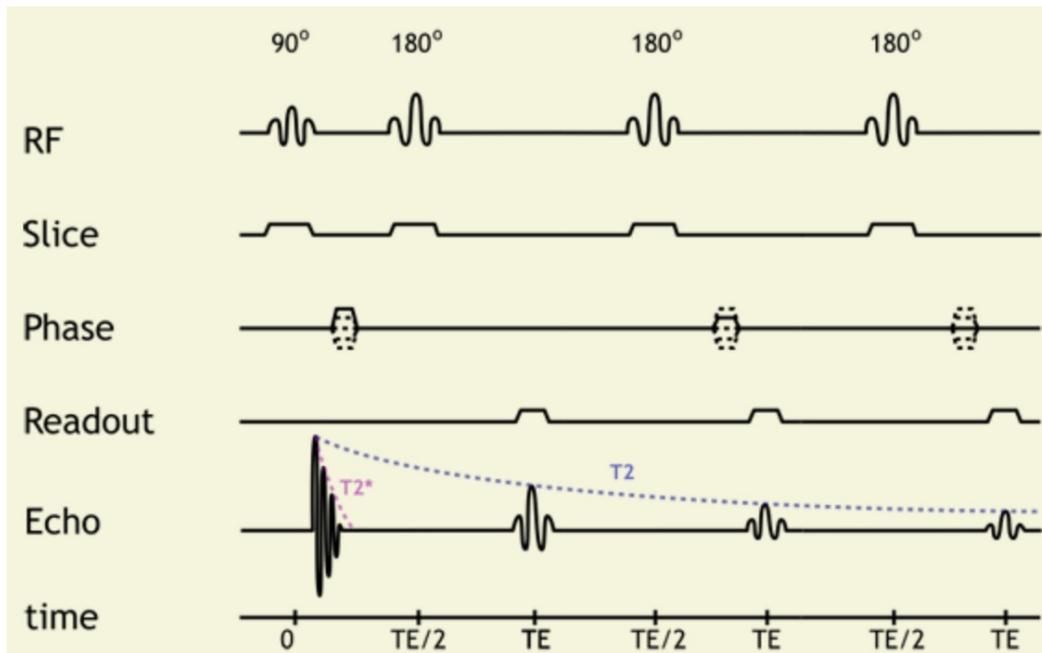
fMRI methods & tech considerations

- Review the participant characterization per usual
- Review experimental design
 - How was HRF assessed?
 - Duration of condition/condition block, duration of fixation
 - Stimulus presentation – bear in mind, laying on your back in a tube

Mini-est of MRI physics lessons



Mini-est of MRI physics lessons



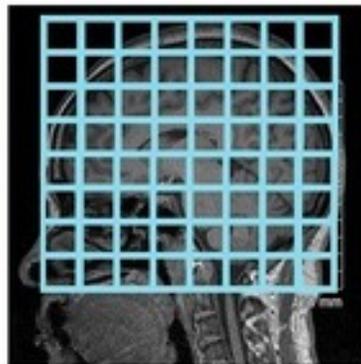
Time to Echo (TE):
Time between RF pulse and echo signal

Repetition time (TR):
Time between RF pulse repetitions at same slice

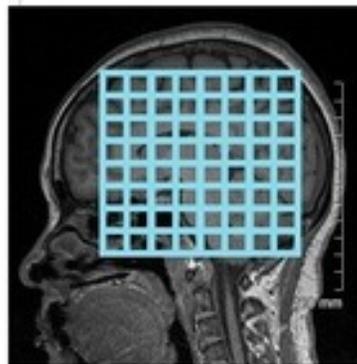
	Short TR	Long TR
Short TE	T1 	PD
Long TE	Poor contrast 	T2

fMRI methods & tech considerations

- Imaging protocol
 - Machine used – important to note strength of MRI, 3T common
 - 3D Anatomical images
 - Often T1-weighted using MPRAGE sequence → **T1 relaxation:** Usually short TE & TR times
 - Pay attention to field of view (FOV)

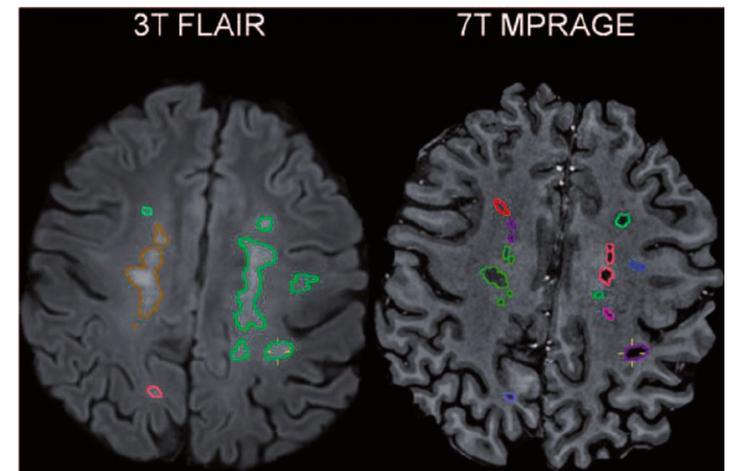


Large FOV



Small FOV

Same number of pixels, but a different size field of view.



fMRI methods & tech considerations

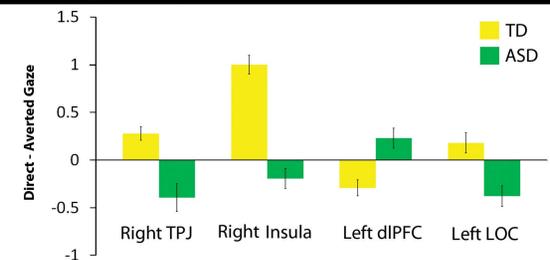
- Imaging protocol
 - Machine used – important to note strength of MRI, 3T common
 - 3D Anatomical images
 - Often T1-weighted using MPRAGE sequence
 - *High-resolution, T1-weighted anatomical images were acquired using an MPRAGE sequence (TR = 1630 ms; TE = 2.48 ms; FOV = 20.4 cm; $\alpha = 8^\circ$; image matrix = 256^2 ; voxel size = 0.8~ 0.8~ 0.8 mm; 224 slices).*
 - 2D Functional images
 - *Whole-brain functional images were acquired using a single-shot, gradient-recalled echo planar pulse sequence (TR = 2000 ms; TE = 30 ms; $\alpha = 73^\circ$; FOV = 20.4 cm; image matrix = 642; voxel size = 3.2~ 3.2 ~ 3.2 mm; 35 slices) sensitive to blood oxygenation level-dependent (BOLD) contrast. We acquired one run of **211 successive brain volumes**.*

fMRI methods & tech considerations

- Processing of data
 - *Data were preprocessed and analyzed using the BrainVoyager QX 1.9 software package (Brain Innovation, Maastricht, The Netherlands). Preprocessing of the functional data included **slice time correction** (using cubic spline interpolation), alignment of slices (using cubic spline interpolation to the first nondiscarded scan time within a scan run), **3-dimensional motion correction** (using trilinear interpolation), **spatial smoothing** with a 4-mm Gaussian kernel, **linear-trend removal**, and **temporal high-pass filtering** (fast-Fourier transform based with a cutoff of 3 cycles/time course).*
 - *The functional data sets were **coregistered** to the Talairach-transformed (Talairach & Tournoux, 1988), within-session, T1-weighted anatomical image series to create 4-dimensional data sets. Estimated motion plots and cine loops were examined for each participant in order to identify movements and eliminate runs in which the participant displayed a deviation in the estimated center of mass (in any dimension) or a rotation that was greater than 3 mm.*
- 

fMRI methods & tech considerations

- **A common analytic approach:** Conduct multiple linear regression of the HRF time course. Extract β values per condition
 - *Model predictors for each gaze condition were defined by convolving an ideal boxcar response with a double gamma function model of the hemodynamic response (Friston, Holmes, Worsley, Poline, Frith, & Frackowiak, 1995). Boxcar values were equal to 1.0 during the 6-second time period when the male figure was enacting direct gaze or averted gaze, and were otherwise 0.*
- Identify voxels in reliable clusters that showcase the predicted HRF (“contrast”)
 - List regions with spatial location in coordinate space (MNI, Talarach), extent of activation (#voxels)



HRF

Cond A

Cond B

Examples of contrasts

Cond A -
Cond B

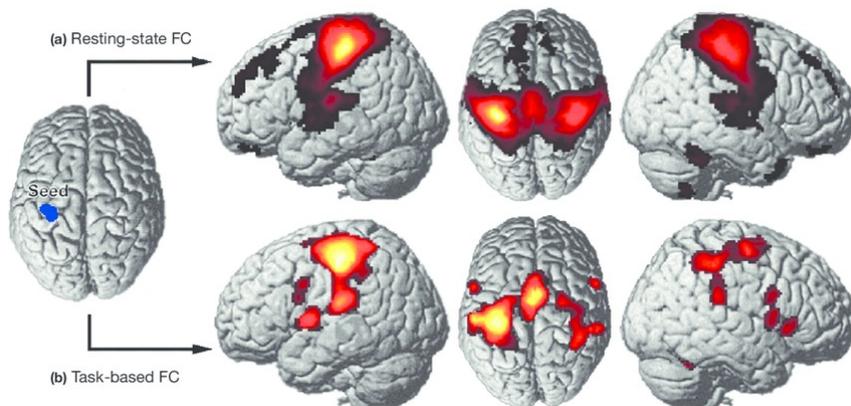
Cond A – Cond B
& Cond A – Cond C

fMRI methods & tech considerations

- Considerations:
 - Whole brain mask? Remove erroneous areas? Only target a priori regions?
 - Do you use all participants for HRF? Only clinical group?
 - Test for multiple comparisons

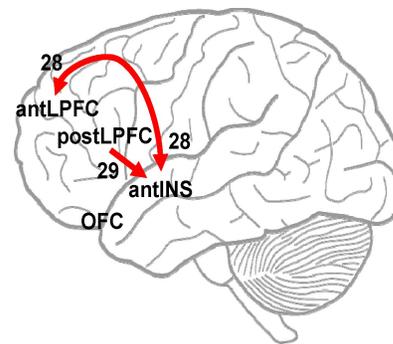
More complex analytics

Seed-based functional connectivity

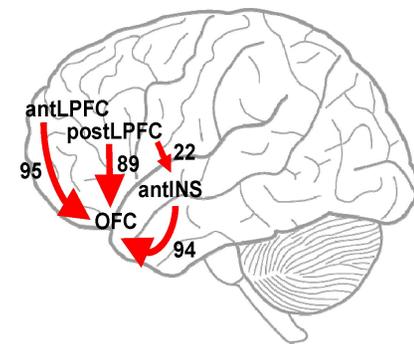


Causality mapping (effective connectivity)

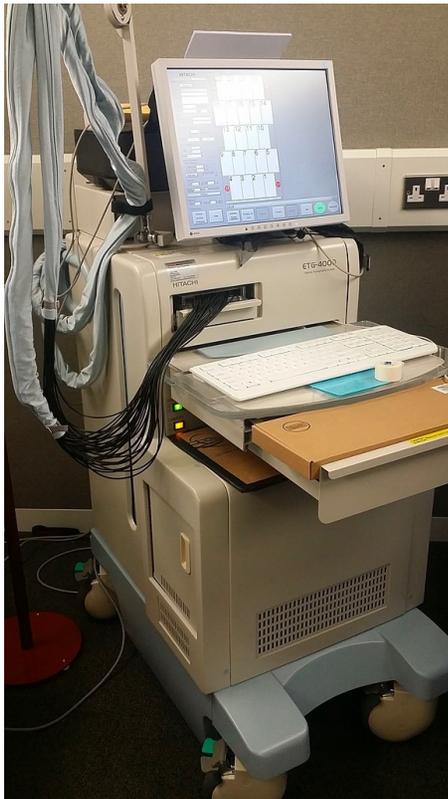
A Intensity



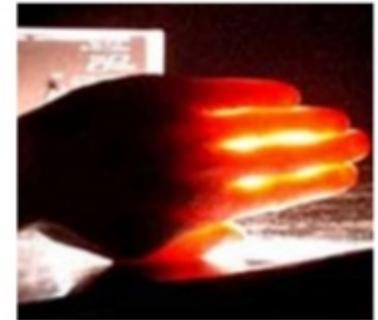
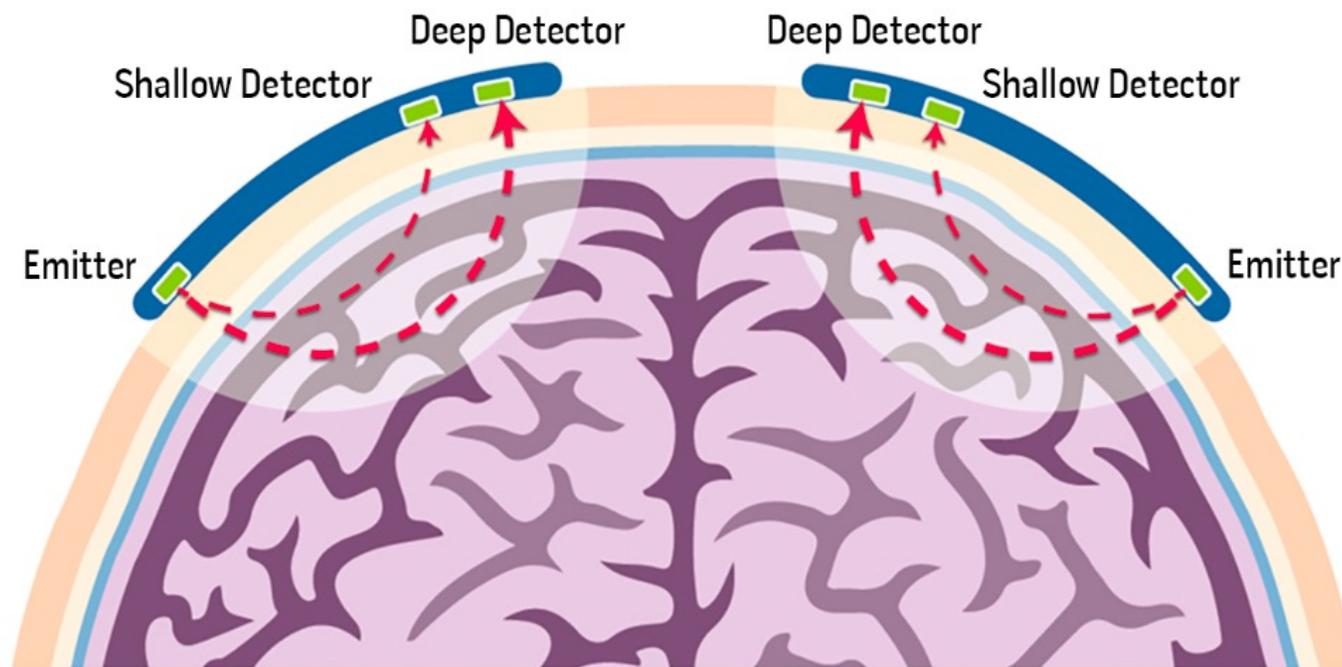
B Pleasantness



Near-infrared spectroscopy



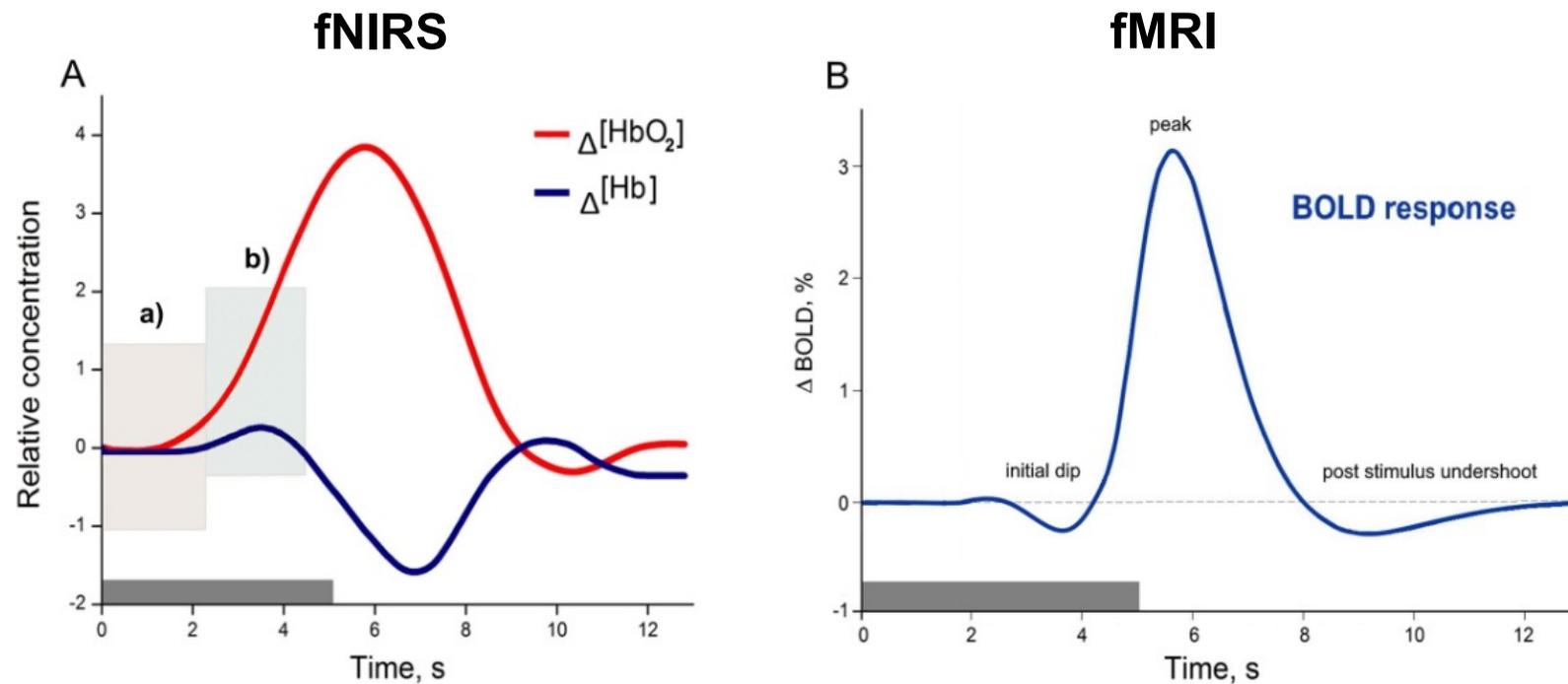
Near-infrared spectroscopy



Red light penetrating in biological tissue



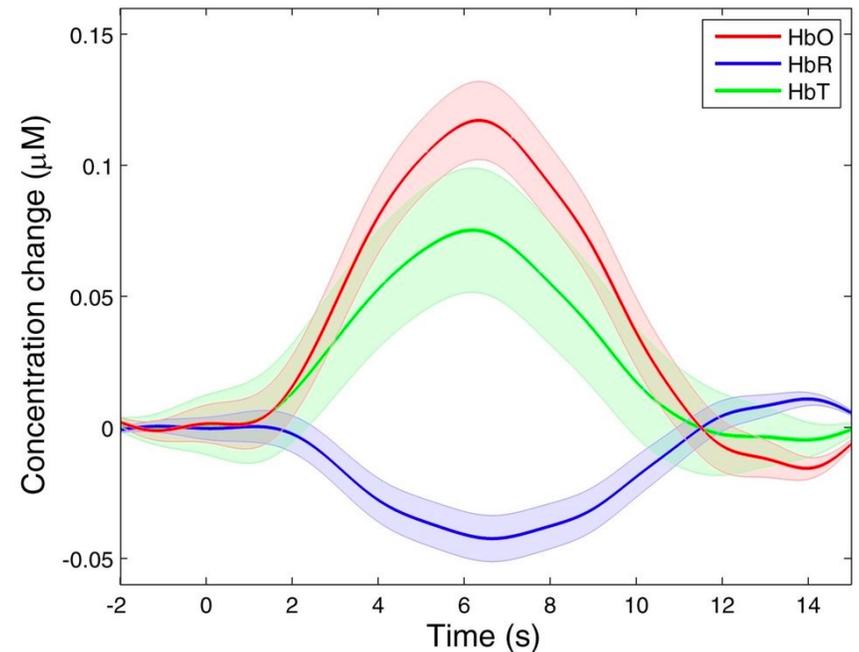
Hemodynamic response function (HRF)



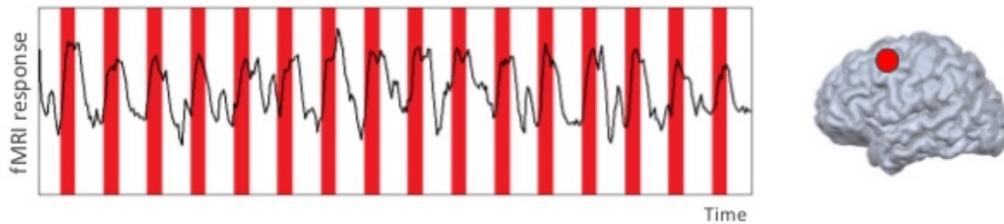
Cincuit, 2019, *Brain and Cognition*

fNIRS HRF

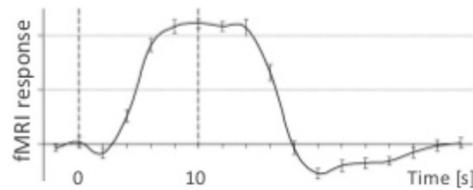
- Advantage of measuring 3 outcomes of the HRF
 - **HbO** = Oxygenated hemoglobin
 - **HbR** = de-oxygenated hemoglobin
 - **HbT** = Hemoglobin total



fNIRS: Experimental designs similar to fMRI



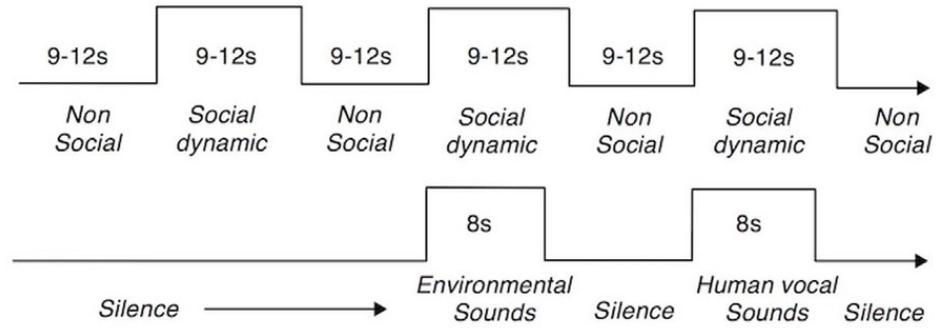
- Resting periods (20s)
- Motor-imagery periods (10s)



**VISUAL
STIMULI**

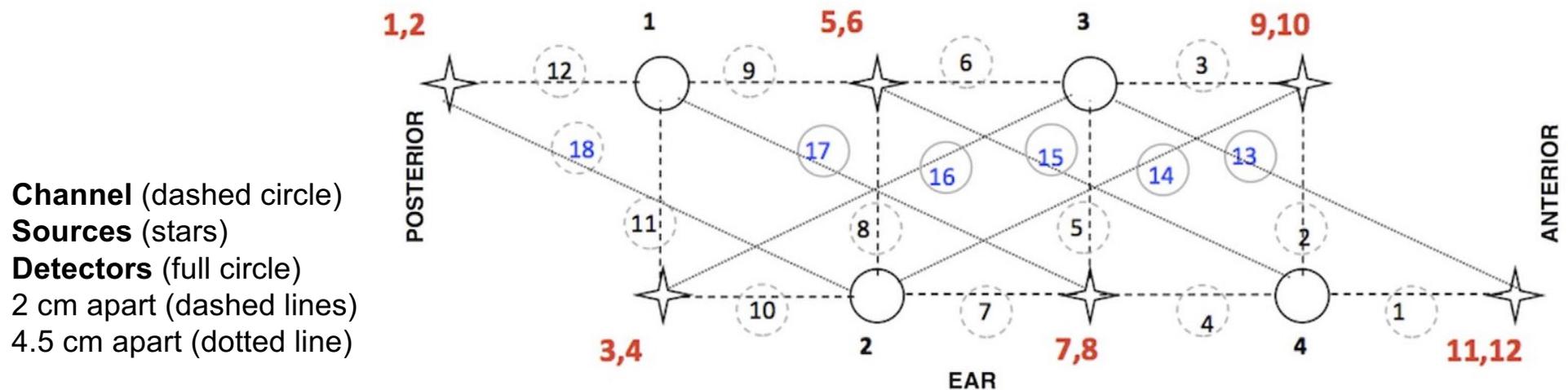
**AUDITORY
STIMULI**

**VISUAL-SOCIAL
CONDITION** **NON-VOCAL
CONDITION** **VOCAL
CONDITION**



Reading fNIRS papers: Location of optodes

- fNIRS can be “DIY” so it is important to know locations as channels can be in different locations between sources and detectors



fNIRS methods & tech considerations

- Review the participant characterization, per usual
- Review experimental design
 - How was HRF assessed?
 - Duration of condition/condition block, duration of fixation
 - Stimulus presentation
 - Optode locations
- Processing of data
 - Channel rejection for artifacts using automatic or manual strategies

fNIRS methods & tech considerations

- **A common analytic approach:**

- Grand-average HRF → verify time windows, especially if new developmental group
- Extract HbO, HbR, HbT

- For each channel, the **maximum change (or amplitude) in HbO₂ (increase in chromophore concentration) and/or HHb (decrease in chromophore concentration)** in response to each experimental condition was assessed relative to baseline during the specified time window. Either a significant increase in HbO₂ concentration, or a significant decrease in HHb, is commonly accepted as an indicator of cortical activation in infant work[8]. During statistical analyses, **if HbO₂ and HHb were either to increase or decrease significantly in unison, the signal was considered inconsistent** with a haemodynamic response to functional activation[59] and not reported in the analyses (for further discussion of physiological changes reported in infant fNIRS work see[8,13]).

- **Considerations:**

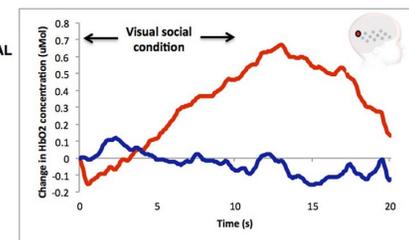
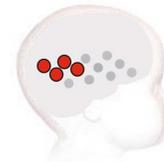
- Test for multiple comparisons



VS



VISUAL SOCIAL > NON-SOCIAL



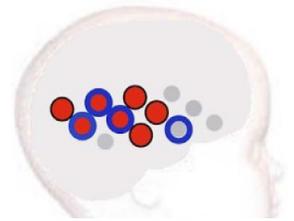
Reading fNIRS papers: Location of optodes

- Opportunities for spatial tuning of conditions:

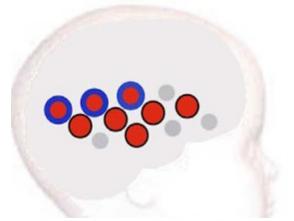
Table 2 | The channel-by-channel t-test (two-tailed) analysis for the contrast between each of the experimental conditions (auditory: vocal and non-vocal; visual only) and the baseline (silence). For each contrast the results for the significant increase in HbO₂ and/or decrease in HHb concentration are displayed. Channel tests that would not survive a False Discovery Rate analysis are highlighted (*)

HbO ₂ (uM)				HHb (uM)				HbO ₂ (uM)				HHb (uM)			
Ch	t	p	df	Ch	t	p	df	Ch	t	p	df	Ch	t	p	df
Voice Condition vs Baseline								Non-Voice Condition vs Baseline							
5	4.16	0.00038	23	4	3.02	0.006	23	2*	2.62	0.016	23	6*	2.23	0.0356	
6	3.08	0.00053	23	8*	2.42	0.024	23	5	3.60	0.0015	23	9	3.85	0.0008	
7*	3.88	0.044	23	9	3.46	0.002	23	6	3.83	0.00085	23	12*	2.37	0.026	
8	6.66	<0.00001	23	11*	2.08	0.049	23	7*	2.43	0.023	23				
9	5.30	0.00002	23	17*	7.46	0.018	6	8	9.36	<0.00001	23				
11	8.47	<0.00001	23					9	6.47	<0.00001	23				
12	5.40	0.000017	23					11	6.02	<0.00001	23				
15*	2.37	0.049	9					12	3.45	0.0022	23				
16	8.07	0.004	7												
17	8.48	0.0136	6												
Visual Condition vs Baseline								Vocal > Non-Vocal Condition							
9*	2.68	0.013	23									2*	2.09	0.049	23
11	3.39	0.0025	23									10*	2.15	0.042	23
12	3.89	0.00075	23									11*	2.29	0.031	23
17	7.49	0.0017	8												
18*	4.97	0.038	6												

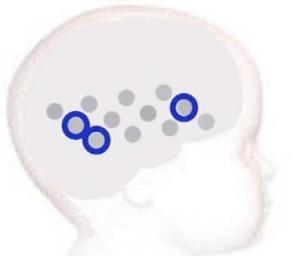
VOCAL vs
BASELINE



NON-VOCAL vs
BASELINE

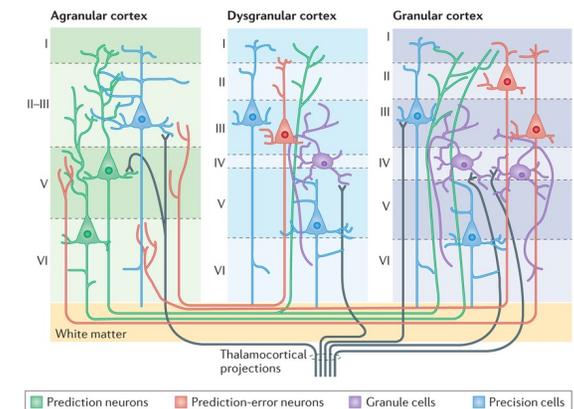
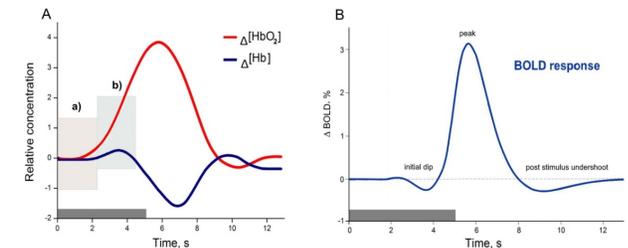


VOCAL > NON-VOCAL
SELECTIVE RESPONSES



Revisit: Issues for affective neuroscience experiments?

- **HRF is slow**
 - ~10-12 seconds
- **Reliant on organized microcolumns of neurons**
 - “Wired together, fired together”
 - Yet, many emo/aff regions are granular
 - Insula, thalamus
 - Cerebellum



Questions? Chat?

