Behavioral/Cognitive

Repetition Probability Effects Depend on Prior Experiences

Mareike Grotheer[1,2] **and Gyula Kovács**[1,2,3]

[1]Institute of Psychology and [2]DFG Research Unit Person Perception, Friedrich-Schiller-University of Jena, 07743 Jena, Germany, and [3]Department of Cognitive Science, Budapest University of Technology and Economics, 1111 Budapest, Hungary

The magnitude of repetition suppression (RS) in the Fusiform Face Area is influenced by the probability of repetitions of faces (Summerfield et al., 2008), implying that perceptual expectations affect repetition-related processes. Surprisingly, however, macaque single-cell (Kaliukhovich and Vogels, 2011) and human fMRI (Kovács et al., 2013) studies have failed to find repetition probability [P(rep)] modulations of RS with nonface stimuli in the occipitotemporal cortex, suggesting that the effect is face specific. One possible explanation of this category selectivity is that the extensive experience humans have with faces affects the neural mechanisms of RS specifically, creating P(rep) modulatory effects. To address this question, we used fMRI to test the P(rep) effects for another well trained stimulus category, upright letters of the roman alphabet as well as for unfamiliar false fonts. We observed significant RS for both stimulus sets in the Letter Form Area as well as in the caudodorsal part of the lateral occipital complex. Interestingly, the influence of P(rep) on RS was dependent on the stimulus: while we observed P(rep) modulations for the roman letters, no such effects were found for the unfamiliar false fonts in either area. Our findings suggest that P(rep) effects on RS are manifest for nonface stimuli as well, but that they depend on the experience of the subjects with the stimulus category. This shows, for the first time, that prior experience affects the influence of contextual predictive information on RS in the human occipitotemporal cortex.

Key words: expectation; fMRI; learning; letter; prediction; repetition suppression

Introduction

The repetition of a stimulus elicits a reduced neuronal response, when compared with its first presentation, a phenomenon termed repetition suppression (RS; Henson, 2003). Although the neural mechanisms of RS remain unclear (for review, see Grill-Spector et al., 2006; Krekelberg et al., 2006; Gotts et al., 2012; Malach, 2012), recent results suggest that RS reflects a reduced prediction error in the context of predictive coding (PC) models (Rao and Ballard, 1999). Interestingly, the probability of repetition [P(rep)] of face stimuli in different contexts (blocks) influences the magnitude of RS in the Fusiform Face Area (FFA; Kanwisher et al., 1997) (Summerfield et al., 2008; Kovács et al., 2012; Larsson and Smith, 2012), suggesting that higher order contextual expectations modulate prediction error (but see Ewbank and Henson, 2012, for further discussion of contextual vs perceptual predictions). However, P(rep) modulations could not be found for chairs or everyday objects in human neuroimaging (Kovács et al., 2013) or for fractal patterns and everyday objects in monkey single-cell recording experiments of the inferior temporal cortex (IT; Kaliukhovich and Vogels, 2011). The reasons behind this category specificity are unclear and auditory studies make the face specificity of such effects unlikely (Todorovic and

de Lange, 2012). One hypothesis suggests that P(rep) modulations are stronger for visual stimuli of high expertise, such as faces (Bukach et al., 2006). Indeed, stimulus familiarity has been shown to interact with repetition-related responses for faces and symbols (Henson et al., 2000) as well as words (Henson, 2001; Fiebach et al., 2005). Furthermore, the acquisition of expertise leads to enhanced associations among features or objects, suggesting the interaction of predictions and expertise (for review, see Cheung and Bar, 2012). Meyer and Olson (2011) used an extensive training and compared the single-cell activity of macaques for associated stimulus pairs with that for nonassociated and nontrained stimulus pairs. Authors found a strong "surprise" effect where untrained and therefore unpredicted pairs evoked stronger neuronal activity in IT when compared with trained pairs. This suggests that experience can lead to predictions, which manifest in neuronal responses. Interestingly, associative facilitations by context and experience have also been explained by other models, involving the interaction of top-down and bottom-up information, similarly to the PC models (Bar, 2004).

This suggests that experience influences predictions, which, in turn, alter neuronal responses. To test the effects of prior experience on the P(rep) modulation of RS we used the same fMRI paradigm as previous studies (Summerfield et al., 2008), presenting another stimulus category with which humans are well experienced: characters of the roman alphabet (RL), as well as unfamiliar false fonts (FF). Briefly, we observed P(rep) effects on RS in the Letter Form Area (LFA; Thesen et al., 2012) and in the caudodorsal part of the lateral occipital complex (LO; Malach et al., 1995; Grill-Spector et al., 1999) for the well trained RL, but not for the unfamiliar FF, suggesting that prior experience affects
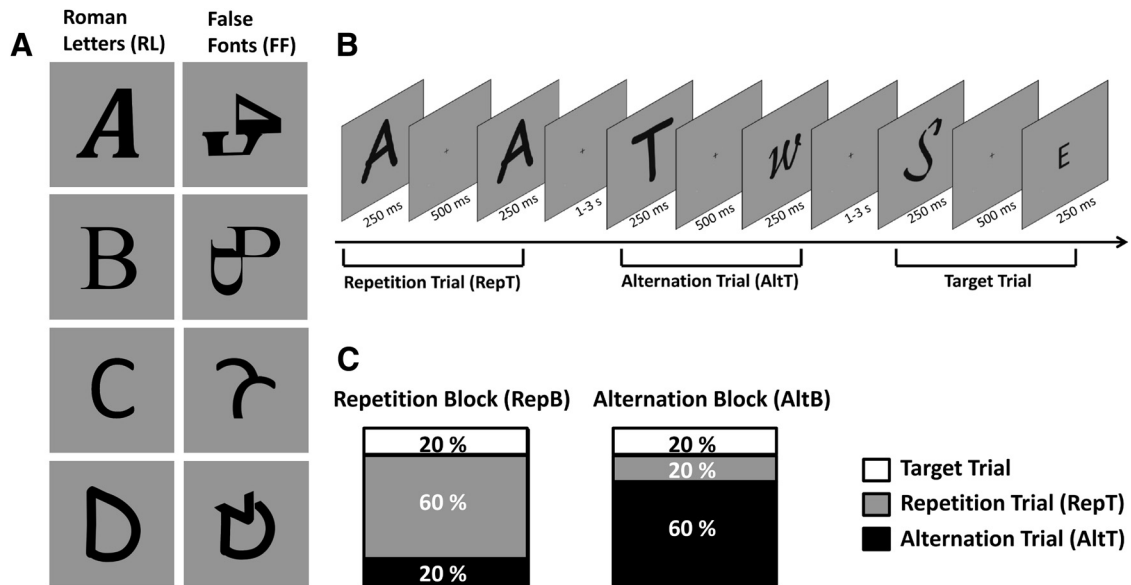
Figure 1. *A*, Examples of the stimuli used in the experiment. Left column, RLs in different fonts. Right column, FFs created by relocating parts of the RL. *B*, Stimulation parameters and arrangements. An RL Repetition Trial (RepT), an RL Alternation Trial (AltT), and a target trial are illustrated. *C*, The composition of the repetition (RepBs) and alternation blocks (AltBs). During a run, RepBs and AltBs were presented randomly, each repeating four times.

the influence of high-level, contextual predictions on RS in the ventral visual pathway.

Materials and Methods

Subjects. Twenty healthy volunteers (16 female; 15 right-handed; mean age (±SD): 21(2) years) participated in the experiment. Three subjects were excluded from the analysis on the basis that two subjects failed to perform the behavioral task during scanning and that we could not reliably locate the LFA in one subject. Therefore the current study is based on the data of 17 subjects. All subjects had normal or corrected to normal vision and gave informed written consent in accordance with the protocols approved by the Ethical Committee of the Friedrich-Schiller-University of Jena.

Stimulation and procedure. The experimental design of the current study was similar to what has previously been used to test P(rep) modulations (Summerfield et al., 2008; Kaliukhovich and Vogels, 2011; Kovács et al., 2012; 2013; Larsson and Smith, 2012), with the exception that two sets of letter-like characters with 240 exemplars each were used as stimuli. One set consisted of capital RLs, whereby every alphabetic character (except the letters I and U, being similar in shape to L and V) was presented 10 times. Each letter was presented in 10 different font styles (Times New Roman, Calibri, Comic Sans MS, Britannic Bold, Forte, Bradly Hand ITC, Informal Roman, Pristina, Surgeon Bold Script, and Cambria Bold Italic), so that they had different shapes and were trial unique during a run. These stimuli were used for creating the FF stimulus set. For this, 1–4 components of a particular letter in a given font were moved randomly to a different position, using Gimp 2.6 (for examples of RL and FF see Fig. 1*A*). The resulting FF stimuli were comparable to those of previous studies (Moore and Price, 1999; Ben-Shachar et al., 2007; Vinckier et al., 2007; Thesen et al., 2012) and were of similar size (height of 2.4° visual angle), contrast, and complexity as the original RLs, but they were novel shapes, previously unknown to the subjects. Stimuli were presented in the center of the screen on a gray background. They were back-projected via an LCD video projector onto a translucent circular screen, placed inside the scanner bore. Stimulus presentation was controlled via MATLAB (MathWorks), using Psychtoolbox (Version 3.0.9).

Stimuli were presented pairwise, for 250 ms each, separated by an interstimulus interval randomized between 0.4 and 0.6 ms, and followed randomly by a 1 s or 3 s long intertrial interval (Kovács et al., 2013). The first stimulus (S1) was either identical to (Repetition Trial, RepT) or different from the second stimulus (S2; Alternation Trial, AltT). To re-

duce local feature adaptation, the size of either S1 or S2 (chosen randomly) was reduced by 18% during each trial (height of 2° visual angle). The participants' task was to maintain central fixation throughout the trials and to signal the occurrence of 60% smaller (height of 0.96° visual angle) target stimuli by pressing a button.

In addition to the different trial types, two different types of blocks were presented to the subjects (Summerfield et al., 2008). In the Repetition Blocks (RepB), 75% of the trials were Repetition Trials while 25% were Alternation Trials. In the Alternation Blocks (AltB), 75% of the trials were Alternation Trials and 25% were Repetition Trials. With the exception of the first four trials of each block, which always consisted of the more frequent trial type of that block (RepT in RepB and AltT in AltB), Repetition Trials and Alternation Trials were presented randomly within a block. In addition, 20% of all trials were target trials, which were either Alternation Trial or Repetition Trial with the same relative probability. Both Alternation Blocks and Repetition Blocks contained 20 trials and were repeated four times during each run, so that a run contained 160 trials. The different blocks were separated from each other by a 7 s pause during which the words "Short Break. Next block in…" were presented centrally together with a countdown. The trial and block structures are depicted in Figure 1, *B* and *C*. During an experiment two RL and two FF runs were presented across subjects in a counterbalanced order.

Imaging parameters and data analysis. A 3 T MR scanner (Siemens Magnetom Trio) was used. During the functional blocks, we continuously acquired images (34 slices, 10° tilted relative to axial, T2* weighted EPI sequence, TR = 2000 ms; TE = 30 ms; flip angle = 90°; 64 × 64 matrices; in-plane resolution: 3 × 3 mm; slice thickness: 3 mm). To additionally obtain a 3D structural scan, high-resolution sagittal T1-weighted images were acquired using a magnetization EPI sequence (MP-RAGE; TR = 2300 ms; TE = 3.03 ms; 1 mm isotropic voxel size). Details of preprocessing and statistical analysis were described previously (Cziraki et al., 2010; Kovács et al., 2013). Briefly, the functional images were realigned, normalized to the MNI-152 space, resampled to 2 × 2 × 2 mm resolution, and spatially smoothed with a Gaussian kernel of 8 mm FWHM (SPM8, Welcome Department of Imaging Neuroscience, London, UK). Separate functional localizer runs [480 s long, 20 s epochs of RLs and FFs (different from main experiment, Arial font style) and Fourier randomized images, interleaved with 20 s of blank periods, 2 Hz stimulus repetition rate; 300 ms exposition time; 200 ms blank] were used to determine regions of interest (ROIs), which were analyzed using MARSBAR 0.42 toolbox for SPM (Brett et al., 2002). Only those subjects

($N = 17$) in whom all ROIs could confidently be determined on the basis of the localizer were included in any further analyses. The LFA (Thesen et al., 2012) of the left hemisphere [average MNI coordinates ($\pm$SE): $-45(1)$, $-66(2)$, $-14(2)$] was determined as responding more intensely to RLs than to FFs and Fourier noise images (Puce et al., 1996; Thesen et al., 2012). The LO [average MNI coordinates ($\pm$SE): $-47(1)$, $-81(2)$, $-8(1)$ for left, 46(1), $-81(2)$, $-6(1)$ and right hemisphere] was determined individually as an area responding stronger to RLs than to Fourier noise images in the localizer scans. The results were visualized using xjView toolbox (http://www.alivelearn.net/xjview) and the approximate average locations of LFA and LO are shown in Figure 2.

The percent signal change of the mean voxel value within the ROIs was extracted from the event-related sessions. The four experimental conditions (AltB_AltT, AltB_RepT, RepB_AltT, and RepB_RepT) as well as the target trials were defined as separate regressors and convolved with the canonical hemodynamic response function of SPM8, for a general linear model analysis of the data. For the LO, we performed repeated-measures ANOVA with hemisphere (2), stimulus type (2), block type (2) and trial type (2) as factors. For the LFA, we performed a three-way within-subject ANOVA with stimulus (2), block (2) and trial (2) as factors. Additionally, we performed individual, two-way within-subject ANOVAs with block type (2) and trial type (2) separately for RLs and FFs in both ROIs. *Post hoc* analyses were performed using Fisher LSD tests.

Results

Performance
Informal questioning at the end of the experiment revealed that, similarly to prior studies, none of the subjects were aware of the different repetition probabilities in the different blocks. Subjects detected the target stimuli on average with 83.92% ($\pm$SE: 13.99%) accuracy and with an average reaction time of 983 ms ($\pm$SE: 79 ms). Neither the performance, nor the reaction times differed in Alternation and Repetition Blocks (main effect of block: $F_{(1,16)} = 0.02$, $p = 0.89$, $\eta_p^2 = 0.001$ and $F_{(1,16)} = 4.10$, $p = 0.06$, $\eta_p^2 = 0.20$) or for RLs and FFs (main effect of stimulus type: $F_{(1,16)} = 4.24$, $p = 0.06$, $\eta_p^2 = 0.21$ and $F_{(1,16)} = 0.55$, $p = 0.47$, $\eta_p^2 = 0.03$), for performance and response times, respectively. This suggests that any difference between the P(rep) conditions or stimulus categories cannot be explained by different task difficulties or allocations of attentional resources.

fMRI results
LFA

We observed significant repetition suppression in the LFA (Fig. 3; $N = 17$) for both RLs (main effect of trial: $F_{(1,16)} = 6.36$, $p = 0.02$, $\eta_p^2 = 0.28$) and FFs (main effect of trial: $F_{(1,16)} = 6.84$, $p = 0.02$, $\eta_p^2 = 0.30$) in separate ANOVAs (see Materials and Methods). In the case of RLs, the observed RS was dependent on the P(rep) (interaction of block and trial: $F_{(1,16)} = 9.99$, $p = 0.006$, $\eta_p^2 = 0.38$), as the blood oxygen-level dependent (BOLD) signal was significantly lower for Repetition Trials when compared with Alternation Trials in Repetition Blocks (Fisher LSD *post hoc* test: $p = 0.0006$), but not in Alternation Blocks (Fisher LSD *post hoc* test: $p = 0.84$). This suggests that P(rep) affects the magnitude of
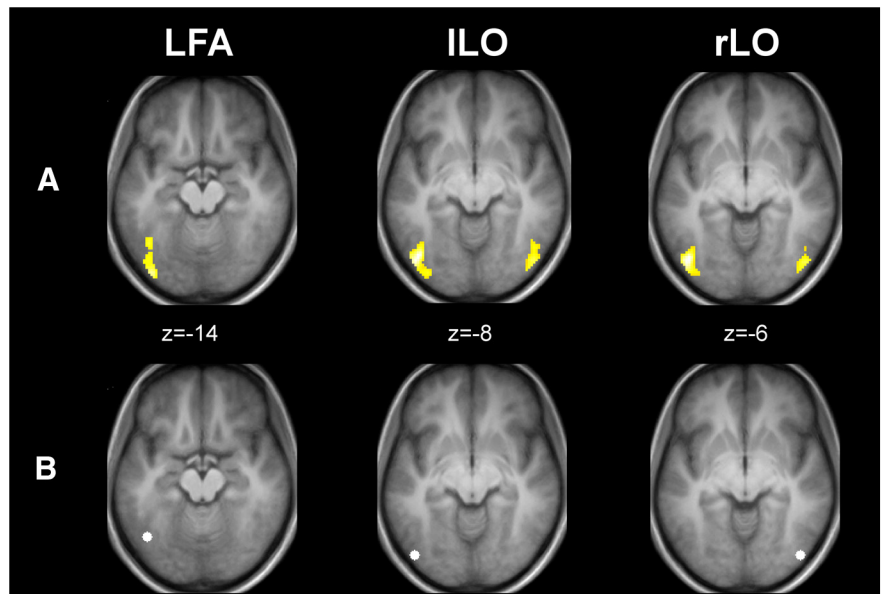

Figure 2. Results of the functional localizer used to determine ROIs. **A**, Average activations contrasting RL with Fourier noise images and FF ($p < 0.0001_{\text{UNCORRECTED}}$ with a cluster extent of >50 voxels) or contrasting RL with Fourier ($p < 0.000001_{\text{UNCORRECTED}}$ with a cluster extent of >50 voxels) for LFA and LO localization, respectively. **B**, A 4 mm sphere around the average center coordinates of LFA [average MNI coordinates ($\pm$SE): $-45(1)$, $-66(2)$, $-14(2)$] and LO [average MNI coordinates ($\pm$SE): $-47(1)$, $-81(2)$, $-8(1)$ for left, 46(1), $-81(2)$, $-6(1)$ and right hemisphere] ROIs. lLO, left lateral occipital cortex; rLO, right lateral occipital cortex.
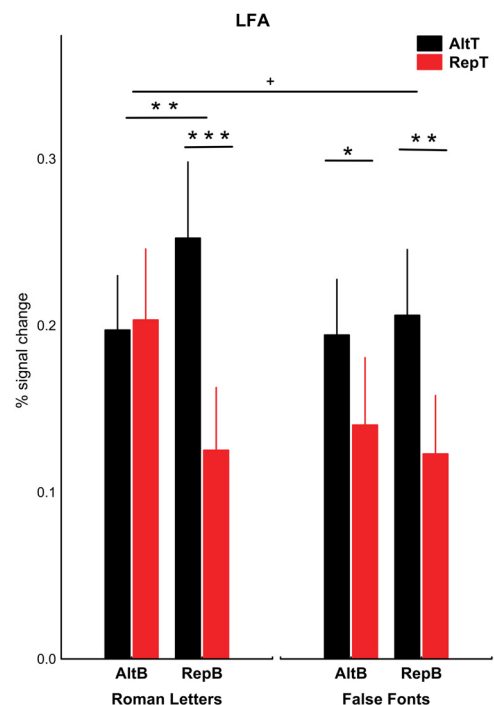

Figure 3. Average peak activation profiles ($\pm$SE) of the LFA for AltTs and RepTs in AltB and RepB, when RLs or FFs were presented; $^+p < 0.1$, $^*p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$.

RS for RLs in the LFA similar to previous findings for face stimuli in the FFA. Interestingly however, no such influence of P(rep) was observed for the FFs in the LFA (block × trial interaction: $F_{(1,16)} = 0.71$, $p = 0.41$, $\eta_p^2 = 0.04$), in which case Repetition Trials lead to similar responses in Repetition Blocks and Alternation Blocks (Fisher LSD *post hoc* test: $p = 0.49$). These observa-
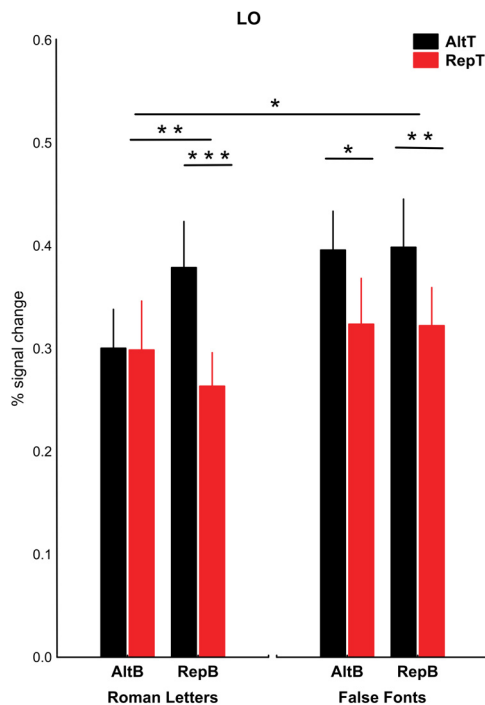
Figure 4. Average peak activation profiles ($\pm$SE) of the LO for AltTs and RepTs in AltB and RepB, when RLs or FFs were presented; *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

Figure 5. Results of the whole-brain analysis showing significant activations for the main effects of trial ($p < 0.0001_{\text{UNCORRECTED}}$; cluster extent $>$20 voxels) for RLs and FFs, as well as for the main effect of block ($p < 0.0001_{\text{UNCORRECTED}}$ with a cluster extent of $>$20 voxels) and for the interaction of the two factors for RLs ($p < 0.05_{\text{FWE}}$ with a cluster extend of $>$50 voxels).

tions were confirmed by the three-way ANOVA with stimulus, block, and trial type as factors, in which the magnitude of RS (main effect of trial: $F_{(1,16)} = 11.3$, $p = 0.004$, $\eta_p^2 = 0.41$) showed a strong tendency for dependence on block-type and stimulus-type (three-way interaction of stimulus, block, and trial: $F_{(1,16)} = 3.23$, $p = 0.09$, $\eta_p^2 = 0.17$), suggesting larger RS in the Repetition Blocks specifically during RL stimulation. These results demonstrate that P(rep) effects in the visual modality are not a unique property of the category of faces; rather they can also be found for nonface stimuli, such as roman characters. The fact, however, that no such effects were found for the unfamiliar FF stimuli suggests a role of prior experiences in determining P(rep) modulatory effects on RS.

LO

LO ($N = 17$) showed no main effect of hemisphere ($F_{(1,16)} = 0.98$, $p = 0.34$, $\eta_p^2 = 0.06$), no interaction of hemisphere with stimulus ($F_{(1,16)} = 4.19$, $p = 0.06$, $\eta_p^2 = 0.21$), with trial ($F_{(1,16)} = 0.0009$, $p = 0.98$, $\eta_p^2 = 0.00005$), or with block ($F_{(1,16)} = 0.01$, $p = 0.92$, $\eta_p^2 = 0.0007$). As in the LFA, we observed significant repetition suppression in the LO (Fig. 4) for RLs (main effect of trial: $F_{(1,16)} = 7.09$, $p = 0.02$, $\eta_p^2 = 0.31$) as well as for FFs ($F_{(1,16)} = 14.32$, $p = 0.002$, $\eta_p^2 = 0.47$). While we also found a significant interaction of RS with P(rep) for RLs ($F_{(1,16)} = 10.61$, $p = 0.005$, $\eta_p^2 = 0.40$), the same analysis led to no significant results for FFs ($F_{(1,16)} = 0.01$, $p = 0.91$, $\eta_p^2 = 0.001$). The P(rep) effects were driven by a lower BOLD signal to Repetition Trials when compared with Alternation Trials in Repetition Blocks (Fisher LSD *post hoc* test: $p = 0.0003$) but not in Alternation Blocks (Fisher LSD *post hoc* test: $p = 0.95$) for the RLs. However, no such effect was observed for FFs where Repetition Trials were significantly lower than Alternation Trials for both Repetition Block and Alternation Block (Fisher LSD *post hoc* test: $p = 0.02$ for AltB, $p = 0.008$ for RepB). Hence, in contrast to previous studies with everyday objects and chairs (Kovács et al., 2013) and similarly to those with faces
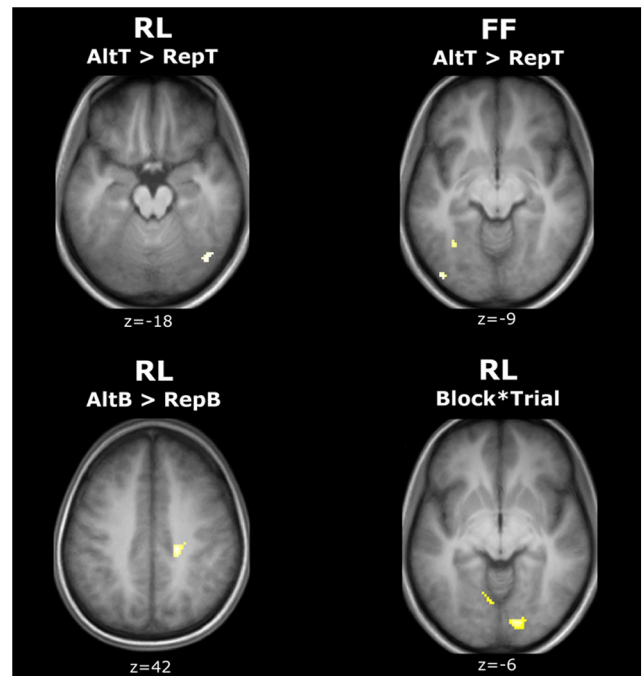
(Summerfield et al., 2008; Kovács et al., 2012; Larsson and Smith, 2012), we could show modulation of RS by P(rep) in LO for characters of the familiar script. However, as in the LFA, this modulation was dependent on the stimulus type (three-way interaction of stimulus, block, and trial: $F_{(1,16)} = 5.69$, $p = 0.03$, $\eta_p^2 = 0.26$). These findings suggest that P(rep) modulations of RS for RLs are not unique to the LFA and support the conclusion that these modulations depend on the prior experiences of the subjects.

Whole-brain analyses

To test whether other areas possibly reflect the repetition probability modulation effects as well, we also performed whole-brain random-effects analyses separately for the RL and FF stimuli. Testing the main effect of trial type (AltT vs RepT) and the main effect of block type (AltB vs RepB) led to no significant activations in additional brain regions at the threshold of $p_{\text{FWE}} < 0.05$ (cluster extent of $>$50) for either stimulus type. Next, to make sure that no area is overlooked by the commonly applied, rigorous FWE corrected threshold we also analyzed our data at a more liberal ($p < 0.0001_{\text{UNCORRECTED}}$; cluster extent of $>$20 voxels) threshold. The AltT $>$ RepT contrast of this analysis (Fig. 5, top) revealed two small clusters (MNI coordinates [x,y,z]: $-46, -86, -8$; cluster size: 22 voxels and $-34, -58, -10$; cluster size: 24 voxels) for FFs and a single cluster for RLs (MNI coordinates [x,y,z]: $42, -74, -18$; cluster size: 40 voxels). While not identical, these coordinates show strong correspondence to those of the average left LO, LFA, and right LO ROIs, respectively. The lack of further clusters showing a main effect of trial type suggests that this effect is specific to these regions. No significant activations were found for the opposite (RepT $>$ AltT) contrast.

The same liberal threshold identified a single cluster for the main effect of block type (AltB $>$ RepB) for RLs (Fig. 5, bottom left) in the medial parietal lobe, at the dorsal posterior cingulate

area (BA 31; MNI coordinates [*x,y,z*]: 20, −30, −42; cluster size: 66 voxels), an area involved in various cognitive functions (for review, see Leech and Sharp, 2014). No significant activations were found for the opposite (RepB > AltB) contrast.

The contrast testing the interaction of trial and block types [(AltB_AltT vs AltB_RepT) vs (RepB_AltT vs RepB_RepT)], i.e., the P(rep) effect on RS, led to two clusters of voxels in the lingual gyrus (Fig. 5, bottom right), corresponding to the early visual areas V1/V2 (MNI coordinates [*x,y,z*]: 12, −88, −6; cluster size: 158 voxels and −8, −70, −2; cluster size: 142 voxels; threshold: $p_{FWE} < 0.05$ with a cluster extent of >50 voxels) for RL stimuli. This activation supports the findings of Larsson and Smith (2012), who found similar interactions for the retinotopically identified V1 and V2 for face stimuli. In accordance with the results of the ROI analysis, the same contrast led to no significant activations for FFs anywhere in the brain, even with the more liberal ($p < 0.0001_{UNCORRECTED}$; cluster extent of >20 voxels) threshold.

Discussion

We observed repetition suppression modulation by repetition probability in the LFA and in the LO. However, these modulations were stimulus dependent; they were observed for well known RLs, but not for unfamiliar FFs. Therefore, the current study suggests that P(rep) effects depend on the subject's prior experiences with the presented stimulus.

LFA

A posterior to anterior increase in processing level during word recognition has recently been demonstrated (Vinckier et al., 2007; Thesen et al., 2012). Thesen et al. (2012) proposed the existence of the LFA, bordering anteriorly on the Visual Word Form Area (VWFA; Cohen et al., 2000, 2002; Dehaene et al., 2002), which accomplishes letter-form processing, but not word-form processing. In our aim to keep our stimulus set comparable to previous studies (Summerfield et al., 2008; Kovács et al., 2013), we tested the RS of the LFA for two reasons. First, we wanted to limit any possible influence of semantic information as present in words. Second, for better comparison with previous studies using single stimuli on a uniform background, we also presented single characters, instead of words consisting of multiple characters. Taking the relatively large interindividual differences into account (Wong et al., 2009; Glezer and Riesenhuber, 2013), activations in the LFA have been found when contrasting single RLs with geometrical lines (Longcamp et al., 2005) and by directing attention (Flowers et al., 2004) or working memory (Libertus et al., 2009) to letters, as opposed to colors and digits, or faces and digits, respectively. These findings suggest the LFA to be sensitive to single letter presentations, a conclusion supported by the current study.

LO

The caudodorsal part of the lateral occipital complex (Malach et al., 1995; Grill-Spector et al., 1999) is commonly described as an area involved in processing objects, but also responds to faces (Puce et al., 1995; Lerner et al., 2001). The current study shows that LO responds to single letters as well.

Previous studies on the interaction of P(rep) with RS analyzed the LO. Larsson and Smith (2012) used retinotopic mapping to localize LO1 and LO2, which both demonstrated P(rep) effects on RS for faces. Others showed P(rep) effects on RS in LO for faces (Kovács et al., 2012), but not for everyday objects and chairs (Kovács et al., 2013). This indicates that P(rep) effects in LO are

dependent on the stimulus category; a result further supported by single-cell recordings of macaque IT, a proposed homolog of the human LO (Denys et al., 2004), which did not show P(rep) effects for fractal patterns and everyday objects (Kaliukhovich and Vogels, 2011).

The expertise hypothesis

Previous studies found P(rep) effects for faces, but not for other visual stimuli (Summerfield et al., 2008; Kovács et al., 2013). Indeed, during the last decades the neural processing of faces has been shown to differ from other objects in many aspects. For example, faces are processed configural and/or holistic, meaning that components are integrated into a holistic unit instead of being decomposed into parts (Young et al., 1987; Tanaka and Farah, 1993; Hole, 1994; Farah et al., 1998; Barton et al., 2001; Le Grand et al., 2001; Maurer et al., 2002). Although the origin of this specificity is strongly debated in the literature (Gauthier et al., 2000; Bukach et al., 2006; McKone et al., 2007, 2012), studies suggest that many face-specific effects might be explained by extensive prior experiences. After all, dog experts show configural processing for their breed similarly to faces (Diamond and Carey, 1986) and subjects trained for novel objects (Greebles; Gauthier and Tarr, 1997) show holistic processing with the onset of expertise (but see Brants et al., 2011 for a different conclusion). In addition to faces, another stimulus category of high expertise is letters of the familiar writing system. Previous studies showed enhanced activity of the LFA for characters of the familiar script, suggesting a role of experience in determining the response magnitude to single characters (Wong et al., 2009). The fact that P(rep) effects on RS have been observed for faces (Summerfield et al., 2008) and RLs (current data), but not for objects (Kovács et al., 2013) and unfamiliar FFs (current data), suggests that P(rep) effects depend on the previous experience participants have with the stimuli. The lack of experience with the stimuli could explain the lack of P(rep) effects in the study of Kaliukhovich and Vogels (2011) as well. Indeed, recent studies on perceptual expertise have revealed that the acquisition of expertise leads to enhanced associations among features or objects in the sense that untrained stimulus pairs evoke much stronger neural activity in IT when compared with trained and therefore predicted pairs (Meyer and Olson, 2011). This suggests that predictions and experiences are connected to each other (for review, see Cheung and Bar, 2012), thereby linking expertise to predictive coding and the origin of RS. One important implication of the present data is that neurons of a given area might have different sensitivity for P(rep) effects on RS, depending on prior experiences with the applied stimulus. It is possible, for example, that prior experiences facilitate the neurons of the LFA in sending expectation-related signals, leading to probability effects on RS. However, testing the neuronal mechanism of the interaction of expertise and expectation-related phenomena will require specific future studies.

Alternative explanations

Attention

Larsson and Smith (2012) showed that P(rep) effects on RS are present only if attention is directed toward the stimuli. Since the monkeys of the Kaliukhovich and Vogels (2011) study performed a passive fixation task, lack of attention could explain the absence of P(rep) effects on RS. However, in the human fMRI study of Kovács et al. (2013), in which P(rep) effects were not observed for objects, subjects performed the same task as in previous studies, which reported P(rep) effects for faces (Kovács et al., 2012). This indicates that different attentional states are unlikely to explain

differences in P(rep) effects, unless the stimuli per se recruit different attentional resources. In fact, there is evidence that faces draw more attention than inanimate objects (Mack et al., 2002; New et al., 2007). This might explain the differences in P(rep) effects on RS observed previously (Summerfield et al., 2008; Kovács et al., 2013). However, to our best knowledge, there is no evidence that letters of the familiar writing system attract more attention than FFs. Further, the fact that our subjects performed their task equally well for both stimulus categories supports similar attentional states. Hence, even though attention cannot be ruled out to explain previous findings, it is very unlikely the source of the P(rep) effect differences observed in the current study.

P(rep) effects on RS as an attribute of different neuronal populations

RLs possibly "recycle" neuronal terrain evolved for face perception (Dehaene and Cohen, 2011), as suggested by the fact that the VWFA partially encodes faces as well (Mei et al., 2010). Hence, in addition to expertise, faces and letters share another factor, which could account for the different P(rep) effects when compared with FF and objects. However, it is very unlikely that the repetition probability effect differences are based on different neuronal population attributes for three reasons. First, the LFA and the LO show P(rep) effects for RL, but not for FF in the current study, suggesting that the same neuronal population may show these effects or not, depending on the stimulus presented. Second, the current study found P(rep) effects for letters in the LO, the same area that did not show P(rep) effects for objects (Kovács et al., 2013). Finally, and above all, predictive coding, and hence the P(rep)-related effect, is proposed to be universal throughout the sensory cortices (Friston, 2005).

Differences in verbal encoding

In addition to familiarity, RLs and FFs vary in another attribute; namely the fact that the former can, but the latter cannot, be verbalized. Therefore, it is possible that for RLs expectation is represented (in addition to the common sensory representation) also by a verbal code, which might enhance RS. Indeed, differential verbal coding could also account for the differences of the macaque and human studies. However, since unfamiliar faces and objects are processed at a similar (basic) categorization level (Engst et al., 2006; Anaki and Bentin, 2009), leading to similar verbal coding, semantic information cannot explain the lack of P(rep) effects for chairs and everyday objects in our previous human fMRI study (Kovács et al., 2013) and is therefore unlikely to modulate P(rep) effects.

In summary, the current study shows that repetition probability-related expectations affect the magnitude of repetition suppression for neurons of the LFA and the LO for letters of the familiar script, but not for novel FFs. This suggests, for the first time, that prior experiences affect the influence of high-level, contextual predictions on RS in the human occipitotemporal cortex. Further studies will reveal the nature of these experiences and show whether mere exposure, intense training, or even evolutionary mechanisms are necessary for these changes to arise.

References

Anaki D, Bentin S (2009) Familiarity effects on categorization levels of faces and objects. Cognition 111:144–149. CrossRef Medline

Bar M (2004) Visual objects in context. Nat Rev Neurosci 5:617–629. CrossRef Medline

Barton JJ, Keenan JP, Bass T (2001) Discrimination of spatial relations and features in faces: effects of inversion and viewing duration. Br J Psychol 92:527–549. CrossRef Medline

Ben-Shachar M, Dougherty RF, Deutsch GK, Wandell BA (2007) Differential sensitivity to words and shapes in ventral occipito-temporal cortex. Cereb Cortex 17:1604–1611. CrossRef Medline

Brants M, Wagemans J, Op de Beeck HP (2011) Activation of fusiform face area by Greebles is related to face similarity but not expertise. J Cogn Neurosci 23:3949–3958. CrossRef Medline

Brett M, Johnsrude IS, Owen AM (2002) The problem of functional localization in the human brain. Nat Rev Neurosci 3:243–249. CrossRef Medline

Bukach CM, Gauthier I, Tarr MJ (2006) Beyond faces and modularity: the power of an expertise framework. Trends Cogn Sci 10:159–166. CrossRef Medline

Cheung OS, Bar M (2012) Visual prediction and perceptual expertise. Int J Psychophysiol 83:156–163. CrossRef Medline

Cohen L, Dehaene S, Naccache L, Lehéricy S, Dehaene-Lambertz G, Hénaff MA, Michel F (2000) The visual word form area: spatial and temporal characterization of an initial stage of reading in normal subjects and posterior split-brain patients. Brain 123:291–307. CrossRef Medline

Cohen L, Lehéricy S, Chochon F, Lemer C, Rivaud S, Dehaene S (2002) Language-specific tuning of visual cortex? Functional properties of the visual word form area. Brain 125:1054–1069. CrossRef Medline

Cziraki C, Greenlee MW, Kovács G (2010) Neural correlates of high-level adaptation-related aftereffects. J Neurophysiol 103:1410–1417. CrossRef Medline

Dehaene S, Cohen L (2011) The unique role of the visual word form area in reading. Trends Cogn Sci 15:254–262. CrossRef Medline

Dehaene S, Le Clec'H G, Poline JB, Le Bihan D, Cohen L (2002) The visual word form area: a prelexical representation of visual words in the fusiform gyrus. Neuroreport 13:321–325. CrossRef Medline

Denys K, Vanduffel W, Fize D, Nelissen K, Peuskens H, Van Essen D, Orban GA (2004) The processing of visual shape in the cerebral cortex of human and nonhuman primates: a functional magnetic resonance imaging study. J Neurosci 24:2551–2565. CrossRef Medline

Diamond R, Carey S (1986) Why faces are and are not special: an effect of expertise. J Exp Psychol Gen 115:107–117. CrossRef Medline

Engst FM, Martín-Loeches M, Sommer W (2006) Memory systems for structural and semantic knowledge of faces and buildings. Brain Res 1124: 70–80. CrossRef Medline

Ewbank MP, Henson RN (2012) Explaining away repetition effects via predictive coding. Cogn Neurosci 3:239–240. CrossRef Medline

Farah MJ, Wilson KD, Drain M, Tanaka JN (1998) What is "special" about face perception? Psychol Rev 105:482–498. CrossRef Medline

Fiebach CJ, Gruber T, Supp GG (2005) Neuronal mechanisms of repetition priming in occipitotemporal cortex: spatiotemporal evidence from functional magnetic resonance imaging and electroencephalography. J Neurosci 25:3414–3422. CrossRef Medline

Flowers DL, Jones K, Noble K, VanMeter J, Zeffiro TA, Wood FB, Eden GF (2004) Attention to single letters activates left extrastriate cortex. Neuroimage 21:829–839. CrossRef Medline

Friston K (2005) A theory of cortical responses. Philos Trans R Soc Lond B Biol Sci 360:815–836. CrossRef Medline

Gauthier I, Tarr MJ (1997) Becoming a "Greeble" expert: exploring mechanisms for face recognition. Vision Res 37:1673–1682. CrossRef Medline

Gauthier I, Skudlarski P, Gore JC, Anderson AW (2000) Expertise for cars and birds recruits brain areas involved in face recognition. Nat Neurosci 3:191–197. CrossRef Medline

Glezer LS, Riesenhuber M (2013) Individual variability in location impacts orthographic selectivity in the "visual word form area." J Neurosci 33: 11221–11226. CrossRef Medline

Gotts SJ, Chow CC, Martin A (2012) Repetition priming and repetition suppression: a case for enhanced efficiency through neural synchronization. Cogn Neurosci 3:227–237. CrossRef Medline

Grill-Spector K, Kushnir T, Edelman S, Avidan G, Itzchak Y, Malach R (1999) Differential processing of objects under various viewing conditions in the human lateral occipital complex. Neuron 24:187–203. CrossRef Medline

Grill-Spector K, Henson R, Martin A (2006) Repetition and the brain: neural models of stimulus-specific effects. Trends Cogn Sci 10:14–23. CrossRef Medline

Henson RN (2001) Repetition effects for words and nonwords as indexed by event-related fMRI: a preliminary study. Scand J Psychol 42:179–186. CrossRef Medline

Henson RN (2003) Neuroimaging studies of priming. Prog Neurobiol 70: 53– 81. CrossRef Medline

Henson R, Shallice T, Dolan R (2000) Neuroimaging evidence for dissociable forms of repetition priming. Science 287:1269–1272. CrossRef Medline

Hole GJ (1994) Configurational factors in the perception of unfamiliar faces. Perception 23:65–74. CrossRef Medline

Kaliukhovich DA, Vogels R (2011) Stimulus repetition probability does not affect repetition suppression in macaque inferior temporal cortex. Cereb Cortex 21:1547–1558. CrossRef Medline

Kanwisher N, McDermott J, Chun MM (1997) The fusiform face area: a module in human extrastriate cortex specialized for face perception. J Neurosci 17:4302–4311. Medline

Kovács G, Iffland L, Vidnyánszky Z, Greenlee MW (2012) Stimulus repetition probability effects on repetition suppression are position invariant for faces. Neuroimage 60:2128–2135. CrossRef Medline

Kovács G, Kaiser D, Kaliukhovich DA, Vidnyánszky Z, Vogels R (2013) Repetition probability does not affect fMRI repetition suppression for objects. J Neurosci 33:9805–9812. CrossRef Medline

Krekelberg B, Boynton GM, van Wezel RJ (2006) Adaptation: from single cells to BOLD signals. Trends Neurosci 29:250–256. CrossRef Medline

Larsson J, Smith AT (2012) fMRI repetition suppression: neuronal adaptation or stimulus expectation? Cereb Cortex 22:567–576. CrossRef Medline

Leech R, Sharp DJ (2014) The role of the posterior cingulate cortex in cognition and disease. Brain 137:12–32. CrossRef Medline

Le Grand R, Mondloch CJ, Maurer D, Brent HP (2001) Neuroperception. Early visual experience and face processing. Nature 410:890. CrossRef Medline

Lerner Y, Hendler T, Ben-Bashat D, Harel M, Malach R (2001) A hierarchical axis of object processing stages in the human visual cortex. Cereb Cortex 11:287–297. CrossRef Medline

Libertus ME, Brannon EM, Pelphrey KA (2009) Developmental changes in category-specific brain responses to numbers and letters in a working memory task. Neuroimage 44:1404–1414. CrossRef Medline

Longcamp M, Anton JL, Roth M, Velay JL (2005) Premotor activations in response to visually presented single letters depend on the hand used to write: a study on left-handers. Neuropsychologia 43:1801–1809. CrossRef Medline

Mack A, Pappas Z, Silverman M, Gay R (2002) What we see: inattention and the capture of attention by meaning. Conscious Cogn 11:488–506. CrossRef Medline

Malach R (2012) Targeting the functional properties of cortical neurons using fMR-adaptation. Neuroimage 62:1163–1169. CrossRef Medline

Malach R, Reppas JB, Benson RR, Kwong KK, Jiang H, Kennedy WA, Ledden PJ, Brady TJ, Rosen BR, Tootell RB (1995) Object-related activity revealed by functional magnetic resonance imaging in human occipital cortex. Proc Natl Acad Sci U S A 92:8135–8139. CrossRef Medline

Maurer D, Grand RL, Mondloch CJ (2002) The many faces of configural processing. Trends Cogn Sci 6:255–260. CrossRef Medline

McKone E, Kanwisher N, Duchaine BC (2007) Can generic expertise explain special processing for faces? Trends Cogn Sci 11:8–15. CrossRef Medline

McKone E, Crookes K, Jeffery L, Dilks DD (2012) A critical review of the development of face recognition: experience is less important than previously believed. Cogn Neuropsychol 29:174–212. CrossRef Medline

Mei L, Xue G, Chen C, Xue F, Zhang M, Dong Q (2010) The "visual word form area" is involved in successful memory encoding of both words and faces. Neuroimage 52:371–378. CrossRef Medline

Meyer T, Olson CR (2011) Statistical learning of visual transitions in monkey inferotemporal cortex. Proc Natl Acad Sci U S A 108:19401–19406. CrossRef Medline

Moore CJ, Price CJ (1999) Three distinct ventral occipitotemporal regions for reading and object naming. Neuroimage 10:181–192. CrossRef Medline

New J, Cosmides L, Tooby J (2007) Category-specific attention for animals reflects ancestral priorities, not expertise. Proc Natl Acad Sci U S A 104: 16598–16603. CrossRef Medline

Puce A, Allison T, Gore JC, McCarthy G (1995) Face-sensitive regions in human extrastriate cortex studied by functional MRI. J Neurophysiol 74:1192–1199. Medline

Puce A, Allison T, Asgari M, Gore JC, McCarthy G (1996) Differential sensitivity of human visual cortex to faces, letterstrings, and textures: a functional magnetic resonance imaging study. J Neurosci 16:5205–5215. Medline

Rao RP, Ballard DH (1999) Predictive coding in the visual cortex: a functional interpretation of some extra-classical receptive-field effects. Nat Neurosci 2:79–87. CrossRef Medline

Summerfield C, Trittschuh EH, Monti JM, Mesulam MM, Egner T (2008) Neural repetition suppression reflects fulfilled perceptual expectations. Nat Neurosci 11:1004–1006. CrossRef Medline

Tanaka JW, Farah MJ (1993) Parts and wholes in face recognition. Q J Exp Psychol A 46:225–245. CrossRef Medline

Thesen T, McDonald CR, Carlson C, Doyle W, Cash S, Sherfey J, Felsovalyi O, Girard H, Barr W, Devinsky O, Kuzniecky R, Halgren E (2012) Sequential then interactive processing of letters and words in the left fusiform gyrus. Nat Commun 3:1284. CrossRef Medline

Todorovic A, de Lange FP (2012) Repetition suppression and expectation suppression are dissociable in time in early auditory evoked fields. J Neurosci 32:13389–13395. CrossRef Medline

Vinckier F, Dehaene S, Jobert A, Dubus JP, Sigman M, Cohen L (2007) Hierarchical coding of letter strings in the ventral stream: dissecting the inner organization of the visual word-form system. Neuron 55:143–156. CrossRef Medline

Wong AC, Jobard G, James KH, James TW, Gauthier I (2009) Expertise with characters in alphabetic and nonalphabetic writing systems engage overlapping occipito-temporal areas. Cogn Neuropsychol 26:111–127. CrossRef Medline

Young AW, Hellawell D, Hay DC (1987) Configurational information in face perception. Perception 16:747–759. CrossRef Medline