

# Frontal Midline Theta Co-ordinates Spatial Memory Retrieval

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## Theta and Spatial Memory

Theta oscillations dominate the rodent hippocampal LFP during translational movement [Vanderwolf 1969, O'Keefe and Recce 1993]

In humans, hippocampal theta power correlates with episodic memory performance [Guderian et al. 2009]

Theta oscillations are observed in frontal midline regions during a wide variety of behavioural tasks [Mitchell et al. 2008]

However, the function of this frontal midline theta rhythm and its relationship with hippocampal theta is currently unclear

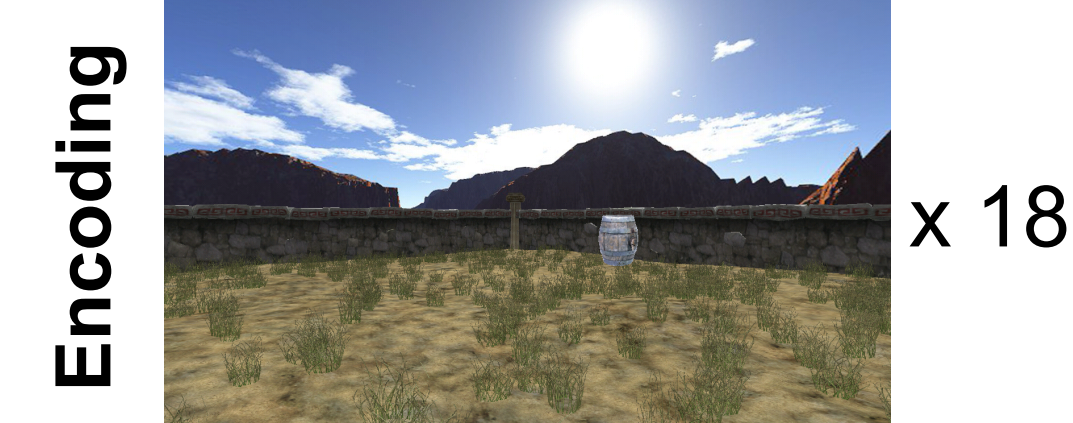
We examine frontal and hippocampal theta during a spatial memory task

## Task Design and Analysis

During each of six encoding sessions, participants were asked to navigate towards and encode the location of six objects, three times each, that were presented sequentially and pseudo-randomly in consistent locations [Doeller et al. 2008; Kaplan et al. 2012]

During six subsequent retrieval trials in each session, participants were cued with an image of one object, and asked to navigate to the previously encoded location of that object and make a response

We contrast 1s of the cue period with preceding 1s quiet fixation period



Seventeen right-handed male participants navigate using a button box

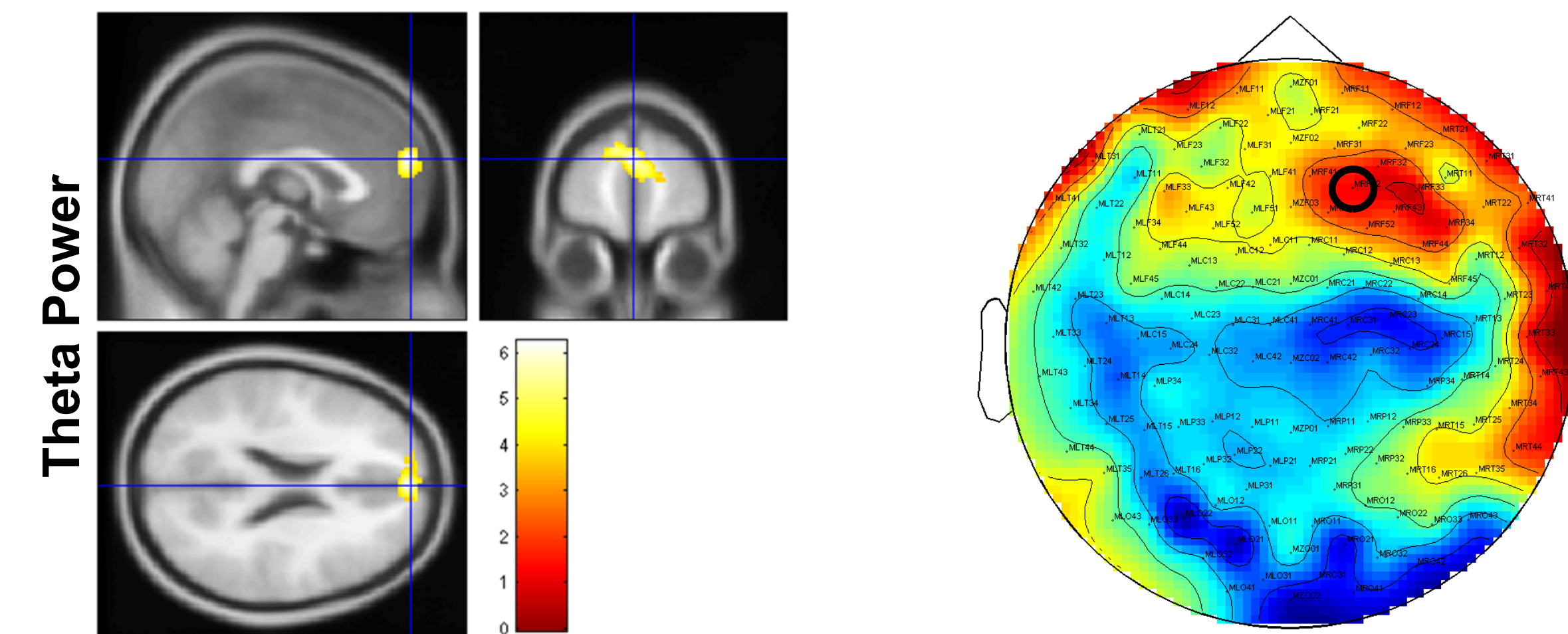
MEG recordings made using a 275 channel CTF system, sampled at 480Hz

Source reconstruction performed using the LCMV beamformer algorithm [Barnes and Hillebrand 2003]

Statistical analyses performed in SPM8

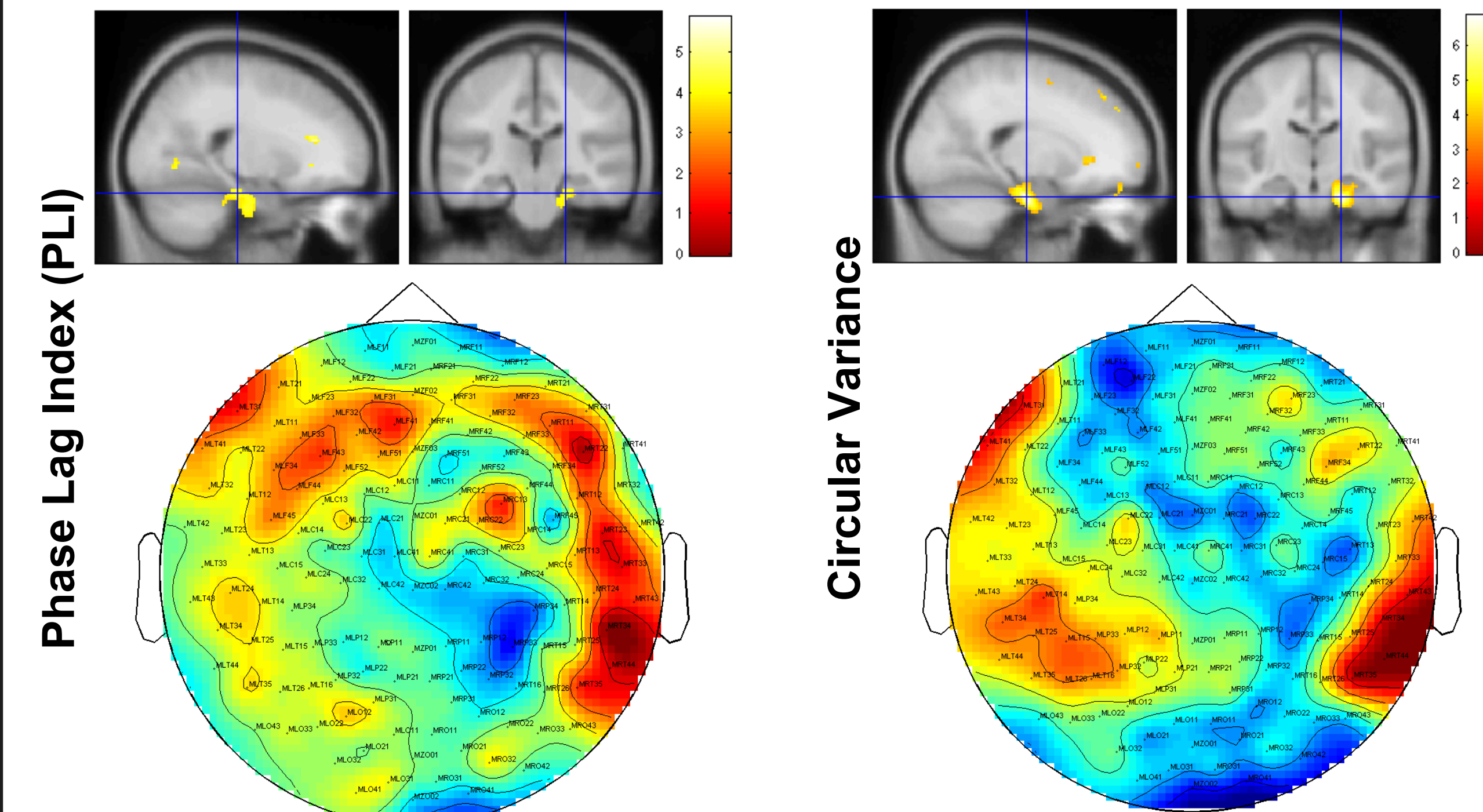
## Theta Power and Phase Coupling

We identified an increase in 4-8Hz theta power in the mPFC during the cue period, peaking at [0 58 22],  $p < 0.05$  FWE corrected



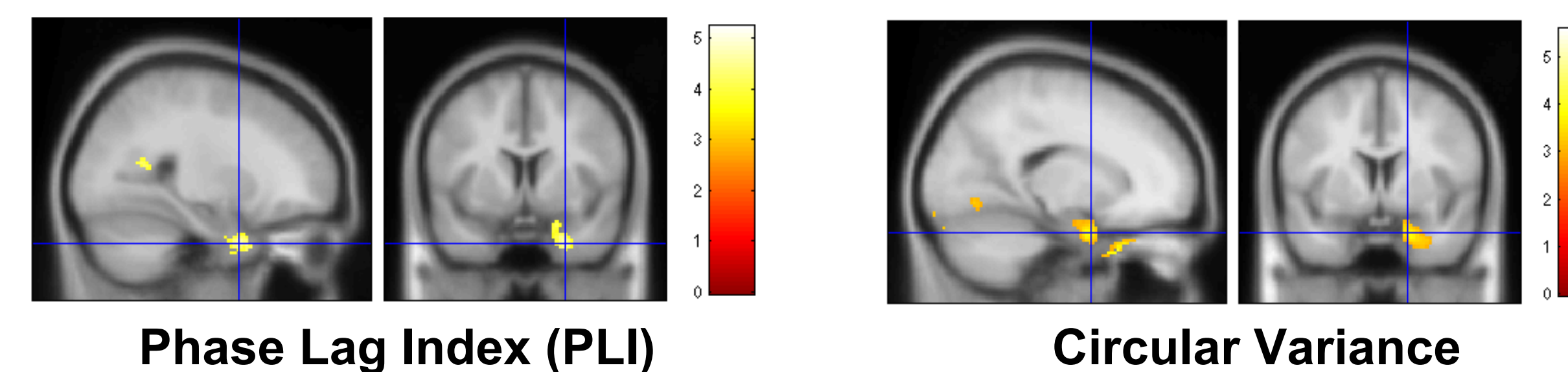
We then used the mPFC voxel with the greatest theta power contrast between baseline and cue periods for each participant within 20mm of the group peak as a seed to investigate inter-regional theta phase coupling

We identify an increase in theta phase coupling between the mPFC source and right anterior MTL during the cue period,  $p < 0.001$  FWE corrected



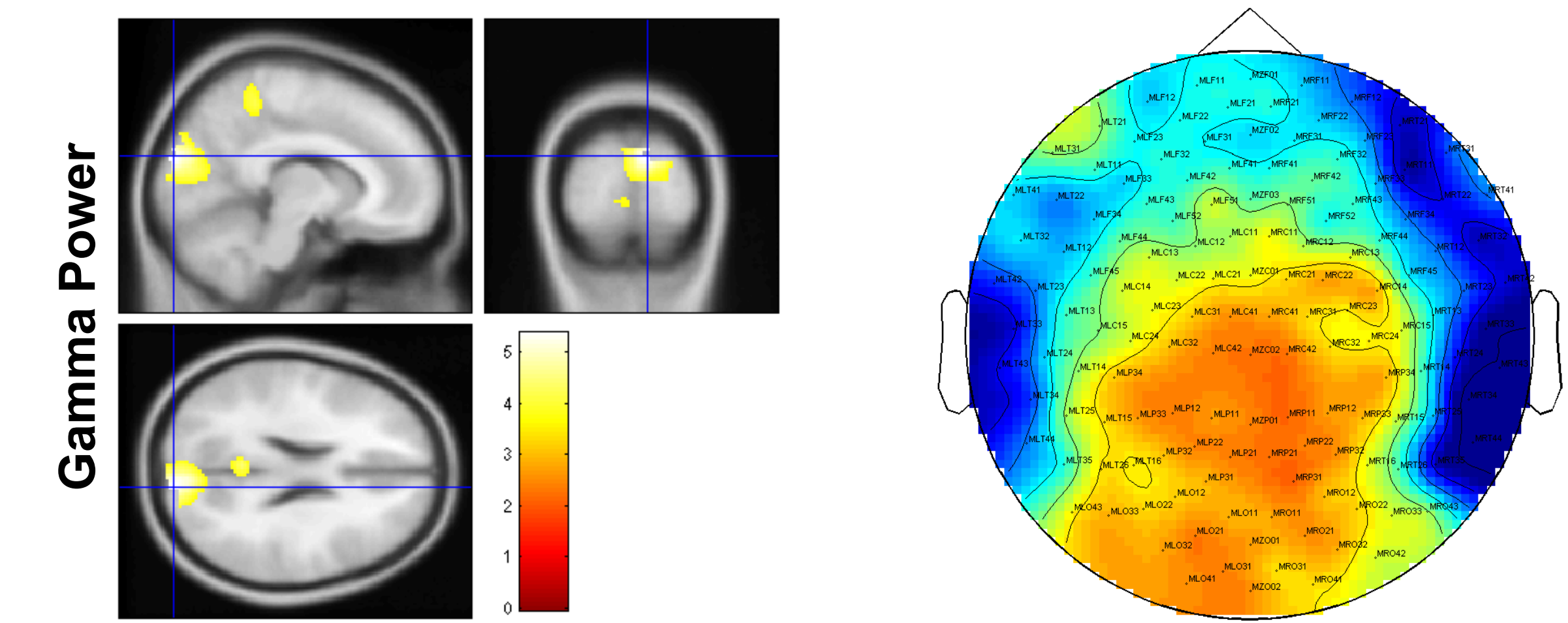
We then split the trials performed by each participant according to whether the distance error is above or below their median performance, in order to identify any subsequent memory effects

We establish that mPFC-aMTL theta phase coupling is stronger during high performance trials,  $p < 0.05$  FWE corrected



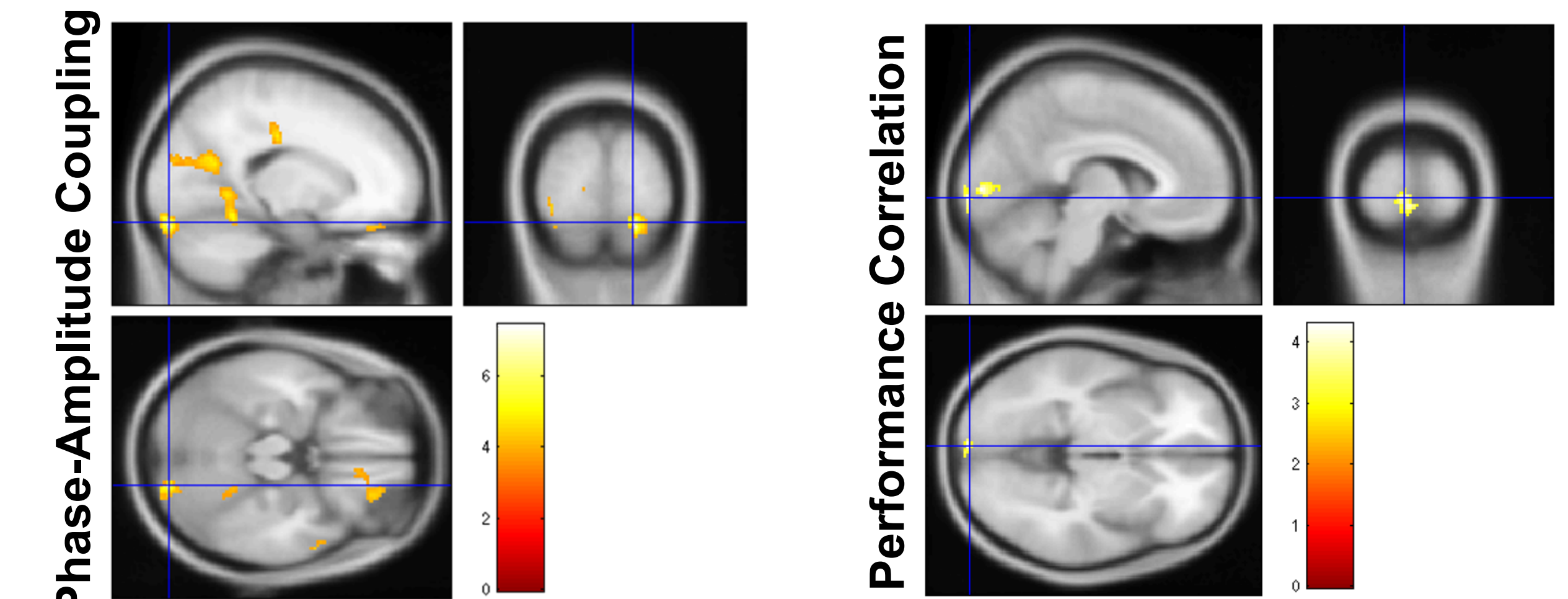
## Gamma and Phase-Amplitude Coupling

We also identified an increase in 65-85Hz occipital gamma power during the cue period, peaking at [10 -92 24],  $p < 0.05$  FWE corrected



This increase in gamma power is accompanied by an increase in theta phase - gamma amplitude coupling between mPFC and occipital sources measured using circular variance,  $p < 0.001$  FWE corrected

Furthermore, frontal-occipital theta phase - gamma amplitude coupling is stronger during high performance trials,  $p < 0.001$  uncorrected



## Conclusions

Increased mPFC / MTL theta coupling during spatial memory retrieval is consistent with previous findings in rodents [Hyman et al. 2005; Jones and Wilson 2005; Siapas, Lubenov and Wilson 2005] and humans [Guitart-Masip et al. 2013]

We provide the first demonstration that the strength of this theta coupling is predictive of subsequent spatial memory performance

We also provide the first demonstration of inter-regional theta phase - gamma amplitude coupling in human MEG, and show that the strength of this coupling is predictive of subsequent spatial memory performance

We hypothesise that frontal midline theta co-ordinates spatial memory retrieval

Vanderwolf CH (1969) Hippocampal electrical activity and voluntary movement in the rat. *Electroencephalography & Clinical Neurophysiology* 26(4): 407-418  
O'Keefe J, Recce ML (1993) Phase relationship between hippocampal place units and the EEG theta rhythm. *Hippocampus* 3(3): 317-330  
Hyman JM, Zili EA, Paley AM, Hasselmo ME (2005) Medial prefrontal cortex cells show dynamic modulation with the hippocampal theta rhythm dependent on behaviour. *Hippocampus* 15(6): 739-749  
Jones MW, Wilson MA (2005) Theta rhythms coordinate hippocampal-prefrontal interactions in a spatial memory task. *PLoS Biology* 3(12): e402  
Siapas AG, Lubenov E, Wilson MA (2005) Prefrontal phase-locking to hippocampal theta oscillations. *Neuron* 46(1): 141-151  
Doeller C, King JA, Burgess N (2008) Parallel striatal and hippocampal systems for landmarks and boundaries in spatial memory. *PNAS* 105(15): 5915-5920  
Mitchell DJ, McNaughton N, Flanagan D, Kirk IJ (2008) Frontal midline theta from the perspective of hippocampal theta. *Progress in Neurobiology* 86(3): 156-185  
Guderian S, Schott BH, Richardson-Klavehn A, Düzel E (2009) Medial temporal theta state before an event predicts episodic encoding success in humans. *PNAS* 106(13): 5365-5370  
Kaplan R, Doeller CF, Barnes GR, Litvak V, Düzel E, Bandettini PA, Burgess N (2012) Movement-related theta rhythm in humans: Coordinating self-directed hippocampal learning. *PLoS Biology* 10(2): e1001267  
Guitart-Masip M, Horner AJ, Fuentes-Milla L, Penny W, Düzel E (in press) Synchronisation of medial temporal lobe and prefrontal rhythms in human decision-making. *Journal of Neuroscience*

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