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Global familiarity of visual stimuli affects repetition-related neural plasticity but not repetition priming

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In this study, we tested the prediction of the *component process model* of priming [Henson, R.N. (2003). Neuroimaging studies of priming. Prog Neurobiol, 70 (1), 53–81] that repetition priming of familiar and unfamiliar objects produces qualitatively different neural repetition effects. In an fMRI study, subjects viewed four repetitions of familiar objects and globally unfamiliar objects with familiar components. Reliable behavioral priming occurred for both item types across the four presentations and was of a similar magnitude for both stimulus types. The imaging data were analyzed using multivariate linear modeling, which permits explicit testing of the hypothesis that the repetition effects for familiar and unfamiliar objects are qualitatively different (i.e., non-scaled versions of one another). The results showed the presence of two qualitatively different latent spatial patterns of repetition effects from presentation 1 to presentation 4 for familiar and unfamiliar objects, indicating that familiarity with an object's global structural, semantic, or lexical features is an important factor in priming-related neural plasticity. The first latent spatial pattern strongly weighted regions with a similar repetition effect for both item types. The second pattern strongly weighted regions contributing a repetition suppression effect for the familiar objects and repetition enhancement for the unfamiliar objects, particularly the posterior insula, superior temporal gyrus, precentral gyrus, and cingulate cortex. This differential repetition effect might reflect the formation of novel memory representations for the unfamiliar items, which already exist for the familiar objects, consistent with the component process model of priming.

Keywords: fMRI; Priming; Multivariate linear models; Objects; Repetition enhancement; Repetition suppression

Repetition priming refers to a behavioral change in the speed, accuracy, or bias of processing a stimulus due to prior exposure to the stimulus (e.g., Tulving and Schacter, 1990). It is a form of *implicit memory* and can occur even when conscious memory for the stimulus is not available (Deeprose and Andrade, 2006; Henson, 2003; Roediger and McDermott, 1993; Schacter and Buckner, 1998; Schacter et al., 1993). Repetition priming is typically measured using indirect tests of memory, which make no explicit reference to the prior encounter with the stimulus. It has been observed both when the same (e.g., Habeck et al., 2006; Henson et al., 2004) or different (Liu and Cooper, 2001; Soldan et al., 2006) tasks are performed during the initial and repeated presentation of a stimulus.

Many neuroimaging studies of repetition priming have demonstrated *repetition suppression (RS)*, a reduction in the neural response to the repeated compared to the first presentation of a stimulus (for reviews, see Henson, 2003; Schacter and Buckner, 1998). These reductions in neural activity tend to occur in a subset of the brain regions that are engaged during the initial analysis of the stimulus. Thus, for visual stimuli, RS tends to be prominent in occipital–temporal cortex, as well as in areas involved in the semantic analysis of stimuli, particularly the inferior frontal gyrus, and is not normally observed in primary visual cortex or in primary motor cortex (Reber et al., 2005; Sayres and Grill-Spector, 2006; Simons et al., 2003; van Turennout et al., 2000; Vuilleumier et al., 2002; Zago et al., 2005). Parallel findings have been demonstrated with single-cell recordings in monkeys, showing a decrease in the neuronal firing rate in inferior temporal cortex and prefrontal cortex for repeated visual stimuli (Desimone, 1996; Ringo, 1996; Sobotka and Ringo, 1994). RS at the neuronal level is stimulus-dependent (Sobotka and Ringo, 1994) and for a given stimulus is largest in neurons that showed the greatest response to that stimulus when it was initially presented (Li et al., 1993).

As both repetition priming and RS are repetition-related phenomena and neither depends on explicit memory retrieval, it has been conjectured that RS reflects the neural plasticity that causes repetition priming (Henson, 2003; Maccotta and Buckner, 2004; Schacter and Buckner, 1998; Wiggs and Martin, 1998; Zago et al., 2005). One model for a mechanism by which RS may give rise to priming was proposed by Wiggs and Martin (1998). They suggested that RS in occipital–temporal areas reflects a "sharpening" of the neuronal population representation of a stimulus, such

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that a repeated stimulus can be represented with fewer neurons. When measured with neuroimaging, this would lead to macroscopic RS, as blood flow signal is thought to be a spatial average over several mm of cortical activity. This more sparse representation is thought to allow for more efficient stimulus processing and hence result in faster behavioral responses (i.e., repetition priming). Others have suggested that the number of neurons representing a repeated stimulus is the same, but their level of activity (Grill-Spector et al., 1999) or duration of activity (Henson and Rugg, 2003) is reduced. This is thought to reflect the increased efficiency in the neural processing of a repeated stimulus, which leads to behavioral priming. Going against both models, there have been a few reports of dissociations between repetition priming and RS in occipital–temporal cortex, as measured by fMRI (Dobbins et al., 2004; Sayres and Grill-Spector, 2006). This suggests that not all aspects of RS may be directly related to repetition priming and that further research is necessary to determine the precise relationship between them.

Most neuroimaging studies in support of the view that repetition priming is mediated by RS have used familiar stimuli, such as pictures of everyday objects, animals, famous faces, and words. However, it is still a matter of debate whether repetition priming for familiar and pre-experimentally unfamiliar stimuli, such as nonsense objects, unfamiliar faces, and pseudowords, is mediated by the same neural mechanism, i.e., RS, and the same brain areas. Consistent with the view that RS is a general mechanism that mediates repetition priming of all stimulus types, independent of stimulus familiarity, several studies have demonstrated repetition priming accompanied by RS in occipital–temporal cortex for nonsense (i.e., non-nameable) objects (Habeck et al., 2006; van Turennout et al., 2000; Vuilleumier et al., 2002) and unfamiliar faces (Pourtois et al., 2005). Other studies examining repetition priming of unfamiliar stimuli have reported increases in neural activity, or *repetition enhancement* (RE), in occipital–temporal cortex for repeated stimuli, including unfamiliar faces (Henson et al., 2000; Thiel et al., 2002), meaningless symbols (Henson et al., 2000), line drawings of novel 3D objects (Schacter et al., 1995), and pseudowords (Fiebach et al., 2005). At least two of these studies (Fiebach et al., 2005; Schacter et al., 1995) only found RE and no RS in occipital–temporal cortex for the unfamiliar stimuli, while Henson et al. (2000) and Thiel et al. (2002) did not report whether there were any regions that showed RS for the unfamiliar stimuli.

Interestingly, both those studies finding RS and those finding RE for unfamiliar stimuli have reported fewer locations of significant neural repetition effects (either RS or RE) for unfamiliar stimuli compared to familiar ones. Thus, those studies reporting RS for both familiar and unfamiliar stimuli within the same task (van Turennout et al., 2000; Vuilleumier et al., 2002) have found that RS for unfamiliar objects was confined to more posterior regions of occipital–temporal cortex, whereas RS for familiar stimuli encompassed both posterior and anterior regions of occipital–temporal regions as well as inferior frontal regions. Similarly, in the context of repetition priming tasks, RE in occipital–temporal regions for unfamiliar stimuli has been reported in very few and relatively small loci, including the anterior fusiform gyrus (Fiebach et al., 2005; Henson et al., 2000; Schacter et al., 1995; Thiel et al., 2002). In addition, Fiebach et al. (2005) showed that within the same task, familiar stimuli (words) elicited RS in large areas of occipital–temporal cortex, as well as in frontal and parietal regions, whereas unfamiliar stimuli (pseudowords) produced RE in only a subset of occipital–temporal areas.

In order to integrate these findings into a coherent framework, Henson (2000, 2003) proposed in his *component process* model of priming that “repetition suppression occurs whenever the same process is performed on prime [the first presentation of a stimulus] and target [a repeated stimulus], whereas repetition enhancement occurs whenever priming causes a new process to occur on the target that did not occur on the prime” (Henson, 2003, p. 71). With respect to the issue of stimulus familiarity, this model further suggests that RE for unfamiliar stimuli indexes processes related to the formation of new, or abstracted (i.e., high-level) representations, which can occur after a single stimulus presentation. These new high-level representations, in addition to RS-related mechanisms affecting more low-level processes common to both familiar and unfamiliar stimuli, would facilitate stimulus processing on subsequent encounters and thereby contribute to repetition priming effects (Fiebach et al., 2005; Gruber and Müller, 2005). For familiar stimuli, repetition would modulate both lower level and established high-level perceptual and lexical/semantic representations (and hence lead to RS) throughout wide areas of cortex (Henson, 2003), which would all contribute to repetition priming. Note that although the component process model emphasizes anterior occipital–temporal cortex as a location where differential RS/RE effects would be expected for familiar and unfamiliar stimuli, such effects could occur in other brain regions as well, provided that some process occurs for the unfamiliar items that does not occur for the familiar ones. Thus, not only new perceptual, but also semantic or lexical representations might be created for unfamiliar stimuli.

Because the component process model has RS occurring for familiar stimuli, while for unfamiliar stimuli there would be RS in a subset of these regions and RE or no repetition effects in other regions, it predicts that repetition effects for familiar and unfamiliar stimuli should be associated with qualitatively different brain activation patterns. Although past results (Fiebach et al., 2005; Henson et al., 2000; Thiel et al., 2002; van Turennout et al., 2000; Vuilleumier et al., 2002), taken together, suggest that this prediction has been borne out, the imaging analysis approaches they employed (i.e., statistical parametric mapping; SPM) are not appropriate to test it. The reason is that even pure scaling differences between conditions could lead to the existence of true voxel-wise intensity differences between these conditions (see Fig. 1 for an illustration). Likewise, two thresholded SPM maps (one per brain activation pattern) can look quite distinct from each other even when the latent spatial patterns are identical to within a scaling factor. In contrast, a different type of test based on singular value decomposition of brain activation patterns, multivariate linear modeling (MLM), can validly assess whether brain activation patterns are qualitatively different by explicitly determining the number of latent spatial patterns required to summarize them (Worsley et al., 1997; for applications of MLM, see Zarahn et al., 2005, 2007).

We used MLM to test the prediction of the *component process model* that repetition effects, as measured with BOLD fMRI, associated with line drawings of familiar real-world objects and unfamiliar items have qualitatively different brain activation patterns. Unlike prior studies on this topic, which reported non-significant or less priming for the unfamiliar items, the magnitude of priming in this study was comparable for both item types (Hilton et al., 2006), facilitating interpretation of differential neural repetition effects between item types. Furthermore, because the component process model does not differentiate between familiarity for the global object structure and familiarity for local object