



Published in final edited form as:

*J Cogn Neurosci.* 2011 April ; 23(4): . doi:10.1162/jocn.2010.21501.

## The Price of Fame: The Impact of Stimulus Familiarity on Proactive Interference Resolution

Ranjani Prabhakaran and Sharon L. Thompson-Schill

University of Pennsylvania

### Abstract

Interference from previously learned information, known as proactive interference (PI), limits our memory retrieval abilities. Previous studies of PI resolution have focused on the role of short-term familiarity, or recency, in causing PI. In the present study, we investigated the impact of long-term stimulus familiarity on PI resolution processes. In two behavioral experiments and one event-related fMRI experiment, long-term familiarity was manipulated through the use of famous and nonfamous stimuli, and short-term familiarity was manipulated through the use of recent and nonrecent probe items in an item recognition task. The right middle frontal gyrus demonstrated greater sensitivity to famous stimuli, suggesting that long-term stimulus familiarity plays a role in influencing PI resolution processes. Further examination of the effect of long-term stimulus familiarity on PI resolution revealed a larger behavioral interference effect for famous stimuli, but only under speeded response conditions. Thus, models of memory retrieval—and of the cognitive control mechanisms that guide retrieval processes—should consider the impact of and interactions among sources of familiarity on multiple time scales.

### INTRODUCTION

The impact of previously learned information on future attempts to learn and remember, generally referred to as proactive interference (PI), has been the focus of much research because of the demonstration that this phenomenon limits our ability to retrieve from STM (Bennett, 1975; Keppel & Underwood, 1962). What are the mechanisms underlying the resolution of PI? And more generally, what are the factors that affect our ability to retain information in working memory? The answers to these questions have the potential to inform our understanding of the processing principles involved in several domains of cognition, as working memory has been shown to play an important role in language processing, problem solving, and reasoning (Federenko, Gibson, & Rohde, 2006; Jonides & Nee, 2006; Van Dyke & McElree, 2006; Just & Carpenter, 1992).

One can draw a distinction between two types of PI effects that have been reported in the literature: item-nonspecific PI, which refers to the buildup of interference from items once remembered for previous trials but which are now irrelevant, and item-specific PI, which refers to interference caused by stimulus overlap from one trial to the next (see Postle, Brush, & Nick, 2004). The current study focuses on item-specific PI, which will henceforth be referred to simply as PI. Efforts to investigate the mechanisms underlying PI in short-term recognition memory have typically used a variant of the item recognition task (Sternberg, 1966). In this task, subjects are presented with items in a target set. After a delay, a probe item is presented, and the subject is asked to determine whether the probe

matches an item that was presented in the target set of the current trial. PI is induced via manipulation of the recency of the probe such that “recent negative” (RN) probes, which were presented in the previous (recent) but not in the current (negative) target set are typically associated with increased RTs and error rates relative to “nonrecent negative” (NN) probes, which have not been encountered for several trials (Monsell, 1978). These behavioral consequences of RN trials will be referred to as the “RN effect.” Monsell (1978) interpreted these findings as indicating an important role for recency in STM judgments, thus opening the door for further research on the mechanisms through which recency impacts memory. In addition, these results demonstrate an interaction between short-term and long-term memory, as the recency manipulation, which exceeds traditionally defined temporal windows of STM, was shown to have a significant impact on STM retrieval.

Following Monsell’s (1978) work and similar findings by McElree and Doshier (1989), neuroimaging studies have investigated the neural substrates that mediate PI resolution. Several of these studies have shown greater activation of ventrolateral and dorsolateral pFC (VLPFC and DLPFC) for RN relative to NN trials (a neural RN effect; Nee, Jonides, & Berman, 2007; Badre & Wagner, 2005; Postle et al., 2004; Mecklinger, Weber, Gunter, & Engle, 2003; Nelson, Reuter-Lorenz, Sylvester, Jonides, & Smith, 2003; D’Esposito, Postle, Jonides, & Smith, 1999; Jonides, Smith, Marshuetz, Koeppe, & Reuter-Lorenz, 1998). In particular, several of these studies have focused on the role of left VLPFC, corresponding approximately to Brodmann’s area (BA) 45, in resolving PI. A role for left VLPFC in mediating PI resolution has garnered additional support through converging neuropsychological (Hamilton & Martin, 2005; Thompson-Schill et al., 2002) and TMS (Feredoes & Postle, 2010) evidence.

A large body of literature has implicated a critical role for VLPFC and DLPFC in mediating cognitive control processes, such as resolving conflict between competing incompatible stimulus representations, across a variety of different tasks (e.g., Bedny, McGill, & Thompson-Schill, 2008; Badre & Wagner, 2007; Metzler, 2001; Milham et al., 2001; Miller & Cohen, 2001; Duncan & Owen, 2000; Smith & Jonides, 1999; Thompson-Schill, D’Esposito, & Kan, 1999; Gabrieli, Poldrack, & Desmond, 1998; Robinson, Blair, & Cipolotti, 1998; Thompson-Schill, D’Esposito, Aguirre, & Farah, 1997). The convergent finding of pFC involvement in PI resolution across neuroimaging, neuropsychological, and TMS studies suggests that general cognitive control processes may function to resolve PI during memory retrieval. However, the precise nature of this process has been the subject of debate. Several studies (e.g., Nelson et al., 2003; Thompson-Schill et al., 2002; D’Esposito et al., 1999; Jonides et al., 1998) argue in favor of a PI resolution mechanism that operates via inhibition of irrelevant familiarity information evoked by the RN probe. Alternatively, increased pFC activation has been characterized as the consequence of increased demands associated with determining the temporal context of RN probe items, which induce competition among incompatible contextual details from both the previous and the current trial (e.g., Nee et al., 2007; Badre & Wagner, 2005; Jonides, Marshuetz, Smith, Reuter-Lorenz, & Koeppe, 2000).

Investigations of the behavioral and neural correlates of PI across different stimulus domains may shed light on the factors that influence PI resolution and thereby provide constraints on theories of PI resolution mechanisms. The majority of previous studies of PI (e.g., Nee et al., 2007; Nelson et al., 2003; Thompson-Schill et al., 2002; Bunge, Ochsner, Desmond, Glover, & Gabrieli, 2001; D’Esposito et al., 1999; Jonides et al., 1998; Monsell, 1978) have focused primarily on PI resolution in verbal working memory, where the stimuli in the item recognition task consist of letters or words. Studies of PI resolution in nonverbal working memory reveal a somewhat different pattern of results, particularly in terms of the extent of pFC activity associated with nonverbal stimuli (e.g., Badre & Wagner, 2005; Leung &

Zhang, 2004; Postle et al., 2004; Mecklinger et al., 2003). For example, Mecklinger et al. (2003) found similar behavioral RN effects for letters and abstract objects; however, the neuroimaging data revealed a greater neural RN effect for letters than for objects in the left inferior frontal junction (BA 6/8/44). In addition, the right middle frontal gyrus (RMFG) demonstrated a neural RN effect only for letters. Mecklinger et al. suggested that the increased familiarity and verbalizability for letters compared with abstract objects may have increased demands on interference resolution, reflected by increased pFC activation for letter RN effects. Badre and Wagner (2005) also investigated the domain generality of the behavioral and neural correlates of PI resolution through the use of verbal (words) and nonverbal (abstract visual patterns) stimuli in the item recognition task. Although a behavioral RN effect was found for both words and abstract visual patterns, a reliable neural RN effect in BA 45 was only found for words; however, overall poorer performance for the pattern trials complicates interpretation of this null finding.

A closer inspection of the stimuli used in these studies reveals that verbalizability is confounded with the long-term familiarity of the stimuli. For example, the verbal stimuli (letters and words) are highly familiar, whereas the nonverbal stimuli (abstract objects and abstract visual patterns) are unfamiliar. As the role of familiarity in PI resolution is primarily investigated in terms of recency in STM, the effect of long-term stimulus familiarity on PI resolution remains unclear. The present study addressed this issue by directly investigating the effect of long-term stimulus familiarity on PI resolution processes. An item recognition task was used in which long-term stimulus familiarity was manipulated by using famous and nonfamous face stimuli. Famous stimuli corresponded to highly familiar modern-day actors and actresses, and nonfamous stimuli corresponded to unfamiliar people. As verbal coding of the stimuli may play a role in potential differences between processing of famous and nonfamous faces, famous and nonfamous name stimuli were also included in Experiments 1 and 2. Experiments 1 and 3 investigated the behavioral effects of the long-term stimulus familiarity manipulation on PI resolution. In Experiment 2, event-related fMRI was used to investigate the neural RN effect during the probe portion of trials in anatomically defined ROIs in pFC, namely, bilateral inferior frontal gyri (IFG), bilateral middle frontal gyri (MFG), and ACC on the basis of previous neuroimaging results (Nee et al., 2007; Badre & Wagner, 2005; Mecklinger et al., 2003; Nelson et al., 2003; Bunge et al., 2001; D'Esposito et al., 1999; Jonides et al., 1998). An exploratory whole-brain random-effects analysis was also performed. Neural RN effects for each stimulus category, the interaction between long-term familiarity and recency, and the relationship between behavioral and neural RN effects were evaluated.

What might be the effects of the manipulation of long-term stimulus familiarity on PI resolution processes? And how might these results shed light on previous studies of PI resolution in verbal and nonverbal working memory? The combination of the effects of long-term stimulus familiarity and recency may serve to enhance activation of the famous RN probe item, resulting in increased difficulty to reject the probe as a member of the current target set. Consequently, we predicted a larger behavioral and neural RN effect for highly familiar famous compared with unfamiliar nonfamous stimuli. This prediction is consistent with the speculation that increased neural RN effects for verbal compared with nonverbal stimuli reflect, in part, the greater long-term familiarity of the verbal materials used in previous experiments investigating the domain generality of PI resolution mechanisms.

## METHODS: EXPERIMENTS 1 AND 2

### Subjects

Fifty-three subjects (46 women, 7 men; age = 18–30 years) participated in Experiment 1 of this study. Data from one additional behavioral subject were excluded because of at-chance performance in one of the test blocks of the experiment. Sixteen subjects (9 women, 7 men; age = 21–33 years) participated in Experiment 2. Data from four additional subjects were excluded because of failure to complete the experiment and technical difficulties with data collection. All subjects were right-handed, native English speakers, and were not taking any psychoactive medications. In addition, all fMRI subjects in Experiment 2 possessed no bodily metal. Subjects were recruited from the University of Pennsylvania campus and gave informed consent before participating in the experiments according to guidelines established by the institutional review board of the University of Pennsylvania.

All subjects were prescreened to determine their familiarity with current famous movie actors and actresses before experimental participation. Each subject in Experiments 1 and 2 was given two prescreening questionnaires composed of 20 faces and 20 names (10 famous and 10 nonfamous in each questionnaire) not featured in the experiments. Subjects were instructed to indicate the familiarity of each face and name according to a scale from 1 to 3 (with 1 = *not familiar* and 3 = *very familiar*). Only those subjects who rated at least 70% of the famous movie stars with a familiarity rating of “3” were allowed to participate in each experiment.

### Stimuli

Four stimulus categories were used in Experiments 1 and 2: famous faces, famous names, nonfamous faces, and nonfamous names. Pictures of famous and nonfamous faces were obtained from Internet Web sites. Nonfamous name stimuli were created by the authors. Famous and nonfamous name stimuli were equated for the number of syllables and letters. All stimuli were normed via a familiarity-rating questionnaire that was administered to 12 individuals. Twenty stimuli (10 men, 10 women) that were consistently rated as “very familiar” were selected for each famous stimulus category, and 20 stimuli (10 men, 10 women) consistently rated as “not familiar” were selected for each nonfamous stimulus category.

### Behavioral Procedures

Subjects performed an item recognition task composed of a total of eight blocks, with two blocks of each of the four stimulus categories. The timing parameters and block and trial orders were identical for Experiments 1 and 2 (Figure 1). In each trial, a target set of four faces or names (depending on the block) was presented for 3 sec, followed by a delay period of 3 sec. The probe portion of the trial then followed, in which a single face or name was presented for 3 sec. The subject was instructed to indicate whether the single face or name was among the four faces or names presented at the beginning of the current trial. Subjects were instructed to press one of two buttons using a keyboard to indicate either a “yes” or a “no” response. An intertrial interval of 9 sec followed the probe portion of each trial.

Each block consisted of 30 trials, with the first two trials of each block composed of a “no” and a “yes” trial. The remaining 28 trials consisted of an equal number of the following four trial types: recent no (RN), nonrecent no (NN), recent yes (RY), and nonrecent yes (NY). In the RN trials, the probe was not a member of the current target set but did occur in both of the previous two target sets. In the NN trials, the probe stimulus did not occur in the current target set, nor did it occur in either of the two previous target sets. In the RY trials, the probe occurred as a member of the target set both in the current trial as well as in the previous trial.

In NY trials, the probe stimulus occurred as a member of the target set in the current trial but not in the preceding trial. To eliminate the possibility of the repetition of stimuli serving as a cue to the trial type, two stimuli (one man and one woman) repeated from one target set to the next. For those blocks in which semantically related celebrities co-occurred, these celebrities were assigned to different trials to prevent subjects from using semantic strategies to perform the task. All subjects were presented with a fixed pseudorandomized order of trials, and each face and name stimulus was seen approximately an equal number of times.

Each subject performed four practice blocks (one for each stimulus category) to familiarize them with all of the stimuli before beginning the experiment. Each practice block consisted of 30 trials (15 “yes” and 15 “no” trials), in which there was no interference manipulation. The experiment was run using E-prime software (Schneider, Eschman, & Zuccolotto, 2002). After the experiment, subjects were given separate familiarity-rating questionnaires for the faces and names and were instructed to rate the pre-experimental familiarity of each stimulus according to the scale described above (see Subjects section). Subjects were also instructed to write down any verbal labels that they may have used for the faces while doing the task.

### Functional Imaging Procedures (Experiment 2)

Anatomical and functional images were acquired using a 3-T Siemens MRI scanner with a standard four-channel head coil.<sup>1</sup> Before experimental runs, a three-dimensional, high-resolution anatomical MPRAGE data set was acquired for each subject. Functional images were then acquired during 8 blocks of the item recognition task (repetition time = 3000 msec, echo time = 30 msec, voxels =  $3 \times 3 \times 3$  mm), with each block lasting about 9 min. Forty-four slices per volume (slice thickness = 3 mm) were acquired in an interleaved fashion for each subject in the axial orientation. A total of 184 volumes were acquired in each block of the item recognition task. Each experimental block was preceded by 12 sec of “dummy” pulses to allow the scanner to reach steady-state magnetization. Subjects were instructed to make bimanual responses on a four-button fiber-optic response pad to indicate a “yes” or “no” response.

### fMRI Data Analysis

Offline fMRI data analysis was carried out using VoxBo ([www.voxbo.org](http://www.voxbo.org)) and SPM2 ([www.fil.ion.ucl.ac.uk](http://www.fil.ion.ucl.ac.uk)). Each subject’s data were realigned, thresholded, and spatially smoothed using a 9-mm FWHM Gaussian kernel. For whole-brain analyses, each subject’s anatomical and functional data were also normalized in SPM2, using a standard template in Montreal Neurological Institute space. Non-normalized anatomical images and functional data were reoriented to the coronal orientation from the axial orientation to facilitate ROI analyses (see next section). Each subject’s reoriented coronal data files were submitted to a general linear model (GLM) for serially correlated error terms (Worsley & Friston, 1995). Separate GLMs were run on each subject’s axial functional data for whole-brain analyses. For all correct trials, two orthogonal covariates were included in the GLM modeling the first second of the target memory set (modeled according to stimulus type: famous face, famous name, nonfamous face, and nonfamous name) and the first second of the probe/response component (modeled according to stimulus type and trial type: RN, NN, RY, and NY) of each trial. A separate covariate was also included to model the intertrial interval (baseline) component for all correct trials. Additional separate covariates were included to model the target set and probe/response components of incorrect trials as well as those trials that did not meet the appropriate familiarity criteria for a given subject.<sup>2</sup> All covariates of interest

---

<sup>1</sup>Three of the 16 subjects were scanned using a standard eightchannel head coil because of the unavailability of the four-channel head coil at the time of scanning.

were convolved with a standard hemodynamic response function. The following nuisance covariates were included in each subject's GLM: trial effects, global signal, and spike covariates. A  $1/f$  noise model derived from the first run of each subject's data was also included in the model. Beta values derived from each subject's first-level model were used to carry out second-level random effects analyses. Data analyses were restricted to the covariates modeling the probe component of the trial, as this is the trial component associated with PI (D'Esposito et al., 1999).

### Regions of Interest

Bilateral IFG, MFG, and ACC ROIs were drawn using the Duvernoy Brain Atlas as a reference (Duvernoy, 1991). Because of reported intersubject variability in the location of anatomical landmarks defining the boundaries of IFG (Amunts et al., 1999), masks were drawn for all ROIs on each subject's nonnormalized anatomical coronal brain image to preserve individual differences. The posterior and ventral-most portion of BA 44 of the IFG corresponding to the frontal operculum was excluded from IFG masks.<sup>3</sup>

For each subject, those voxels showing a greater neural response to the probe portion for all correct trials (including both "yes" and "no" trials) relative to baseline were first determined at a threshold of  $t = 2$ . These voxels will be referred to as "task-responsive voxels." Within each anatomical ROI, the time series for task-responsive voxels were averaged. Within this set of voxels, secondary contrasts were performed comparing activation for the probe portion of RN relative to NN trials for each stimulus type. The beta values, or regression weights, for each secondary contrast for each subject were submitted to one-sample  $t$  tests to determine the reliability of these deviations from zero.

## RESULTS: EXPERIMENTS 1 AND 2

RN Effects correspond to the difference between RN and NN trials on each measure of interest (RTs, percent error rates, and beta values). As in previous studies (e.g., Badre & Wagner, 2005), failures to respond were coded as errors. Results from only RN and NN trials are presented for each experiment, as these trials constitute the primary trials of interest (Table 1). RN effects across all subjects for each stimulus condition are presented in Figure 2. Only correct responses were included in the analyses of median RTs and the fMRI data.

### Experiment 1

Planned paired  $t$  tests revealed a significant RT RN effect for famous names,  $t(52) = 6.34$ ,  $p < .001$ , famous faces,  $t(52) = 6.18$ ,  $p < .001$ , nonfamous names,  $t(52) = 5.81$ ,  $p < .001$ , and nonfamous faces,  $t(52) = 6.28$ ,  $p < .001$  (Figure 2A, left). However, although a significant RN effect was found within each stimulus category, the magnitude of the RN effect did not vary as a function of fame ( $F < 1$ ). Subjects showed significantly longer RTs for nonfamous compared with famous stimuli, collapsing across stimulus type (face, name) and recency,  $F(1, 52) = 9.89$ ,  $p < .01$ .<sup>4</sup>

<sup>2</sup>Those trials containing famous probe stimuli that were rated as unfamiliar by the subject were removed from the behavioral and fMRI analysis for that subject's data. The same procedure was followed for those nonfamous probe stimuli that were rated as being very familiar by the subject.

<sup>3</sup>Cytoarchitectural studies have demonstrated that the frontal operculum and adjacent ventral premotor cortex (BA 6) have similar agranular cytoarchitectonic properties and thus may differ from the rest of dysgranular BA 44 and granular BA 45 with respect to function (Friederici, 2006; Amunts et al., 1999).

<sup>4</sup>In light of this result, data were also analyzed in terms of proportional RN effects. This analysis similarly showed that proportional RN effects did not vary as a function of fame.

Planned paired  $t$  tests showed a significant percent error RN effect for famous names,  $t(52) = 4.58, p < .001$ , famous faces,  $t(52) = 5.34, p < .001$ , nonfamous names,  $t(52) = 2.99, p < .01$ , and nonfamous faces,  $t(52) = 5.90, p < .001$  (Figure 2A, right). However, as for the RT data, although significant RN effects were found within each stimulus category, the interaction between fame and recency failed to reach significance ( $F < 1$ ). Subjects made significantly more errors on nonfamous compared with famous trials, collapsing across stimulus type (face, name) and recency,  $F(1, 52) = 7.67, p < .01$ , and more errors for face compared with name trials, collapsing across fame and recency,  $F(1, 52) = 21.72, p < .001$ . A Stimulus Type  $\times$  Recency interaction was found, resulting from a larger percent error RN effect for face compared with name trials,  $F(1, 52) = 7.19, p < .05$ . However, the three-way interaction effect between fame, stimulus type, and recency failed to reach significance for both RTs and percent error rates ( $F_s < 1$ ), indicating that there was no significant difference in the magnitude of the RN effect difference between famous and nonfamous names and famous and nonfamous faces.

## Experiment 2

**Behavioral Results**—As in Experiment 1, no significant Fame  $\times$  Recency interaction effect was found in either RT or percent error data ( $F_s < 1.3$ ). Planned paired  $t$  tests revealed significant RT RN effects for famous names,  $t(15) = 2.39, p < .05$ , famous faces,  $t(15) = 4.67, p < .001$ , nonfamous names,  $t(15) = 2.13, p < .05$ , and a marginally significant RN effect for nonfamous faces,  $t(15) = 2.04, p = .06$  (Figure 2B, left).

Planned paired  $t$  tests revealed a significant percent error RN effect for famous names,  $t(15) = 2.72, p < .05$ , and nonfamous faces,  $t(15) = 3.53, p < .01$  (Figure 2B, right). Although subjects tended to make more errors for RN compared with NN trials for the famous faces and nonfamous names conditions, these differences failed to reach significance ( $p_s > .2$ ) (Figure 2B, right). As in Experiment 1, the three-way interaction effect between fame, stimulus type, and recency failed to reach significance for both RTs and percent error rates ( $F_s < 1.7$ ).

## fMRI Results

**Main effects of recency:** When we collapsed the data across all four stimulus conditions, we found a reliable neural RN effect (i.e., more activity for RN compared with NN trials) for task-responsive voxels in the left IFG (LIFG),  $t(15) = 3.73, p < .01$  (Figure 3A), and left MFG (LMFG),  $t(15) = 3.40, p < .01$  (Figure 3B). Although task-responsive voxels in the right IFG (RIFG; Figure 3C), RMFG (Figure 3D), and ACC (Figure 3E) demonstrated greater activity for RN compared with NN trials, these RN effects failed to reach significance ( $p_s > .1$ ). For famous stimuli (collapsed across faces and names), we found reliable RN effects in the LIFG,  $t(15) = 2.17, p < .05$ , LMFG,  $t(15) = 2.65, p < .05$ , RMFG,  $t(15) = 2.38, p < .05$ , and a marginal RN effect in the RIFG,  $t(15) = 1.82, p = .09$ . For nonfamous stimuli (collapsed across faces and names), we found reliable RN effects only in *left* lateral pFC regions: LIFG,  $t(15) = 4.79, p < .001$ ; LMFG,  $t(15) = 3.04, p < .01$ ; the RN effect in *right* lateral pFC regions did not approach significance ( $p_s > .5$ ). Most of the RN effects for individual stimulus conditions did not reach significance; the two exceptions were the marginally significant RN effects for nonfamous faces in the LIFG,  $t(15) = 1.99, p = .07$ , and LMFG,  $t(15) = 2.05, p = .06$ .

**Does fame matter?:** An examination of the impact of long-term stimulus familiarity on PI resolution failed to reveal significant Fame  $\times$  Recency interaction effects in our frontal ROIs (all  $p_s > .1$ ). However, the results of several post hoc analyses suggest that rejection of the hypothesis that long-term stimulus familiarity impacts PI resolution would be premature. We describe each of these analyses below.

**ROI results: binomial test:** Although the Fame  $\times$  Recency interaction effects did not reach significance in any ROI, we were struck by the consistency of the pattern of the (nonsignificant) differences between famous and nonfamous trials: Out of 10 comparisons (two pairs of famous vs. nonfamous effects in each of five ROIs), 8 famous RN effects demonstrated greater activity compared with nonfamous RN effects. The binomial probability that 8 of 10 comparisons would appear in the same direction by chance is  $p = .04$ . As we will return to below, the two contrasts that showed the reverse pattern were in left pFC. Therefore, although none of the individual contrasts yielded a reliable difference between famous and nonfamous RN effects, the overall pattern is inconsistent with a null effect of fame.

**Individual differences analysis:** A consistent pattern across the ROI results was the considerable variability observed across subjects in terms of the magnitude of neural RN effects. To explore whether this variability in the magnitude of neural RN effects was related to the variability in behavioral RN effects, we calculated correlations between these measures for each ROI and each stimulus condition. We predicted that those regions sensitive to the long-term familiarity of a stimulus (i.e., fame in the current study) should demonstrate activity that is related to the extent of behavioral interference in response to famous stimuli. To ensure robustness of the individual differences analysis results, we report only those correlations for which both Pearson's  $r$  and Spearman's rho coefficients were significant.

A significant negative correlation was found between the percent error RN effect and the neural RN effect for famous face stimuli in the RMFG (Pearson  $r = -.76, p < .01$ ; Spearman's rho =  $-.61, p < .05$ ) (Figure 4A and B). That is, those subjects who demonstrated a greater RMFG famous face neural RN effect also demonstrated a *smaller* behavioral percent error RN effect in response to famous faces. In contrast to the result obtained for famous faces, the percent error RN effect in response to nonfamous faces did not predict the RMFG nonfamous faces neural RN effect (Pearson  $r = -.09, p = .74$ ; Spearman's rho =  $.03, p = .92$ ) (Figure 4C). In addition, the strength of the relationship between behavioral and neural RN effects for famous faces was found to be significantly greater than for nonfamous faces in RMFG ( $r = -.76$  vs.  $r = -.09, z = -2.32, p < .05$ ). It is interesting to note that Mecklinger et al. (2003) found reliable RN effects only for familiar stimuli in the RMFG. Although the interaction between fame and recency was not significant in this region, we do note that the RN effect was only reliable for famous stimuli, which is consistent with the findings of Mecklinger et al.

One difference between famous and nonfamous faces is that subjects are more likely to verbally recode (i.e., label) famous stimuli. Thus, the high correlation between behavioral and neural RN effects for famous face stimuli in the RMFG could be driven by this verbal strategy. However, this explanation of the pattern of individual differences in RMFG appears unlikely for the following reasons. Although subjects labeled a greater percentage of famous faces (mean = 84.0%) compared with nonfamous faces (mean = 73.4%), this labeling difference failed to reach significance,  $t(15) = 1.61, p = .13$ . To determine the contribution of verbalization of the famous faces to the correlation between behavioral and neural famous face RN effects in RMFG, we calculated a partial correlation to control for the variance accounted for by the percentage of famous faces labeled by each subject. Even after controlling for labeling of famous faces, the relationship between behavioral and neural RN effects in response to famous face stimuli in RMFG remained statistically significant (partial  $r = -.77, p < .01$ ). Thus, it appears that verbalization of the famous face stimuli cannot explain the pattern of results obtained in RMFG.

**Exploratory whole-brain random effects analysis:** The results of exploratory whole-brain analyses are shown in Figure 5 at an uncorrected threshold of  $p < .001$  for the following contrasts (collapsing across stimulus type): famous RN effect (Figure 5A) and nonfamous RN effect (Figure 5B). Perhaps the most striking feature of the whole-brain analyses is the lateralization of activity for famous and nonfamous RN effects. Whereas famous RN effects appear to be mediated by right pFC, nonfamous RN effects appear to be mediated by left pFC.

To further explore the lateralization of RN effects, we investigated the presence of Fame  $\times$  Recency  $\times$  Hemisphere interactions in our ROI results. A significant Fame  $\times$  Recency  $\times$  Hemisphere interaction effect was found for the MFG,  $F(1, 15) = 5.78$ ,  $p < .05$ , because of a larger famous versus nonfamous RN effect in RMFG compared with LMFG. Although the RIFG demonstrated a larger famous versus nonfamous RN effect compared with LIFG, the Fame  $\times$  Recency  $\times$  Hemisphere interaction for IFG failed to reach significance ( $F < 1.6$ ).

Although exploratory in nature, these results, along with the greater sensitivity of RMFG to famous RN effects, point toward a role for long-term stimulus familiarity in impacting PI resolution processes.

### EXPERIMENT 3

On the basis of the results of Experiment 1 alone, it would appear that the long-term familiarity (i.e., fame) of the stimuli does not impact the magnitude of short-term recency effects in the RNs paradigm. In contrast, the results of Experiment 2 appear somewhat mixed. Although we failed to find reliable Fame  $\times$  Recency interaction effects in frontal neural regions, the results of several post hoc analyses, which indicate an impact of long-term stimulus familiarity on neural short-term recency effects, make us uncomfortable rejecting the hypothesis that there is an interaction between these two sources of familiarity. One explanation for the discrepancy between the behavioral and the neural results and also for the weak neural evidence for an interaction between long-term familiarity and short-term recency is that this interaction may occur only during the initial stages of evaluating the probe. Under this explanation, we may have been unable to capture this interaction using behavioral methods alone in Experiment 1, as subjects were not placed under time pressure to indicate their response. The behavioral results of Experiment 2 fall under the same limitation. In contrast, the neural results of Experiment 2 may reflect our ability to capture the initial interaction between long-term familiarity and short-term recency using neuroimaging methods. However, as the fMRI signal integrates the neural response over a longer time scale, it is perhaps not surprising that the fMRI results provide weak evidence for an impact of long-term stimulus familiarity on PI resolution. Experiment 3 was designed to test the hypothesis that long-term and short-term familiarity would interact in a time course dependent fashion. That is, we predicted that by creating a situation that encourages familiarity-based responses, we would be better able to capture the interaction between long-term and short-term familiarity.

A great deal of prior research indicates a relationship between the time course and the type of recognition memory processing mechanism invoked in a given situation. Dualprocess theories of recognition memory propose that familiarity and recollection both play important roles in influencing recognition judgments (e.g., Rugg & Yonelinas, 2003; Yonelinas, 1994; Mandler, 1980; Atkinson & Juola, 1974). These two processes have also been shown to operate on differential time courses: familiarity operating as a fast, global assessment early in retrieval and recollection involving the slower recovery of episodic details (e.g., Curran, 2000; McElree, Dolan, & Jacoby, 1999; Hintzman & Curran, 1994; McElree & Doshier, 1989). Öztekin and McElree (2007) investigated the effects of item-nonspecific PI across

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

trials drawn from the same semantic category on familiarity versus recollective processes. The RN effect was used as an index of subjects' reliance on familiarity assessments, with a larger RN effect indicating a greater reliance upon familiarity. Öztekin and McElree found that item-nonspecific PI (because of the buildup of interference from items in the same semantic category) resulted in a reduction of the magnitude of the RN effect, but only at shorter response deadlines. As Experiments 1 and 2 of the current study used a long response deadline of 3000 msec, the RN effects observed in these experiments may reflect the recovery of episodic information rather than subjects' reliance on fast familiarity assessments. That is, on the basis of Öztekin and McElree's results, it is possible that long-term stimulus familiarity functions similarly to item-nonspecific PI in that both sources of semantic similarity may impact subjects' reliance on fast assessments of familiarity, but only at shorter response deadlines. Consequently, the use of longer response deadlines may have resulted in the lack of a behavioral interaction effect between long-term stimulus familiarity and recency in Experiments 1 and 2. However, our finding of greater neural sensitivity to famous stimuli in RMFG using fMRI in Experiment 2 may reflect the initial conflict arising from reliance upon fast familiarity assessments. To gain a greater understanding of long-term stimulus familiarity's impact on PI resolution processes in Experiment 3, we manipulated both the long-term stimulus familiarity and the response deadline using the item recognition task, with response deadline as a between-subjects factor. Thus, some subjects were given only 500 msec in which to make their decision about the probe item, whereas other subjects were given 3000 msec to make this decision. On the basis of the findings of Öztekin and McElree, we predicted that an interaction effect between long-term stimulus familiarity and recency would emerge under speeded response conditions, where subjects are more likely to rely upon fast assessments of familiarity.

## Methods

Sixty-four subjects (47 women, 17 men; age = 19–32 years) participated in Experiment 3. All subjects met the requirements listed above for Experiments 1 and 2. Subjects performed an item recognition task composed of a total of eight blocks, with four blocks of famous face trials interleaved with four blocks of nonfamous face trials. Some subjects in Experiments 1 and 2 reported only reading the first or last name of the famous and nonfamous name stimuli. Consequently, we did not include the name stimuli in Experiment 3, as speeded response conditions would only increase the likelihood that subjects would read only the first or last name of the name stimuli, thus compromising the fame manipulation. Behavioral procedures were modeled after Öztekin and McElree (2007) (Figure 6). Subjects saw a fixation cross for 500 msec, followed by four faces (target set), with each face presented for 500 msec in a serial fashion. Subjects were then presented with a scrambled visual pattern mask for 500 msec, followed by the probe stimulus. The duration of the probe stimulus served as a between-subjects variable, where half of the subjects were presented with the probe for 500 msec, and the other half were presented with the probe for 3000 msec. After probe presentation, a 50-msec tone sounded, cueing subjects to respond. Subjects were instructed to indicate their response by pressing one of two buttons using a keyboard to indicate either a “yes” or “no” response within 500 msec of the onset of the tone.

Each block was composed of 66 trials, the first two of which were “yes” and “no” trials. The remaining 64 trials were composed of equal numbers of each of the trial types employed in Experiments 1 and 2. Subjects were presented with a fixed pseudorandomized order of trials, where trials were designed with the same constraints as employed in Experiments 1 and 2. All subjects completed two practice blocks of 60 trials (one block for each stimulus category) with no interference to familiarize them with all of the stimuli as well as the task procedure. After the experiment, subjects completed a familiarity-rating questionnaire for the face stimuli.

## Results

The mean of median RTs and percent error rates for RN and NN trials in each stimulus condition are presented in Table 2. Each subject's behavioral RN effects for each stimulus condition were submitted to two-way mixed ANOVAs for the within-subject factors of fame (famous vs. nonfamous) and recency (recent vs. nonrecent) and the between-subjects variable of response deadline (500 vs. 3000 msec). The RT data demonstrated a significant Fame  $\times$  Recency  $\times$  Deadline interaction,  $F(1, 62) = 7.09, p = .01$ , because of a larger RT RN effect for famous compared with nonfamous trials in the 500-msec deadline condition. This is further evidenced by a significant Fame  $\times$  Recency interaction for RT RN effects in the 500-msec deadline condition,  $F(1, 31) = 4.81, p < .05$ . However, no significant Fame  $\times$  Recency interaction effect was observed for RT RN effects in the 3000-msec deadline condition,  $F(1, 31) = 2.76, p = .11$ . This result suggests a differential effect of fame on RN effects as a function of response deadline condition. However, it should be noted that the RT data may reflect the speed of subjects' motor responses rather than the speed of their retrieval process, particularly in the 3000-msec deadline condition. Thus, as a more sensitive test of the impact of fame on RN effects at different deadlines, we focus our discussion of the results on Fame  $\times$  Recency interaction effects observed in the percent error data (Figure 7).

Critically, we found a significant Fame  $\times$  Recency  $\times$  Deadline interaction,  $F(1, 62) = 5.62, p < .05$ , suggesting a differential impact of fame on the percent error RN effect for the different response deadline conditions. Significant main effects of fame, recency, and deadline were also found. Subjects showed higher percent error rates for nonfamous compared with famous trials, collapsing across both recency and deadline,  $F(1, 62) = 35.35, p < .001$ , as well as a significant percent error RN effect, collapsing across both fame and deadline,  $F(1, 62) = 196.93, p < .001$ . Collapsing across both recency and fame, percent error rates were higher for the 500-msec deadline condition compared with the 3000-msec deadline condition,  $F(1, 62) = 13.84, p < .001$ .

Separate ANOVAs were performed for the percent error data within each response deadline condition to further explore the observed interaction effects with response deadline. In the 500-msec deadline condition, a significant Fame  $\times$  Recency interaction emerged because of a larger percent error RN effect for famous compared with nonfamous stimuli,  $F(1, 31) = 6.83, p < .05$ . Significant main effects of fame and recency were also found. Percent error rates were significantly higher for nonfamous compared with famous trials, collapsing across recency,  $F(1, 31) = 25.25, p < .001$ , and there was a significant percent error RN effect, collapsing across fame,  $F(1, 31) = 83.66, p < .001$ . In contrast to the 500-msec deadline condition, no significant Fame  $\times$  Recency interaction was found for percent error rates in the 3000-msec deadline condition ( $F < 1$ ). However, significant main effects of fame and recency were found. Percent error rates were significantly higher for nonfamous compared with famous stimuli, collapsing across recency,  $F(1, 31) = 11.48, p < .01$ , and there was a significant percent error RN effect, collapsing across fame,  $F(1, 31) = 134.48, p < .001$ .

**Verbal Labeling Analysis**—Name stimuli were not included in Experiment 3 for the reason stated above. However, the inclusion of only famous and nonfamous face stimuli in Experiment 3 reintroduced the potential confound with verbalizability that we sought to avoid in Experiments 1 and 2. Consequently, we performed analyses by both subject and probe item to assess the contribution of verbalizability to the Fame  $\times$  Recency interaction effect observed in the 500-msec response deadline condition.

Subjects labeled a greater percentage of famous faces (mean = 70.2%) compared with nonfamous faces (mean = 45.1%),  $t(31) = 4.76, p < .001$ . To investigate the relationship

between percentage of famous faces labeled by each subject and the magnitude of subjects' percent error RN effect for famous faces, we calculated the correlation between these measures. This correlation failed to reach significance ( $r = -.01, p = .96$ ). The correlation between the percentage of nonfamous faces labeled and the magnitude of the percent error RN effect for nonfamous faces also failed to reach significance ( $r = -.28, p = .12$ ).

We also investigated the impact of verbalizability on percent error rates (averaged across subjects) for those probe items that occurred in both recent no and nonrecent no conditions, where verbalizability was calculated as the percentage of subjects that gave a verbal label for each probe face. As expected, the verbalizability of famous face probe items was significantly higher than for nonfamous face probe items,  $t(56) = 9.59, p < .001$ . Although this method of analysis does not take the verbalizability of the faces in the target set into account, it allowed us to determine whether those probe faces that were given a greater number of verbal labels were also associated with a larger percent error RN effect. A marginally significant effect of recency was found, such that percent error rates were higher for probe items when they appeared in the recent no compared with the nonrecent no condition,  $F(1, 56) = 3.10, p = .08$ . In addition, a main effect of verbalizability was found, such that those probe items that were more verbalizable were associated with lower percent error rates,  $F(1, 56) = 8.19, p < .01$ . However, the interaction effect between recency and verbalizability was not significant ( $F < 1$ ), suggesting that verbalizability of the probe faces did not affect their corresponding percent error RN effect. As evident in Figure 8, there was no monotonic effect of verbalizability for the percent error RN effect associated with famous face probe items (Pearson  $r = -.33, p = .09$ ) or nonfamous face probe items (Pearson  $r = .15, p = .42$ ); indeed, for famous faces, the trend is in the opposite direction as predicted by a verbalizability account of their effects. The distributions of the percent error RN effects for famous and nonfamous probe items in Figure 8 demonstrate a great deal of variability along with a greater range of verbalizability for the nonfamous compared with famous probe items. Although several factors may have impacted the percent error RN effects for famous and nonfamous probe items, the results of the analyses reported above suggest that the Fame  $\times$  Recency interaction effect in the 500-msec deadline condition is not entirely due to verbalizability.

## DISCUSSION

In light of previous studies of PI that have focused on short-term familiarity in the form of recency, the present set of experiments investigated the impact of long-term stimulus familiarity on PI resolution processes. We observed greater sensitivity to the RN effect associated with famous stimuli in RMFG. In addition, we found a larger behavioral RN effect for famous compared with nonfamous stimuli, but only under speeded response conditions. Potential implications for theories of PI resolution as well as for previous studies of domain generality of PI will be discussed in turn.

### Long-term Stimulus Familiarity and PI Resolution Mechanisms

The novel component introduced by the present study involves the investigation of how long-term stimulus familiarity impacts the processes that mediate PI resolution. The neuroimaging results from Experiment 2 suggested that long-term stimulus familiarity impacts PI resolution in the form of greater right pFC sensitivity to famous compared with nonfamous stimuli. We were able to resolve the discrepancy between our neural findings in Experiment 2 and the lack of modulation of behavioral RN effects by fame in Experiment 1 through a more fine-grained examination of the time course of long-term familiarity in Experiment 3. In sum, these results suggest that long-term familiarity plays an important

role in PI resolution. These findings raise the following question: How does long-term stimulus familiarity impact the putative PI resolution mechanisms carried out by pFC?

Jonides and Nee (2006) have proposed that PI resolution mechanisms can be viewed using the framework of the biased competition model (Desimone & Duncan, 1995; see also Kan & Thompson-Schill, 2004). This model contends that selection between multiple competing perceptual representations occurs through the use of an attentional template that contains goal-relevant information pertinent to the current trial. Biases are assigned to representations based on the extent to which they match the information contained in the attentional template. Similarly, Jonides and Nee suggested that PI resolution mechanisms may operate through the assignment of bias to representations of probe items based on the extent to which they match the contextual features of the current trial. The attentional template may consist of any combination of the following sources of information: temporal and spatial information regarding the current trial, familiarity, as well as semantic and episodic features of other members of the target set of the current trial (Jonides & Nee, 2006). These sources of information, when incompatible, can compete in the assignment of bias to the probe item as either a match or a nonmatch to the attentional template of the current trial.

One key distinction between the famous and nonfamous stimuli used in the present study lies in the richness of the semantic representations that they evoke. Studies investigating famous face recognition have proposed that famous face perception automatically induces access to information from semantic and episodic memory stores (e.g., Dietl et al., 2005; Douville et al., 2005; Nessler, Mecklinger, & Penny, 2005; Bernard et al., 2004; Leveroni et al., 2000; Bruce & Young, 1986). However, the nonfamous stimuli used in the present experiment are not likely to be associated with rich semantic or episodic long-term memories. When resolving PI among famous stimuli, the long-term familiarity of famous RN probe items, by virtue of their semantic similarity to the target set items of the current trial, may provide further evidence and boost the strength of a “match” classification of the probe. This leads to increased competition between incompatible sources of information, namely, between episodic familiarity and semantic similarity supporting a “match” classification and temporal context supporting a “nonmatch” classification of the RN probe item. We propose that the larger behavioral and neural RN effects for famous stimuli reflect this increased competition.

To enhance our understanding of the nature of PI resolution mechanisms, it is also necessary to consider the time course on which different types of information are considered. McElree and Doshier (1989) showed larger false alarm RN effects, reflecting reliance upon familiarity information, early in retrieval (response deadlines less than 900 msec). The attenuation of these large RN effects later in retrieval was suggested to reflect the recovery of episodic information. Semantic similarity has also been shown to impact subjects’ tendency to false alarm. For example, McElree (1998) showed that semantic similarity of unstudied lures to studied list items resulted in high false alarm rates early in retrieval. Öztekin and McElree (2007) also found that item-nonspecific PI across three trials from the same semantic category results in a reduction in the RN effect, but only early in retrieval. As items from the same semantic category tend to have similar levels of familiarity, item-nonspecific PI (through stimulus category repetition) functions to make familiarity an insufficient cue for determining whether the probe item was a member of the current target set. Consequently, Öztekin and McElree contend that subjects reduce their reliance on fast assessments of familiarity early in retrieval when making recognition judgments, reflected by a reduction in the RN effect.

These previous studies suggest a potential reason for our finding of an interaction effect between long-term stimulus familiarity and recency in Experiment 3, but not in Experiment

1. At the longer response deadline (3000 msec) used in Experiment 1 and for half of the subjects in Experiment 3, subjects may have relied on episodic information rather than fast familiarity assessments to make a probe judgment. Although we used the same paradigm in Experiments 1 and 2, the neural effects that we observed in Experiment 2 may reflect early long-term stimulus familiarity-based conflict, which we were unable to capture on the basis of RT and percent error rates alone in Experiment 1. This hypothesis was confirmed in Experiment 3, where those subjects given only 500 msec of exposure to the probe stimulus demonstrated larger RN effects for famous compared with nonfamous faces.

In addition to differing in terms of their long-term stimulus familiarity, famous and nonfamous stimuli may also differ in terms of recollective information. For example, the greater semantic information available for famous stimuli may boost the contextual binding of the famous target sets. This associative context information may serve as an additional source of recollective information for famous probe items, thereby facilitating their PI resolution under longer response deadline conditions. In support of this idea, we observed a numerically smaller percent error RN effect for famous compared with nonfamous faces at the longer response deadline in Experiment 3. Although this effect did not approach significance, the numerical pattern of results suggests that this effect should be pursued in further research (see also McElree et al., 1999). In addition, greater recollective information available for famous stimuli may have attenuated the impact of long-term stimulus familiarity at the longer response deadlines used in Experiments 1 and 2, thereby explaining the lack of behavioral evidence and weak neural evidence for Fame  $\times$  Recency interaction effects in these experiments.

A superficial comparison of the experimental manipulations employed by Öztekin and McElree (2007) and in Experiment 3 of the current study may lead one to mistakenly characterize our results as at odds with theirs. However, there are important differences in the nature of these experimental manipulations. Öztekin and McElree's study involved a manipulation of item-nonspecific PI, where trials were drawn from the same semantic category. This semantic manipulation functioned to *reduce* the high familiarity of RN probe items, thus leading to smaller RN effects at short response deadlines. Furthermore, in a neuroimaging study, Öztekin, Curtis, and McElree (2009) found that the buildup of item-nonspecific PI resulted in the elimination of the neural RN effect in LIFG, in line with the behavioral results reported in Öztekin and McElree. In contrast, our manipulation of long-term stimulus familiarity in the current study functioned to *increase* the familiarity of RN probe items, thus leading to larger RN effects for famous faces at the short response deadline. Another difference between these experimental manipulations involves the greater recollective information available for famous compared with nonfamous faces, as noted above. Furthermore, item-nonspecific PI, which served as the source of familiarity in Öztekin and McElree as well as Öztekin et al., is associated with poorer memory performance overall. In contrast, the behavioral results from Experiments 1 and 3 show that our subjects had shorter RTs and lower percent error rates for famous compared with nonfamous trials, collapsing across recency. Thus, in the current study, long-term stimulus familiarity tended to result in an overall *advantage* in performance. One possible reason for this advantage may be deeper encoding of famous faces as a result of their higher long-term stimulus familiarity compared with nonfamous faces. Better encoding may have facilitated classification of the probe item as either matching or not matching an item from the target set. On RN trials, however, any facilitation afforded by deeper encoding of famous target items is insufficient to overcome the combined effects of episodic familiarity and semantic similarity on probe judgments. As subjects are more likely to rely upon familiarity assessments early in retrieval, both episodic familiarity and semantic similarity may contribute more to the recognition judgment compared with temporal context information, which is recovered with a slower time course. Thus, early in retrieval, both episodic

familiarity and semantic similarity may increase the activation level of famous RN probe items, making it more difficult to reject the probe. This leads to larger behavioral RN effects for famous stimuli and may also explain our finding of increased sensitivity to long-term familiarity in right pFC. As noted above, it is likely that our manipulation of long-term stimulus familiarity impacted both encoding and retrieval-related processing. Thus, it is possible that our finding of greater right pFC sensitivity to famous stimuli reflects, in part, differences in encoding for famous versus nonfamous stimuli given the temporal proximity of the encoding and probe components of trials in our paradigm. Interestingly, Öztekin et al. focused on LIFG as a frontal ROI and found that the buildup of item-nonspecific PI resulted in the elimination of the RN effect in this neural region. In contrast to Öztekin et al., we found significant neural RN effects for stimuli with both high and low long-term familiarity; however, long-term familiarity did not modulate the magnitude of neural RN effects in this region. Rather, we found greater sensitivity to the long-term familiarity of stimuli in the RMFG. We next discuss the implications of this finding.

### **Familiarity and Domain Generality of PI**

An additional goal of the present study was to investigate the impact of long-term stimulus familiarity on PI resolution mechanisms to shed light on results from previous studies investigating domain generality of PI (e.g., Badre & Wagner, 2005; Postle et al., 2004; Mecklinger et al., 2003). A consistent thread running through prior results is reduced or unreliable neural RN effects in pFC for nonverbal stimuli, such as abstract objects or visual patterns, relative to those obtained with verbal stimuli, such as letters or words. Although we had expected to find a Fame  $\times$  Recency interaction in left VLPFC, our results indicated greater right pFC sensitivity to the effect of long-term stimulus familiarity on PI resolution. In the current study, we found a significant Fame  $\times$  Recency  $\times$  Hemisphere interaction because of a larger Fame  $\times$  Recency interaction effect in RMFG compared with LMFG. Although the RMFG demonstrated greater activity for famous compared with nonfamous RN effects, a significant Fame  $\times$  Recency interaction effect did not emerge in this region. However, the considerable variability across subjects in terms of the magnitude of neural RN effects may have obscured our ability to detect this interaction effect. Indeed, a closer examination of the variability of neural RN effects in RMFG demonstrated a high correlation between behavioral and neural famous face RN effects in this region. That is, the extent of PI experienced in response to famous face stimuli predicted the level of activity evoked in the RMFG. In addition, this relationship between behavioral and neural RN effects in response to famous faces was stronger than the corresponding correlation for nonfamous face stimuli.

Our finding of greater RMFG sensitivity to famous face RN effects bears a striking resemblance to the results obtained by Mecklinger et al. (2003), in which RMFG demonstrated a significant RN effect for letter stimuli, but not in response to abstract objects. Furthermore, our finding of a negative correlation between behavioral and neural RN effects in RMFG is supported by a previous study by Bunge et al. (2001) that used familiar letters as stimuli and reported a similar negative correlation between brain and behavioral measures of PI resolution in this region. Thus, as noted by Mecklinger et al., it is possible that RMFG mediates PI resolution only for familiar stimuli.

It is important to note that previous studies have tended to confound verbalizability of stimuli with their long-term familiarity, such that the verbal stimuli that have been used are highly familiar, whereas the nonverbal stimuli tend to be unfamiliar. This confound complicates interpretation of these previous studies, as one cannot determine whether differences in results for verbal versus nonverbal stimuli stem from differences in the verbalizability or the long-term familiarity of the stimuli or perhaps some combination of these factors.

One may question whether differences in verbalizability of famous versus nonfamous faces are the main factor driving the current set of results. However, if this were the case, we might have expected to find a larger difference between the magnitude of the RN effect for famous and nonfamous faces compared with the difference between the magnitude of the RN effects for famous and nonfamous names. However, we did not find a three-way interaction between fame, stimulus type, and recency in either Experiment 1 or 2. In addition, if verbalizability of the famous face stimuli were responsible for the high correlation between behavioral and neural RN effects for famous faces in the RMFG, we would have expected that controlling for the variance explained by verbalizability would have reduced the strength of this correlation. However the partial correlation between behavioral and neural famous face RN effects, controlling for the verbalizability of famous faces, remained significant. Furthermore, no significant positive correlations were found between verbalizability of famous faces and corresponding RN effects (either by subject or by probe item) in Experiment 3. As a result, it appears unlikely that the larger behavioral and neural RN effects for famous versus nonfamous stimuli are entirely driven by differences in verbalizability.

What then are the implications of the current set of results on studies of domain generality of PI resolution mechanisms? Reexamining previous studies with these results in mind, it is possible that the differences in neural RN effects for verbal versus nonverbal stimuli may stem, in part, from differences in their long-term familiarity. That is, different neural profiles of activity for nonverbal stimuli, such as abstract objects or visual patterns (e.g., Badre & Wagner, 2005; Mecklinger et al., 2003), may reflect the lower long-term familiarity of these stimuli rather than the content specificity of pFC on the basis of verbalizability. Although it is possible that such content specificity exists (see Leung & Zhang, 2004), the suggestion that areas of pFC may be specialized for PI resolution in the verbal domain appears premature in light of the current set of results.

## Conclusions

In the present series of experiments, we have demonstrated that long-term stimulus familiarity affects the extent of PI that subjects experience, but only early in retrieval. These findings indicate important roles for both short-term and long-term familiarity in impacting PI resolution processes. The results of the current study also suggest that the extent of right pFC involvement in PI resolution may depend on the long-term familiarity of the stimuli involved. Further studies are necessary to gain a greater understanding of domain generality of PI resolution mechanisms, and the present study suggests that stimulus familiarity is an important factor that must be taken into account in the selection of stimuli.

## Acknowledgments

This research was supported by NIH grants MH60414 and MH67008 and a National Science Foundation Graduate Research Fellowship. The authors thank W. Quale for assistance with experimental design.

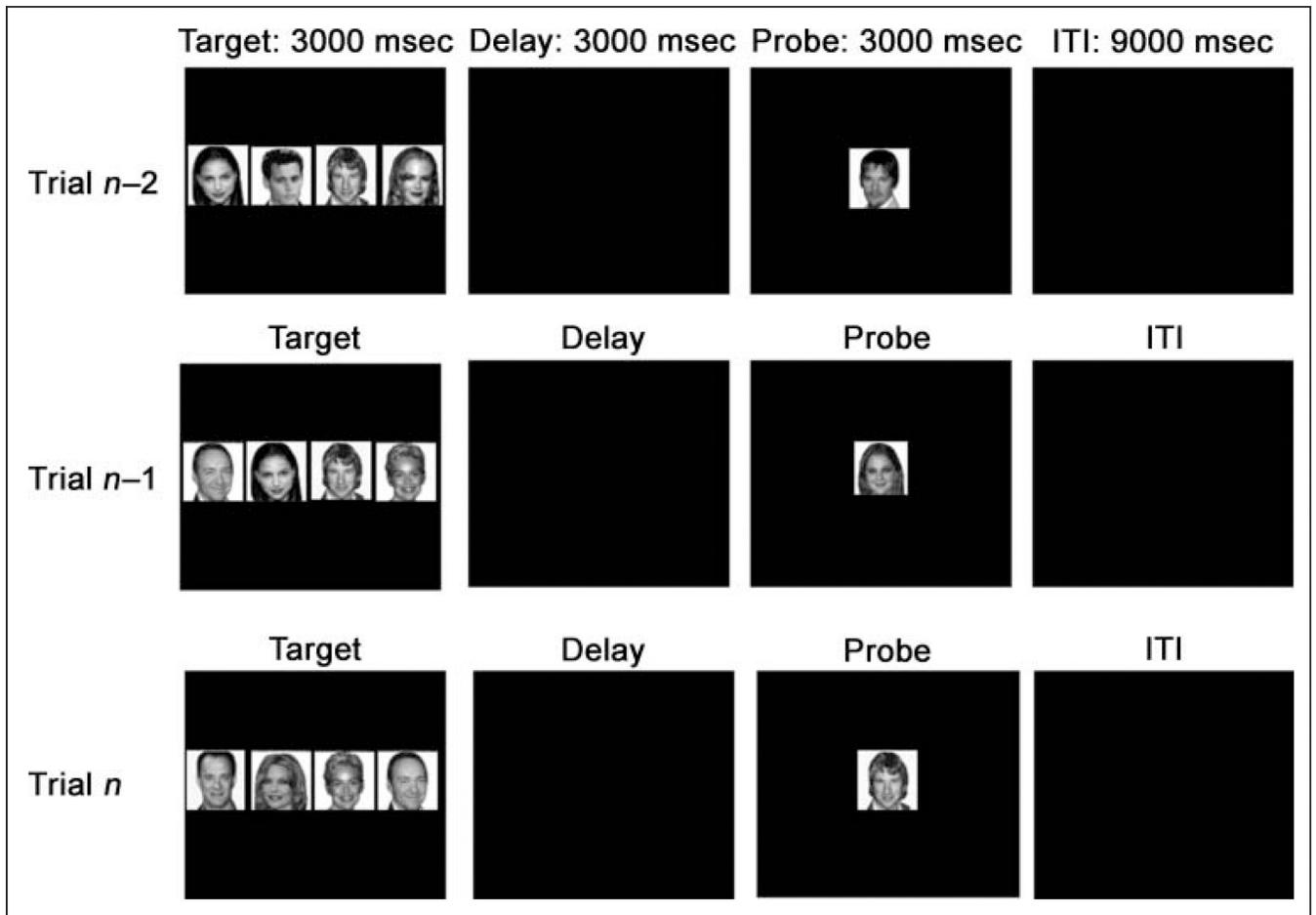
## REFERENCES

- Amunts K, Schleicher A, Bürgel U, Mohlberg H, Uylings HBM, Zilles K. Broca's region revisited: Cytoarchitecture and intersubject variability. *Journal of Comparative Neurology*. 1999; 412:319–341. [PubMed: 10441759]
- Atkinson, RC.; Juola, JG. Search and decision processes in recognition memory. In: Atkinson, RC.; Luce, RD.; Krantz, DH.; Suppes, P., editors. *Contemporary developments in mathematical psychology*. San Francisco, CA: Freeman; 1974. p. 243-293.
- Badre D, Wagner AD. Frontal lobe mechanisms that resolve proactive interference. *Cerebral Cortex*. 2005; 15:2003–2012. [PubMed: 15788702]

- Badre D, Wagner AD. Left ventrolateral prefrontal cortex and the cognitive control of memory. *Neuropsychologia*. 2007; 13:2883–2901. [PubMed: 17675110]
- Bedny M, McGill M, Thompson-Schill SL. Semantic adaptation and competition during word comprehension. *Cerebral Cortex*. 2008; 18:2574–2585. [PubMed: 18308708]
- Bennett RW. Proactive interference in short-term memory: Fundamental forgetting processes. *Journal of Verbal Learning and Verbal Behavior*. 1975; 14:123–144.
- Bernard FA, Bullmore ET, Graham KS, Thompson SA, Hodges JR, Fletcher PC. The hippocampal region is involved in successful recognition of both remote and recent famous faces. *Neuroimage*. 2004; 22:1704–1714. [PubMed: 15275926]
- Bruce V, Young A. Understanding face recognition. *British Journal of Psychology*. 1986; 77:305–327. [PubMed: 3756376]
- Bunge SA, Ochsner KN, Desmond JE, Glover GH, Gabrieli JDE. Prefrontal regions involved in keeping information in and out of mind. *Brain*. 2001; 124:2074–2086. [PubMed: 11571223]
- Curran T. Brain potentials of recollection and familiarity. *Memory and Cognition*. 2000; 28:923–938. [PubMed: 11105518]
- Desimone R, Duncan J. Neural mechanisms of selective visual attention. *Annual Review of Neuroscience*. 1995; 18:193–222.
- D’Esposito M, Postle BR, Jonides J, Smith EE. The neural substrate and temporal dynamics of interference effects in working memory as revealed by event-related fMRI. *Proceedings of the National Academy of Sciences, U.S.A.* 1999; 96:7514–7519.
- Dietl T, Trautner P, Staedtgen M, Vannuchi M, Mecklinger A, Grunwald T, et al. Processing of famous faces and medial temporal lobe event-related potentials: A depth electrode study. *Neuroimage*. 2005; 25:401–407. [PubMed: 15784418]
- Douville K, Woodard JL, Seidenberg M, Miller SK, Leveroni CL, Nielson KA, et al. Medial temporal lobe activity for recognition of recent and remote famous names: An event-related fMRI study. *Neuropsychologia*. 2005; 43:693–703. [PubMed: 15721182]
- Duncan J, Owen AM. Common regions of the human frontal lobe recruited by diverse cognitive demands. *Trends in Neurosciences*. 2000; 23:475–483. [PubMed: 11006464]
- Duvernoy, H. *The human brain: Surface, three dimensional anatomy, and MRI*. New York: Springer-Verlag; 1991.
- Federenko E, Gibson E, Rohde D. The nature of working memory capacity in sentence comprehension: Evidence against domain-specific working memory resources. *Journal of Memory and Language*. 2006; 54:541–553.
- Feredoes E, Postle BR. Prefrontal control of familiarity and recollection in working memory. *Journal of Cognitive Neuroscience*. 2010; 22:323–330. [PubMed: 19400678]
- Friederici AD. Broca’s area and the ventral premotor cortex in language: Functional differentiation and specificity. *Cortex*. 2006; 42:472–475. [PubMed: 16881252]
- Gabrieli JDE, Poldrack RA, Desmond JE. The role of left prefrontal cortex in language and memory. *Proceedings of the National Academy of Sciences, U.S.A.* 1998; 95:906–913.
- Hamilton AC, Martin RC. Dissociations among tasks involving inhibition: A single-case study. *Cognitive, Affective, and Behavioral Neuroscience*. 2005; 5:1–13.
- Hintzman DL, Curran T. Retrieval dynamics of recognition and frequency judgments: Evidence for separate processes of familiarity and recall. *Journal of Memory and Language*. 1994; 33:1–18.
- Jonides J, Marshuetz C, Smith EE, Reuter-Lorenz PA, Koeppel RA. Age differences in behavior and PET activation reveal differences in interference resolution in verbal working memory. *Journal of Cognitive Neuroscience*. 2000; 12:188–196. [PubMed: 10769315]
- Jonides J, Nee DE. Brain mechanisms of proactive interference in working memory. *Neuroscience*. 2006; 139:181–193. [PubMed: 16337090]
- Jonides J, Smith EE, Marshuetz C, Koeppel RA, Reuter-Lorenz PA. Inhibition in verbal working memory revealed by brain activation. *Proceedings of the National Academy of Sciences, U.S.A.* 1998; 95:8410–8413.
- Just MA, Carpenter PA. A capacity theory of comprehension: Individual differences in working memory. *Psychological Review*. 1992; 99:122–149. [PubMed: 1546114]

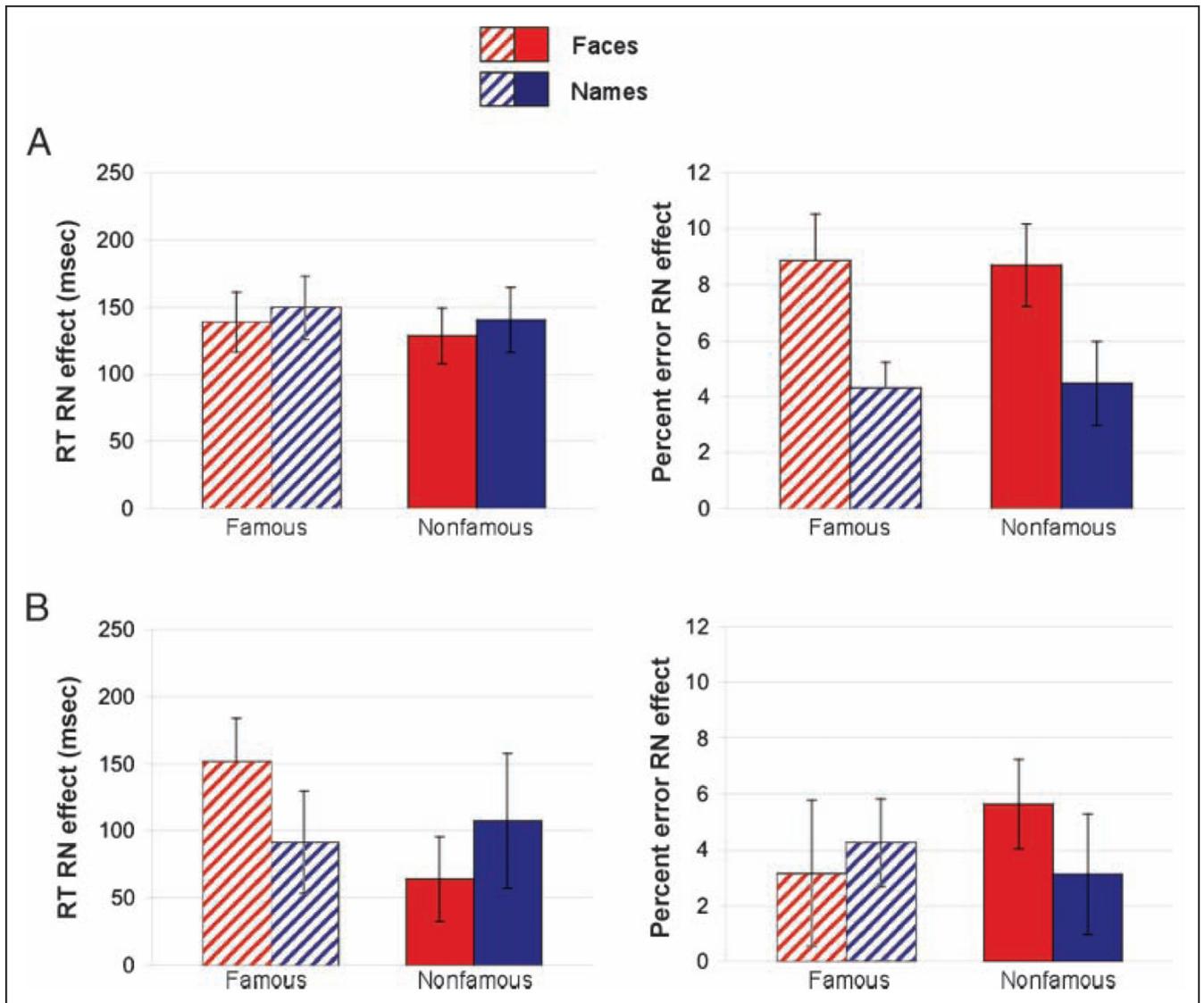
- Kan IP, Thompson-Schill SL. Selection from perceptual and conceptual representations. *Cognitive, Affective, and Behavioral Neuroscience*. 2004; 4:466–482.
- Keppel G, Underwood BJ. Proactive inhibition in short-term retention of single items. *Journal of Verbal Learning and Verbal Behavior*. 1962; 1:153–161.
- Leung H, Zhang JX. Interference resolution in spatial working memory. *Neuroimage*. 2004; 23:1013–1019. [PubMed: 15528101]
- Leveroni CL, Seidenberg M, Mayer AR, Mead LA, Binder JR, Rao SM. Neural systems underlying the recognition of familiar and newly learned faces. *Journal of Neuroscience*. 2000; 20:878–886. [PubMed: 10632617]
- Mandler G. Recognizing: The judgment of previous occurrence. *Psychological Review*. 1980; 87:252–271.
- McElree B. Attended and non-attended states in working memory: Accessing categorized structures. *Journal of Memory and Language*. 1998; 38:225–252.
- McElree B, Dolan PO, Jacoby LL. Isolating the contributions of familiarity and source information to item recognition: A time course analysis. *Journal of Experimental Psychology: Learning, Memory, and Cognition*. 1999; 25:563–582.
- McElree B, Doshier BA. Serial position and set size in short-term memory: The time course of recognition. *Journal of Experimental Psychology: General*. 1989; 118:346–373.
- Mecklinger A, Weber K, Gunter TC, Engle RW. Dissociable brain mechanisms for inhibitory control: Effects of interference content and working memory capacity. *Cognitive Brain Research*. 2003; 18:26–38. [PubMed: 14659494]
- Metzler C. Effects of left frontal lesions on the selection of context-appropriate meanings. *Neuropsychology*. 2001; 15:315–328. [PubMed: 11499987]
- Milham MP, Banich MT, Webb A, Barad V, Cohen NJ, Wszalek T, et al. The relative involvement of anterior cingulate and prefrontal cortex in attentional control depends on nature of conflict. *Cognitive Brain Research*. 2001; 12:467–473. [PubMed: 11689307]
- Miller EK, Cohen JD. An integrative theory of prefrontal cortex function. *Annual Review of Neuroscience*. 2001; 24:167–202.
- Monsell S. Recency, immediate recognition memory, and reaction time. *Cognitive Psychology*. 1978; 10:465–501.
- Nee DE, Jonides J, Berman MG. Neural mechanisms of proactive interference-resolution. *Neuroimage*. 2007; 4:740–751. [PubMed: 17904389]
- Nelson JK, Reuter-Lorenz PA, Sylvester CC, Jonides J, Smith EE. Dissociable neural mechanisms underlying response-based and familiarity-based conflict in working memory. *Proceedings of the National Academy of Sciences, U.S.A.* 2003; 100:11171–11175.
- Nessler D, Mecklinger A, Penney TB. Perceptual fluency, semantic familiarity, and recognition-related familiarity: An electrophysiological exploration. *Cognitive Brain Research*. 2005; 22:265–288. [PubMed: 15653299]
- Öztekin I, Curtis CE, McElree B. The medial temporal lobe and the left inferior prefrontal cortex jointly support interference resolution in verbal working memory. *Journal of Cognitive Neuroscience*. 2009; 21:1967–1979. [PubMed: 18855551]
- Öztekin I, McElree B. Proactive interference slows recognition by eliminating fast assessments of familiarity. *Journal of Memory and Language*. 2007; 57:126–149.
- Postle BR, Brush LN, Nick AM. Prefrontal cortex and the mediation of proactive interference in working memory. *Cognitive, Affective, and Behavioral Neuroscience*. 2004; 4:600–608.
- Robinson G, Blair J, Cipolotti L. Dynamic aphasia: An inability to select between competing verbal responses? *Brain*. 1998; 121:77–89. [PubMed: 9549489]
- Rugg MD, Yonelinas AP. Human recognition memory: A cognitive neuroscience perspective. *Trends in Cognitive Sciences*. 2003; 7:313–319. [PubMed: 12860190]
- Schneider, W.; Eschman, A.; Zuccolotto, A. E-prime user's guide. Pittsburgh: Psychology Software Tools Inc; 2002.
- Smith EE, Jonides J. Storage and executive processes in the frontal lobes. *Science*. 1999; 283:1657–1661. [PubMed: 10073923]

- Sternberg S. High speed scanning in human memory. *Science*. 1966; 153:652–654. [PubMed: 5939936]
- Thompson-Schill SL, D’Esposito M, Aguirre GK, Farah MJ. Role of the left inferior prefrontal cortex in retrieval of semantic knowledge: A reevaluation. *Proceedings of the National Academy of Sciences, U.S.A.* 1997; 94:14792–14797.
- Thompson-Schill SL, D’Esposito M, Kan IP. Effects of repetition and competition on activity in left prefrontal cortex during word generation. *Neuron*. 1999; 23:513–522. [PubMed: 10433263]
- Thompson-Schill SL, Jonides J, Marshuetz C, Smith EE, D’Esposito M, Kan IP, et al. Effects of frontal lobe damage on interference effects in working memory. *Cognitive, Affective, and Behavioral Neuroscience*. 2002; 2:109–120.
- Van Dyke JA, McElree B. Retrieval interference in sentence comprehension. *Journal of Memory and Language*. 2006; 55:157–166. [PubMed: 18209744]
- Worsley KJ, Friston K. Analysis of fMRI time-series revisited—Again. *Neuroimage*. 1995; 2:173–182. [PubMed: 9343600]
- Yonelinas AP. Receiver-operating characteristics in recognition memory: Evidence for a dual-process model. *Journal of Experimental Psychology: Learning, Memory, and Cognition*. 1994; 20:1341–1354.

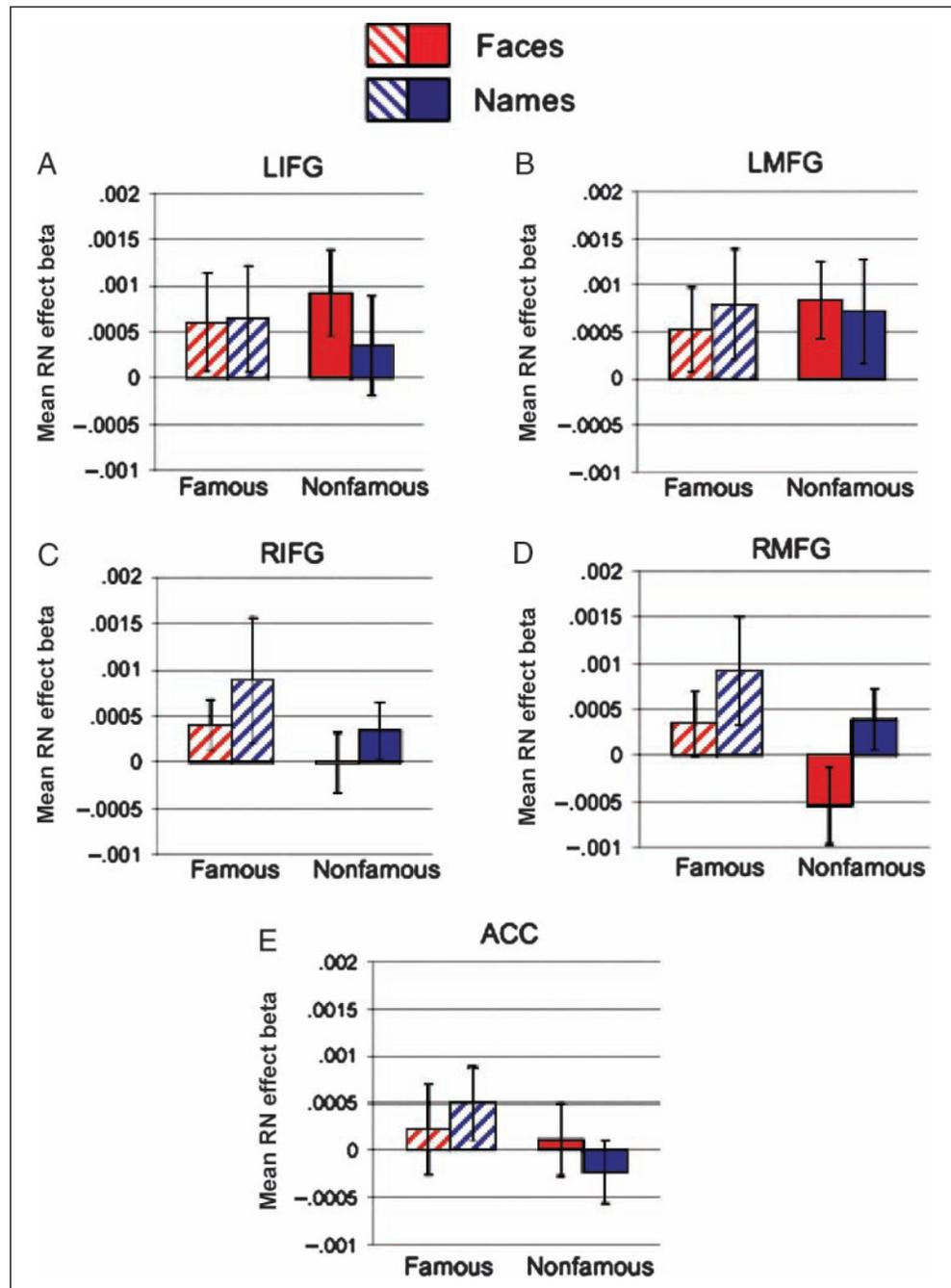


**Figure 1.**

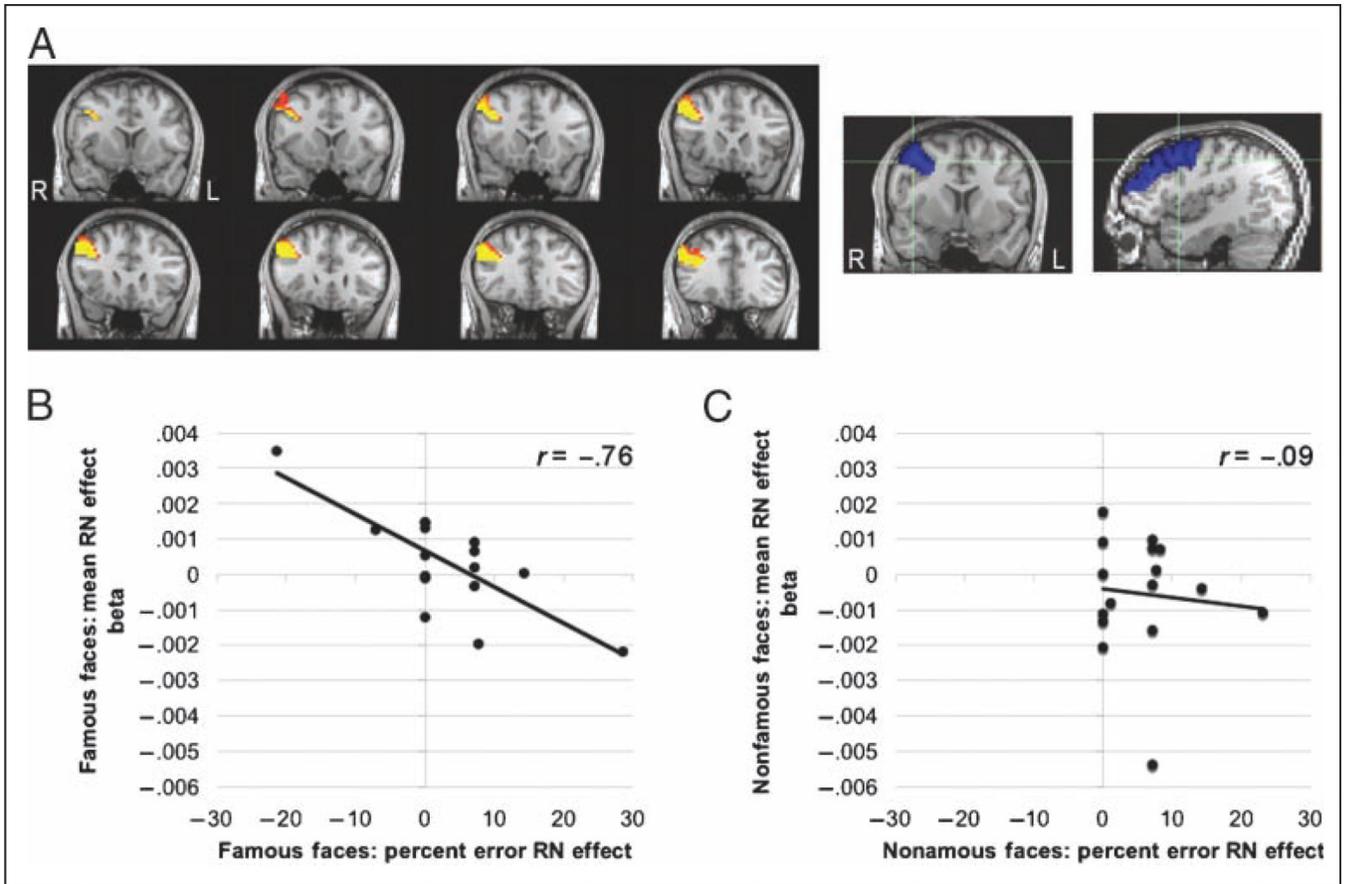
Trial design for Experiments 1 and 2. Subjects performed two blocks of each stimulus category: famous faces, famous names, nonfamous faces, and nonfamous names. A sample famous faces trial is shown. Subjects were presented with four faces in the target set for 3000 msec, a delay period for 3000 msec, and the probe face for 3000 msec. Subjects were instructed to make their response before the probe disappeared from the screen. An intertrial interval (ITI) of 9000 msec followed the probe, with the last 1000 msec of the ITI consisting of a fixation cross. Trial  $n$  represents a recent negative (RN) trial, where the probe (Richard Gere) did not occur in the current target set but did appear in the previous two target sets (of Trials  $n-1$  and  $n-2$ ). Half of the subjects performed the blocks in the following order: famous names, famous faces, nonfamous names, and nonfamous faces, with this order of blocks repeating once more (for a total of eight blocks). The other half of subjects performed the blocks in the reverse order.



**Figure 2.** Mean RT RN effect (RN – NN) in milliseconds and mean percent error RN effect for each stimulus category for Experiments 1 and 2. (A) Experiment 1 ( $n = 53$ ). (B) Experiment 2 ( $n = 16$ ). Error bars represent the *SEM*. See Table 1 for RT and percent error data for RN and NN trials in each stimulus category.

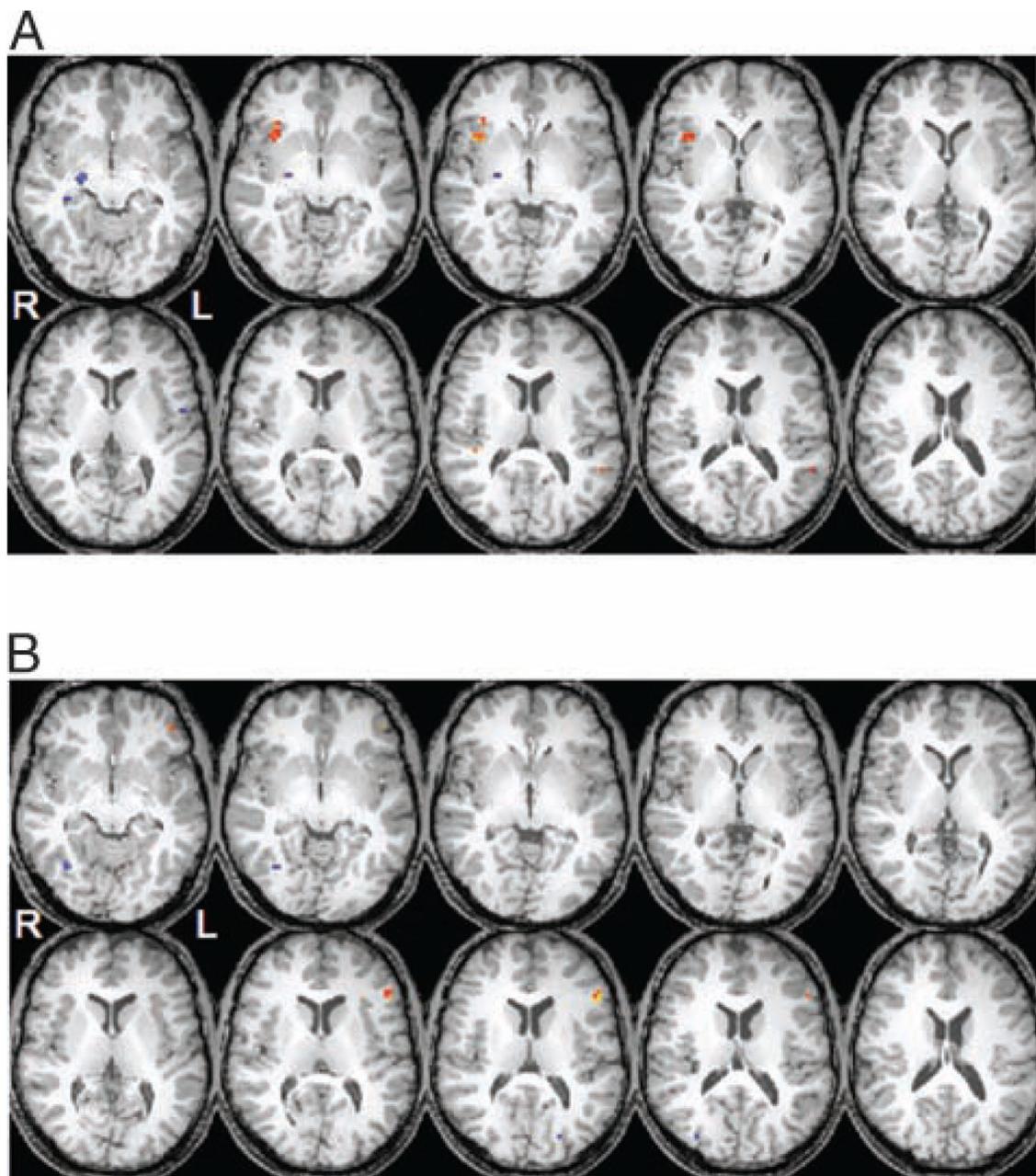


**Figure 3.** Mean RN Effect beta values for each stimulus category for each ROI. (A) LIFG; (B) LMFG; (C) RIFG; (D) RMFG; (E) ACC. Error bars represent the *SEM*.



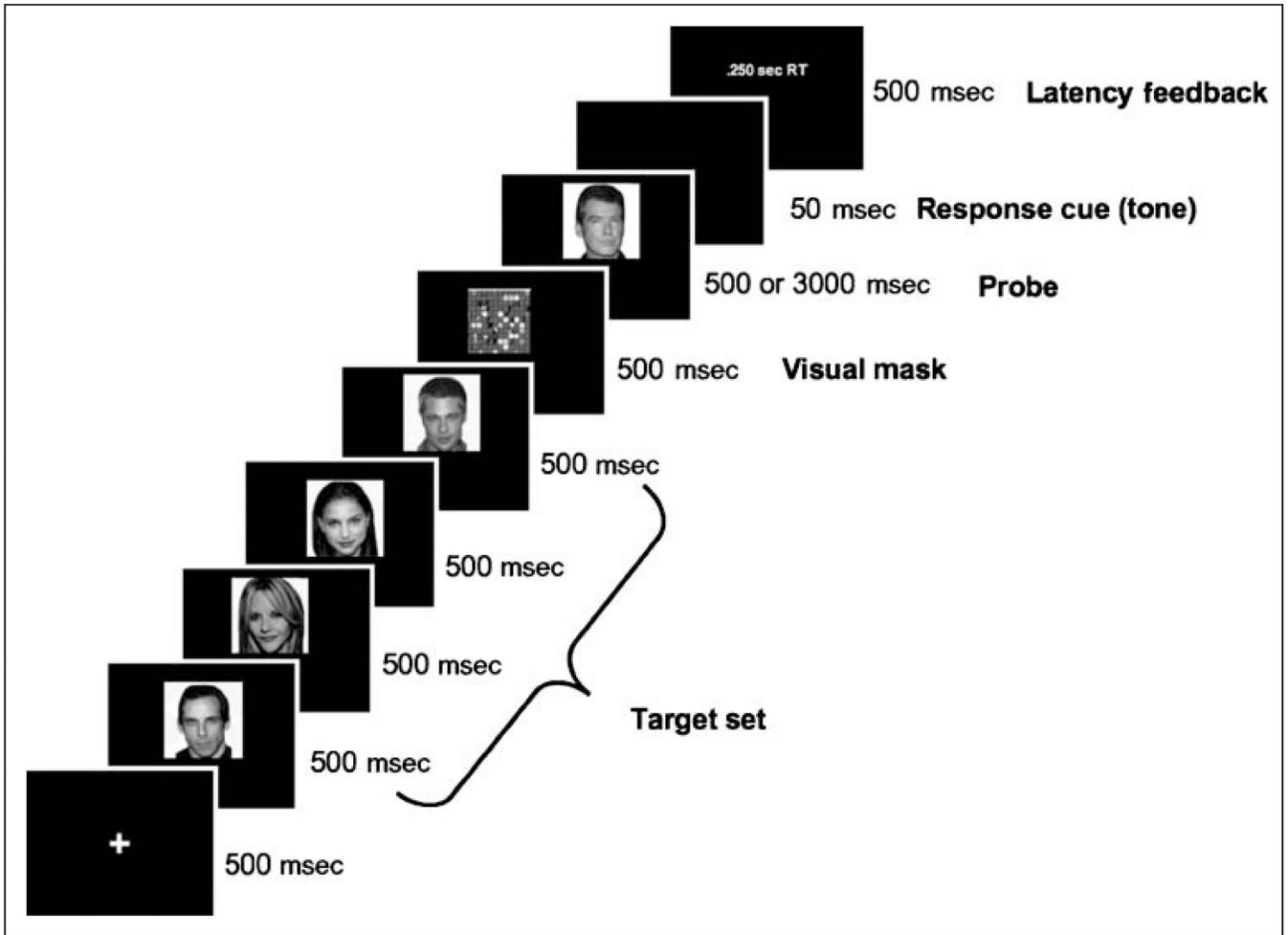
**Figure 4.**

Individual differences in RMFG ROI. (A) Sample coronal slices showing active voxels in RMFG in a representative subject's nonnormalized coronal brain image for the contrast of all correct probe items versus baseline (ITI) at a threshold of  $t = 2.0$ . Coronal and sagittal slices show area covered by anatomically defined RMFG mask (shown in blue). (B) Correlation between percent error RN effect and mean RN Effect beta value in RMFG (in those voxels described in panel A) for famous face stimuli. (C) Correlation between percent error RN effect and mean RN effect beta value in RMFG (in those voxels described in panel A) for nonfamous face stimuli.



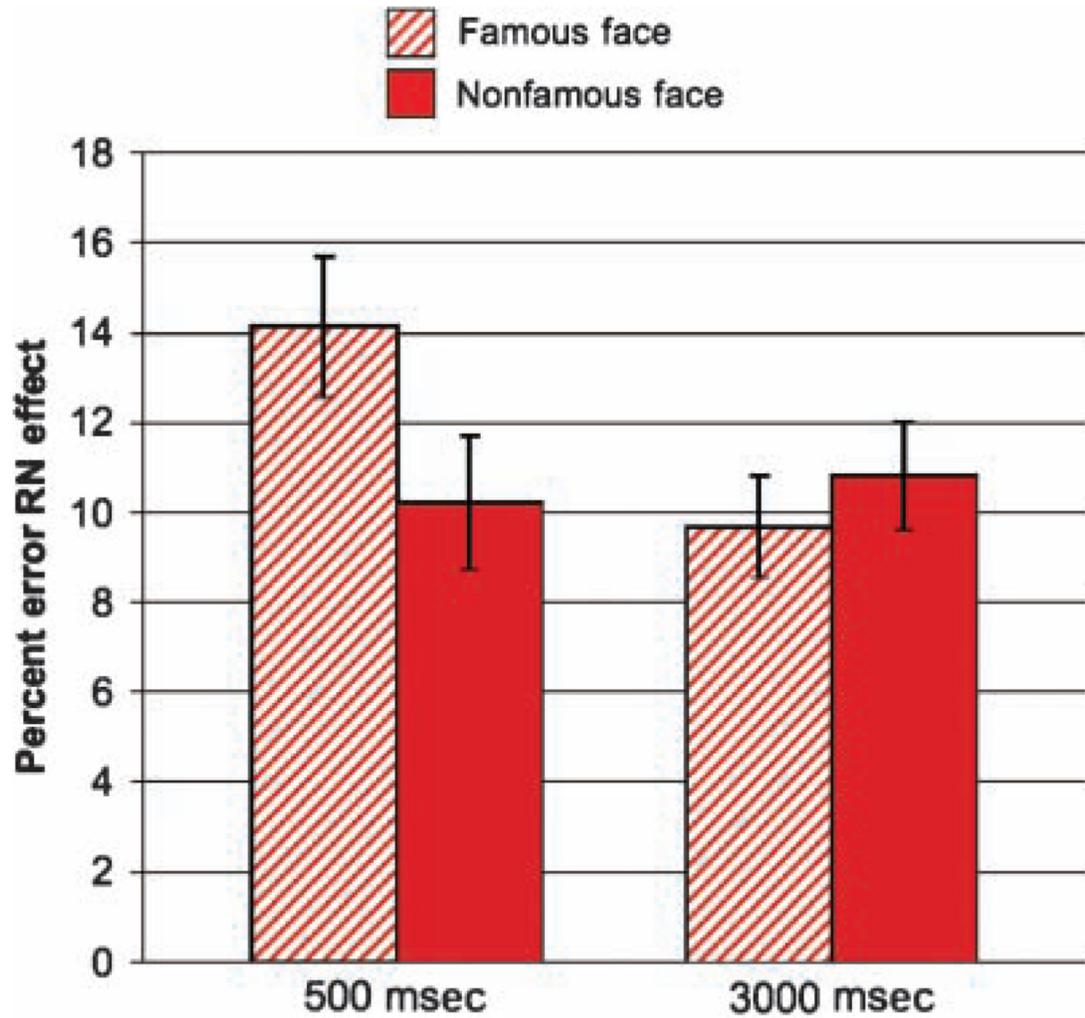
**Figure 5.**

Exploratory whole-brain random effects analysis results displayed on the normalized anatomical scan of one subject. All areas of activation are significant at  $t(15) = 4.073$ ,  $p < .001$  (uncorrected) (warm colors correspond to greater activity for RN vs. NN trials; cool colors correspond to greater activity for NN vs. RN trials). (A) Famous RN effect (collapsed across faces and names); (B) nonfamous RN effect (collapsed across faces and names).

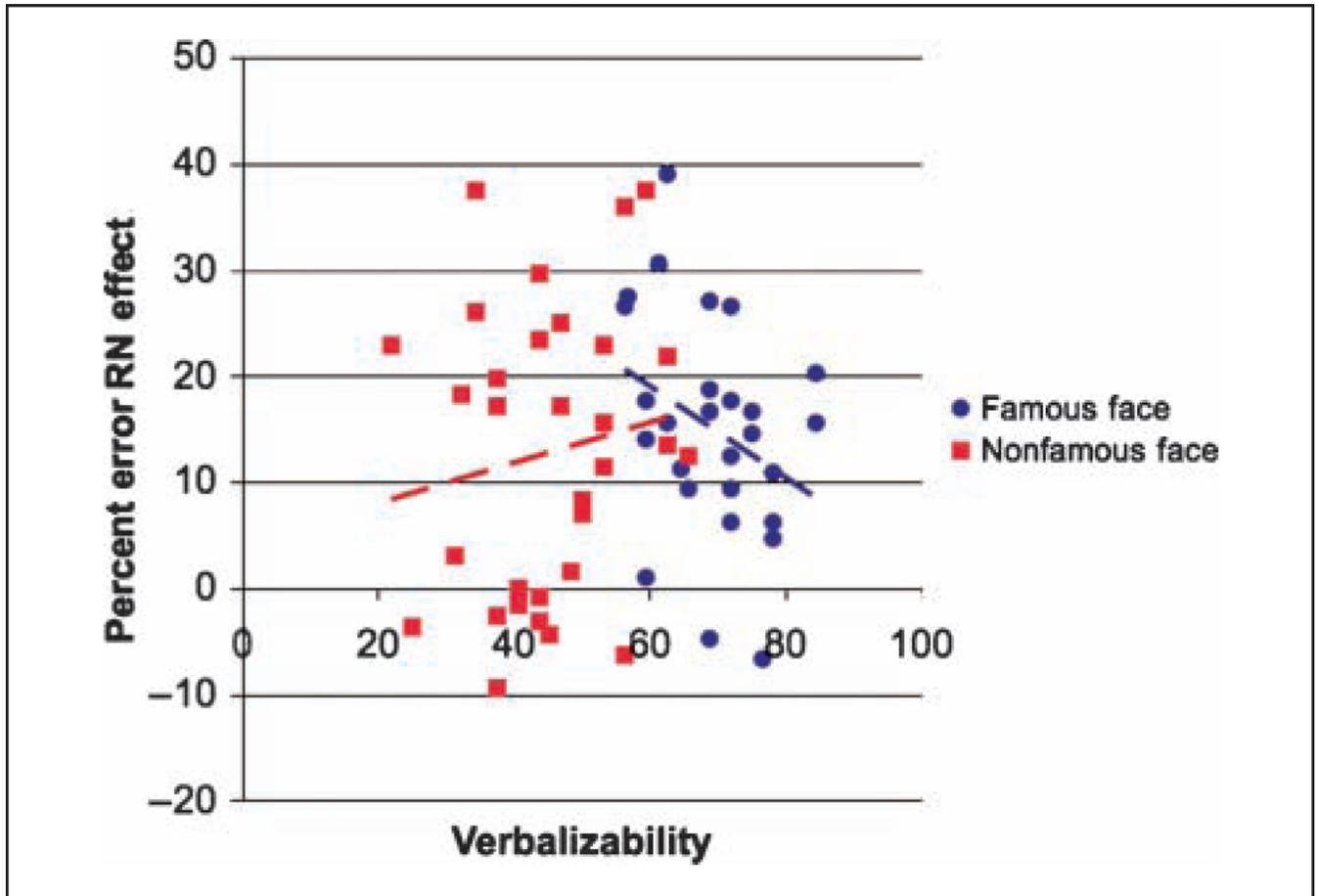


**Figure 6.**

Trial design for Experiment 3 (modeled after Öztekin McElree, 2007). Subjects performed four blocks of each stimulus category: famous faces and nonfamous faces. Half of the subjects were presented with a block of nonfamous face trials first, and the other half were presented with a block of famous face trials first. Subjects were presented with a fixation cross for 500 msec followed by serial presentation of the four target faces, each for 500 msec. A scrambled visual pattern mask was presented for 500 msec followed by the probe stimulus, which was presented for 500 msec for half the subjects and 3000 msec for the other half. After the probe, a 50-msec tone was presented, cueing the subjects to respond. Subjects were given 500 msec to respond after the onset of the tone. After making a response, subjects were given feedback as to how quickly they had responded.



**Figure 7.** Mean percent error RN Effect for each stimulus category for Experiment 3 (500-msec deadline:  $n = 32$ ; 3000-msec deadline:  $n = 32$ ; total  $N = 64$ ). Error bars represent the *SEM*. See Table 2 for RT and percent error data for RN and NN trials in each stimulus category.



**Figure 8.**

Relationship between verbalizability of famous and nonfamous probe items and their corresponding percent error RN effects in Experiment 3. Dashed lines indicate trend lines for famous faces (blue) and nonfamous faces (red). Correlation between verbalizability of probe items and their corresponding percent error RN effects: famous faces (Pearson  $r = -.33$ ,  $p = .09$ ) and nonfamous faces (Pearson  $r = .15$ ,  $p = .42$ ).

**Table 1**

Mean of Median RT in Milliseconds and Mean Percent Error Rate for Recent No and Nonrecent No Trial Types in Each Stimulus Condition for Experiments 1 and 2

Condition	Experiment 1 (n = 53)		Experiment 2 (n = 16)	
	RT (msec)	Percent Error Rate	RT (msec)	Percent Error Rate
Famous face	Recent no	1069 (35)	1314 (85)	6.3 (2.1)
	Nonrecent no	930 (28)	1162 (70)	3.2 (1.5)
Famous name	Recent no	1061 (49)	1227 (80)	5.2 (1.8)
	Nonrecent no	911 (35)	1135 (70)	0.89 (0.61)
Nonfamous face	Recent no	1110 (32)	1311 (89)	9.6 (2.0)
	Nonrecent no	982 (25)	1246 (89)	4.0 (1.3)
Nonfamous name	Recent no	1102 (45)	1265 (97)	6.3 (2.2)
	Nonrecent no	961 (32)	1157 (78)	3.1 (1.1)

SEM in parentheses.

**Table 2**

Mean of Median RT in Milliseconds and Mean Percent Error Rate for Recent No and Nonrecent No Trial Types in Each Stimulus Condition for Experiment 3 (Total  $n = 64$ )

Condition	500-msec Deadline (n = 32)		3000-msec Deadline (n = 32)		
	RT (msec)	Percent Error	RT (msec)	Percent Error	
Famous face	Recent no	179 (10)	21.8 (2.0)	197 (4.5)	14.1 (1.6)
	Nonrecent no	164 (10)	7.7 (1.1)	198 (4.6)	4.4 (0.74)
Nonfamous face	Recent no	180 (8.9)	24.6 (2.2)	197 (4.6)	17.9 (1.2)
	Nonrecent no	176 (9.6)	14.4 (1.3)	195 (4.5)	7.1 (0.96)

*SEM* in parentheses.