Supporting Methods

Ghuman *et al.* 10.1073/pnas.0710674105

SI Text

Subjects. Participants (mean age = 21 years, range 18–25) were recruited through flyers and advertisements at local colleges and universities and received $100 for their participation. Participants were screened by using a short medical questionnaire to ensure that they were free from current psychiatric or neurological disorder, any history of brain injury or excessive drug or alcohol use. Written informed consent was obtained from each participant before the experimental session. The Human Subjects Committees of Boston University School of Medicine and the Veterans Affairs Healthcare System approved all procedures.

Recording. Each triplet is comprised of two orthogonal planar gradiometers and one magnetometer, thereby providing three independent measurements of the magnetic field at each sensor triplet. Bidirectional electrooculograms (EOG) were recorded to detect and discard trials containing eye movement and blink artifacts. Additionally, to exclude the possibility that our results were due to eye movements, we compared the output of the EOG channels between the novel and repeated conditions and no significant differences ($p >$. 1 corrected, at all time points) were seen.

Before the subject entered the shielded room, the positions of multiple points on the scalp were measured in a head coordinate system defined by anatomical landmarks by using a Polhemus FastTrack 3-D digitizer (Polhemus), to allow subsequent coregistration with MR images. The signal was sampled at 600 Hz and down-sampled off-line to 150 Hz for computational efficiency. Structural MR images of each subject's brain was acquired with a 3.0T Siemens system.

Phase-Locking Validation (PLS). To exclude the possibility that the phase synchrony was solely due to common, coincidental phase locking of the signals to the presentation of the stimulus, phase locking statistics [PLS; (5)] were determined. If phase locking was due solely to common locking of the signals to the stimulus, then the signals should not only be phase locked within a particular trial, but also the signal from one ROI should be phase locked to the signal from all trials in the second ROI. Therefore we used a resampling method in which the phase values of one site were reshuffled across trials relative to the other site and the PLVs were calculated between these reshuffled trials. This reshuffling was done 500 times and the PLS was defined as the proportion of these reshuffled PLVs which were greater than the original PLV. In this study, we used a significance criterion of PLS $<$ .05 to exclude the possibility that PLVs could be explained by independent and coincidental phase locking to the stimulus presentation. For PLS values to be considered reliable, we required statistical significance ($P < 0.05$) to be achieved over at least one full oscillatory cycle. This conservative threshold for considering a value reliable was used to reduce the possibility of false positives in our analysis.

It is important to note that the phase locking analysis is correlational in nature. Any phase locking between the PFC and temporal cortex could be due to either direct communication between these regions or due to a third region undetected in the whole cortex analysis driving both the PFC and temporal cortex with a shorter delay to one or the other. Lesion or TMS studies would be required to fully explore whether the communication between regions is direct or mediated by a third region.

Inverse Solution. The precise location of the cortical current sources cannot be precisely determined by using the measured magnetic fields from outside the head, and therefore is estimated by using cortically constrained MNE, described extensively elsewhere (1, 6). Briefly, a linear inverse operator W is applied to the measured signal to calculate the MNE: $y(t) = Wx(t)$, where $x(t)$ represents the MEG channel data at time t, and $y(t)$ is the corresponding current projected onto the cortical surface. The expression of W is defined as $W = RA^T (ARA^T + \lambda^2 C)^{-1}$, where C and R are the noise and source covariance matrices respectively. A is the free source orientation solution of the forward problem calculated by using the boundary element method (7, 8). To compensate for the bias toward superficial currents of the MNE a scaling factor (i.e., depth weighting) of .75 is applied to A (9). λ^2 is a regularization parameter (1, 10).

To estimate the time course and statistical significance of the cortical MEG activity, noise normalized values were calculated at each time point and each dipole location (1). This transforms power values into dynamic statistical parametric values and makes the point spread function of the estimated signal relatively uniform across cortical dipoles (10). For all non-phase-locking analyses, these dSPM values are used to describe neural activity.

Additional ROI Analyses and ROI Validation. In addition to the ROI definition described in the main body of the manuscript, ROIs were defined based on regions in the PFC and temporal cortex that demonstrated greater MEG activity for novel relative to repeated stimuli (i.e., repetition reduction). The PLVs derived from these ROIs demonstrated a strong trend ($P < 0.1$) for greater phase locking for repeated compared to novel stimuli peaking at 14 Hz and ≈220 ms after stimulus onset. Although these PLVs failed to reach statistical significance, these results do suggest that there is a connection between neural response reductions and increased synchrony seen with repetition.

We further validated our results using an all-conditions (including novel stimuli) vs. baseline ROI definition to allay any potential concerns that using the third presentation to define our ROIs may be tuned to find effects that occur only with repetition, rather than effects that may be present for repeated or novel trials. This method can be compared favorably with using an all-conditions versus fixation/baseline contrast in ROI analysis of fMRI data. Similar to the ROI definition based on the third presentation, a reference ROI was chosen based on the PFC location that showed greatest power for the all vs. baseline comparison. A target ROI in the temporal cortex was defined as the region that demonstrated greatest phase locking for the all vs. baseline condition and these ROIs were then used to compare phase locking novel and repeated objects from the test phase of the experiment. The results of this analysis show significantly stronger synchrony for repeated than novel objects from 190 to 280 ms after stimulus onset (very similar to the results reported for ROIs tuned by using the third presentation).

1. Dale AM, *et al.* (2000) Dynamic statistical parametric mapping: combining fMRI and MEG for high-resolution imaging of cortical activity. *Neuron* 26:55–67.
2. Dhond RP, Buckner RL, Dale AM, Marinkovic K, Halgren E (2001) Spatiotemporal maps of brain activity underlying word generation and their modification during repetition priming. *J Neurosci* 21:3564–3571.
3. Marinkovic K, *et al.* (2003) Spatiotemporal dynamics of modality-specific and supramodal word processing. *Neuron* 38:487–497.
4. Puce A, Allison T, McCarthy G (1999) Electrophysiological studies of human face perception. III: Effects of top-down processing on face-specific potentials. *Cereb Cortex* 9:445–458.

5. Lachaux JP, Rodriguez E, Martinerie J, Varela FJ (1999) Measuring phase synchrony in brain signals. *Hum Brain Mapp* 8:194–208.
6. Hamalainen MS, Hari R (2002) Magnetoencephalographic characterization of dynamic brain activation: Basic principles and methods of data collection and source analysis. *Brain Mapping: The Methods*, eds Toga AV, Mazziotta JC (Academic, San Diego), pp 227–254.
7. Hamalainen MS, Sarvas J (1989) Realistic conductivity geometry model of the human head for interpretation of neuromagnetic data. *IEEE Trans Biomed Eng* 36:165–171.
8. Oostendorp TF, van Oosterom A (1989) Source parameter estimation in inhomogeneous volume conductors of arbitrary shape. *IEEE Trans Biomed Eng* 36:382–391.
9. Lin FH, *et al.* (2004) Spectral spatiotemporal imaging of cortical oscillations and interactions in the human brain. *NeuroImage* 23:582–595.
10. Liu AK, Dale AM, Belliveau JW (2002) Monte Carlo simulation studies of EEG and MEG localization accuracy. *Hum Brain Mapp* 16:47–62.

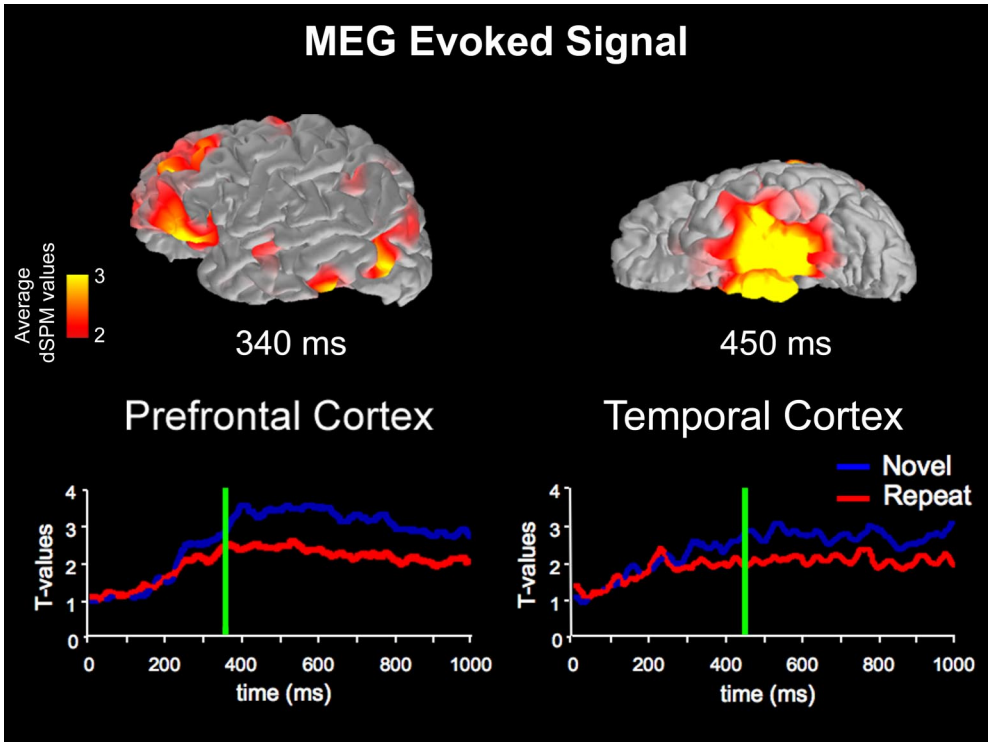

Fig. S1. Evoked MEG signal as measured by dynamical statistical parametric mapping values (1) demonstrating significantly greater evoked activity for novel versus repeated stimuli in both the PFC and temporal cortex. The result of reduced PFC and temporal activity in the 250- to 450-ms range, with PFC reductions preceding or co-occurring with temporal reductions for repeated compared to novel stimuli is supported by previous studies (1–4). Green lines (*Lower*) correspond to the time points shown on the dSPM maps (*Upper*). In addition to the PFC and temporal cortex, more dorsal PFC, lateral occipital, and parietal regions also showed significant dSPM signal for the novel vs. repeat comparison, although the time courses in these regions differed from the PFC and temporal cortex.

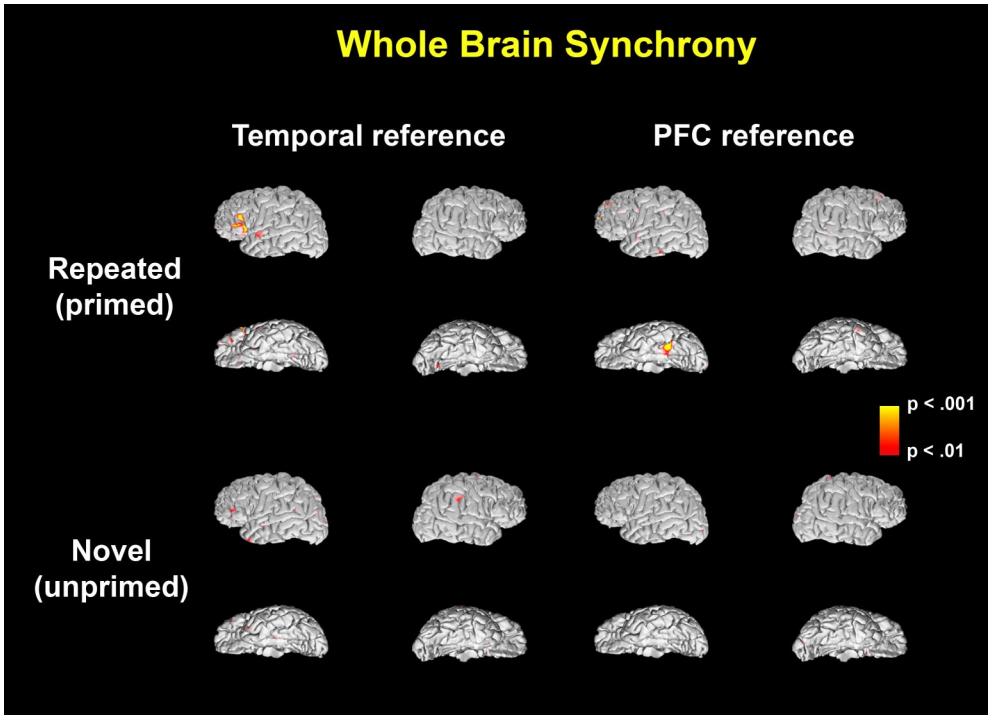

Fig. S2. Peak synchrony (14 Hz, 215 ms) between a single reference ROI and the entire brain relative to prestimulus baseline synchrony. These other views support that, for a reference ROI in the temporal cortex, significant synchrony is seen in a relatively localized region of the PFC for primed, but not novel, objects. For a reference ROI in the PFC, significant synchrony is seen in a relatively localized region of the temporal cortex for primed, but not novel, objects.