

Interactive report

Activity in fusiform face area modulated as a function of working memory load¹

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Abstract

Previous fMRI results suggest that extrastriate visual areas have a predominant role in perceptual processing while the prefrontal cortex (PFC) has a predominant role in working memory. In contrast, single-unit recording studies in monkeys have demonstrated a relationship between extrastriate visual areas and visual working memory tasks. In this study we tested whether activity in both the PFC and fusiform face area (FFA) changed with increasing demands of an *n*-back task for gray-scale faces. Since stimulus presentation was identical across conditions, the *n*-back task allowed us to parametrically vary working memory demands across conditions while holding perceptual and motor demands constant. This study replicated the result of PFC areas of activation that increased directly with load *n* of the task. The novel finding in all subjects was FFA activation that also increased directly with load *n* of the task. Since perceptual demands were equivalent across the three task conditions, these findings suggest that activity in *both* the PFC and the FFA vary with face working memory demands. © 2001 Elsevier Science B.V. All rights reserved.

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Topic: Cognition; Learning and memory: systems and functions

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1. Introduction

Pathology studies of prosopagnosic patients introduced the notion that a brain area might exist which is specialized for the perception of human faces [19]. Prosopagnosic patients have selectively impaired recognition and perception of faces compared with other visual images. These patients frequently demonstrate lesions in occipitotemporal areas of visual cortex, usually showing right-lateralized or bilateral damage. Primate single-unit recording experiments subsequently documented the presence of both face-selective and object-selective neurons in the inferior temporal cortex (IT) and superior temporal sulcus (STS) [8,9,27,40,43,49]. In humans, the fusiform face area (FFA) is the suggested functional and anatomical homologue to

primate face-selective IT [3,32,41,42]; portions of human STS showing face- and gaze-selectivity are believed homologous to primate STS [30]. Investigations of the FFA have generally identified a small area of the fusiform gyrus which shows a greater response to visually presented faces than other visual stimuli [3,32,41,42,44]. Recent experiments have described the FFA as an 'expert' processor [25], but there is little evidence that this region might have functions beyond perception. With the exception of studies looking at the effects of attention in the FFA [38,47], the FFA has been exclusively examined as a perceptual module.

We believe that the functions of the FFA should extend beyond the perception of faces or other stimuli requiring expert processing. Current models of object working memory predict a significant role for the FFA in working memory for faces. Working memory has been broadly defined as a cognitive system that permits short-term, active maintenance and manipulation of stimulus information when that information is not available in the

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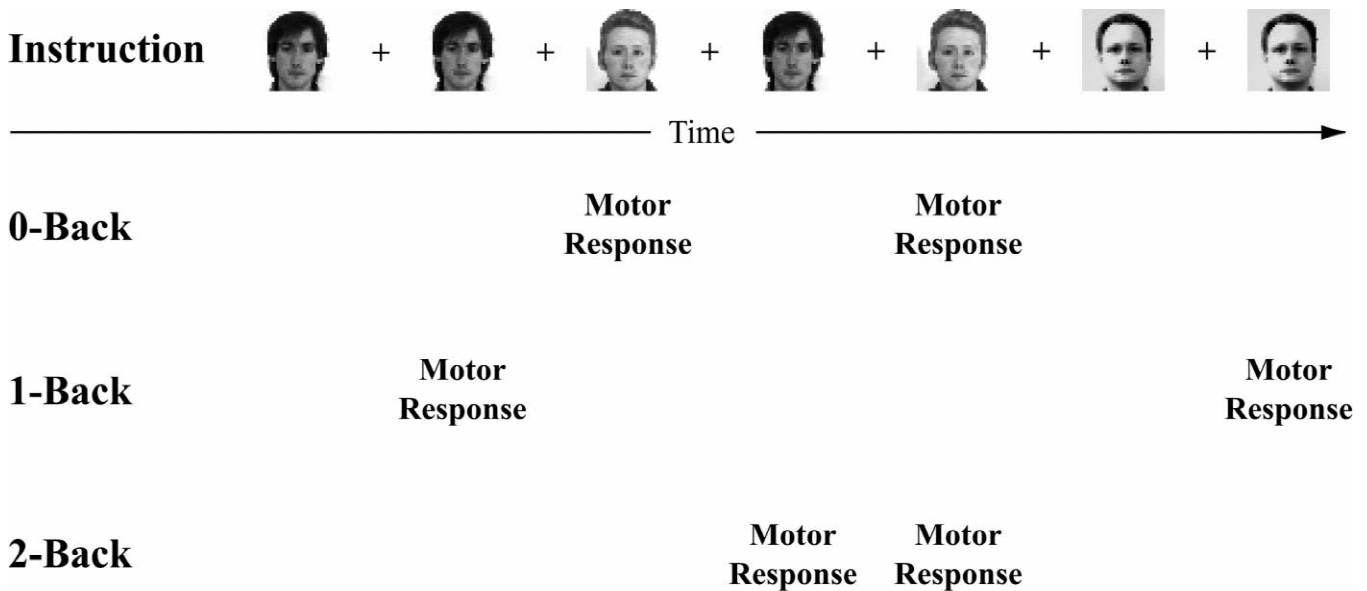


Fig. 1. A block of stimuli representative of the n -back task for faces. Following a task instruction, a series of faces appeared for 1 s at a time with 1 s of fixation between faces. Subjects gave a motor response according to the instruction given at the beginning of each block. For 0-back, the response was to a predetermined target face. For 1-back, the response was when a face matched the face presented one ago. For 2-back, the response was when a face matched the face presented two ago. Conditions were balanced for perceptual and motor demands. For display purposes, responses are shown to the same block of seven stimuli; during the actual experiment, blocks of stimuli were not repeated and consisted of thirteen stimuli per block.

environment [4,5]. Data from primate lesion [7,21,24] and single-unit recording studies [15,23,24,33,35–37] have described different but complementary roles for IT and PFC in object working memory. While PFC neurons robustly maintain stimulus-specific information across the delay period of a working memory task [23,24,35], IT neurons show more subtle delay effects [15] and robust stimulus-specific effects at target presentation [24,33,36,37]. The response properties of neurons in these two regions suggest that activity in IT is biased in favor of behaviorally relevant stimuli by virtue of top-down feedback from prefrontal structures [14,18]. If the FFA is homologous to face-selective regions of IT then FFA should have working memory properties similar to IT when the task involves face stimuli.

In the present study, we hypothesized that the FFA would demonstrate increased activity with increased working memory load for human faces. If a positive bias on a subgroup of neurons within the FFA is associated with maintaining a behaviorally relevant face, it is reasonable to believe that maintenance of more faces would involve recruitment of additional subgroups of FFA neurons. Previous work has suggested the involvement of fusiform gyrus in face working memory [17,26,28,29,50], but in various ways these inferences have been confounded by the perceptual demands of the task. As the FFA is known to be active under conditions of face perception, these confounds make it difficult to state whether working memory was the source of the FFA activity in these studies. Since the present study used a working memory task which controlled for perceptual demands across task

conditions, we were in a position to make stronger statements about changes in FFA activity specific to working memory.

To test our hypothesis, we used fMRI to measure neuronal activity in humans performing an n -back task for gray-scale faces (Fig. 1). Given the similarity to previous visuospatial n -back studies, we expected to replicate previous findings of increased activity with load in the PFC and posterior parietal areas [10,11,16,31]. The novel aspects of the experiment were: (1) the use of face stimuli in the n -back task, and (2) a separate experiment to functionally define the FFA. These features allowed us to simultaneously analyze the PFC and the FFA, an easily identifiable portion of extrastriate visual cortex. Using the same logic employed by other investigators to correlate activity in frontal and parietal regions with working memory, we were able to determine that working memory load for faces modulated FFA activity.

2. Materials and methods

2.1. Subjects

Nine right-handed subjects (age range 21–27, 5 male and 4 female) were recruited from the University of Pennsylvania Medical School. All participants were screened against medical, neurological, and psychiatric illnesses, and also for use of prescription medications. The day prior to the scan, subjects were behaviorally trained to an overall 85% performance criterion.

2.2. Behavioral task (Fig. 1)

Subjects were presented with an instruction (0-back, 1-back, or 2-back) for 4 s, followed by a sequence of 13 faces. The face stimuli were full-face, above-the-neck, gray-scale photographs obtained from a yearbook. Faces appeared for 1 s at a time, followed by 1 s of a fixation crosshair. In the 0-back condition, subjects responded with a button press to a predetermined target face. In the 1-back condition, subjects responded when a face matched the previous face. In the 2-back condition, subjects responded when a face matched the one presented two faces prior in the sequence. Motor responses were balanced across conditions so that 33% of stimuli required a motor response. The experiment was structured in 30-s condition blocks presented in a pseudo-randomized order.

2.3. MRI technique

Imaging was carried out on a 1.5T SIGNA scanner (GE Medical Systems) equipped with a prototype fast gradient system for echo-planar imaging. A standard radiofrequency (RF) head coil was used with foam padding to comfortably restrict head motion. High-resolution sagittal and axial T1-weighted images were obtained in every subject. A gradient echo, echoplanar sequence (TR=2000 ms, TE=50 ms) was used to acquire data sensitive to the blood oxygen level dependent (BOLD) signal. Resolution was 3.75 mm×3.75 mm in plane, and 5 mm between planes (21 axial slices were acquired). Twenty seconds of gradient and RF pulses preceded data acquisition to allow steady-state tissue magnetization. Subjects viewed a backlit projection screen from within the magnet bore through a mirror mounted on the head coil.

2.4. Data preparation

Off-line data processing was performed on SUN Ultra workstations using programs written in Interactive Data Language (Research Systems, Boulder, CO). Initial data preparation proceeded in the following steps: image reconstruction; sinc interpolation in time (to correct for the fMRI slice acquisition sequence); motion correction (six-parameter, rigid-body, least-squares alignment); slice-wise motion compensation (to remove spatially coherent signal changes via the application of a partial correlation method to each slice in time) [2,20,51]. The data were not spatially smoothed. Since fMRI data are temporally autocorrelated under the null-hypothesis [51], statistical analyses were conducted within the framework of the modified general linear model for serially correlated error terms [48]. In the convolution matrix [48] was placed a time-domain representation of the expected 1/f power structure [51] and a notch filter that removed frequencies above 0.245 Hz (i.e.,

at or around the Nyquist frequency) and below 0.02 Hz (i.e., the portions of highest power in the noise spectrum). Due to the low frequency of the paradigm, the data were smoothed temporally with an idealized model of the hemodynamic response function [48].

2.5. Identifying regions of interest (Fig. 2)

The FFA was identified in a separate experiment where subjects passively viewed 20-s blocks of gray-scale faces and objects over a single scan. Based on individual sulcal and gyral anatomy, a fusiform gyrus region of interest (ROI) was identified for each subject. The FFA was subsequently defined as all voxels in the fusiform gyrus ROI showing statistically significant activation in a contrast of faces against objects. In contrast, the fusiform object area (FOA) was defined as all voxels in the fusiform gyrus showing a statistically significant activation in a contrast of objects against faces. The FOA was generally located medial to the FFA, consistent with category-related topography observed by other investigators [12].

2.6. Analysis for linear trends

The three task conditions appeared in pseudo-randomized 30 s blocks with a total of 32 blocks per condition. Within the context of the modified general linear model, the trial portion of each block was modeled as an individual event convolved by an idealized hemodynamic response function. The instruction periods for all of the blocks were used as the baseline. Considering each block as a covariate of interest, a mean parameter estimate (β) was obtained for each block giving 32 parameter estimates per condition. Intuitively speaking, each β is a scale factor that reflects changes in fMRI signal attributed to both task specific-effects and block-specific confounds. Linear regression of the β 's onto a numerical index of load n (0, 1, or 2) gave a magnitude for any linear trend and a statistical significance of that trend. This type of regression analysis allowed a separation of the block-specific confounds from the parametric effects of varying load n . The two types of linear trend analyses performed were: (1) a ROI analysis within the functionally-defined FFA and FOA, and (2) a map-wise random effects analysis.

The first analysis focused on identification of linear trends within the functionally-defined FFA (Fig. 3). A voxel-wise analysis identified individual voxels showing linear trends within the FFA. A parallel analysis averaged the time series from each voxel within a ROI into a single composite time series across the ROI. The average time series was then tested for linear effects as previously described. As a control, the same analysis was performed within the functionally-defined FOA.

The second analysis was a map-wise random effects

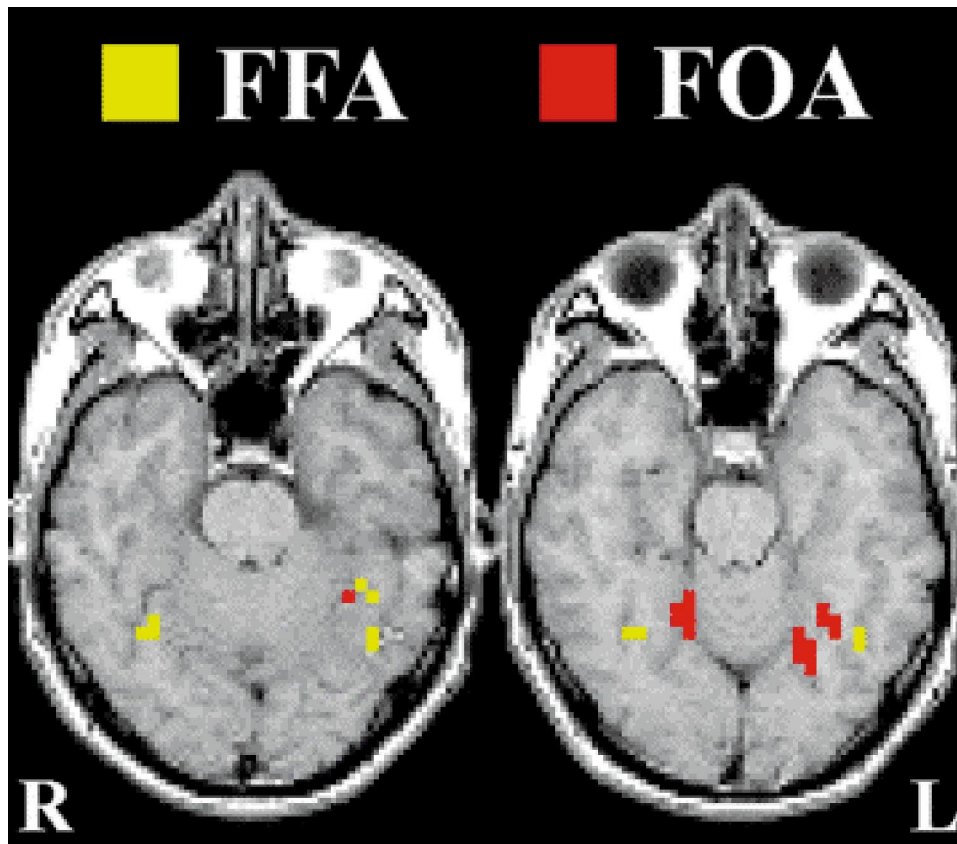


Fig. 2. The FFA and FOA identified from a single representative subject. Images are shown in radiological convention (L=R). Regions more activated by faces than by objects (FFA) are shown in yellow, whereas more activated by objects than by faces (FOA) are shown in red.

analysis to identify regions showing reliable examined all nine subjects as a group (Fig. 4). In the random effects analysis, a whole-brain map of t -values associated with the linear trend was generated for each subject. The t -map for each subject was normalized to the template found in SPM96b (<http://www.fil.ion.ucl.ac.uk/spm>) by applying a 12-parameter affine transformation with non-linear deformations routine [20]. Normalized t -maps were then smoothed using a Gaussian smoothing kernel (7.5 mm full-width at half-maximum). For each voxel in Talairach space [46], the group of nine t -values (one derived from each of the nine subjects) were one-way t -tested for a significant difference from zero. The threshold for significance [$t(8) > 6.39$] was adjusted for multiple comparisons given the smoothness of the map to correct to a mapwise $P < 0.05$. The result was a whole-brain Talairach-normalized map of voxels that showed linear increases in activation with load n across subjects.

3. Results

3.1. Behavioral results

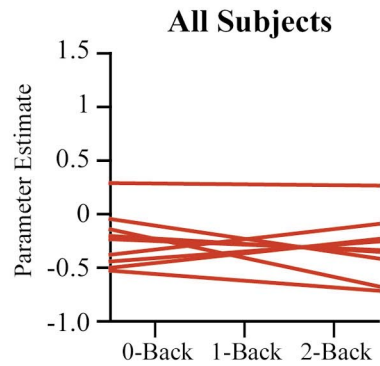
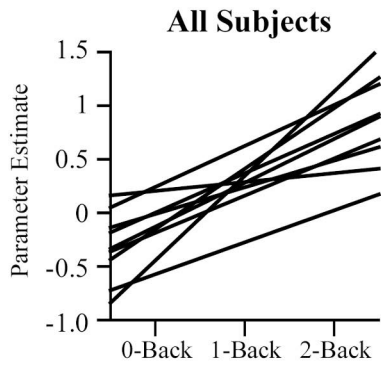
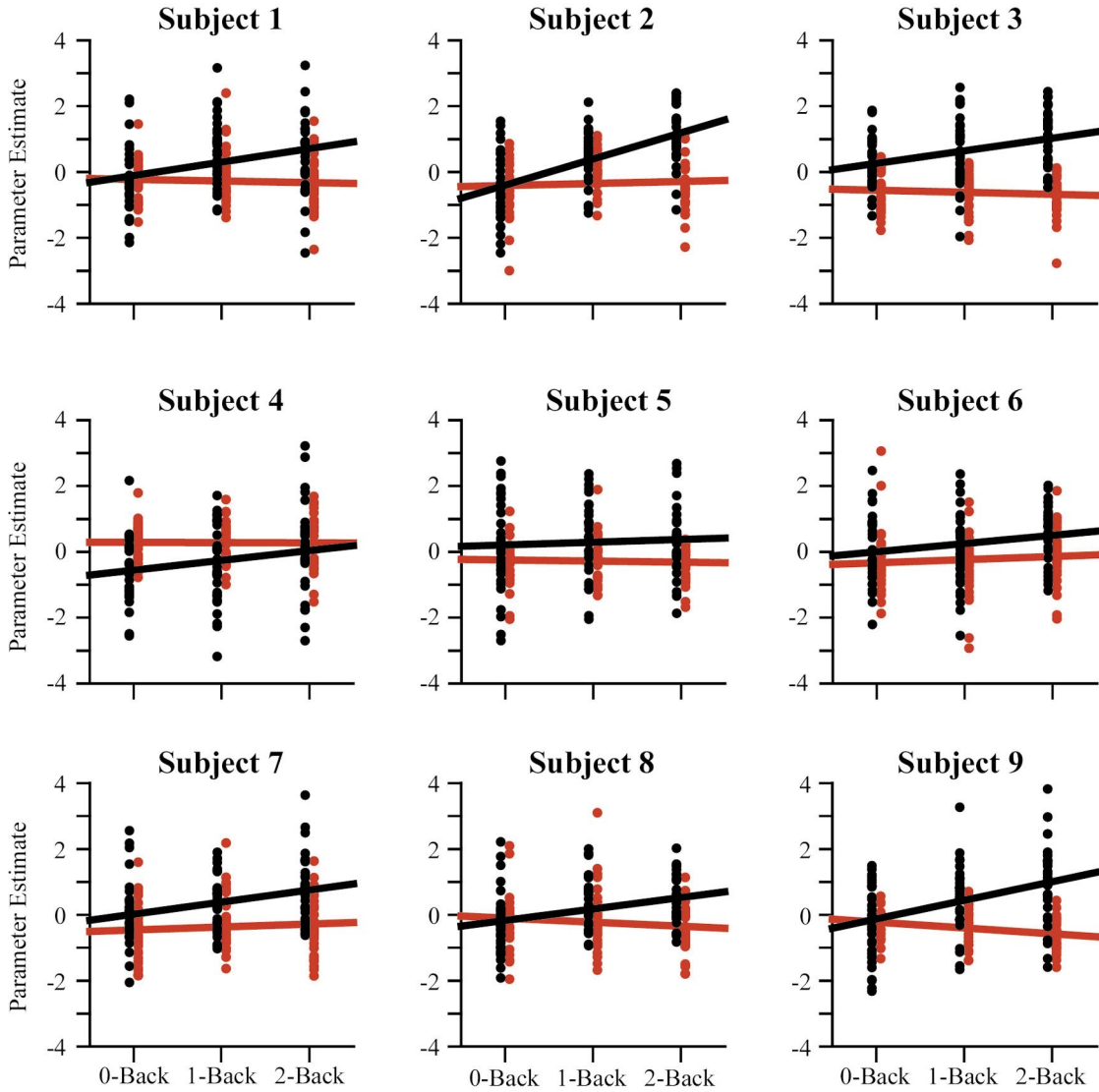
Behavioral results are summarized in Table 1. As expected, subjects indicated that the 2-back task was much more difficult than either the 0-back or 1-back task. This increased difficulty is reflected in the lower accuracy and higher reaction time for the 2-back task. The overall accuracy of $86.2 \pm 3.2\%$ was close to the 85% criterion used for training the subjects.

3.2. fMRI results in fusiform face area and fusiform object area

The FFA was identified in a separate localizer run in all nine subjects (Fig. 2). The FFA was defined as the set of voxels within the fusiform gyrus showing greater activity

Fig. 3. Regression of parameter estimates for the condition blocks against an index of condition (0, 1, or 2) for all nine subjects. Parameter estimates were z -normalized to a common scale for all subjects. In the FFA, all nine subjects had increased activity with load n . The FFA linear trend was statistically significant in eight of nine subjects. In the FOA, no reliable relationship between activity and load was observed. The FOA linear trend was only significant in one of nine subjects.

■ FUSIFORM FACE AREA
■ FUSIFORM OBJECT AREA



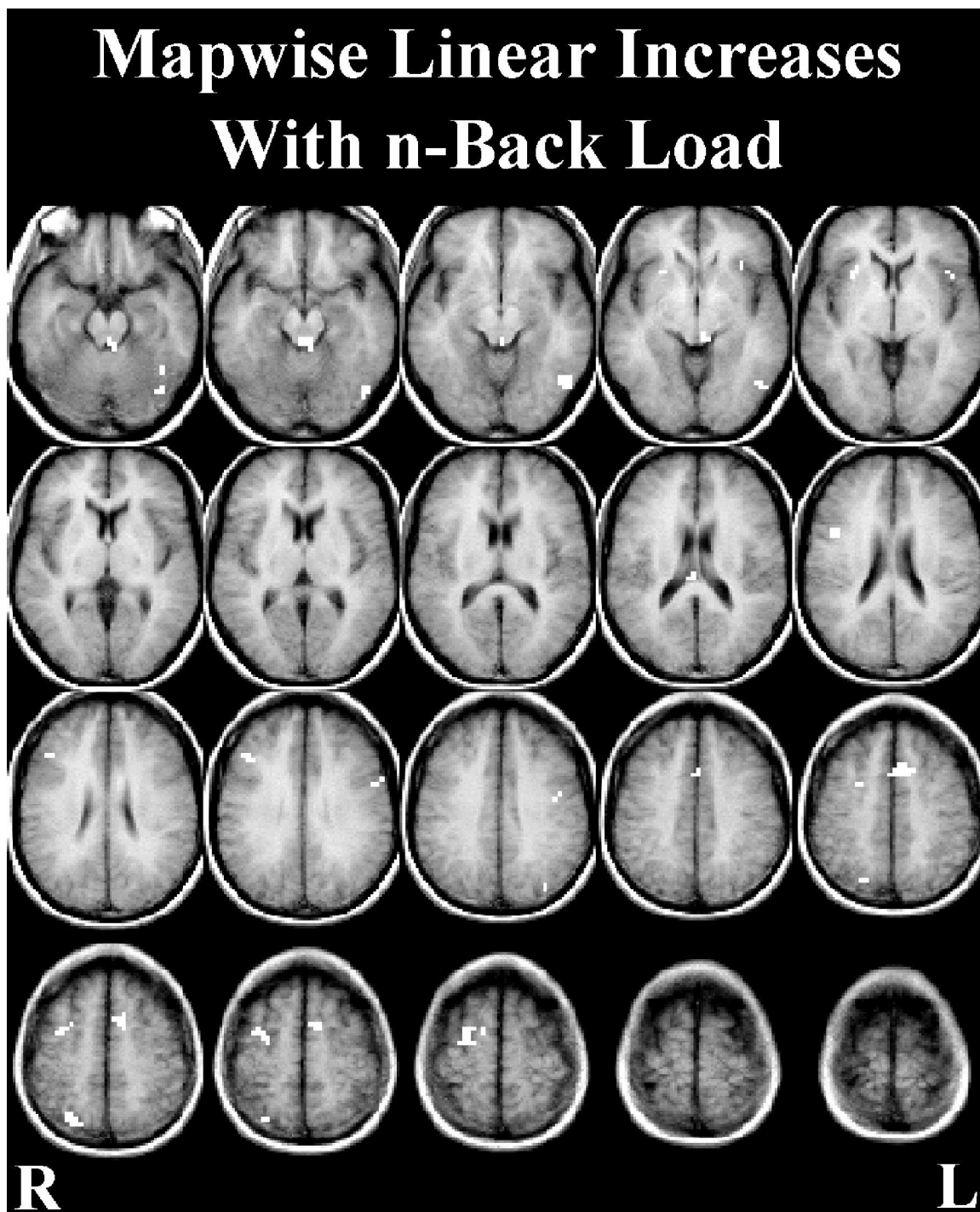


Fig. 4. Map-wise random effects analysis searching for increases in activity with n of the task. White voxels correspond to $t(8) > 6.39$, $P < 0.05$. Images are shown in radiological convention (L=R).

Table 1
Behavioral data from scanning

	Mean accuracy (% Correct \pm Standard Error)	Reaction time (ms \pm Standard Error)
0-Back	99.1 \pm 0.1	505.4 \pm 3.9
1-Back	89.0 \pm 0.3	526.6 \pm 4.3
2-Back	70.5 \pm 1.1	585.2 \pm 6.4

in a contrast of faces against objects. In seven of the nine subjects, there were voxels within the FFA that demonstrated a statistically significant linear increase with load n . The location of these voxels frequently overlapped those voxels which showed the highest t -values in the FFA localizer run. When time series were averaged across all voxels within the FFA, increases with n of the task were

Table 2
Linear trends across FFA and FOA regions of interest

	FFA parameter estimates (β)	FOA parameter estimate (β)
Subject 1	0.45**	-0.05
Subject 2	0.81****	0.06
Subject 3	0.26***	-0.04
Subject 4	0.65*	-0.02
Subject 5	0.15	0.06
Subject 6	0.49*	0.19
Subject 7	0.44**	-0.11
Subject 8	0.48**	-0.17
Subject 9	0.56****	-0.18**
One-way <i>t</i> -test	7.34****	-0.72

****indicates $P < 0.0001$; ***indicates $P < 0.001$; **indicates $P < 0.01$; *indicates $P \leq 0.05$.

found in all nine subjects (Fig. 3). In eight of the nine subjects, these increases were significant at $P = 0.05$ (Table 2). Furthermore, the subject with the non-significant linear increase (Subject 5) also had the poorest behavioral performance on the 2-back task (accuracy = 65.1%). A one-way *t*-test of the FFA parameter estimates from all nine subjects was significant at $P < 0.0001$. To control for the possibility that the increases might be a by-product of a more general modulation of the extrastriate visual areas, a control area that we call the fusiform object area (FOA) was also examined. In the localizer run, the FOA was identified as the set of voxels within the fusiform gyrus showing greater activity in a contrast of objects against faces. When collapsed across the entire FOA, linear increases with n of the task were only found in three subjects (Fig. 3 and Table 2), and these increases were not statistically significant. A one-way *t*-test of the FOA parameter estimates from all nine subjects was also not significant ($P = 0.76$).

3.3. Random effects imaging analysis (Fig. 4)

When tested at a whole-brain level across subjects,

Table 3
Talairach coordinates of map-wise linear increases

Anatomy	Laterality	Talairach coordinates		
		X	Y	Z
Middle frontal gyrus	Right	-34	-4	55
Superior parietal lobule	Right	-30	-68	50
Supplementary motor area	Left/midline	4	11	45
Angular gyrus	Left	34	-79	35
Precentral gyrus	Left	41	-8	35
Precentral gyrus	Left	56	0	30
Middle frontal gyrus	Right	-45	23	25
Insula	Right	-30	19	-5
Insula	Left	34	26	-10
Middle occipital gyrus	Left	49	-64	-15
Superior colliculus	Left/midline	4	-34	-20
Fusiform gyrus	Left	41	-56	-25

linear increases with n of the task were consistently found in left middle occipital gyrus, left fusiform gyrus, bilateral insular cortex, right superior parietal lobule, right middle frontal gyrus, and bilateral supplementary motor area (Table 3). The right fusiform gyrus did not appear as a significant result in this analysis, although we noted a small activation in that area before the *t*-threshold was corrected for multiple comparisons. On a map-wise level, the lack of a strong effect in the anatomic location of the functionally-defined FFA was not surprising. The small size and anatomic variability of the module made co-registration across normalized brains unlikely. Additionally, any positive effect in the FFA was being smoothed into areas of little or no effect in immediately adjacent cortex.

4. Discussion and references

The *n*-back task is an elegant paradigm that has allowed experimenters to isolate areas of the brain which vary with working memory load-dependent aspects of the task [10,11,16,31]. In *n*-back experiments, subjects perform a working memory task where they decide when a serially-presented stimulus matches the one presented n stimuli ago. By parametrically varying n , the task highlights processes that vary with the load of information maintained and/or manipulated in working memory. As a general class of experiment, parametric designs do not need to assume a pure insertion of the process of interest since only the magnitude of the process of interest is altered [1]. In the case of the *n*-back task, the perceptual and motor demands of the task are similar across levels of n , as the only difference between conditions is the instruction given to the subject. Given these features, the consensus from previous experiments has been that areas of increased activity with load n are involved with a load-dependent aspect of working memory. While there has been some discrepancy as to the exact locations of these activations, the bulk of the results have implicated bilateral middle frontal gyrus (MFG), superior frontal sulcus (SFS), superior frontal gyrus (SFG), and when they have been imaged, posterior parietal areas [10,11,16,31].

The results of this study replicate findings of other visuospatial *n*-back studies in frontal and parietal regions, but additionally demonstrate that working memory load modulates activity in the FFA, an extrastriate visual area. While the FFA may be important in the perception of face stimuli, this area also functions in maintaining and/or manipulating that face information in a working memory task for faces. Previous visuospatial working memory studies have suggested that performance of these tasks is subserved by spatially distributed network of cortical areas [10,11,16,31,45]. The present finding supports that idea but additionally suggests that the network of cortical areas activated is highly specific to the stimulus set involved.

While the notion of working memory for faces modulating fusiform activity is not new to the literature [17,26,28,29], prior studies have suffered from perceptual confounds of their working memory tasks. Haxby [29] and Grady [26] found decreased fusiform activity with increasing length of delay in a delay-match-to-sample task. Unfortunately, both experiments were structured such that blocks with shorter delays contained more face stimuli. As the authors acknowledged, the decrease in fusiform activity at long delays clearly resulted from decreased perceptual demands. Thus, any effects of the working memory manipulation were masked by that perceptual confound. Courtney [17] and Haxby [28] conducted an event-related experiment, which examined the encoding, delay, and response periods of a face recognition task. While they found significant delay period activity within the fusiform, the statistical analysis was structured in a way that the encoding period (where faces are visually presented) might influence the delay covariate. Simulations have shown that a delay covariate placed temporally close to the encoding period can be influenced by activity that occurs at encoding [50]. Thus, it is impossible to determine if the 'memory' effects seen in these studies results from perception of the stimuli or maintenance of the face information. By eliminating the perceptual confounds found in prior studies, we can be confident that modulation of FFA activity in the present study results from variation in working memory load.

The biased-competition model of attention seems to predict the result of the present study [14,18]. This model, developed in the context of visual search paradigms, suggests that presentation of a face would activate a population of FFA cells tuned to the features of that face. After the stimulus disappears from the screen, this population of cells would be positively-biased by top-down feedback projections from the prefrontal cortex. The feedback biases inhibitory competition in IT in favor of cells representing the relevant face, and cells representing irrelevant faces are ultimately suppressed. In the case of a match, there is no competition to suppress activity in the population of cells representing the relevant face.

This model would predict an increase in FFA activity with increasing load during the n -back task. In the 0-back case, there would be no feedback from the PFC as there is no face being held in working memory. In the 1-back case, there would be feedback from the PFC to bias the one population of cells representing the one face being maintained in working memory. In the 2-back case, there would be feedback to bias two populations of cells representing the two faces being maintained in working memory. Even though the perceptual demands of the tasks are the same, this difference in FFA neural activity would result from the increased prefrontal bias with the load of the task. In a standard delay response task, this bias should manifest itself as delay-specific activity within the FFA.

The involvement of FFA in working memory for faces

might have been predicted as a natural extension of a recent mental imagery study for faces [39]. In this study, FFA activity was observed under a condition where subjects were prompted to imagine the face associated with a famous name. One could argue that this imagery task qualitatively resembled the delay component of a working memory task for faces; in both cases, the subject maintained a mental representation of a face not present in the environment. While the imagery task only examined mental representations of a single face, it seems reasonable that increasing the number of faces maintained would require additional activity among the neurons associated with the extra faces.

The general effects of task 'difficulty' must also be given some consideration since the higher load conditions demonstrated slower reaction times and reduced accuracy. Previous working memory experiments have used perceptual degradation to control reaction time as a non-specific index of task difficulty [6]. Interpretation of such studies is complicated by the fact that such a non-specific control task may not only increase 'mental effort' but may also recruit other more specific cognitive processes (i.e. object parsing, manipulation, or binding). Operationally, task difficulty could be defined as comprising both non-specific (effort and arousal) and specific (attention) processes. The lack of linear effect in the FOA constituted an important control in discounting a non-specific modulation of activity in extrastriate visual regions. The control clearly demonstrated that load n for faces modulated activity in an area sensitive to faces, but not in another area sensitive to higher level object processing. In contrast, attention has been demonstrated to broadly modulate activity in lower-level primate visual areas [34]. Studies of V4 and V5 have shown that activity in these areas can be specifically modulated by attention to motion and color, respectively [13]. Given this result, one might question whether different attention loads for faces could specifically modulate activity in the FFA. While covert attention specifically modulates activity in the FFA [47], it remains unclear whether this modulation is a pure effect of attention since face stimuli were still present in the visual field. Again, it would not be surprising if increased attention for faces modulated activity in the FFA since the biased-competition model blurs the distinction between working memory and attention.

While we acknowledge the benefits of the n -back task in identifying brain regions involved with working memory, we must also point out that it neglects the idea that a working memory task can be divided into a number of sub-components. A principled way of dividing these tasks is into: (1) encoding of stimulus information, (2) maintenance and manipulation of that information across a delay, and (3) retrieval of information for the response. Since the n -back task is a continuous working memory process with no inter-trial intervals, it is impossible to determine which sub-component might be contributing to the modulation of

activity in the FFA. Event-related investigations will be necessary to make such distinctions.

As knowledge of the human brain grows, it will become increasingly important to conduct neuroimaging studies that examine the brain as a whole unit. This system of working memory for faces is a specific example of the distributed active memory networks described by Fuster [22]. In this network view, memory is a cognitive function that requires the interplay of the cerebral cortex as a whole; comparatively, its concrete contents (i.e. the visual representation of a face) are localized to the cortex that mediates that modality. While there may be brain areas that appear to exhibit modular specialization, our results emphasize that these areas interact and may subserve a number of functions.

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