

available at [www.sciencedirect.com](http://www.sciencedirect.com)[www.elsevier.com/locate/brainres](http://www.elsevier.com/locate/brainres)
**BRAIN  
RESEARCH**

## Research Report

# MEG correlates of bimodal encoding of faces and persons' names

P. Pazo-Alvarez<sup>a</sup>, P.G. Simos<sup>b</sup>, E.M. Castillo<sup>a</sup>, J. Juranek<sup>a</sup>, A.D. Passaro<sup>a</sup>,  
Andrew C. Papanicolaou<sup>a,\*</sup>

<sup>a</sup>Department of Pediatrics University of Texas, Center for Clinical Neuroscience, Health Science Center, Houston, TX 77030, USA

<sup>b</sup>Department of Psychology, University of Crete, Crete, Greece

### ARTICLE INFO

#### Article history:

Accepted 2 July 2008

Available online 9 July 2008

#### Keywords:

Magnetoencephalography

Learning

Memory

Language

Associative encoding

Auditory

Visual

Occipital cortex

### ABSTRACT

Learning associations between people's faces and names is a universal cognitive function with important social implications. The goal of the present study was to examine brain activity patterns associated with cross-modal encoding of names and faces. Learning face-name pairs was compared to unimodal learning tasks using the same visual and auditory stimuli. Spatiotemporal brain activation profiles were obtained with magnetoencephalography using an automated source estimation method. Results showed activation foci in left (for names) and right (for faces) temporal lobe perisylvian cortices, predominantly right-hemisphere occipital and occipitotemporal regions (for faces), and right hemisphere dorsolateral prefrontal regions during the encoding phase for both types of stimuli presented in isolation. Paired (face-name) stimulus presentation elicited bilateral prefrontal and temporal lobe perisylvian activity for faces and enhanced visual cortex activation in response to names (compared to names in the unpaired condition). These findings indicate distinct patterns of brain activation during the formation of associations between meaningful visual and auditory stimuli.

Published by Elsevier B.V.

## 1. Introduction

Many common cognitive tasks, such as relating a person's name with his face, involve the establishment of new associations between auditory and visual input. Initial, unimodal processing of either type of input shares many components with the mechanism responsible for the formation of memories based on that input. Thus, processing of a person's name (i.e. engaging in the analysis and registration of linguistic features) engages many of the same brain regions which are also involved when a name is processed for the explicit purpose of memorization and future retrieval. These regions are primarily located in the superior and middle temporal cortices in the left hemisphere (in the majority of

right-handers; for a discussion of the brain substrates of encoding as part of the function and mechanism of memory see Papanicolaou et al., 2006).

Functional brain imaging studies have shown that perception of and memory for faces is mediated by a mechanism that involves neurophysiological processes that take place in several brain regions. Distinct components of this mechanism appear to be located in visual extrastriate cortex, including the inferior occipital gyri (probably involved in the early extraction of facial features; Haxby et al., 2000) and the fusiform gyrus, especially in the right hemisphere, probably involved in processing invariant aspects of faces (Clark et al., 1996; Haxby et al., 1991; Kanwisher et al., 1997). Additional structures in the medial temporal lobe (Grady et al., 1998;

\* Corresponding author.

E-mail address: [andrewc.papanicolaou@uth.tmc.edu](mailto:andrewc.papanicolaou@uth.tmc.edu) (A.C. Papanicolaou).

Haxby et al., 1996) and the prefrontal cortices (Kelley et al., 1998) are likely involved in consolidation and retrieval of information regarding faces.

In view of the fact that initial processing (encoding) of faces and names engages different brain mechanisms, the question arises as to how these mechanisms work together to support the formation of associations between stored traces of these two types of stimuli. Most of the functional imaging studies addressing this issue have explored face-name associative memory within the visual domain. PET (Herholz et al., 2001) and fMRI (Kirwan and Stark, 2004; Sperling et al., 2001) studies have shown the engagement of medial temporal, prefrontal and ventral occipitotemporal structures in the formation of associative memories. Other regions, such as the middle frontal gyrus, the inferior frontal gyrus and the supramarginal gyrus of the inferior parietal lobe have also been shown to be involved in tasks requiring integration of face-name stimuli as compared to tasks involving within category associations such as face-face or name-name associations (Campanella et al., 2001). Surprisingly, few studies have been conducted to explore the brain activation profiles engaged during the much more common task of forming bimodal face-name associations. Along these lines, an event related potentials (ERP) study reported differences in the characteristics of the evoked electrical response to spoken names and faces which were predictive of subsequent retrieval performance (Guo et al., 2005). Further, an fMRI study that focused on hippocampal activity (Small et al., 2001) showed that the distribution of activity across the long axis of the hippocampus associated with processing of face-name pairs was not accounted by the simple summation of the activation produced by the encoding of isolated names or faces. The findings from both studies seem to indicate that lateral and mesial temporal regions show distinct patterns of activation when

cross-modal memory formation is required. However, the low spatial resolution of scalp recordings of electrical potentials and the restricted scope of fMRI data to the hippocampal formation in the Small et al. (2001) study, did not allow a clear identification of the specific brain activation patterns related to associative bimodal encoding.

The present study employs Magnetoencephalography (MEG) to investigate the spatio-temporal profiles of activity elicited by brain areas engaged in the encoding of visual (faces) and auditory (names) stimuli that define a person's identity, either separately or in a task that requires bimodal integration. The study extends previous investigations of cross-modal processing (Baier et al., 2006; Johnson and Zatorre, 2005) by experimentally recreating a common phenomenon involving meaningful stimuli. In order to ensure that cognitive processes engaged during presentation of each face stimulus did not involve retrieval, each stimulus was only presented once during each phase of the experiment. The present study was designed on the premise that formation of new associations between faces and names depends on neurophysiological processes that take place in more than one brain regions. The latter may include modality-specific cortices, which are also engaged during encoding of each type of stimulus presented in isolation, as well as modality non-specific cortices.

## 2. Results

### 2.1. In scanner performance

Participants correctly recalled  $76.4 \pm 6.9\%$  of the person's names and correctly recognized  $88.9 \pm 8.1\%$  of the faces during Phase 1 of the experiment. During Phase 2 participants correctly recalled the name that was paired with a given face in  $42.7 \pm 14.5\%$  of the trials.

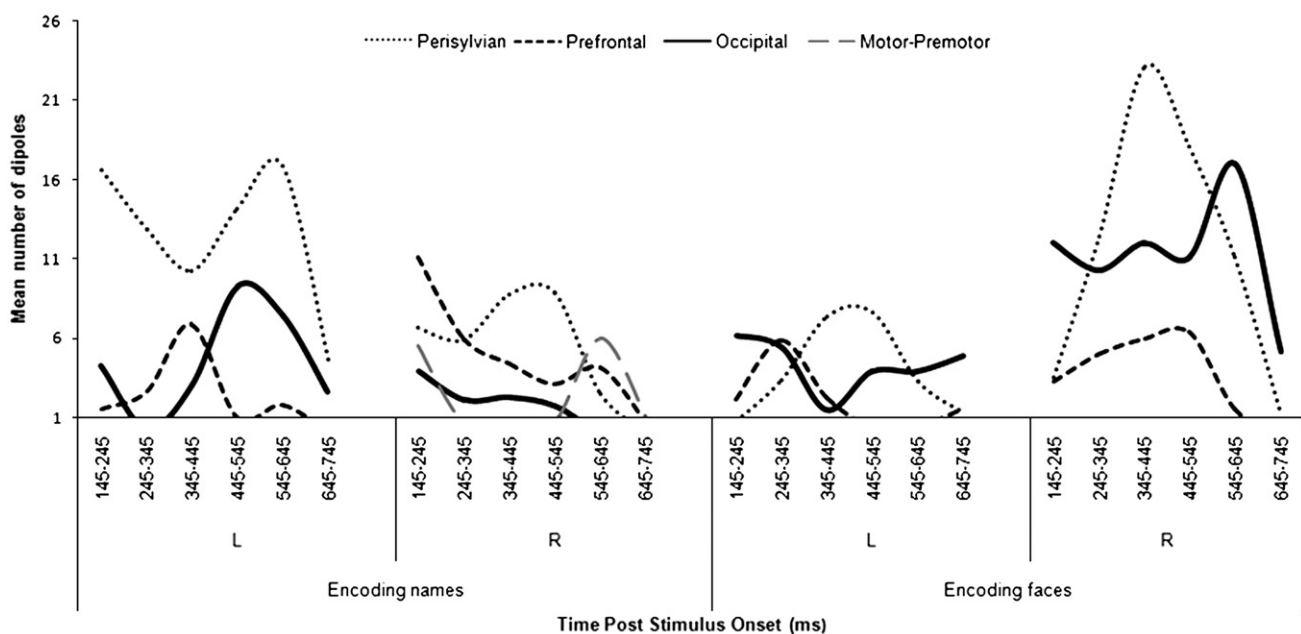


Fig. 1 – Time course of regional magnetic activity in eight ROIs which consistently showed activity sources during non-associative encoding of names and faces.

## 2.2. Meg data: non associative encoding

The time course of magnetic activity in the 8 ROIs which met the criterion described in the Methods (of at least one activity source per 100 ms) is shown in Fig. 1 separately for names and faces. In response to persons' names presented alone, perisylvian areas showed early activity which persisted in the vicinity of the auditory cortex for 200 ms or so after the peak of the N1m response. Subsequent peaks were noted at 600 ms in the left and 500 ms in the right hemisphere. Activity in prefrontal regions peaked early in the right (~200 ms) and somewhat later in the left hemisphere (~400 ms). Occipital regions showed predominant activity in the left hemisphere peaking at approximately 550 ms. Finally, motor-premotor activity in response to person's names was consistently active only in the right hemisphere, peaking at 600 ms.

The encoding of faces presented in isolation elicited Perisylvian temporal lobe activation with a maximum around 500 ms in both hemispheres. In the left hemisphere prefrontal regions were maximally activated at 250–350 ms, whereas in the right hemisphere the activation was more sustained with a maximum around 450–550 ms. After the expected early wave of occipital activity, magnetic sources in this regions were subsequently noted with a right hemisphere peak between 550–650 ms. Activity sources were also found in the right hemisphere cingulate gyrus peaking between 450 and 550 ms. Motor-premotor activity did not reach significance in either hemisphere.

Significant main effects or two-way interactions were found in six ROIs. GEE analysis results revealed significant stimulus main effects in ventral occipitotemporal ( $\chi^2 [1]=12.01, p=.001$ , scale deviance=1.07—names<faces), and anterior temporal cortices ( $\chi^2 [1]=8.14, p=.004$ , scale deviance=.40—names>faces), Hemisphere effects in the Motor-premotor ( $\chi^2 [1]=6.69, p=.01$ , scale deviance=.57—L<R) and inferior frontal ROIs ( $\chi^2 [1]=4.93, p=.026$ , scale deviance=.37—L<R), and Stimulus by Hemisphere interactions in Perisylvian temporal lobe cortices ( $\chi^2 [1]=4.72, p=.03$ , scale deviance=.71) and occipital areas ( $\chi^2 [1]=6.79, p=.009$ , scale deviance=.60). Simple main effects tests revealed non-significant trends for greater activity for faces than names in the right hemisphere ( $p=.08$ ) and for names greater than faces in the left hemisphere ( $p=.07$ ). Similar tests on data from the occipital region indicated significantly greater activity for faces than names in the right hemisphere ( $\chi^2 [1]=14.91, p=.0001$ , scale deviance=.40) and similar amounts of activity in the left hemisphere ( $p=.9$ ).

## 2.3. Meg data: associative encoding

Listening to person's names in the associative encoding phase elicited a profile of activity that included persisting early activity in the perisylvian-temporal regions bilaterally, with subsequent late peaks at approximately 450 (left) and 600 ms (right hemisphere). Prefrontal activity was relatively sparse and more prominent in the right hemisphere. Perhaps the most prominent feature of the activation profile was occipital activity that showed a double peak in the left hemisphere (at ~300 and 600 ms) and more sustained activity between approximately 200 and 500 ms in the right hemisphere. Motor-premotor activity did not reach significance in either hemisphere.

The profile of activity that was found for faces during the associative encoding phase (meeting the criterion of one activity source per 100 ms) featured perisylvian-temporal activation that was more prominent between approximately 350 and 650 ms in the left hemisphere and between 300–600 ms in the right hemisphere. Sustained occipital activity was observed in the left hemisphere with a shallow peak at 350 ms, whereas in the right hemisphere following early occipital activity which dissipated by about 350 ms, a later prominent peak was noted at approximately 550 ms. Again prefrontal activity was relative sparse and distributed throughout the epoch. Motor-premotor activity did not reach significance.

GEE analysis with hemisphere (left and right), ROI (perisylvian, occipital and prefrontal regions) and stimulus type (i.e. names, faces) as within subject factors were performed. Results produced a good fit to the data (scaled deviance=1.25 and a scaled Pearson  $\chi^2=0.90$ ), but failed to reveal significant effects involving hemisphere or stimulus material.

## 2.4. Meg data: associative vs. non associative encoding

The most striking finding of the present study was the unexpected late, occipital activation found during the encoding of person's names (see Table 1). This region was significantly active during auditory presentation in both associative and non associative tasks. However the degree of activation observed during associative encoding was considerably larger than that observed during encoding the auditory names in isolation. This impression was confirmed by GEE analysis with hemisphere (left and right), stimulus type (names, faces), and encoding condition (associative, non-associative) as within-subject factors. Results revealed a Condition by Stimulus type interaction ( $\chi^2 [1]=16.63, p=.0001$ , scale deviance=.51). Further tests indicated greater occipital activation during associative than non-associative encoding of person's names ( $\chi^2 [1]=30.48, p=.0001$ , scale deviance=.37), and greater activity for faces than names during non-associative encoding ( $\chi^2 [1]=7.22, p=.007$ , scale deviance=.41).

## 3. Discussion

The brain activation profile elicited by the encoding of unfamiliar faces and names presented in isolation for later retrieval confirms previous results that showed greater activity in ventral occipitotemporal cortices in response to faces, with a right hemisphere predominance (Halgren et al., 2000; Lee et al., 2005; Swithenby et al., 1998). A trend for greater activity for faces in the right posterior middle/superior

**Table 1 – Mean Talairach coordinates for occipital activity**

		Left hemisphere			Right hemisphere		
		x	y	z	x	y	z
Associative	Faces	-20	-74	23	24	-68	7
	Names	-19	-71	11	18	-69	22
Non-associative	Faces	-17	-74	16	21	-65	10
	Names	-23	-76	9	16	-62	25

temporal lobe was also found, whereas an opposite trend was observed for persons' names. These results are in line with previous findings (Gorno-Tempini et al., 1998; Kim et al., 1999) of right-hemisphere predominant temporal-lobe activation during memory formation of faces (Kelley et al., 1998), and left temporal activation during processing of verbal stimuli (Kirchhoff et al., 2000).

During associative encoding, responses to faces engaged similar regions than during initial processing of (and memory formation for) faces in isolation. Compared to non-associative encoding of the same stimuli, however, the right hemisphere predominance in the degree of activity was not evident when the task involved arbitrary pairing of these unfamiliar faces with names. Reduced right hemisphere predominance in the degree of activity in response to faces was observed in occipital (including both primary and association cortices), motor-premotor, prefrontal, and posterior middle/superior temporal cortices. It has been shown that the integration of verbal and visual information, at least within the visual domain, produces changes in the activation lateralization profiles. For example, Herholz et al. (2001) observed that learning visual face-name associations activated the fusiform gyrus with a left hemisphere predominance, whereas greater right hemisphere activity was observed during the presentation of isolated faces. These findings have been interpreted as reflecting the engagement of neurophysiological processes responsible for the integration of verbal and visual information during the presentation of face-name pairs.

In response to names, task demands for associative encoding induced a similar tendency of reduced (left hemisphere, in this case) predominance in the degree of activation. But more surprisingly, the encoding of spoken persons' names was associated with pronounced activation of occipital cortices similar in magnitude to the occipital response observed during the encoding of faces. This activity took place during late processing of the auditory stimuli (therefore it was not likely to reflect persisting visual cortex activation in response to the preceding face stimuli) and was significantly enhanced in the associative condition. The consistent engagement of visual cortices during associative encoding opens the possibility that these regions may also play a role in cross-modal encoding processes. Previous functional brain imaging studies (i.e. Ishai et al., 2002) have shown that visual perception and visual imagery share common neural substrates. They found that visual imagery of famous faces generated strong activation in regions that included bilateral calcarine cortices, especially when imagery was evoked from short term memory (vs. long term memory). Recently, Ryan et al. (2008) provided further evidence supporting the hypothesis that prior experiences may influence processing of faces and names such that perception encompasses more than what is imparted on the senses.

Occipital (visual) cortex activation was also found during non-associative encoding of persons' names, with a significantly smaller magnitude than both the response to faces in isolation and to names during associative encoding. The involvement of visual regions, especially in the vicinity of the fusiform gyrus in the right hemisphere, during verbal visual processing has been previously reported (Nobre et al., 1994). Although less common, left hemisphere activation of

this region have been also shown during auditory verbal processing (Balsamo et al., 2006). It is likely that extrastriate regions may be involved in processes which are common to both visual and auditory verbal material, such as semantic processing (Binder et al., 1997). Our results extend previous findings of enhanced BOLD signal in occipital cortices in response to stimuli that were learned in multisensory (audio-visual) format (Murray et al., 2005) and is in agreement with microelectrode data demonstrating the existence of neurons in the primate extrastriate visual cortex that preferentially respond to multimodal stimulus presentations (Gibson and Maunsell, 1997). The results of a recent fMRI study investigating visual cueing effects in a cross-modal paradigm are also relevant to the current study. Baier et al. (2006) simultaneously presented non-meaningful, visual-auditory stimulus pairs preceded by a visual cue. They noted increased BOLD signal in lateral extrastriate cortices in response to audiovisual stimuli when the auditory stimulus was task-relevant and was cued by a visual stimulus compared to the same stimuli that were not cued.

Lateral prefrontal activity was also found during both associative and non-associative encoding of faces and person's names in agreement with the key role the prefrontal lobe plays in memory formation (Buckner et al., 1999). Hemispheric asymmetries in prefrontal activity during memory tasks are often interpreted in the context of differential hemispheric contribution to component memory operations, such as encoding and retrieval (Tulving et al., 1994). Alternatively it has been suggested that the prefrontal cortices show a hemispheric bias dependent upon stimulus type (i.e. right hemisphere preference for memorization of unfamiliar faces, left hemisphere predominance for encoding of verbal stimuli, and bilateral activation for namable objects; Kelley et al., 1998). In our study we found that encoding of either unfamiliar faces or persons' names elicited prefrontal activity with a right hemisphere predominance. This asymmetry was reduced when the same stimuli were presented for a second time during the associative encoding phase of the experiment, raising the possibility that changes in the familiarity of the stimuli may have been responsible for this finding.

The procedure used by previous studies exploring the neural substrates of cross-modal formation of associations is generally similar to the procedure used in the present study with the exception that face and name stimuli were presented simultaneously during associative encoding. A successive presentation of face and name stimuli was opted for in the present study making it easier to directly compare activation profiles in the two phases of the experiment, given that these profiles were associated with identical stimuli. Moreover, many studies involved repetition of face-name pairs during the encoding phase making it difficult to disentangle encoding from retrieval processes. Thus, to ensure that we measured pure encoding processes we used a single learning episode per item. A potential confound in all studies investigating learning when it is deemed important to obtain activation profiles to the same stimuli studied under different conditions. A relatively long interval between the two conditions of the experiment was chosen in order to reduce this effect. A similar effect is expected, however, to take place for auditory stimuli, making it difficult to explain the main findings of the study simply in terms of familiarity.



In conclusion, memory formation engages an extended network of brain regions including primary and association visual areas, temporal lobe regions along the lateral banks of the Sylvian fissure and prefrontal cortices. The profile of activation during non associative encoding of visual and verbal material featured lateralized activity in occipital and temporal lobe perisylvian regions. When the task required formation of associations between the two types of stimuli, however, cortical activation was bilaterally symmetric in these key regions and the encoding of persons' names involved pronounced activity in the visual cortices, suggesting that even

prospective integration of visual and auditory representations may require the engagement of visual cortices.

#### 4. Experimental procedures

##### 4.1. Participants

Ten right handed volunteers (6 female; mean age=34.7±10 years) without history of neurological or psychiatric disorders and with normal or corrected-to-normal vision

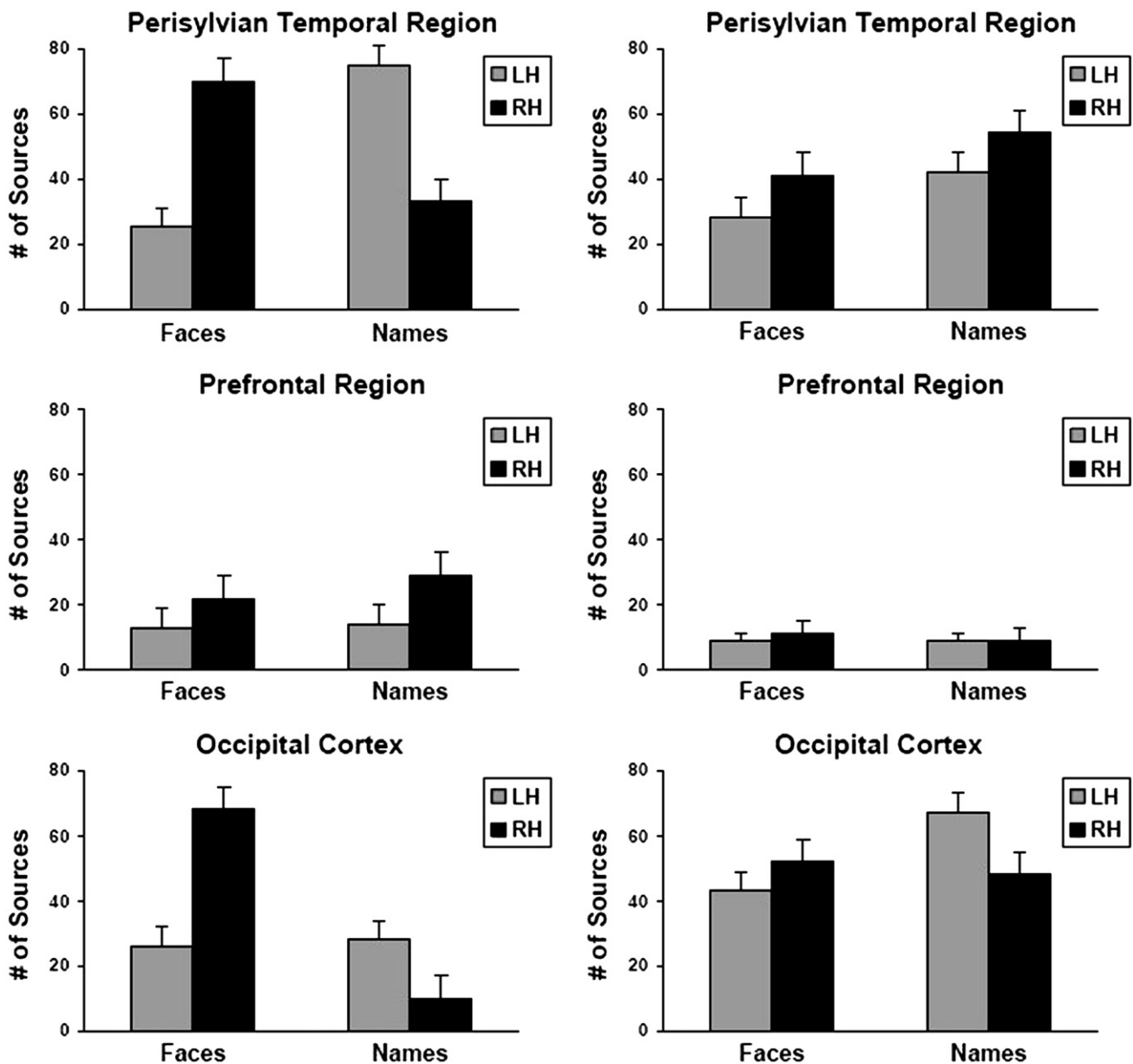


Fig. 2 – Degree of magnetic activity (#: average number of consecutive activity sources) in three bilaterally active ROIs in response to persons' names and faces during the two encoding conditions. Left: During the non-associative encoding condition, greater activity in ventral occipitotemporal cortices was found to faces as compared to names with a right hemisphere predominance. A trend for greater activity for faces in the right posterior middle/superior temporal lobe was also found, whereas an opposite trend was observed for persons' names. Right: Activity was bilaterally symmetric during associative encoding of both faces and names.

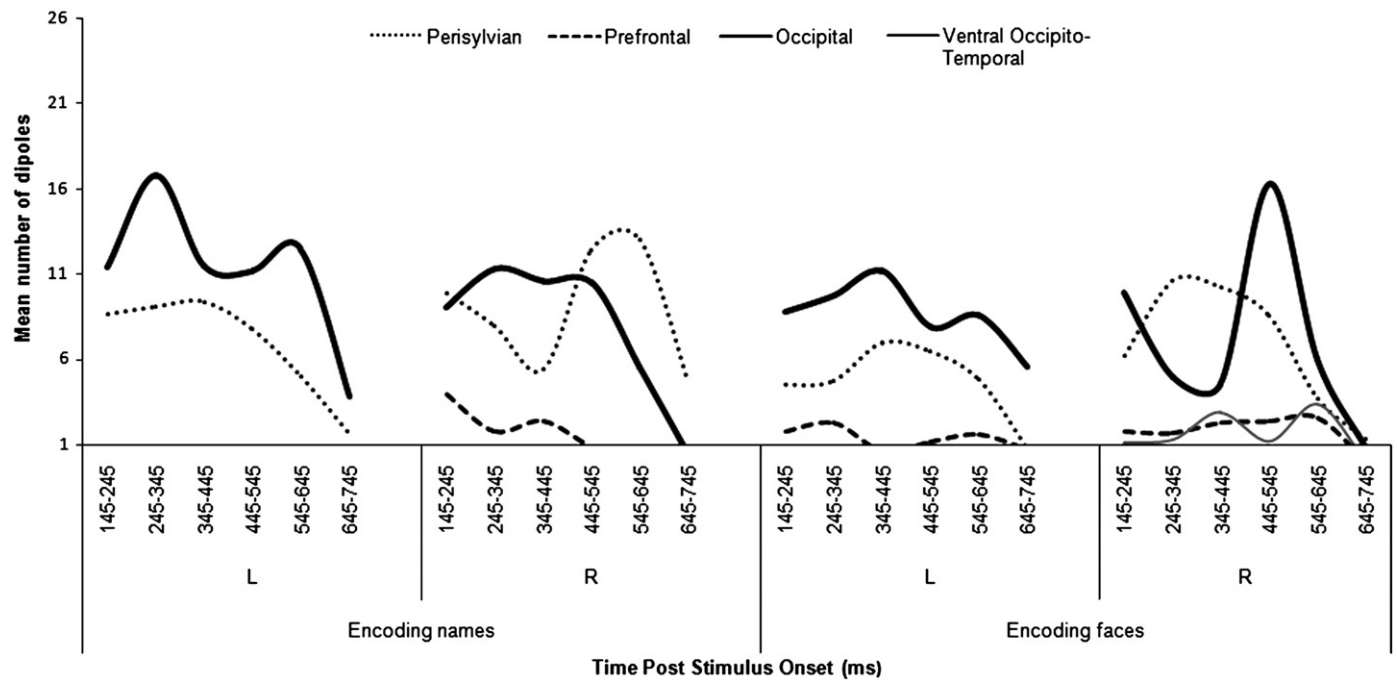


Fig. 3 – Time course of regional magnetic activity in seven ROIs which consistently showed activity sources during associative encoding of names and faces.

participated in the study. Eight of the subjects (4 female and 4 were male; mean age  $31.6 \pm 8.1$  years) in the first experiment also volunteered for a second experimental session. All subjects provided written informed consent.

#### 4.2. Procedures

Phase 1 of the study (Non-Associative Encoding) assessed brain activation patterns associated with the encoding of auditory (common names) or visual stimuli (faces) separately, for later verbal recall or recognition, respectively. In the name encoding task, stimuli were presented in 18 blocks of 6 names each (including three female and three male names) with a randomly varied ISI between 2 and 3 s, for a total of 108 trials per task. Participants were asked to memorize the names from each block and verbally recall them (in any order) immediately after each block. In the face encoding task, faces were arranged in 18 blocks (with six different faces in each block) and presented for 1.5 s (with the ISI varying randomly between 2 and 3 s). After each block, a recognition memory test was administered, consisting of 6 faces, three of which were included in the immediately preceding encoding block and three that were new. Recognition blocks consisted of six faces, each one presented for 1.5 s and followed by a blank screen with a question mark (subtending 0.5 deg) placed at the fixation point. Subjects were requested to verbally indicate whether the faces were or were not included in the immediately previous encoding block. No information was given about the number of different faces to be presented during the learning block.

In phase 2 of the study (Associative Encoding) profiles of brain activity were examined during encoding of pairs of stimuli consisting of the picture of a face followed by a person's name (in the auditory modality). Participants were asked to form an association between each face and its corresponding name and try to memorize them. Face-name pairs were arranged in 18 blocks (six pairs per block) that always consisted of a face, presented for 1.5 s, followed after a 500–700 ms randomly varying ISI, by a spoken common name. The inter-trial interval varied randomly between 2 and 3 s. The same auditory (108 spoken auditory names) and visual stimuli (108 faces) used in the first phase of the experiment were used in the second phase. Names and faces were randomly assigned to pairs but were always gender-matched.

Immediately after each learning block, participants were presented with a cued-recall test for names, in which face stimuli were presented for 1.5 s followed by a small question mark (subtending 0.5° of visual angle) that remained at the center of the screen for 2 s. They were instructed to orally produce the correct name when cued with each of the faces they had seen during the previous encoding block. Responses were allowed only during the presentation of the question mark, immediately after the disappearance of the face from the screen. Presentation order of faces during the cued-recall blocks was different than during the encoding session. In order to ensure that brain activation during these sessions reflected solely encoding process and not automatic retrieval within each phase we used a single learning episode per item in each task.

The two phases of the experiment were separated by a period of at least one month minimizing the probability of

recognition of the faces participants had seen during the first phase of the experiment. Magnetic activity was recorded during the encoding sessions of both phases of the experiment. Responses to both faces and names were recorded during the Associative Encoding Phase (Figs. 2 and 3).

Visual stimuli consisted of 108 photographs depicting 108 unfamiliar faces (half male and half female) extracted from the AR Face Database (Martinez and Benavente, 1998). Images were cropped and resized with ImageMagick (<http://www.imagemagick.org>) to  $152 \times 184$  pixels and converted to grey level images. An oval mask was then applied so that only facial features were visible. All faces carried a neutral expression. Face stimuli were projected through an LCD projector onto a white screen located about 0.5 m in front of the participant, subtending 4.5 and 5.5° of horizontal and vertical visual angle, respectively.

Auditory stimuli consisted of 108 common American names (54 male and 54 female), with a duration ranging between 500 and 700 ms, spoken by a female voice and delivered at a randomly varying ISI (2–3 s) binaurally through two 5-m-long plastic tubes terminating in ear inserts, at an intensity of 80 dB SPL at the participant's outer ear. Stimulus presentation and task control were performed by the "Presentation" software (Neurobehavioral Systems, Inc.).

#### 4.3. Meg data acquisition and reduction

Magnetic recordings were performed with a whole-head neuromagnetometer (4D Neuroimaging, San Diego, CA.) equipped with 248 gradiometer sensors and housed in a magnetically shielded room designed to reduce environmental magnetic noise. The recording sessions required the participants to lie as still as possible, on a bed with their head inside the helmet-like device for approximately 30 min. The recorded signals were filtered online with a band pass between 0.1 and 100 Hz, and digitized at a rate of 500 Hz. The records of magnetic activity time locked to each face or name stimulus, or Event-related Magnetic Fields (EMFs) were then submitted to a series of computer routines performing artifact rejection, averaging, and magnetic source estimation, as follows.

First, those MEG channels presenting random drift beyond a preset criterion (correlation with adjacent channels  $\leq 0.6$ ) were identified and were excluded from further processing. Second, EMFs were inspected, and those containing magnetic artifacts (defined as a peak-to-peak amplitude greater than 2 pT) were excluded from further analysis. Third, artifact-free EMFs were averaged selectively on the basis of encoding operation (associative and non associative), and the stimulus material type (auditory and visual), producing four separated EMFs: Simple Encoding of faces, Simple Encoding of names, Associative Encoding of faces, and Associative Encoding of names.

To identify the brain areas producing the averaged EMFs, the intracranial sources that may have accounted for their amplitude at successive points during their temporal unfolding (typically every 4 ms) were modeled as equivalent current dipoles embedded in a spherical conductor using an automated magnetic source estimation procedure. This automated procedure has been reliably applied in a previous MEG study and presents advantages over other validated single dipole methods

since it reduces substantially the amount of analysis time and eliminates any subjective judgments in the process of deriving the activation profiles (Papanicolaou et al., 2006). The Automated Channel Group selection (ACGS™) consists of two steps. This routine first determines (at a given latency) the appropriate channel grouping by calculating the planar gradients of the field map from the measured data for each channel using the channel and its nearest neighbors. For purposes of choosing the channel groups, the gradient could be calculated for either a single latency of the data or the average gradient over a range of latencies, which could be chosen based on the underlying characteristic of the signal being analyzed. In general, sources are located below the maximum of the planar gradients of the field. Center channels of the channel groups were selected based on the local maxima of the calculated gradient pattern. Up to five were selected at each time point, or EMF latency. Any maxima that were less than 10% of the strongest maximum were rejected.

Once a maximum in the planar field was found its width was estimated by fitting it to a Gaussian function. This was a fit of the 'hill' in the planar gradient distribution that was calculated from the fields measured. The size of the Gaussian parameter (typically labeled sigma) was a rough estimate of the width of this 'hill', or maximum. All of this estimation was done in a two-dimensional plane corresponding to a local flattening of the array around the maximum. This width of the maximum was then compared to widths of maxima calculated in the same way from field patterns generated from a single dipole forward model. Based on this comparison the extent of the channel group was inferred. This was done by a linear fit of the width versus channel group extent from the simulated data. The range between a minimal and maximal diameter was enforced simply by clipping this estimating function. This adjustment was limited such that the radius of the resulting channel-group was always greater than 7 cm and less than 9.5 cm. From this comparison the extent of the channel group was determined. Finally, to help reject maxima that would often occur near the edge of the array due to edge effects, the resulting channel group was inspected to make sure it extended across a zero line in the field data. If either of the number channels having positive or negative field values was less than 10% of the total number of channels, then the group was rejected.

Next, the single dipoles that accounted for surface dipolar maps were derived using the standard model (Sarvas, 1987) and the entire procedure was repeated at successive latency points until the entire EMF duration was exhausted. Finally dipolar sources that met our criteria of acceptability (Correlation  $\geq 0.92$ , Confidence volume  $\leq 10 \text{ cm}^3$ ) were selected for constructing the activation profiles through co-registration with normalized structural MRI's involving the following steps: Dipolar sources that were automatically computed with reference to the MEG Cartesian coordinate system mentioned above were coregistered on T1-weighted, magnetic resonance (MR) images (TR 13.6 ms; TE 4.8 ms; recording matrix  $256 \times 256$  pixels, 1 excitation, 240 mm field of view, and 1.4 mm slice thickness) obtained from a subset of the participants. For those participants that did not volunteer for an MRI scan we used the MRIs of others on the basis of similarity in their digitized head shape files. Transformation

of the MEG coordinate system into MRI-defined space was achieved with the aid of three lipid capsules inserted into the ear canals and attached to the nasion, which could be easily visualized on the MRIs, using the MR Overlay tool which is part of the 4-D Neuroimaging software.

To allow comparison and averaging of results across subjects, activity source locations were transformed into MNI-standard (Montreal Neurological Institute) coordinate space. After registration of the subject's MEG data with the MRI, MEG-coordinate locations were determined for three reference points: the Anterior Commissure (AC), Posterior Commissure (PC), and a point on the Falx Cerebri (F). In conjunction with brain dimensions measured along a set of axes parallel to the AC-PC line, these reference points were used to translate, rotate, and scale activity source locations into universal coordinates. Spatially normalized activity sources were then averaged across subjects within a given experimental condition and sorted into 41 Regions of Interest (ROIs) defined within the MNI synthetic brain, with no overlap between ROIs. Regions were based on the Anatomical Automatic Labelling atlas (Tzourio-Mazoyer et al., 2002) and Brodmann areas.

#### 4.4. Data analysis

The number of early (<140 ms) and late (>145 ms) activity sources in each ROI provided a measure of that region's involvement in the processing of the stimuli and served as the dependent variable in the analyses described below. Therefore, the index of the degree of regional activation was the total number of successive activity sources in a particular area or group of areas.

To ensure that the profiles of activity reflected the engagement of neurophysiological operations that take place after the initial sensory processing of the visual and auditory stimuli only late activity sources (>145 ms) were included in the analysis. The inclusion of activity after 145 ms also ensures that the face specific activity in occipito-temporal cortices that generally takes place at 140–200 ms after stimulus onset is included in the analysis (Lee et al., 2005).

**Table 2 – ROIs that showed more than one activity source per 100 ms**

Task	Stimulus	ROI	Hem
Non associative	Names	Perisylvian	R L
		Occipital	R L
		Prefrontal	R L
	Faces	Motor/premotor	R
		Perisylvian	R L
		Occipital	R L
		Prefrontal	R L
Associative	Names	Cingulate	R
		Perisylvian	R L
		Occipital	R L
	Faces	Prefrontal	R
		Perisylvian	R L
		Occipital	R L
		Prefrontal	R L
	Ventral occipito-temporal	R	



To determine whether a region was consistently active or not, we modelled the number of late dipolar activity sources using a generalized estimating equation (Zeger and Liang, 1986) approach. This procedure was deemed necessary because the measurements of interest (i.e. number of dipoles per source) consisted of discrete data (i.e., frequency counts), which are positively skewed with a clustering of values at the lower end of the range. GEE models are derived from generalized linear models (McCullagh and Nelder, 1989): general linear models (regression, ANOVA) that are not limited by normality considerations and can be applied to data fitting exponential-family distributions (binomial, Poisson, negative binomial, etc). With this approach the data are modeled using a generalized linear model along with a link function that makes the relation between the predictors in the model and the outcome approximately linear (such as a log function for the Poisson or negative binomial, or the logit function for the binomial distribution). The data in the current study were fitted using a negative binomial distribution model, which provides control for the over-dispersion of these distributions, with a log link function. Since the time frame for measurements was not equal for all subjects, we used an offset in the model to produce estimates per 100 ms. An ROI displaying significantly more than one activity source per 100 ms was considered to be consistently active (see (Papanicolaou et al., 2006)). The following broader cortical regions in both hemispheres met this criterion (see Table 2). The Temporal lobe-Perisylvian ROI encompassed Heschl's gyrus, the superior temporal gyrus and the medial temporal region. The Prefrontal ROI included dorsolateral prefrontal and inferior frontal cortices, whereas the Occipital ROI included primary and association visual cortices (Brodmann Areas 17, 18 and 19 excluding the fusiform gyrus). In addition to these bilateral ROIs, significant activation was detected in the following right hemisphere regions: Motor-Supplementary cortex (during non-associative encoding of names), the cingulate gyrus (during non-associative encoding of faces), and the fusiform gyrus (during associative encoding of faces).

In order to evaluate the main distinctive features of the activation profile associated with each condition (associative, non-associative) GEE analyses were performed separately for each ROI (significantly active regions across all conditions) with hemisphere (left, right) and stimulus material type (names, faces) as the within-subject factors. Next, to evaluate differences between the two encoding conditions, an additional GEE analysis was performed by adding Condition to the within-subjects factors listed previously. The number of late activity sources served as the dependent variable in these analyses.

## Acknowledgments

This study was supported in part by Grant NS46588-01A2 from the National Institutes of Health, to the corresponding author.

## REFERENCES

Baier, B., Kleinschmidt, A., Muller, N.G., 2006. Cross-modal processing in early visual and auditory cortices depends on expected statistical relationship of multisensory information. *J. Neurosci.* 26, 12260–12265.

- Balsamo, L.M., Xu, B., Gaillard, W.D., 2006. Language lateralization and the role of the fusiform gyrus in semantic processing in young children. *Neuroimage* 31, 1306–1314.
- Binder, J.R., Frost, J.A., Hammeke, T.A., Cox, R.W., Rao, S.M., Prieto, T., 1997. Human brain language areas identified by functional magnetic resonance imaging. *J. Neurosci.* 17, 353–362.
- Buckner, R.L., Kelley, W.M., Petersen, S.E., 1999. Frontal cortex contributes to human memory formation. *Nat. Neurosci.* 2, 311–314.
- Campanella, S., Joassin, F., Rossion, B., De Volder, A., Bruyer, R., Crommelinck, M., 2001. Association of the distinct visual representations of faces and names: a PET activation study. *Neuroimage* 14, 873–882.
- Clark, V.P., Keil, K., Maisog, J.M., Courtney, S., Ungerleider, L.G., Haxby, J.V., 1996. Functional magnetic resonance imaging of human visual cortex during face matching: a comparison with positron emission tomography. *Neuroimage* 4, 1–15.
- Gibson, J.R., Maunsell, J.H., 1997. Sensory modality specificity of neural activity related to memory in visual cortex. *J. Neurophysiol.* 78, 1263–1275.
- Gorno-Tempini, M.L., Price, C.J., Josephs, O., Vandenberghe, R., Cappa, S.F., Kapur, N., Frackowiak, R.S., 1998. The neural systems sustaining face and proper-name processing. *Brain* 121, 2103–2118.
- Grady, C.L., McIntosh, A.R., Rajah, M.N., Craik, F.I., 1998. Neural correlates of the episodic encoding of pictures and words. *Proc. Natl. Acad. Sci. U. S. A.* 95, 2703–2708.
- Guo, C., Voss, J.L., Paller, K.A., 2005. Electrophysiological correlates of forming memories for faces, names, and face-name associations. *Brain Res. Cogn. Brain Res.* 22, 153–164.
- Halgren, E., Raji, T., Marinkovic, K., Jousmaki, V., Hari, R., 2000. Cognitive response profile of the human fusiform face area as determined by MEG. *Cereb. Cortex* 10, 69–81.
- Haxby, J.V., Grady, C.L., Horwitz, B., Ungerleider, L.G., Mishkin, M., Carson, R.E., Herscovitch, P., Schapiro, M.B., Rapoport, S.I., 1991. Dissociation of object and spatial visual processing pathways in human extrastriate cortex. *Proc. Natl. Acad. Sci. U. S. A.* 88, 1621–1625.
- Haxby, J.V., Hoffman, E.A., Gobbini, M.I., 2000. The distributed human neural system for face perception. *Trends Cogn. Sci.* 4, 223–233.
- Haxby, J.V., Ungerleider, L.G., Horwitz, B., Maisog, J.M., Rapoport, S.I., Grady, C.L., 1996. Face encoding and recognition in the human brain. *Proc. Natl. Acad. Sci. U. S. A.* 93, 922–927.
- Herholz, K., Ehlen, P., Kessler, J., Strotmann, T., Kalbe, E., Markowitsch, H.J., 2001. Learning face-name associations and the effect of age and performance: a PET activation study. *Neuropsychologia* 39, 643–650.
- Ishai, A., Haxby, J.V., Ungerleider, L.G., 2002. Visual imagery of famous faces: effects of memory and attention revealed by fMRI. *Neuroimage* 17, 1729–1741.
- Johnson, J.A., Zatorre, R.J., 2005. Attention to simultaneous unrelated auditory and visual events: behavioral and neural correlates. *Cereb. Cortex* 15, 1609–1620.
- Kanwisher, N., McDermott, J., Chun, M.M., 1997. The fusiform face area: a module in human extrastriate cortex specialized for face perception. *J. Neurosci.* 17, 4302–4311.
- Kelley, W.M., Miezin, F.M., McDermott, K.B., Buckner, R.L., Raichle, M.E., Cohen, N.J., Ollinger, J.M., Akbudak, E., Conturo, T.E., Snyder, A.Z., Petersen, S.E., 1998. Hemispheric specialization in human dorsal frontal cortex and medial temporal lobe for verbal and nonverbal memory encoding. *Neuron* 20, 927–936.
- Kim, J.J., Andreasen, N.C., O'Leary, D.S., Wiser, A.K., Ponto, L.L., Watkins, G.L., Hichwa, R.D., 1999. Direct comparison of the neural substrates of recognition memory for words and faces. *Brain* 122, 1069–1083.
- Kirchhoff, B.A., Wagner, A.D., Maril, A., Stern, C.E., 2000. Prefrontal-temporal circuitry for episodic encoding and subsequent memory. *J. Neurosci.* 20, 6173–6180.

- Kirwan, C.B., Stark, C.E., 2004. Medial temporal lobe activation during encoding and retrieval of novel face-name pairs. *Hippocampus* 14, 919–930.
- Lee, D., Simos, P., Sawrie, S.M., Martin, R.C., Knowlton, R.C., 2005. Dynamic brain activation patterns for face recognition: a magnetoencephalography study. *Brain Topogr.* 18, 19–26.
- Martinez, A.M., Benavente, R., 1998. The AR Face Database. CVC Technical Report 24.
- McCullagh, P., Nelder, J.A., 1989. *Generalized Linear Models*. Chaman and Hall, London.
- Murray, M.M., Foxe, J.J., Wylie, G.R., 2005. The brain uses single-trial multisensory memories to discriminate without awareness. *Neuroimage* 27, 473–478.
- Nobre, A.C., Allison, T., McCarthy, G., 1994. Word recognition in the human inferior temporal lobe. *Nature* 372, 260–263.
- Papanicolaou, A.C., Pazo-Alvarez, P., Castillo, E.M., Billingsley-Marshall, R.L., Breier, J.I., Swank, P.R., Buchanan, S., McManis, M., Clear, T., Passaro, A.D., 2006. Functional neuroimaging with MEG: normative language profiles. *Neuroimage* 33, 326–342.
- Ryan, J.D., Moses, S.N., Ostreicher, M.L., Bardouille, T., Herdman, A.T., Riggs, L., Tulving, E., 2008. Seeing sounds and hearing sights: the influence of prior learning on current perception. *J. Cogn. Neurosci.* 20, 1030–1042.
- Sarvas, M., 1987. Basic mathematical and electromagnetic concepts of the biomagnetic inverse problem. *Phys. Med. Biol.* 32, 11–22.
- Small, S.A., Nava, A.S., Perera, G.M., DeLaPaz, R., Mayeux, R., Stern, Y., 2001. Circuit mechanisms underlying memory encoding and retrieval in the long axis of the hippocampal formation. *Nat. Neurosci.* 4, 442–449.
- Sperling, R.A., Bates, J.F., Cocchiarella, A.J., Schacter, D.L., Rosen, B.R., Albert, M.S., 2001. Encoding novel face-name associations: a functional MRI study. *Hum. Brain Mapp.* 14, 129–139.
- Swithenby, S.J., Bailey, A.J., Brautigam, S., Josephs, O.E., Jousmaki, V., Tesche, C.D., 1998. Neural processing of human faces: a magnetoencephalographic study. *Exp. Brain Res.* 118, 501–510.
- Tulving, E., Markowitsch, H.J., Kapur, S., Habib, R., Houle, S., 1994. Novelty encoding networks in the human brain: positron emission tomography data. *Neuroreport* 5, 2525–2528.
- Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., Mazoyer, B., Joliot, M., 2002. Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. *Neuroimage* 15, 273–289.
- Zeger, S.L., Liang, K.Y., 1986. Longitudinal data analysis for discrete and continuous outcomes. *Biometrics* 42, 121–130.