

Repetition-Induced Changes in BOLD Response Reflect Accumulation of Neural Activity

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Abstract: Recent exposure to a stimulus improves performance with subsequent identification of that same stimulus. This ubiquitous, yet simple, memory phenomenon is termed priming and has been linked to another widespread phenomenon called repetition suppression, which is a repetition-induced reduction in human brain activation as measured using fMRI. Here, competing models of the neural basis of repetition suppression were tested empirically. In a backward masking paradigm, we found that effectively masked object stimuli showed repetition *enhancement* of brain activation instead of suppression. This finding is consistent with an Accumulation model, but is inconsistent with a Suppression model of neural activity. Enhanced activation and the improved behavioral performance usually associated with priming are both explained by a shift in peak latency of the population neural activity elicited during identification. *Hum Brain Mapp* 27:37–46, 2006. © 2005 Wiley-Liss, Inc.

Key words: fMRI; object recognition; perception; vision

INTRODUCTION

Recent visual exposure to an object stimulus causes changes in both behavioral response measures and in measures of brain activity when that stimulus is subsequently presented. Effects on behavior are generally called priming and usually improve response time and/or accuracy on a variety of implicit tasks, such as naming. The effect is largest when the repeated stimulus is an exact copy of the initial object, which is then termed repetition priming [for review, see Roediger and McDermot, 1993; Schacter et al., 1993].

Human neuroimaging studies as early as 1992 measured changes in brain activation associated with repeated presentation of stimuli [Squire et al., 1992]. That study, and a majority of subsequent neuroimaging studies found that objects or words stimulated less blood oxygen level-dependent (BOLD) brain activation after repeated exposure than upon initial exposure [for review, see Cabeza and Nyberg, 2000; Schacter and Buckner, 1998; Wiggs and Martin, 1998]. This effect has come to be called repetition suppression [Henson, 2003], reflecting its predictable, experience-driven decrease in brain activation. Brain regions that show repetition suppression differ between experiments, but in general the regions that show suppression are those that are involved in processing the stimulus in question. For instance, object-selective cortex in the occipito-temporal region is suppressed with repeated exposure to object stimuli. Several researchers suggest that repetition suppression and priming are associated [Buckner et al., 1998a; Henson et al., 2004; James et al., 2000; Schacter and Buckner, 1998; Ungerleider, 1995; Wiggs and Martin, 1998], but the exact relationship between priming effects and repetition suppression effects remains controversial [Grill-Spector and Malach, 2001; Henson, 2003].

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Single-neuron recordings in the inferior temporal lobe (IT) of nonhuman primates also provide information about changes in brain activity related to experience. Although there are fewer data than with human neuroimaging, some evidence suggests that object stimuli produce less activity after repeated exposures than upon initial exposure [Li et al., 1993; Miller et al., 1991]. This effect is also called repetition suppression [Desimone, 1996] or sometimes response suppression [Brown and Xiang, 1998; Henson, 2003]. In the absence of more direct data, the pattern of response after repetition in neurons in human IT can be inferred on the basis of this animal work, and suggests that a subset of neurons in IT decrease their activity with repeated exposure to objects.

The experimental conditions under which response suppression in single-units and repetition suppression in neuroimaging is found are quite different, although the phenomena are similar. Both record a decrease in activation related to repeated exposure to a visual stimulus. Several researchers, therefore, have proposed models of BOLD repetition suppression that are based on single-unit response suppression [Desimone, 1996; Grill-Spector and Malach, 2001; Wiggs and Martin, 1998]. Furthermore, one of these models has been extended to describe the interrelation of repetition suppression, response suppression, and priming [Wiggs and Martin, 1998]. Thus, converging evidence from priming experiments, single-unit recordings, and human neuroimaging has spawned a model of object repetition that links behavioral facilitation (priming) with a general suppressive neural effect in object-selective regions of the cortex that manifests in both single-unit and population measures in human and nonhuman primates [Wiggs and Martin, 1998]. We will call this the Suppression model. Specifically, objects are represented by a subset of neurons in IT that code the diagnostic and nondiagnostic features of the object. Repeated exposures cause suppression of activity in neurons coding nondiagnostic features, while the diagnostic neurons continue their strong activity. Eventually, repeated exposure causes the nonessential cells to drop out. As nondiagnostic neurons drop out of the representation, the representation is sharpened or tuned, because the cells that continue to respond are the ones that code the most relevant features for identification. Looking at IT as a population of neurons, the net effect of tuning would be reduced activity; therefore, neuroimaging signals would be suppressed (Fig. 1). Sharpening would also make the object representation more efficient, which would explain the behavioral facilitation of priming.

The general acceptance of the homology between repetition priming, human repetition suppression in neuroimaging, and single-unit response suppression in monkeys appears to ignore several important findings that depart from the typical pattern of results [Dolan et al., 1997; George et al., 1999; Grill-Spector et al., 2000; Henson et al., 2000; James et al., 2002b; Malach et al., 1995; Schacter et al., 1995]. These idiosyncratic experiments all describe results in which repeated exposure to an object caused an *increase* in activation,

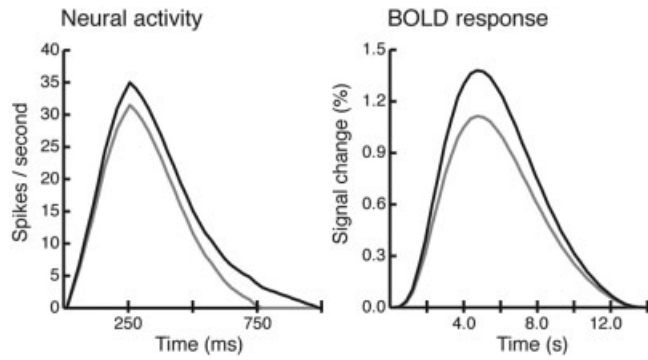


Figure 1.

Suppression model. The right graph illustrates a simulated neural response to a single repeated (gray) and nonrepeated (black), nondegraded stimulus. The left graph illustrates a simulated BOLD response to those same stimuli. Note that the neural activity and BOLD response graphs use different time scales. The primed neural activity is suppressed and produces a smaller BOLD response.

not the typical *decrease* in activation. The studies are of two types, those that used non-nameable stimuli such as novel objects [Henson et al., 2000; James et al., 2002b; Schacter et al., 1995], and those that used degraded stimuli that were initially difficult to name [Dolan et al., 1997; George et al., 1999; Grill-Spector et al., 1999; Malach et al., 1995]. In the experiments with degraded stimuli, it is likely that the increase in fMRI signal was related to an increase in recognition accuracy. More recent experiments [Ress and Heeger, 2003] have determined that successful discrimination of a stimulus stimulates more activity in visual cortex than unsuccessful discrimination. Therefore, if the probability of successful identification is greater for primed objects than for nonprimed objects, the average activation across a group of primed objects will be greater. When identification is constant across priming conditions, such as when performance is at a ceiling, the common decrease in activation prevails.

The second set of experiments is more diverse and the reasons for their atypical repetition effects are less clear. These experiments all used novel objects or nonfamous faces as stimuli [Henson et al., 2000; James et al., 2002b; Schacter et al., 1995]. One of the experiments [Henson et al., 2000] used famous faces as well as nonfamous faces. The famous faces in that study produced the typical suppressive repetition effect while novel faces led to an enhancement following repetition. Therefore, because suppression and enhancement were found in the same study where stimulus and scanning parameters were equated, this rules out an account based on methodological differences. It is tempting to speculate that the novelty of the objects could account for the enhancement effects. There are, however, at least three reports of typical suppressive repetition effects with novel objects [James et al., 2002a; van Turennout et al., 2000; Vuilleumier et al., 2002]. Nevertheless, examination of the spe-

cific types of stimuli used in different studies reveals differences in the homogeneity of the object sets, suggesting that novelty may contribute to the atypical effects, but only when combined with a high degree of perceptual similarity. Experiments that used perceptually diverse novel stimuli showed the typical suppressive repetition effect [James et al., 2002a; van Turennout et al., 2000; Vuilleumier et al., 2002], whereas experiments that used perceptually similar novel stimuli showed an atypical repetition enhancement effect [Henson et al., 2000; James et al., 2002b; Schacter et al., 1995].

Regardless of the explanation, it is clear that the Suppression model has difficulty accounting for the atypical results, in addition to several other unresolved problems [for review, see Henson, 2003]. What is needed is another model of the relationship between priming that facilitates behavioral response measures, and repetition suppression, which decreases hemodynamic response as measured using neuroimaging. Here, we propose an Accumulation model to account for the relationship between priming and repetition suppression. Accumulation models are derived from models of reaction time data [Luce, 1986] and are well suited for describing both behavioral response measures [Nosofsky and Palmeri, 1997] and neural activity [Gold and Shadlen, 2001; Perrett et al., 1998; Schall, 2003]. To model object recognition times with an Accumulation model, recognition is considered a process that accumulates evidence over time until a critical level of evidence is reached, at which time recognition is achieved, the process is terminated, and a response is made. To model neural activity with an Accumulation model, the population of neurons that underlie the recognition process accumulate activity until a critical level is reached [Gold and Shadlen, 2001; Hanes and Schall, 1996], at which time the process is complete and activity returns to baseline. A neural simulation of word priming [Becker et al., 1997] showed that repeated presentation of a stimulus caused a strengthening of the word's representation, which in turn caused the network to settle more quickly. Therefore, priming effects can be modeled as a shift in time of peak activity, which leads to shorter recognition times. Typically, the BOLD response is considered proportional to the *cumulative* underlying neural activity [Boynton et al., 1996; Henson et al., 2002; Rees et al., 2000]. As shown in Figure 2, when two activity functions have different peak times, but the same postpeak rate of decay, the function with the earlier peak has the smaller cumulative activity. The primed activity function peaks earlier and shows a smaller BOLD response. Therefore, an Accumulation model can explain the relationship between priming effects and repetition suppression.

But can Accumulation account for the atypical results reported above? Accumulation would predict that repeated objects in these experiments would have *longer* peak times and that the behavioral priming effect would be in the wrong direction. That is, repetition enhancement should accompany a performance deficit. Unfortunately, the experiments in question did not acquire behavioral performance measures that are useable in this type of analysis. However,

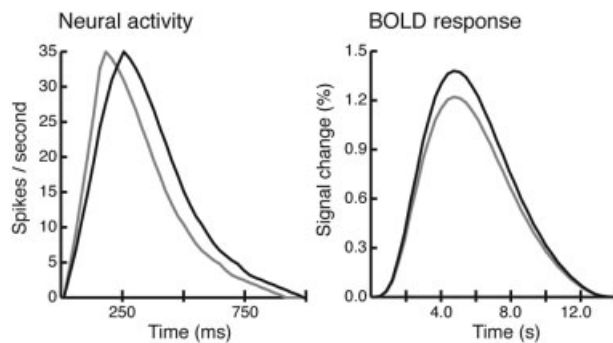


Figure 2.

Accumulation model. The right graph illustrates a simulated neural response to a single repeated (gray) and nonrepeated (black), nondegraded stimulus. The left graph illustrates a simulated BOLD response to those same stimuli. Note that the neural activity and BOLD response graphs use different time scales. The primed neural activity is shifted leftward in time and produces a smaller BOLD response.

unpublished data from our laboratory support this hypothesis. Using a gradual presentation technique reported previously [James et al., 2000], we measured BOLD time courses to primed and nonprimed novel objects. Identification times were faster for nonprimed objects, which also had a *faster* rise to peak activation. The Accumulation model, therefore, has the potential to explain a wider range of results than the Suppression model.

The Accumulation model suggests that differences between primed and nonprimed activation are due to differences in the temporal dynamics of the underlying neural activity. At least three studies [Henson et al., 2002; James et al., 1999, 2000] have used functional MRI (fMRI) to explore the temporal dynamics of visual object priming in humans. All of these studies found that priming shortened the time to reach peak BOLD and hypothesized that this reflected a similar pattern in the underlying neural activity: that priming enhanced the rate of accumulation of neural activity following stimulus onset. But fMRI is not the best neuroimaging technique for resolving the timing of neural events. The temporal resolution of magnetoencephalography (MEG) is much greater than that of fMRI. There are at least two MEG studies [Dale et al., 2000; Noguchi et al., 2004] that explored the temporal dynamics of visual object priming. One of these studies [Dale et al., 2000] found that nonprimed objects produced more activity than primed objects after 385 ms poststimulus onset. This effect is similar to the late positive effect reported in many event-related potential (ERP) studies of priming [for review, see Rugg, 1995]. The MEG study, however, did not investigate the possibility that primed objects could produce more activity than nonprimed objects at some other point in the time course. Examination of the raw images suggests that earlier than 185 ms primed objects produced more activity than nonprimed objects in posterior cortex. This supposition is supported by another more recent MEG study [Noguchi et al., 2004]. In that study,

activity for primed objects peaked earlier than for non-primed objects and activity for nonprimed objects persisted longer than for primed objects. In other words, primed objects initially produced more activity, but were eventually overtaken by the nonprimed objects once the primed object activity reached its peak. Of interest was the finding that the primed peak was also reduced in magnitude compared to the nonprimed peak, suggesting that repetition suppression may reflect a combination of Accumulation and Suppression models. This idea is further explored below and in the Discussion section.

Single-unit recordings also have high temporal resolution compared to fMRI. The neurophysiological studies reported above [Li et al., 1993; Miller et al., 1991] found suppression of single-unit activity upon repeated exposure to an object stimulus, with little evidence for accumulation. Several other neurophysiological studies, however, have found the opposite result [for example, see Bichot and Schall, 1999, 2002], suggesting that response suppression is not ubiquitous and that repetition effects in single-units may be sensitive to the contexts and demands of different experimental procedures.

In summary, the Suppression and Accumulation models both relate priming effects to repetition suppression and both models are supported by neurophysiological evidence. There is growing evidence that Accumulation may account for more priming phenomena than Suppression [Henson and Rugg, 2003], but to date there has been no empirical test of the two models using fMRI. Here, we used fMRI in combination with backward masking to evaluate the contribution of preidentification processes to the BOLD response. As illustrated in Figures 1 and 2, measuring BOLD responses with successfully identified objects *does not* dissociate the Accumulation and Suppression models. Both models predict a reduction in BOLD response with repetition. As Figure 3 demonstrates, however, when the objects are effectively masked and processing is terminated before identification occurs, the Accumulation and Suppression models make opposite predictions. The Suppression model predicts that effectively masked primed objects will produce *less* activation than nonprimed objects, whereas the Accumulation model predicts that effectively masked primed objects will produce *more* activation than nonprimed objects.

Three assumptions are necessary for this prediction. The first assumption is that effective masking implies truncation of neural activity. Backward masking phenomena are complex and the effects on neural activity are not completely understood. Nevertheless, neurophysiological studies find that masked stimuli produce less activity than unmasked stimuli [Macknik and Livingstone, 1998; Rolls et al., 1999], suggesting that masking does truncate neural activity. The second assumption is that the decay functions for primed and nonprimed objects must be equivalent for effectively masked stimuli. A previous MEG study [Noguchi et al., 2004] showed that nonprimed activation functions are wider than primed functions, suggesting that peak activation may persist for nonprimed objects. The objects in that study, however, were all successfully recognized

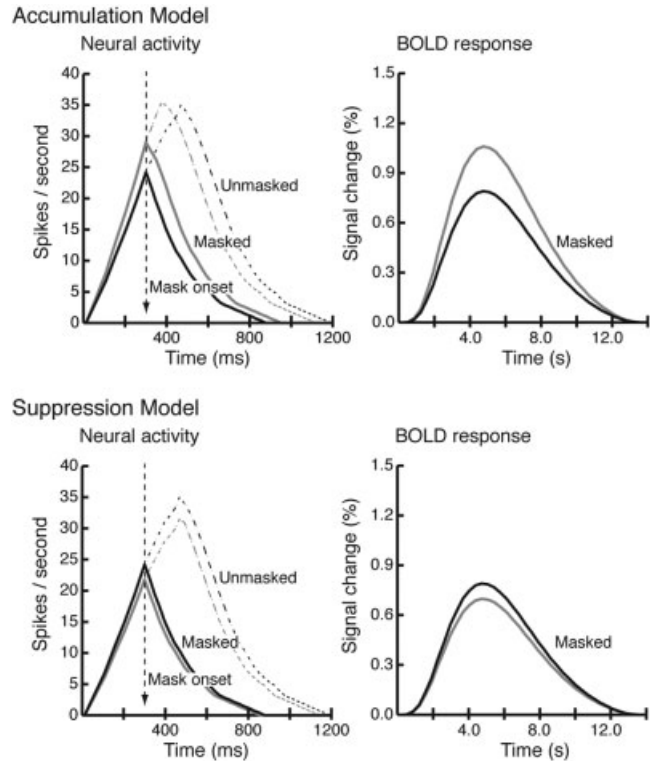


Figure 3.

Backward masking predictions. The right graphs illustrate a simulated neural response to a single repeated (gray) and nonrepeated (black), stimulus embedded in noise and masked. The left graphs illustrate a simulated BOLD response to those same stimuli. Note that the neural activity and BOLD response graphs use different time scales. Termination of activity due to masking produces opposite results in BOLD response for Accumulation and Suppression models.

and it is likely that the persistence reflected postrecognition cognitive operations such as differential deployment of attention to primed and nonprimed objects. With effectively masked objects, primed and nonprimed stimuli cannot be distinguished because they do not reach awareness. In this case, primed and nonprimed objects will not be subjected to different cognitive operations; therefore, equating their decay functions seems a reasonable assumption. With successfully identified objects, different cognitive operations performed on nonprimed and primed objects may cause a shallower decay slope for nonprimed objects than for primed. The effect of this shallower nonprimed decay slope, however, would be to exaggerate the effect already predicted by the Accumulation model. Because our predictions are qualitative, not quantitative, we did not use different decay slopes for nonprimed and primed successfully identified objects. The third assumption is that the peak magnitude of the neural activity function for primed and nonprimed objects is equivalent. The MEG study described above [Noguchi et al., 2004] suggested that peak magnitude for primed objects was lower than for nonprimed

and concluded that a combination of Accumulation and Suppression models accounted best for their results. Although a quantitative fit of the data may benefit from a combination of the two models, for our qualitative predictions we wanted to maximally dissociate the Accumulation and Suppression models. Therefore, the Accumulation model did not include changes in peak magnitude and, likewise, the Suppression model did not include changes in peak latency. In short, our study is a test of whether the Suppression model alone can account for repetition suppression in fMRI—ruling this out would not exclude the possibility that a combination of the two models may be a better fit for the data than the Accumulation model alone.

SUBJECTS AND METHODS

Participants

Of the nine participants, six were male and three were female. They were postdoctoral fellows, research assistants, graduate students, or undergraduate students attending Vanderbilt University. None had any reported history of neurological disorder and all reported normal or corrected-to-normal vision. The Vanderbilt University institutional review board approved the protocol and all participants signed informed consent.

Stimuli

Images of 162 familiar objects were selected from Hemera Photo-Objects images II (Hemera; <http://www.hemera.com>). Objects were selected such that no two objects shared the same common name (e.g., chair). During the LOC localizer runs, 81 of the 162 objects were presented as undegraded, full contrast images. The remaining 81 objects were also presented, but were scrambled on a 20×20 grid (Fig. 4). During the event-related runs, all 162 objects were presented intact (not scrambled), but they were degraded by reducing their contrast to either 0.08, 0.18, or 0.40, and by embedding them in random noise that was normally distributed with a standard deviation equal to one-eighth of the possible luminance range (Fig. 5A). When presented in the scanner, viewed through a set of Visuastim XGA goggles (MRI Devices, Waukesha, WI), images subtended 17.6° of visual angle. The subset of 81 objects that was intact or scrambled was counterbalanced across participants, which effectively counterbalanced the primed and nonprimed object sets.

Procedures

Imaging runs were divided into three LOC localizer runs and six event-related masking runs. For the three LOC localizer runs, images were presented in a blocked design paradigm with six 18-s stimulation blocks and seven 9-s rest blocks per run. Stimuli were full-contrast images of objects, both intact and scrambled (Fig. 4). In each run there were three intact and three scrambled blocks, with nine images per block, each presented for 2 s. During the three runs each of the 81 intact and 81 scrambled images was presented only

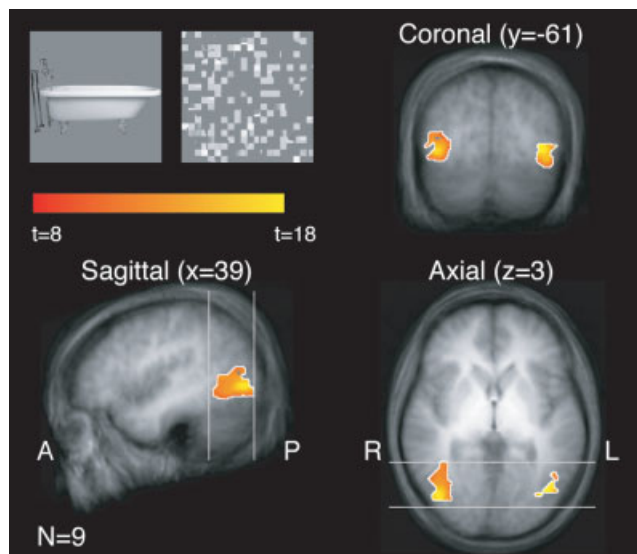


Figure 4.

Lateral occipital complex. Stimuli used in the localizer runs were high-contrast intact and scrambled images of familiar objects. Brain images show the extent of the acquired functional data and, within that area, the location of group LOC averaged across nine observers (stereotaxic coordinates: $x = 39$, $y = -61$, $z = 3$; $x = -39$, $y = -64$, $z = -1$). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

once. Participants passively viewed the objects for the localizer runs and were not told that the objects would be seen again in the following runs.

The six masking runs always followed the localizer runs. For the masking runs, images were presented in an event-related design. Half of the objects presented in these six runs were the 81 intact objects used in the localizer runs (primed) and half were the 81 scrambled objects (nonprimed). Images of these objects were presented at three levels of contrast and were embedded in noise (Fig. 5A). There were 27 trials per run; each trial consisted of an 800-ms warning cross, 83-ms stimulus presentation, and 117-ms mask, followed by 8 s of rest. On each trial, participants attempted to silently name the object and responded with a four choice confidence judgment about the name they were able to generate. Their choices were 1) definitely identified the object; 2) fairly sure they identified it, but not definite; 3) not sure what it was, but saw something or could guess; 4) definitely did not identify it, could not guess, or saw only noise. Choices were made using a four-button response pad with the four fingers of the right hand.

Imaging Parameters

All imaging was done using a 3 T, whole-body GE MRI system and a birdcage head coil located at the Vanderbilt University Medical Center (Nashville, TN). The field of view was $24 \times 24 \times 6.3$ cm, with an in-plane resolution of 64×64 pixels and 9 contiguous coronal scan planes per volume,

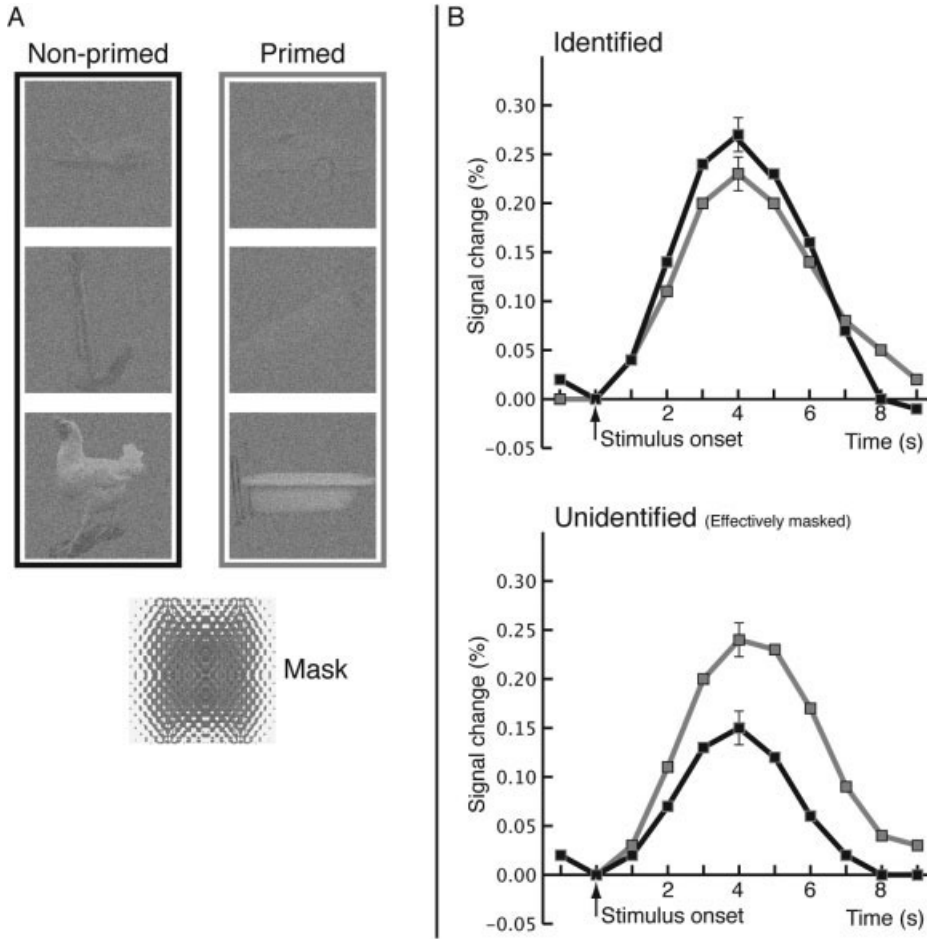


Figure 5.

Backward masking results. Stimuli used in the event-related runs, shown in **A**, were images of familiar objects presented at three levels of contrast and embedded in Gaussian noise. Half of the images were pre-exposed during the localizer runs (primed). Stimulus presentation (83 ms) was preceded by a warning fixation cross (800 ms) and followed by the mask stimulus (117 ms), then followed by 8 s of rest. Activation time courses are shown in **B** for identified (top) and unidentified or effectively masked (bottom) objects. Black lines: nonprimed; gray lines: primed. Error bars are square root of MSE/n. Accumulation predictions for the upper and lower graphs can be found in Figures 2 and 3, respectively.

resulting in a voxel size of $3.75 \times 3.75 \times 7.0$ mm. Images were collected using a T_2^* -weighted EPI acquisition (TE = 25 ms, TR = 1000 ms, flip angle = 70°) for blood oxygen level-dependent (BOLD)-based imaging. High-resolution T_1 -weighted anatomical volumes were also acquired using a 3D fast spoiled grass (FSPGR) acquisition (TI = 400 ms, TE = 4.18 ms, TR = 10 ms, flip angle = 20°). The imaging data were preprocessed using the Brain Voyager 3D analysis tools. Functional data underwent 3D motion correction, 3D spatial Gaussian smoothing (full-width at half-maximum 6 mm), temporal Gaussian smoothing (FWHM 2.8 s), linear trend removal, and slice scan-time correction.

RESULTS

Confidence judgments recorded during the six masking runs were analyzed using a 3×2 two-way ANOVA with stimulus contrast and preexposure as factors. As the dependent measure, we calculated percentage recognition as the number of objects rated “identified” relative to the combined number of objects rated “identified” or “unidentified” (Table I). The analysis revealed a significant main effect of stimulus contrast ($F_{(2,7)} = 14.3, P < 0.005$). The lowest contrast images were recognized worst (13%) and the highest

contrast images were recognized best (78%). A planned comparison between primed and nonprimed objects collapsed across contrast found a small, but reliable, priming effect ($t_{(8)} = 2.25, P < 0.05$). Primed objects were rated identified 48% of the time, whereas nonprimed objects were rated identified 43% of the time. Another dependent measure was calculated by averaging the confidence ratings (1–4) for each object and showed the same pattern of results. Response times did not show a priming effect, but identified judgments were made more quickly than unidentified judgments ($t_{(8)} = 2.73, P < 0.05$, paired). The lack of a priming effect in response times was expected, due to the nonspeeded nature of the task. The confidence judgment task was not designed to infer neural processing time of primed and nonprimed

TABLE I. Percent identified as a function of preexposure and contrast

	Contrast			Mean
	0.08	0.18	0.40	
Nonprimed	12%	41%	74%	43%
Primed	14%	49%	80%	48%
Mean	13%	45%	77%	

objects, but instead was designed to categorize trials based on whether or not objects were identified. Furthermore, it has been suggested that increased time-on-task may reflect increased neural effort and is correlated with increased BOLD signal [Buckner et al., 1998b]; therefore, using the nonspeeded confidence judgment task decreased the likelihood that time-on-task was influencing BOLD signal changes.

The lateral occipital complex (LOC) activates more strongly when viewing intact images or line drawings of objects than when viewing other visual stimuli [Malach et al., 1995]; therefore, area LOC is a relatively high-level visual processing center selective for objects. Although many brain regions show evidence of repetition suppression [Buckner et al., 1998a; James et al., 2000], we chose to focus on area LOC because it shows the most consistent and substantial repetition effects [Schacter and Buckner, 1998; Wiggs and Martin, 1998]. The location of the group LOC was found by collapsing data from nine participants and comparing the intact and scrambled object conditions in the three LOC localizer runs using the Brainvoyager GLM analysis tool. Figure 4 shows the location and extent of this region. Time courses were extracted from the left and right group LOC for each participant and were collapsed across trials for primed and nonprimed preexposure conditions and confidence judgments of “identified” and “unidentified” using the Brainvoyager event-related analysis tool. Raw BOLD responses were converted to percent signal change using the activation at stimulus onset as a baseline. The unidentified confidence condition was analyzed because it was the critical condition for dissociating the two models. The identified confidence condition was analyzed because it was considered a good control condition; it was the most similar to conditions used in previous priming studies. Because participants were given four choices for confidence ratings, the likelihood that the unidentified or identified confidence conditions were contaminated with guesses was low. Combining hemisphere, preexposure and confidence as factors produced a $2 \times 2 \times 2$ factorial design. Although the intermediate confidence judgments were not included in the following analysis, we did confirm that the magnitude of the BOLD response for the two intermediate judgments fell between the identified and unidentified conditions, as found in previous research [Bar et al., 2001].

With peak BOLD response as the dependent variable, the three-way ANOVA revealed a two-way interaction between confidence and preexposure ($F_{(1,8)} = 13.8, P < 0.01$) and a main effect of confidence ($F_{(1,8)} = 7.74, P < 0.05$), but no other significant effects. The same ANOVA performed on the mean BOLD response calculated between 2 and 6 s poststimulus onset produced the same result. Likewise, similar results were obtained when data were taken from a cluster 8 times smaller than that shown in Figure 4. This cluster of voxels was completely subsumed by the LOC region shown in Figure 4 and was defined with a t -value of 14. The lack of any interaction with, or main effect of, hemi-

sphere implies that activation in area LOC was not lateralized; therefore, all further tests were performed on data collapsed across hemisphere. The main effect of confidence (recognized/unrecognized) on HR was not interpreted, being superseded by the more interesting confidence by preexposure interaction.

Figure 5B illustrates the interaction between confidence and preexposure. The Accumulation and Suppression models both predicted that BOLD response for the identified confidence condition would be greater for the nonprimed than primed objects (Figs. 1, 2). A one-tailed planned comparison on these means showed that the nonprimed BOLD response was greater than the primed BOLD response ($t_{(8)} = 2.28, P < 0.05$). For the unidentified confidence condition, the Accumulation and Suppression models made opposite predictions (Fig. 3). A two-tailed planned comparison on these means showed that the primed BOLD response was greater than the nonprimed BOLD response ($t_{(8)} = 5.23, P < 0.001$). This result is consistent with the Accumulation model, but is inconsistent with the Suppression model.

Of course, the Accumulation example shown in Figure 3, which matches the data shown in the lower graph in Figure 5B, could be generated with an atypical set of parameters. Similarly, there may be a set of parameters for the Suppression model that would produce the right pattern of activation. To rule out this possibility, we simulated activity using many combinations of parameters. In our simple simulation, activity was zero at stimulus onset and accumulated linearly with a particular slope until a predetermined peak activity was reached. It then decayed linearly back to zero with a particular slope. Our dependent measure was the difference in cumulative activity between a nonprimed and a primed stimulation. For the Accumulation model, primed simulations were the same as their nonprimed partner, except that the accumulation slope for the primed simulation was always greater. For the Suppression model, primed simulations were the same as their nonprimed partner, except that the accumulation slope for the primed simulation was always smaller, reflecting the smaller peak magnitude. The *difference* between nonprimed and primed slopes was treated as parameters, as was the timing of mask onset relative to stimulus onset. Using five accumulation slope values, three primed/nonprimed accumulation slope *difference* values, 13 peak activity values, three mask onset times, and 91 decay slope values produced 53,235 combinations of parameters for each model. For the Suppression model, no simulations produced greater cumulative activity for the primed condition than nonprimed condition, suggesting that the example in Figure 3 is representative of the Suppression model. For the Accumulation model, 53,211 (99.96%) of the simulations produced greater cumulative activity for the primed condition than nonprimed condition, suggesting that the example in Figure 3 is representative of the Accumulation model. Figures 3 and 5B illustrate the expected pattern of results based on an Accumulation model account of priming and repetition suppression.

DISCUSSION

To our knowledge, this experiment is the first empirical test comparing the Accumulation and Suppression models. The results are consistent with the Accumulation model, which predicted greater activation for effectively masked primed objects, and are inconsistent with the Suppression model [Wiggs and Martin, 1998], which predicted lesser activation for primed objects. The results add to the list of insufficiencies attributed to the Suppression model [Henson, 2003] and find support for the alternative Accumulation model. The Accumulation model not only accounts for our results, but also accounts for results from previous fMRI and PET studies [for review, see Cabeza and Nyberg, 2000; Schacter and Buckner, 1998], MEG studies [Dale et al., 2000; Noguchi et al., 2004], neurophysiological studies [Bichot and Schall, 1999, 2002], and a neural network model [Becker et al., 1997]. The Accumulation model may even account for the atypical repetition *enhancement* results that are found occasionally in fMRI studies [Henson et al., 2000; James et al., 2002b; Schacter et al., 1995]. The Accumulation model would predict that enhanced activation was the result of *poorer* performance with primed objects compared with non-primed. This hypothesis is difficult to test post hoc because the relevant experiments all used indirect tasks, which makes it difficult to extract a reliable behavioral estimate of processing time from the data. This does not imply, however, that the hypothesis cannot be tested using neuroimaging techniques, only that it has not been tested to date. Should such an experiment not result in poorer performance correlated with increased BOLD response, there are other plausible accounts of these atypical effects [Henson, 2003] that remain compatible with the Accumulation model.

When the Suppression model was first formalized it was the prevailing theory linking neural and behavioral repetition effects. The Suppression model [Desimone, 1996; Wiggs and Martin, 1998] posited a relationship between priming effects, repetition suppression in fMRI [Schacter and Buckner, 1998], and response (or repetition) suppression in single-unit recordings [Li et al., 1993; Miller et al., 1991]. At that time there was overwhelming evidence from neurophysiology that repeating stimuli caused a decrease in activity of neurons [Brown and Xiang, 1998; Desimone, 1996]. Since the establishment of the Suppression model, new evidence suggests that response suppression is not universal [Bichot and Schall, 1999, 2002]. These later studies found evidence for enhanced accumulation as a result of stimulus repetition. Our data relate only BOLD repetition suppression with priming effects. They do not speak directly to the role of single-unit responses. What, then, is the relationship between single-unit response suppression and Accumulation?

In our experiment, BOLD responses were measured while participants silently named objects. This task was chosen because naming is used extensively in the study of human priming effects, both behavioral and neuroimaging. Naming is an implicit task for which the response does not depend on the preexposure condition [Roediger and McDermot, 1993; Schacter et al., 1993]. In experiments that find response

suppression, delayed match-to-sample and serial recognition tasks are used because these are tasks that monkeys can perform. For serial recognition the monkey differentiates the preexposed (primed) and new stimuli with two separate responses. This task differs markedly from a naming task, requiring explicit recognition of preexposed stimuli and different responses based on preexposure. In delayed match-to-sample, stimuli either match (targets) or do not match (distractors) the sample. Responding to targets is similar to the explicit recognition task just described because the stimulus must be recognized as matching the previously seen sample stimulus. No explicit recognition is required for distractor stimuli, but monkeys are trained to withhold a response to repetitions of the distractors, which makes this task quite dissimilar from the naming task. Thus, response suppression acts during explicit recognition and during suppression of active response, but there is no evidence that it operates during an implicit naming task such as the one used here.

Another speculation about the relationship between single-unit response suppression and accumulation involves a neural network model of priming [Becker et al., 1997]. Becker's model is a recurrent neural network in which measurements are taken of the time taken for the network to settle on a particular object representation. Presenting a stimulus changes the connection strength between highly coactive nodes in the network, which is suggestive of "strengthening" or tuning the representation. The network requires less time to settle on a representation when a repeated (or primed) stimulus is presented. Measures of "single-unit activity" or even "network activity" are not typically analyzed for these models; however, others have speculated that a decrease in settling time in such a network may decrease the time over which the nodes in the representation are maximally activated [Henson, 2003]. Thus, the pattern of activation across the population of nodes could change with repetition in a manner similar to the Accumulation model, but it would not be necessary that every node in the network display the same change. It is quite possible that a population of nodes could display Accumulation changes, but that within that population individual nodes could show suppression, enhancement, or another pattern of change.

As stated above, the Suppression model was, for many years, the prevailing explanation for repetition reduction findings in neuroimaging experiments. A more recent account of the priming-related reduction in hemodynamic response, however, is Response Association [Dobbins et al., 2004; Logan, 1990]. The Response Association model makes the strong claim that changes in neural object representations are not responsible for repetition reduction. Instead, the model suggests that a response is associated with a particular object on the initial presentation and, consequently, input bypasses cortical object representations on subsequent presentations and directly activates the neural structures responsible for generating the associated responses. The model accounts for repetition reduction in neuroimaging because bypassing the object representations

reduces activation in object-selective brain regions. It also accounts for the response facilitation seen in behavior performance because directly accessing an associated response facilitates responding. Like the Suppression model, however, the Response Association model cannot explain the findings of the present study. Specifically, we found priming-induced changes for both identified and unidentified objects, but the Response Association model only predicts a reduction for identified objects; it does not predict an enhancement for unidentified objects. Our results do not rule out the action of response associations, yet they show clearly that priming-induced changes in BOLD response do reflect changes in object representations. Whether these changes are further modified by the action of response associations remains to be studied.

Our data show that the Suppression model alone cannot account for repetition suppression in fMRI, while the Accumulation model could account for the findings. Crucially, our results are consistent with the MEG results of Noguchi et al. [2004] in ruling out that Suppression alone can explain repetition suppression and in suggesting that an Accumulation model is an important factor in accounting for the changes that occur with object repetition. While a Suppression model does not appear necessary to account for our results, it may be that other fMRI findings, as suggested by Noguchi et al., can only be explained by integrating both models.

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