Multimodal imaging of auditory working memory for tones

S. Kumar[1,2], P.E. Gander[3], S. Joseph[2], A.R. Halpern[4], M. Husain[2], K.V. Nourski[3], H. Oya[3], H. Kawasaki[3], M.A. Howard III[3], T.D. Griffiths[1,2]

[1]Newcastle Auditory Group, Newcastle University, Newcastle-Upon-Tyne, UK, [2]Wellcome Trust Centre for Neuroimaging, University College London, London, UK,
[3]Department of Neurosurgery, The University of Iowa, Iowa City, IA, USA,[4]Bucknell University, Lewisburg, PA, USA
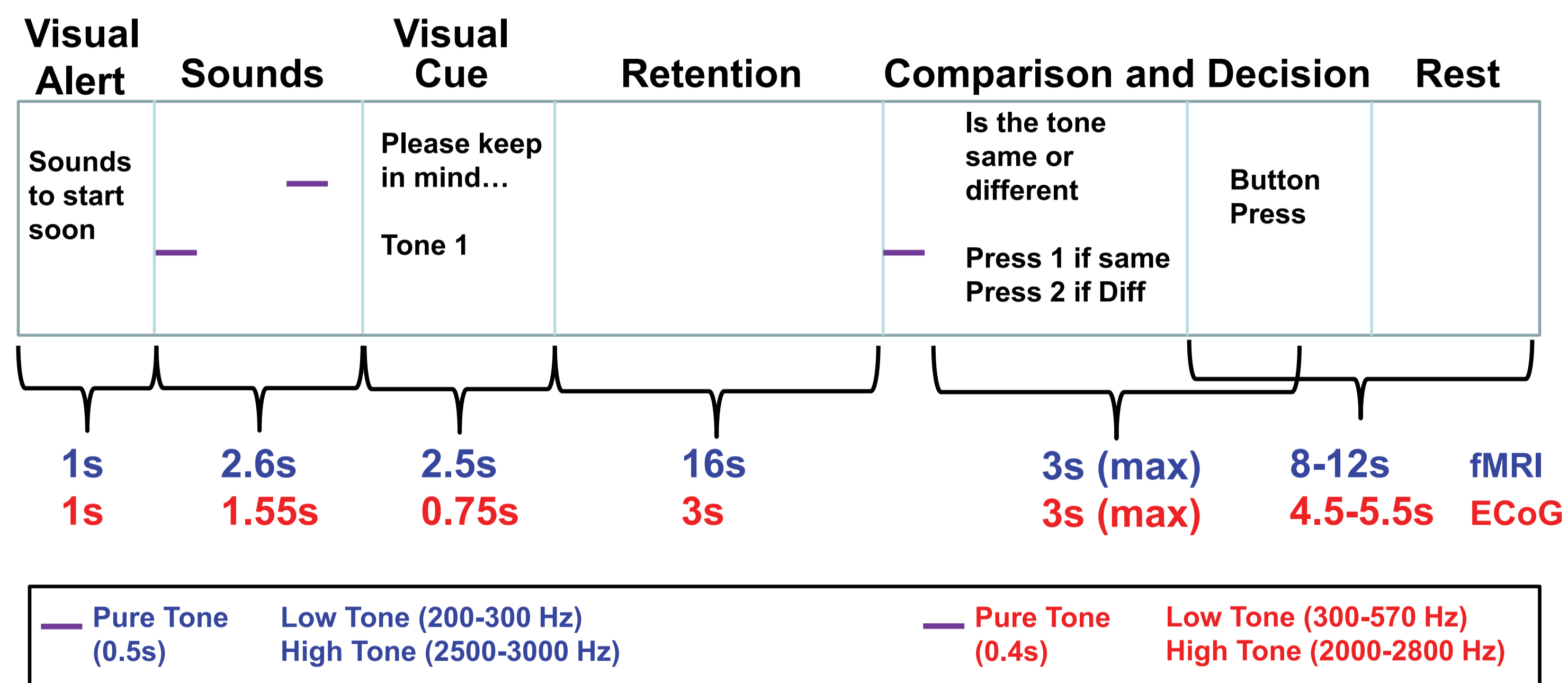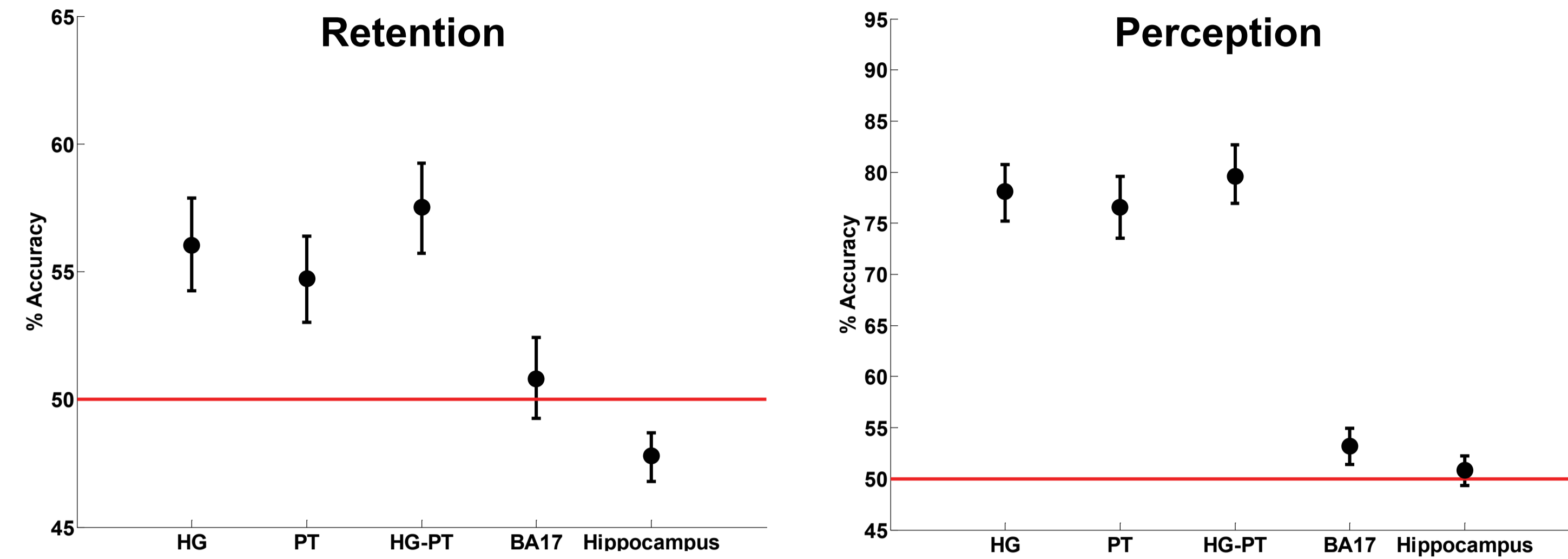
1 Introduction/Methods

- Neural substrates of auditory working memory for auditory stimuli that are not speech or music are not completely understood.
- We measured BOLD signal (17 subjects) and recorded LFPs (ECoG, 3 subjects) during auditory memory for pure tones.

Visual Alert	Sounds	Visual Cue	Retention	Comparison and Decision		Rest
Sounds to start soon		Please keep in mind… Tone 1		Is the tone same or different Press 1 if same Press 2 if Diff	Button Press	
1s	2.6s	2.5s	16s	3s (max)	8-12s	fMRI
1s	1.55s	0.75s	3s	3s (max)	4.5-5.5s	ECoG

Pure Tone (0.5s)	Low Tone (200-300 Hz) High Tone (2500-3000 Hz)	Pure Tone (0.4s)	Low Tone (300-570 Hz) High Tone (2000-2800 Hz)

2 GLM Analysis (fMRI)

- All trials together; Modelled the whole retention period (18.5s); Random effects analysis; $p < 0.05$ (FWE, whole brain); Regressors (4):
  SoundEnc (A) Retention (B) LowToneRecall (C) HighToneRecall (D)

Contrast : Retention Period > Baseline

IFG

Hippo-campus

SMA

Retention Period < Baseline

Visual Cortex

- No auditory cortex activation observed when whole retention period is modelled.
- Retention period broken into three parts (6.17s each); Reten_1,2,3.
- Auditory cortex (HG and PT) changed from negative to positive from Reten_1 to Reten_2 and stayed positive for Reten_3.

Contrast: Reten_1 < Baseline

SupInf Colliculus

Auditory Thalamus

HG/PT

Time Series plot from a voxel in PT during retention interval (beta values vs bin number of FIR model)

Retention Interval Onset →

3 Psychophysiological Interactions PPI (fMRI)

- Using PPI we determined if connectivity of auditory cortex changes from Reten_1 to Reten_3. In two separate PPI analyses we chose HG and PT as seed regions.

HG seed region

4mm sphere around the centre

Change in hippocampal connectivity during retention
$p < 10^{-5}$ (uncorrected)

Change in visual connectivity during retention
$p < 0.05$ (FWE, whole brain)
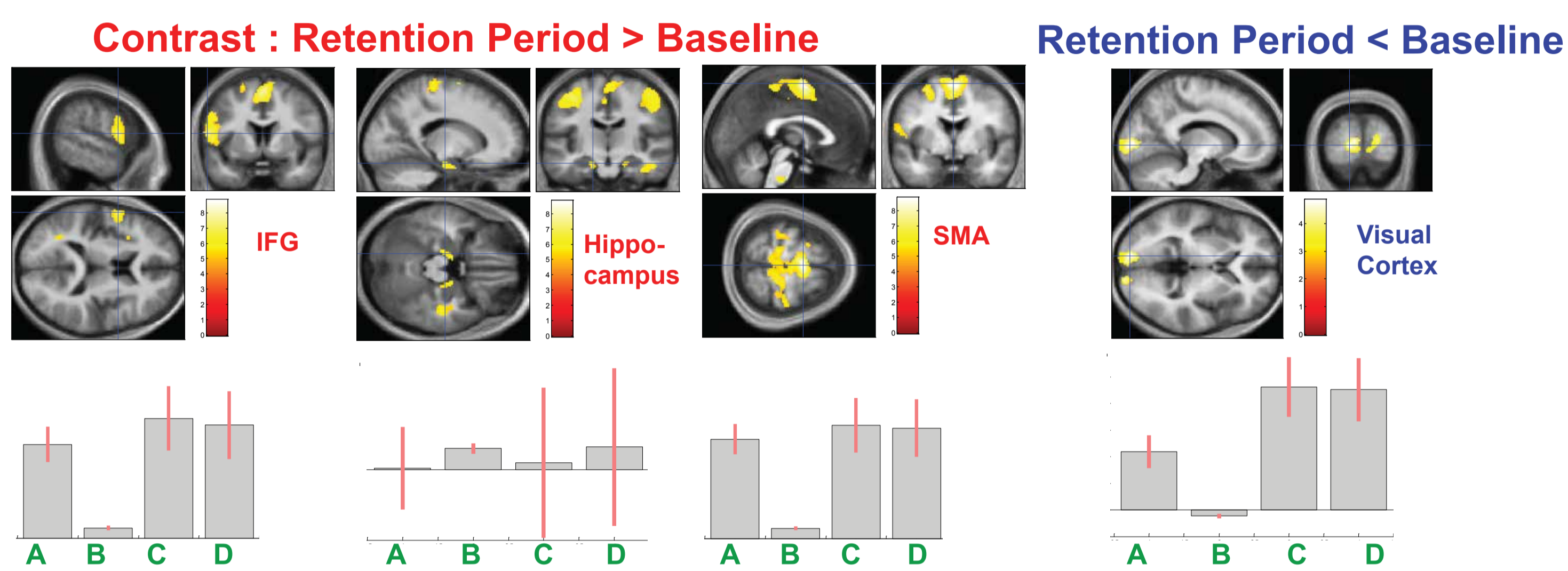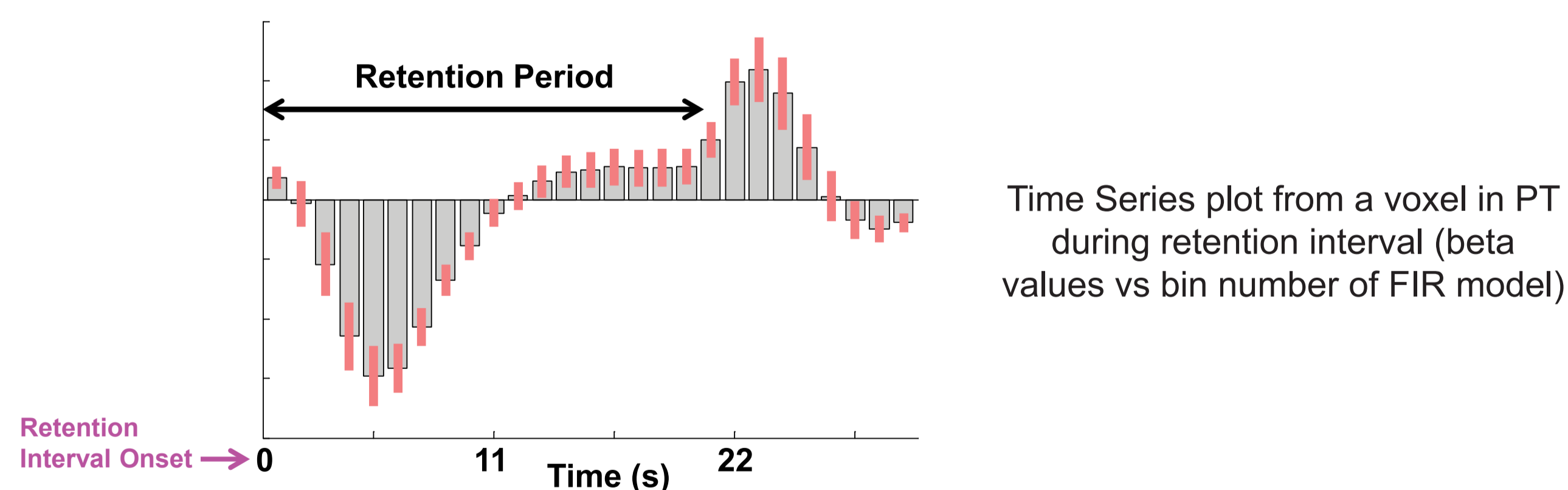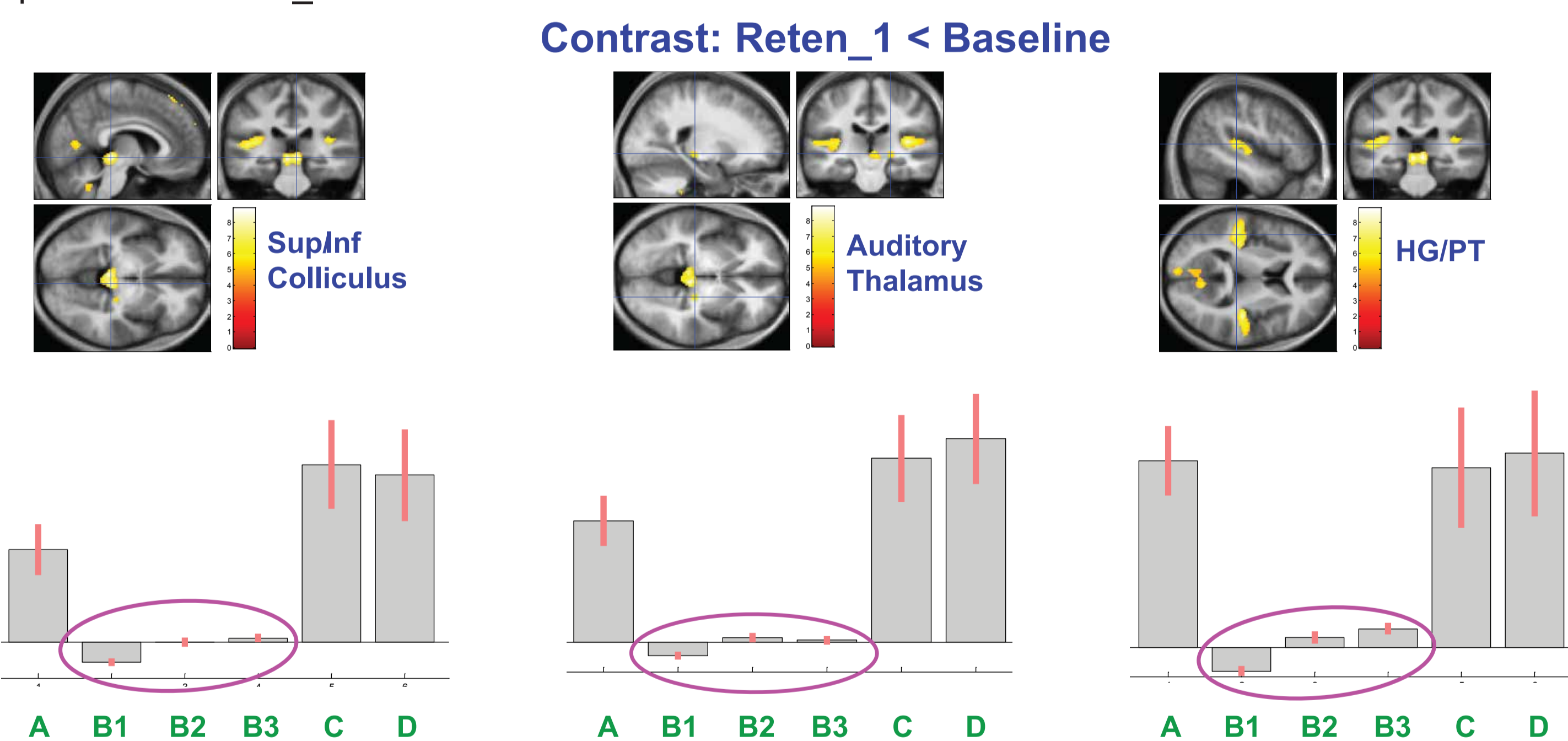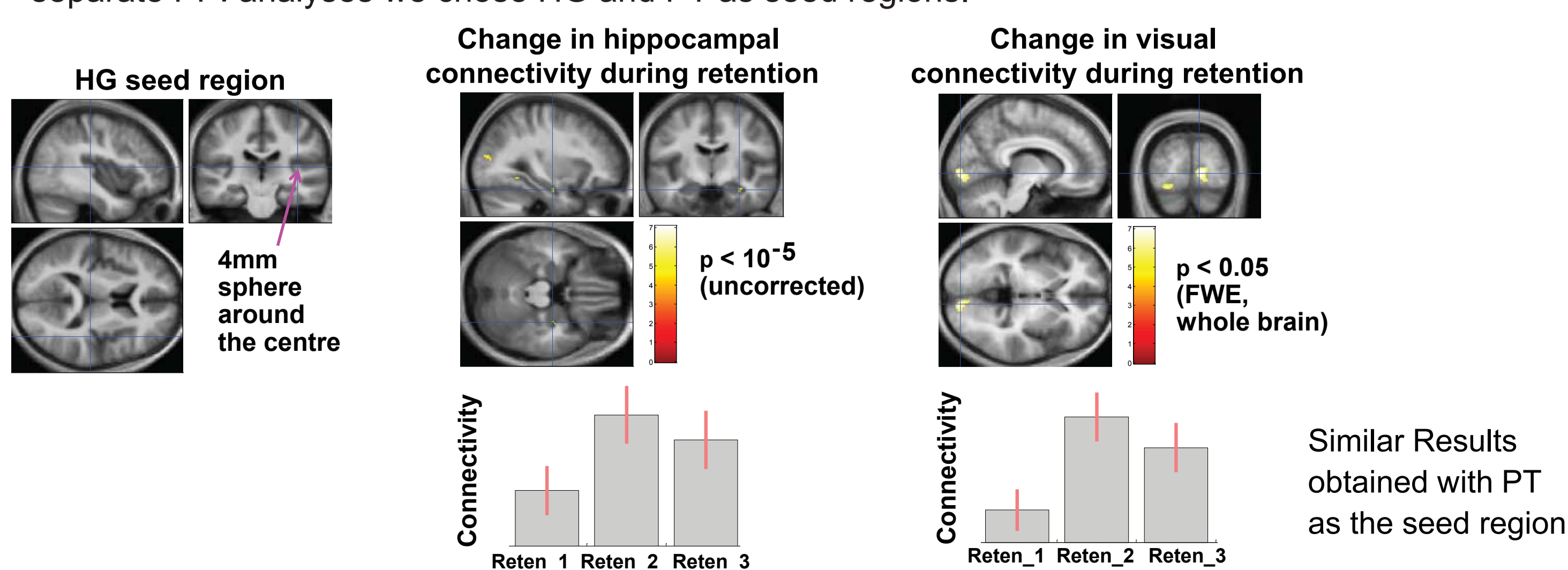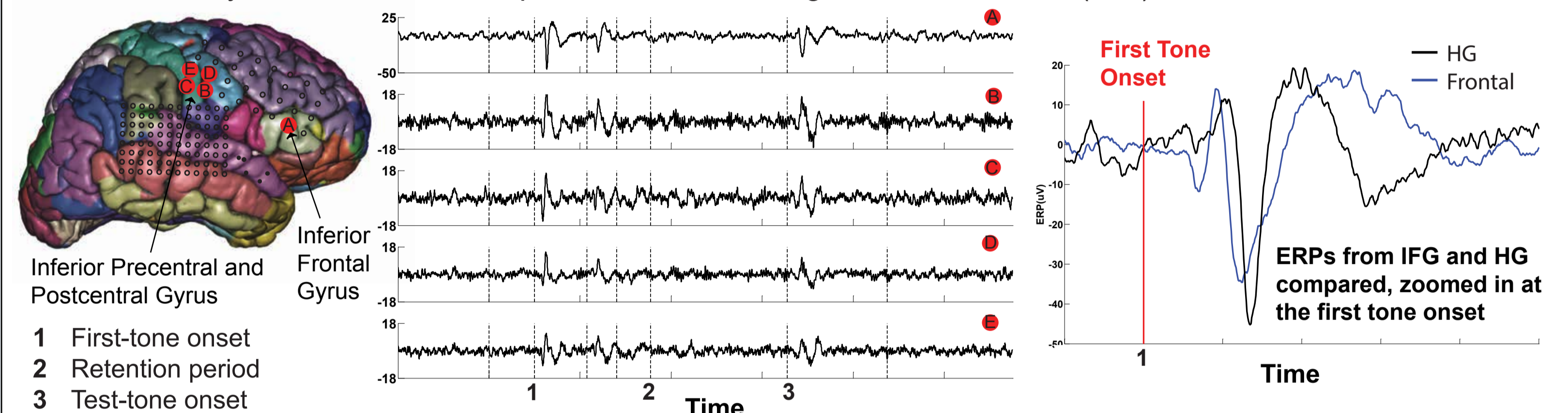
Similar Results obtained with PT as the seed region

4 Multivariate Pattern Analysis (MVPA, fMRI)

- Using GLM analyses we did not find significant differences in activity in any part of the brain during retention of low and high tones.
- We applied MVPA to check if patterns of BOLD activity could be used to decode which tone (low or high) is held in mind. A separate classifier was also trained and tested during perception of low and high tones (Recall period).
- Linear support vector machine; leave one session out; anatomically defined ROIs; classification based on T-images generated using SPM.
- Significant classifier performance during retention in HG and PT.
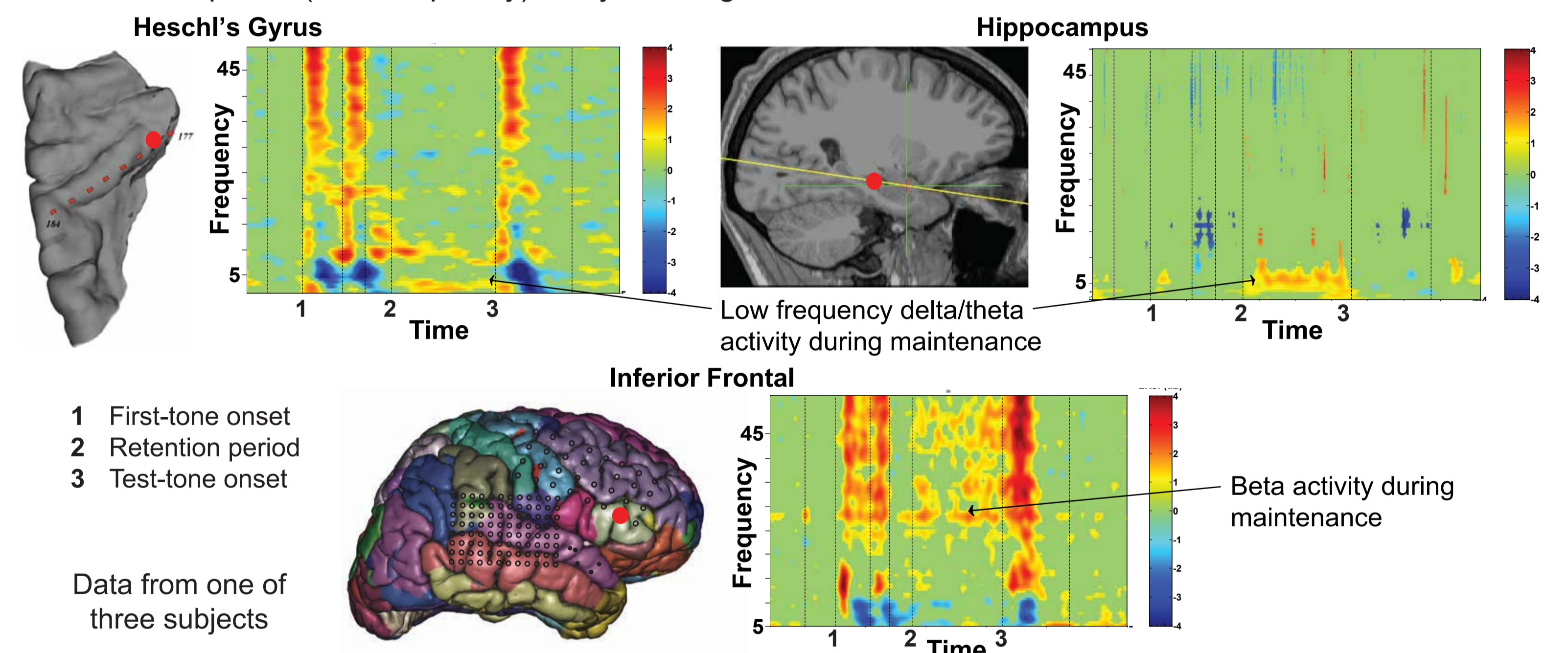

Retention

Perception

5 Intracranial Recordings (LFPs)

Time-locked (ERP) analysis
- We recorded LFPs from three human subjects; paradigm similar to that run using fMRI (see Figure 1). Data for one subject is shown.
- High impedance HG electrodes (70 - 300 kΩ) and low impedance pial electrodes (clinical).
- Recording sites : HG; Temporal grid; Hippocampus; Frontal grid.
- ERP analysis : LFPs downsampled to 500Hz, averaged across all trials (160).

Inferior Precentral and Postcentral Gyrus

Inferior Frontal Gyrus

1 First-tone onset
2 Retention period
3 Test-tone onset

First Tone Onset

HG
Frontal

ERPs from IFG and HG compared, zoomed in at the first tone onset

Induced-response (time-frequency) analysis using Morlet wavelet

Heschl's Gyrus

Hippocampus

Low frequency delta/theta activity during maintenance

1 First-tone onset
2 Retention period
3 Test-tone onset

Data from one of three subjects

Inferior Frontal

Beta activity during maintenance

6 Conclusions

fMRI Study
- Changing BOLD activity was observed in the auditory cortex (HG/PT) during the retention period. This changed from negative to positive during the retention period.
- While the GLM analysis showed no difference in BOLD activity for retention of low and high tones, using multivariate analyses it was possible to decode, from patterns of activity in HG and PT, which tone was held in mind. These structures, therefore, encode specific information about tone identity.
- Sustained BOLD activity occurred throughout the maintenance period in IFG, HC, and SMA. While involvement of IFG (Zatorre et al, 1994) and SMA (Strand et al, 2008) has been shown previously, we are not aware of any prior studies showing a role for hippocampus in auditory WM. The results are in accord with visual studies suggesting a role for HC during WM in the binding of sensory features.
- Connectivity analyses based on BOLD data showed functional connectivity between auditory cortex and hippocampus (and also visual areas).

Intracranial recording Study
- We observed sustained delta and theta band (2-6 Hz) activity in HG during the retention period. The relationship between oscillatory activity and the BOLD signal is not straightforward: low frequencies (up to 20 Hz) correlate negatively; higher frequency bands (above 20 Hz) correlate positively (Mukamel et al, 2005). The theta band activity observed in intracranial recordings is consistent with suppression of BOLD activity during the first part of the maintenance period.
- The involvement of hippocampus in auditory WM is further confirmed by induced LFP activity. Low-frequency sustained theta oscillatory activity (5-8 Hz) during the maintenance period is observed.
- We also observe beta activity during retention in IFG.

Overall Conclusion
- The data support the existence of a system for tone working memory involving auditory cortex, hippocampus and frontal cortex.
- Ongoing systems modelling of both BOLD and electrical data is examining the effective connectivity between these regions in order to define the system.

References
Mukamel et al (2005). Science, 309:951-954.
Strand et al (2008). Brain Research, 1212:48-54.
Zatorre et al (1994). Journal of Neuroscience, 14:1908-1919.

Acknowledgements

Contact information
Sukhbinder Kumar, PhD   sukhbinder.kumar@ncl.ac.uk