

# SPECIFICITY OF PRIMING: A COGNITIVE NEUROSCIENCE PERSPECTIVE

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**Abstract** | Priming is a nonconscious form of memory that involves a change in a person's ability to identify, produce or classify an item as a result of a previous encounter with that item or a related item. One important question relates to the specificity of priming — the extent to which priming reflects the influence of abstract representations or the retention of specific features of a previous episode. Cognitive neuroscience analyses provide evidence for three types of specificity: stimulus, associative and response. We consider empirical, methodological and conceptual issues that relate to each type of specificity, and suggest a theoretical perspective to help in guiding future research.






During the past two decades, an important theme in the cognitive neuroscience of memory has been that memory is not a unitary entity. Instead, it is widely accepted that memory consists of several separate but interacting forms, processes or systems (for reviews, see REFS 1–5). One central piece of evidence for multiple forms of memory comes from the phenomenon known as priming: a change in a person's ability to identify, produce or classify an item as a result of a previous encounter with that item or a related item<sup>6–8</sup>. Whereas traditional explicit or direct memory tests require individuals to think back to a previous experience, and recall or recognize past events, priming is usually assessed using indirect or implicit tests<sup>9,10</sup> in which subjects attempt to identify briefly flashed stimuli, to complete word stems or fragments with the first word that comes to mind, to make decisions about the properties of words or objects, or to produce items from a category in response to a category cue. Performance on all of these tasks is improved when the subject has previously seen or heard the target object or word, even though subjects are not asked to recall the target items.

One reason why priming interests cognitive psychologists and neuroscientists is that priming effects can be dissociated from explicit recall and recognition. For example, patients with amnesia who have damage to the medial temporal lobes (MTL) usually have severely

impaired explicit recall and recognition, but show normal priming effects even when their recognition memory for the same stimuli is at chance levels<sup>11</sup>. Research into the cognitive neuroscience of priming has been greatly influenced during the past decade by neuroimaging studies using positron emission tomography (PET) and functional MRI (fMRI). Such studies have provided important information about the neuroanatomical regions that are involved in priming. Moreover, although neuroimaging studies usually find that explicit retrieval is associated with increased cortical activity, priming is generally associated with decreased activity, and this has led to intense debate about the functional significance of changes in cortical activity<sup>6,7,12,13</sup>.

Here, we focus on an aspect that has been a focal point in recent discussions — the specificity of priming. By this, we mean the extent to which, and sense in which, priming reflects the retention of specific features of a stimulus that was perceived during a study episode, the formation of a specific association between two previously presented stimuli, or a specific response that was made to a previously encountered stimulus. To explain this and place our review in some historical context, consider the cognitive origins of priming research. Researchers who were interested in word recognition provided some of the earliest evidence for priming. They argued that the presentation of a word during an

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Study phase	Test phase
<b>a Stimulus specificity</b> Pleasant or unpleasant? camper pick happen	Complete stems cam ____ (same font) tri ____ (novel item) hap ____ (different font)
<b>b Associative specificity</b> Make a sentence window-reason officer-garden flight-charge	Complete stems window-rea ____ (same pair) second-pai ____ (novel pair) officer-cha ____ (recombined pair)
<b>c Response specificity</b> Bigger than a shoebox?    (same decision)	Smaller than a shoebox?  (novel item)  (different decision)

**Figure 1 | Three types of priming specificity.** Examples of how the three types of specificity have commonly been investigated in priming tasks. These tasks usually include a study and a test phase, which are sometimes presented as separate experiments. **a** | A word stem-completion protocol. During the study phase, participants are asked to indicate whether they find the presented word pleasant or unpleasant. At test they are asked to complete the three-letter stems with the first word that comes to mind; priming occurs when subjects complete stems with the target more often when a word has just appeared in the study list than when it has not. Stimulus specificity is investigated by manipulating the letter font of the words and stems. **b** | An associative word stem-completion protocol. During the study phase, participants are asked to form sentences using the presented, unrelated word pairs. At test they are asked to complete the three-letter word stem with the first word that comes to mind. Associative specificity is investigated by comparing performance on stems paired with the same word that they appeared with during the study phase, or a different word. **c** | A semantic-categorization protocol. During the study phase, participants are asked to indicate whether the object presented is bigger than a shoebox in the real world. At some point, participants are asked to switch their decision and to indicate whether the item is smaller than a shoebox. Response specificity is analysed by comparing the time required to make size decisions for repeated items that require the same decision as when first presented with the time required when a different decision must be made.

experiment primes a long-term lexical representation of the word in semantic memory, resulting in faster reaction times when making decisions about a repeated word<sup>14</sup>, or increased accuracy when attempting to identify a briefly flashed word that has been seen earlier<sup>15</sup>. From this perspective, priming does not reflect retention of specific features of the word or the episode in which it was encountered, but instead reflects the activation of an abstract representation during the study episode. Therefore, it followed that priming could be used as a tool to study the properties of lexical representations (similar reasoning has been applied to object representations<sup>6</sup>). By contrast, subsequent researchers who approached priming as a memory phenomenon showed that the magnitude of priming effects can be

reduced by changing specific features of a studied target, including the typeface or case (upper/lower) in which a word is presented<sup>16</sup>, or whether a word is presented in the same or different associative contexts during study and test<sup>17</sup>. Although this issue is still under debate, there is evidence for both abstract and specific components in priming<sup>18–20</sup>.

Here, we discuss cognitive neuroscience evidence that relates to three types of specificity in priming: stimulus specificity (priming is reduced by changing the physical properties of a stimulus between study and test); associative specificity (priming is reduced when associations between target items are changed between study and test); and response specificity (priming is reduced when subjects make different responses to the same stimulus item at study and test). For each type of specificity, we focus on neuroimaging and neuropsychological evidence (for reviews of purely cognitive studies of specificity effects, see REFS 18,20). FIGURE 1 provides examples of experimental protocols that have been used to study each type of specificity. Discoveries about the nature and properties of each type have important implications for understanding the degree of representation that is required for priming, and the location of brain activity that is involved.

#### Stimulus specificity

Stimulus specificity relates to the effects of changing the perceptual features of stimuli. We first consider modality-specific priming: this occurs when within-modality priming (visual study followed by visual test or auditory study followed by auditory test) is greater than cross-modality priming (auditory study followed by visual test, or visual study followed by auditory test). We then consider within-modality changes, such as the font of a word or the voice of a speaker.

**Modality-specific priming.** Early studies found that patients with amnesia who have MTL damage showed normal priming on the stem-completion task, in which subjects have to complete three-letter word beginnings with the first word that comes to mind<sup>21</sup>. Patients with amnesia also show a normal modality-specific effect on the visual stem-completion task — like control subjects, they show less priming after hearing a word than after seeing it<sup>22–24</sup>. These results indicated that both within- and cross-modality priming depend on structures other than the MTL or diencephalic regions that are damaged in patients with amnesia. By contrast, other studies indicate that patients with amnesia who show robust within-modality priming on a word-fragment completion test (where subjects complete fragments such as A-S--S-N for ASSASSIN) show either marginal or non-existent cross-modality priming<sup>25,26</sup>, indicating that, on this task, cross-modality priming depends on the MTL/diencephalic structures that are damaged in severe amnesia (see also REF 27).

Neuroimaging studies of within-modality visual priming that compared brain activity during primed and unprimed stem completion showed that priming is associated with decreased activity in the posterior and

prefrontal cortical regions, most consistently in the right occipitotemporal EXTRASTRIATE CORTEX<sup>28–32</sup>. These findings raised the possibility that priming-related reductions in extrastriate activity reflect the influence of a modality-specific visual representation: there is less extrastriate activity for primed than unprimed items because visual processing is more efficient for the primed items, perhaps reflecting ‘tuning’ of visual representations by study list exposure<sup>13</sup>. The results of a PET study that directly compared within-modality visual priming to cross-modality priming (in which subjects heard words before being tested on visual stem completion) were consistent with this possibility, showing priming-related reductions in extrastriate activity during within- but not cross-modality priming<sup>33</sup>.

These findings imply that priming-related reductions in extrastriate activity, which might be localized to the right hemisphere, reflect the operation of a perceptual representation system (a presemantic system that represents the form and structure, but not the meaning, of words and objects<sup>8</sup>). Consistent with this idea, patient M.S., who had undergone a right-occipital lobectomy<sup>34</sup>, and patient L.H., who had a bilateral occipital lesion<sup>35</sup>, both failed to show the normal increase from cross-modality to within-modality priming on a visual stem-completion task (both patients also showed impaired visual priming on a word identification test). However, studies using other patients with right occipital lobe lesions indicate that whereas the right occipital region is necessary for visual priming on a standard word stem-completion test, in which subjects can complete stems with several different words, it might not be necessary for visual priming when word stems or fragments can be completed only with a single solution<sup>36</sup>.

Surprisingly, several imaging studies of within-modality auditory stem-completion priming have shown priming-related reductions in activity close to the extrastriate regions that were previously implicated in visual priming<sup>30,37,38</sup> (for patient data, see REF 39). A possible explanation for these results is that part of the extrastriate region (V3A, within BRODMANN'S AREA (BA) 19) might be involved in multimodal functions, perhaps converting perceptual information from one modality to another<sup>37</sup> (see also REFS 30,38,40).

Although the extrastriate cortex does not show a reduction in activity during cross-modality priming, other regions do<sup>33,37,41</sup>: in particular, the left temporoparietal cortex around BA39, which has previously been associated with aspects of phonological processing, and a left temporal region near a cortical area that is associated with amodal processing<sup>30</sup>. More surprisingly, considering that within-modality priming is commonly associated with decreased activity, studies of both visual-to-auditory<sup>37</sup> and auditory-to-visual<sup>33</sup> priming on a word-stem completion test found priming-related increases in activity in a region of the right anterior prefrontal cortex (BA 10) that was previously associated with explicit retrieval. Priming-related activity increases have also been observed in experiments that use novel materials, such as meaningless shapes or unfamiliar faces<sup>6,7</sup>.

The discovery that activity in the anterior prefrontal cortex increases during cross- but not within-modality priming, together with findings that implicate this area in explicit retrieval, support the idea that explicit retrieval is involved in cross-modality priming but not in within-modality priming<sup>27,42</sup>, and converge with studies indicating that patients with amnesia have impaired or marginal cross-modality priming<sup>25,26</sup>. However, these findings do not concur with other findings that cross-modality stem-completion priming can be preserved in patients with amnesia<sup>22–24</sup>.

Some clues to solving this puzzle are provided by the fact that activity in the left temporoparietal cortex decreases during cross-modality priming<sup>33,37,41</sup>, indicating that these changes are related to phonological or lexical processing. Patients with amnesia typically have no phonological or lexical processing deficits, nor do they have damage to the left temporoparietal region, so their ability to rely on this region might account for the preserved cross-modality priming on the stem-completion task in these patients. Overall, the data indicate that there are two ‘routes’ to cross-modality priming: one involving changes in phonological processing, which is available to both patients with amnesia and healthy controls, and the other involving explicit retrieval, which is not available to patients with amnesia. A related idea is that any given priming task might reflect conditions that are optimal for one of several competing processes to dominate behavioural expression<sup>43,44</sup>. If one of these routes can substitute for another, then patients with amnesia can show intact cross-modality priming through a preserved phonological route. This hypothesis predicts that patients with damage to both phonological processing and explicit memory should show impaired cross-modality priming, because both routes to priming are compromised. Consistent with this idea, patients with aphasia who had left hemisphere lesions, which caused phonological deficits and poor explicit memory for verbal material, showed normal within-modality priming and impaired cross-modality priming on a visual stem-completion task<sup>45</sup>.

**Within-modality specificity: word priming.** Changing specific perceptual features of words, such as the typeface or case, between the study session and the test can influence priming. From a cognitive neuroscience perspective, one of the best-documented findings of this kind comes from divided visual-field studies carried out by Marsolek and collaborators using the visual stem-completion task<sup>19,46,47</sup>. After subjects have studied target words displayed across the full visual field, changing the case in which the words or stems are displayed (upper versus lower) reduces priming when test stems are presented to the right cerebral hemisphere (in the left visual field), but not when they are presented to the left cerebral hemisphere (in the right visual field). These results led to the proposal that form-specific priming depends on a subsystem in the right cerebral hemisphere, whereas priming that generalizes across letter case depends on a subsystem in the left cerebral hemisphere.

#### EXTRASTRIATE CORTEX

A belt of visually responsive areas of cortex surrounding the primary visual cortex.

#### BRODMANN'S AREAS

(BA) Korbinian Brodmann (1868–1918) was an anatomist who divided the cerebral cortex into numbered subdivisions on the basis of cell arrangements, types and staining properties (for example, the dorsolateral prefrontal cortex contains subdivisions, including BA 46, BA 9 and others). Modern derivatives of his maps are commonly used as the reference system for discussion of brain-imaging findings.

Consistent with this view, Vaidya *et al.*<sup>48</sup> studied form-specific priming on a visual word-stem completion test by presenting stems in either the same typeface as studied words or a different typeface. Patient M.S., who had undergone a right-occipital lobectomy, failed to show font-specific priming, again indicating that the right occipital lobe is crucial for this effect. A recent fMRI study<sup>49</sup> of masked priming<sup>50,51</sup>, where primes are masked to reduce or preclude conscious perception, also linked case-specific priming and the right extrastriate occipital cortex. Immediately after presentation of a masked prime, subjects had to judge whether a target word referred to a natural or man-made object. When the prime and target words were presented in the same case, there was a priming-related activity reduction in two regions of the right extrastriate occipital cortex, but this did not occur when they were presented in different cases. By contrast, in the left occipital cortex there were similar priming-related reductions in activity in both the same- and different-case conditions (see also REF. 52).

However, in other studies both hemispheres have shown greater priming with words of the same case than with words of different cases on a perceptual-identification test<sup>53–54</sup> and a word-fragment completion test<sup>55</sup>. So, the generality of the finding that case-specific priming is greater in the right hemisphere than in the left is unclear (for a detailed discussion, see REF. 56).

**Within-modality specificity: object priming.** Although most cognitive neuroscience research on priming has used verbal materials, some studies have explored specificity in the priming of visual objects. Neuroimaging studies have implicated the right fusiform cortex as an important source of specific visual-object priming. Repeated processing of visual objects yields reductions in activation in a number of cortical regions, including the fusiform, lateral occipital and inferior prefrontal cortices<sup>57–60</sup>. Koutstaal *et al.*<sup>61</sup> compared object priming effects for identical objects and different exemplars of objects with the same name using a task in which subjects judged whether each object was larger than a 13-inch-square box. Reductions in activation were more pronounced for same than different exemplars in the bilateral middle occipital, parahippocampal and fusiform cortices, paralleling behavioural indications of visually-specific priming. These visually-specific activation reductions for object priming were greater in the right fusiform cortex than in the left<sup>61,62</sup>, consistent with those studies discussed earlier on the laterality of font-specific word priming effects. In a related study<sup>63</sup>, subjects were asked to decide whether pictorial images depicted real or nonsense objects. Repeated stimuli were identical, differed in size or viewpoint, or were different exemplars with the same name. Priming-related reductions in activation in the right fusiform cortex were sensitive to changes in both exemplar and viewpoint. Overall, the fMRI data indicate that priming shows strong visual specificity in the right fusiform region (the extent of visual specificity in the left fusiform region is less clear<sup>62,63</sup>).

**MTL and diencephalic structures.** Studies of within-modality priming specificity in patients with amnesia have produced inconsistent results. Kinoshita and Wayland<sup>64</sup> found that control subjects showed greater priming on a word-fragment completion test for words that appeared in the same typeface at study and test than for words that appeared in different typefaces, but patients with amnesia (who had diencephalic damage associated with Korsakoff's syndrome) did not show such font-specific priming. Schacter *et al.*<sup>65</sup> found that healthy control subjects showed more priming on an auditory word identification test (in which studied and nonstudied words are filtered so that they are difficult to identify) when the speaker's voice was the same at study and test than when it differed. By contrast, patients with amnesia (who had either MTL damage or diencephalic damage) did not show this voice-specific priming effect. These studies raise the possibility that the MTL and diencephalic regions contribute to font- and voice-specific priming. However, Vaidya *et al.*<sup>48</sup> found normal font-specific priming on a visual stem-completion task in patients with amnesia, although the priming effect was small. Furthermore, additional cognitive studies indicate that aspects of explicit memory might contribute to form-specific priming on a visual stem-completion test<sup>66</sup>.

In another study<sup>67</sup>, patients with amnesia who had MTL damage showed normal specific visual priming. Patients with amnesia and control subjects were asked to name pictures of common visual objects in two sessions that were separated by two days. On the second day, pictures could be identical, changed in shading or size, different exemplars of the same objects or entirely new objects. In both patients with amnesia and control subjects, naming times were improved in all conditions for primed objects compared with new objects, but identical objects or objects that had changed only in size were named faster than objects with changes in shading, or than different exemplars of the same objects. In a related study<sup>68</sup>, both patients with Korsakoff's amnesia and control subjects showed greater priming for identical pictures than for different exemplars with the same name.

So, although there is some evidence that MTL and diencephalic structures contribute to font- and voice-specific priming, they are not essential for stimulus specificity in object priming.

#### Associative specificity

We now turn our attention to associative specificity, where associations between items are either the same or changed between study and test.

**Stem-completion tasks.** Research concerning the cognitive neuroscience of associative specificity has its origins in studies that examined whether patients with amnesia show priming of newly acquired associations between unrelated words. In an early study of stem-completion priming<sup>17</sup>, patients with amnesia and control subjects studied pairs of unrelated words (such as window–reason or officer–garden) and then completed stems



paired with study list words (window–rea\_\_\_) or different unrelated words from the study list (officer–rea\_\_\_). Both the patients with amnesia and the control subjects showed more priming when stems were presented with the same words as those in the study task than with different words, indicating that specific information about the association between the two words had been acquired and influenced priming. However, the associative priming effect in this and a subsequent experiment occurred only in those patients with mild memory disorders<sup>69</sup>; patients with severe amnesia failed to show associative priming. Other studies also found that patients with amnesia had impaired priming of new associations in the stem-completion task, and revealed that associative priming is correlated with scores on explicit memory measures from the standardized Wechsler Memory Scale<sup>70–72</sup>. These data converge with cognitive studies of normal subjects, which indicate that priming of new associations on the stem-completion task reflects some aspect of explicit memory<sup>73,74</sup>.

A recent PET study<sup>75</sup> used a blocked-design version of the associative stem-completion task<sup>17</sup>. As in previous behavioural studies, priming was stronger when stems were paired with the same words as in the study period than when they were paired with different words. Both conditions (compared to baseline) were associated with increased blood flow in a left inferior frontal region that is also activated during explicit retrieval<sup>175–79</sup>. The ‘same pairing’ condition also produced greater activation in the right MTL than did the ‘different pairing’ condition. These findings provide further evidence that associative specificity on the stem-completion task reflects aspects of explicit retrieval (for further discussion of the role of the MTL in associative memory, see REFS 1,80–83).

**Decision and identification tasks.** Associative priming on the stem-completion task differs from the perceptual priming effects considered earlier. Some form of semantic encoding during the study episode is necessary for subsequent associative priming, but not for individual-item priming<sup>17</sup>. It is conceivable that associative priming would occur normally in patients with amnesia on tasks where semantic encoding is not required and priming is based on perceptual associations between items. Studies of this subject have produced mixed results<sup>7,84</sup>, with some positive evidence for associative priming in patients with amnesia<sup>85,86</sup>, together with some failures to obtain associative effects using similar tasks<sup>87,88</sup>.

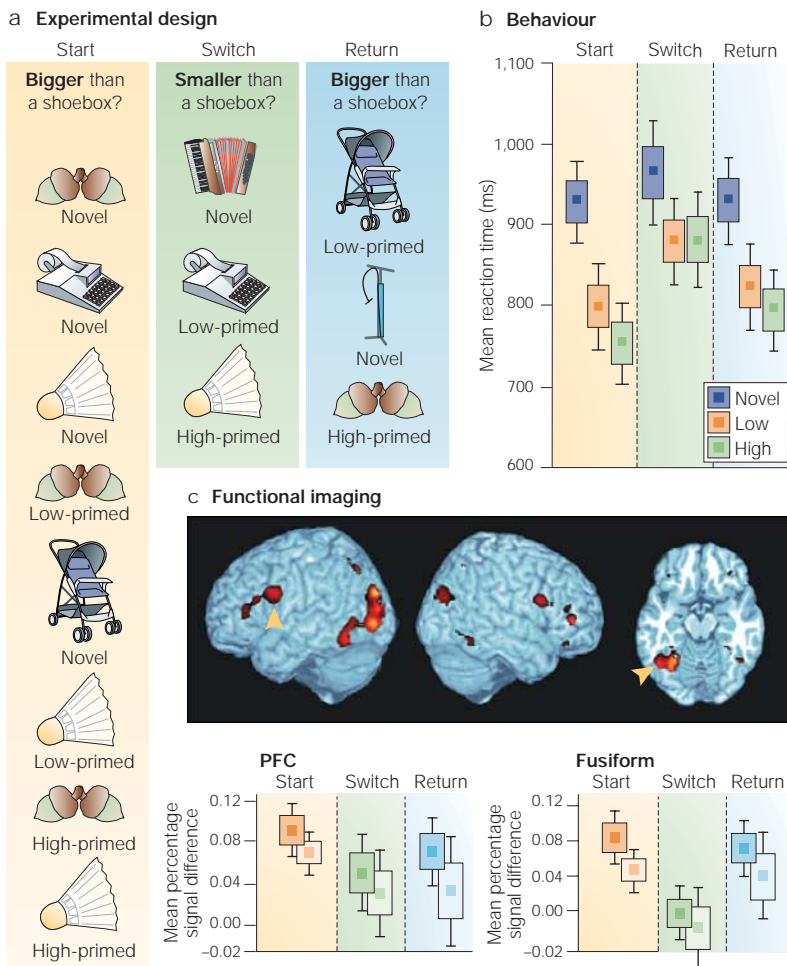
In a more recent study, Goshen-Gottstein *et al.*<sup>89</sup> used, as their implicit task, a lexical-decision test, in which patients and control subjects were shown pairs of words or nonwords, and had to decide whether both items in a pair constituted real words. On the explicit version of the task the same test items were given, but subjects were asked to say whether the words had appeared together previously. During an earlier study task, participants had studied a list of unrelated word pairs by forming sentences that included the pairs. On the lexical-decision task, both patients with amnesia and control subjects responded more quickly to intact pairs

from the study list than to rearranged pairs, showing an associative effect on priming. However, on the explicit version of the test, patients with amnesia showed impaired memory compared with control subjects. By contrast, Yang *et al.*<sup>90</sup> investigated a group of Chinese patients with amnesia who had MTL damage and failed to observe associative priming using a perceptual-identification task in which patients tried to identify briefly-flashed word pairs.

Given the frequent failure to observe normal associative-specificity effects in patients with amnesia, there are at least two interpretations of the corresponding effects in normal subjects. Either these effects reflect the influence of explicit retrieval, intentional or unintentional, on the part of healthy control subjects, or they reflect implicit memory in control subjects for a type of association that depends on the MTL/diencephalic system and is impaired in amnesia. It seems clear that priming of new associations on the stem-completion task fits the former explanation. To argue convincingly for the latter, it is necessary to show that an associative-specificity effect that is impaired in amnesia reflects implicit and not explicit memory in control subjects. This issue remains unresolved among studies that purport to show impaired priming of new associations in amnesia.

#### Response specificity

Changing either the features of a stimulus or associations between stimuli can decrease both behavioural priming and repetition-related reductions in cortical activity. Behaviourally, priming is also reduced when the required responses to a stimulus are changed across repetitions<sup>44,91,92</sup>. However, the possibility that priming-related reductions in cortical activation are sensitive to changes in the required response has typically not been considered in cognitive neuroscience investigations. Most behavioural experiments that use standard priming tasks, such as stem completion or word identification, find that priming occurs when subjects make different responses at study and test, so there has been no reason to suspect a contribution from response learning. Some evidence consistent with the possibility that priming is affected by subjects’ responses has been reported by Wagner *et al.*<sup>93</sup>, who investigated whether simple repetition of target stimuli produced a priming-related reduction in activity in left ventrolateral prefrontal and temporal regions. Repetitions yielded substantial signal reductions only when the semantic judgement task (abstract or concrete) was maintained across exposures. When the semantic task was preceded by a perceptual judgement (uppercase or lowercase), activity was not reduced relative to novel items on repetition (see also REF. 94). Although not a direct demonstration of response specificity, these findings indicate that, even when the stimulus is held constant between study and test, priming can be influenced by changes in the type of cognitive operations that subjects perform. Given these findings of task-specific signal reductions during priming, it is reasonable to propose that response-specific priming reductions might also occur.



**Figure 2 | Response learning.** **a** | Experimental design. Subjects encountered three sequential phases during scanning ('start', 'switch' and 'return'), during which the retrieval cue direction ('bigger than' or 'smaller than' judgement) was reversed or consistent with respect to the start-phase cue. During the start phase (left), objects were seen once ('novel') or three times ('high-primed'). The switch phase (middle) contained novel items, items viewed for the second time ('low-primed') and items viewed for the fourth time ('high-primed'). The return phase (right) used the remaining novel and high-primed items from the start phase and a new set of novel items. **b** | Reaction time data as a function of cue phase. Box indicates one standard error of the between-subjects mean; box plus error bars indicates two standard errors. Behavioural facilitation depended on the match between start and subsequent cues, indicating response specificity. **c** | Brain activation measured by fMRI for novel versus high-primed responses across phases. Typical neural priming was seen in prefrontal (PFC), parietal, inferotemporal and fusiform areas during start phase. A cue reversal during the switch phase disrupted priming, particularly in posterior regions. Returning the cue to its original form (return phase) produced recovery of priming. Top panel, SPM (statistical parametric mapping) interaction map, indicating regions that showed a significant disruption of neural priming signal in the switch relative to start phase. Yellow arrowheads show the approximate location of regions of interest used for box plots. Bottom panel, mean percentage signal difference between novel and high-primed (filled boxes) and novel and low-primed (open boxes) items for each phase. Modified, with permission, from REF. 97 © (2004) Macmillan Magazines Ltd.

the verb-generation task, and this reduction correlated with response stereotypy and reduced reaction times. There are two potential interpretations of these activation reductions: either the semantic analysis of the materials is streamlined with repetition, consistent with a neural tuning account; or semantic analysis of repeated stimuli is largely bypassed in favour of retrieval of previous instances that directly indicate the appropriate response (for relevant behavioural data, see REF. 96).

Recently, we addressed these possibilities in a neuroimaging study<sup>97</sup> by using a modified object-decision priming task in which responses either remained the same or were the opposite of those given during the initial acquisition period. Imaging sessions began with a standard object priming task in which stimuli were either shown once or repeated three times, and subjects indicated whether each stimulus was bigger than a shoebox using a 'yes' or 'no' response (FIG. 2). Later in the scan, a warning screen appeared and then the cue was 'reversed' so that it asked whether each item was 'smaller than a shoebox' for new items and for a subset of those shown previously. Finally, the cue was restored to 'bigger than a shoebox' and subjects were tested on new items and the remaining items from the initial phase. If the priming-related reductions in fusiform activity that are typically produced by this task represent facilitated size processing, then the cue reversal should have little consequence, other than perhaps a disruption in overall task set, which would affect both new and primed items. This is because the same representations regarding object size should be accessed regardless of whether the question reads 'bigger' or 'smaller' than a shoebox. By contrast, if subjects come to rapidly recover prior response instances, and this mechanism bypasses the need to recover size representations, then the cue reversal was predicted to disrupt priming-related reductions, because subjects would have to abandon learned responses and re-engage the material in a deliberate fashion in order to recover size information.

The fMRI data were largely consistent with the latter account. During the initial phase, typical priming-related reductions were observed in the left prefrontal cortex (PFC), fusiform and extrastriate regions. When the cue was reversed, these reductions were eliminated in the left fusiform cortex and there was a concomitant slowing in response times. Furthermore, when the cue was restored to its original format, priming-related reductions in activity returned, particularly in the left fusiform region (FIG. 2), showing that these reductions depended on the ability of subjects to use prior responses during trials. This effect was particularly prominent for items repeated three times before cue reversal. The response-learning account was further supported by multiple regression techniques showing that although reductions in PFC activity predicted the magnitude of behavioural priming for individual subjects, reductions in fusiform activity did not, supporting the idea that these reductions are incidental to the behavioural facilitation.

**Neuroimaging and response specificity.** In an early PET study of language processing, Raichle *et al.*<sup>95</sup> showed that, compared with the simple reading of stimuli, the generation of verbal associates to cue words yielded increased activation in the cingulate, left prefrontal and posterior temporal cortices. This activation declined as subjects became practiced at

**Response specificity and amnesia.** Although there has been considerable research into stimulus specificity and associative specificity of priming in patients with (and without) amnesia, there has been almost no research into response specificity of priming in any neuropsychological patient group. In their review of studies concerning priming of novel information in amnesia, Gooding *et al.*<sup>84</sup> divided studies into those in which there was stimulus–response overlap at study and test, and those in which there was not. The performance of patients with amnesia, relative to that of control subjects, did not differ significantly in the two types of study, indicating that stimulus–response overlap did not interact with the types of priming exhibited by the two groups. Seger *et al.*<sup>98</sup> examined response priming in amnesia using the verb-generation task examined previously by Raichle *et al.*<sup>95</sup>, in which participants generate verbs in response to repeated nouns. Patients with amnesia, like controls, showed decreased verb-generation times to repeated nouns across trials. Importantly, both amnesics and controls showed transfer of priming to novel nouns that tend to elicit the same verb (for example, after generating the verb ‘eat’ in response to the noun ‘fork’, both patients and controls showed reduced time to generate ‘eat’ in response to ‘food’). So, response priming in the verb generation task does not seem to involve a specific link between a particular stimulus and the response; priming seems to be nonspecific in that the response might be more easily accessible to a variety of stimuli that can elicit it.

Although not directly concerned with response specificity in priming, some relevant data have been provided by work on ‘CONTEXTUAL CUEING’ in visual search, which indicates that subjects can rapidly shift from deliberate analysis to more automatic stimulus–response associations. For example, Chun and Phelps<sup>99</sup> used a basic visual array of ‘Ls and ‘T’s in a visual-search task carried out by control subjects and patients with MTL damage. Subjects were required to find the T among Ls and to report its orientation for repeated and new displays. Although both control subjects and patients with MTL damage typically experienced a gain in speed across blocks, indicating a general skill-learning component, only control subjects showed a further advantage that was selective to whether the arrays had been presented before. Control subjects, but not patients with MTL damage, were faster at locating the targets when they were embedded in familiar, rather than new, arrays. Importantly, despite the fact that the contextual learning depended on the integrity of the MTL, it seems to be implicit in that neither group could explicitly identify arrays that they had seen previously as opposed to new arrays<sup>100</sup>. A follow-up study<sup>101</sup> confirmed that the learning exhibited in this protocol depends on MTL structures; however, using a larger patient cohort, it implicated extra-hippocampal regions, such as the parahippocampal gyrus, and not the hippocampal formation itself<sup>101</sup>. To the extent that these contextual-cueing effects depend on mechanisms similar to those found in the response-learning object decision task used in our neuroimaging study<sup>97</sup> (the contextual-cueing protocol

probably also reflects associative specificity), we might expect that patients with amnesia who have MTL damage would not exhibit normal response specificity in the response-learning protocol<sup>97</sup>. Current data from our laboratory are consistent with this expectation.

#### Concluding comments

In this review we have considered a large body of results that reveal the existence of stimulus, associative and response specificity in cognitive neuroscience studies of priming. To conclude, we consider a number of important issues and suggest some theoretical ideas that might help to guide future research.

One fundamental — and unresolved — issue concerns the relationships among the three types of specificity we have discussed. Although we find it heuristically useful to organize the literature from this perspective, it is far from clear whether fundamentally different mechanisms are involved in stimulus, associative and response specificity. For example, one way of thinking about stimulus specificity is in terms of operations that link or bind together several levels of a particular instance (for example, the font in which a word appears and an abstract lexical representation). Stimulus (font)-specific priming might depend on the occurrence of such operations at the time of encoding. Such intra-stimulus binding operations might be the same as, or similar to, those involved in linking together two separate items to produce associative specificity, and could also overlap with the operations involved in linking stimuli and responses to produce response specificity. An alternative way of distinguishing between different types of priming is to consider ‘type A’ priming, which depends on a cortical-perceptual representation system and is preserved in amnesia, and ‘type B’ priming, which involves MTL-based linking or binding operations and is impaired in amnesia<sup>65</sup>.

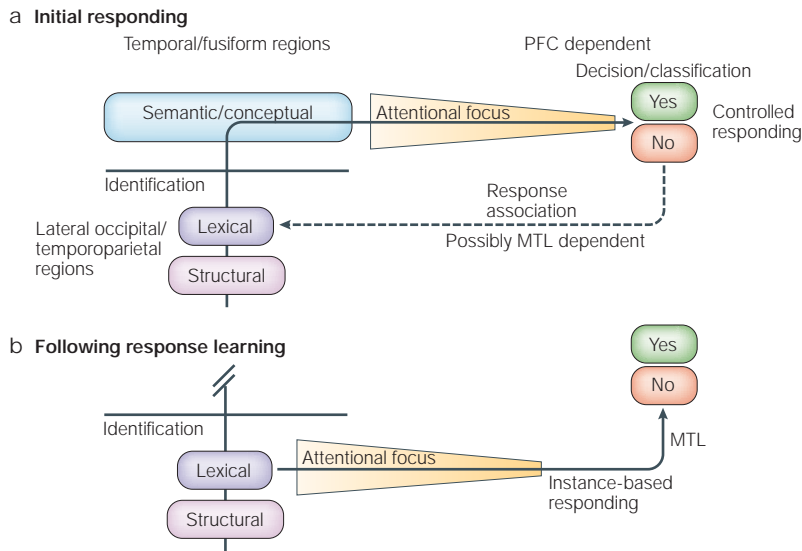
This discussion raises a related point concerning the relationship between stimulus and response specificity. As noted earlier, stimulus specificity can occur even when responses differ at study and test (for example, changes in font influence word priming on a stem-completion test that follows a perceptual-encoding task). However, response specificity has so far been observed under conditions in which an identical stimulus is used at study and test. This observation raises the possibility that stimulus specificity occurs across changes in response specificity, whereas response specificity depends on holding the stimulus constant. If so, response specificity might be more accurately labelled ‘stimulus–response specificity’. However, it is also possible that response-specificity effects occur when properties of the target stimulus are changed between study and test. Future studies should investigate this issue.

To understand the relationships and the extent of mechanistic overlap among the different types of specificity, it will be necessary to undertake neuropsychological and neuroimaging research in which different types of specificity are manipulated and compared in a single study. Few studies<sup>19</sup> have directly compared the different types of specificity. A second important issue concerns

#### CONTEXTUAL CUEING

A model for studying how people learn visual regularities that guide their subsequent responses in perceptual tasks.





**Figure 3 | Hypothetical instance-learning model.** **a** | ‘Initial responding’ on a conceptual level task (for example, deciding whether a pictured object is bigger than a shoebox) requires controlled processing. The prefrontal cortex (PFC) directs attention to conceptual representations that trigger several hierarchical stages of processing in the posterior occipital, fusiform and temporal areas. Furthermore, the PFC mediates classification processes on the basis of recovered evidence. As the task is repeated, medial temporal lobe (MTL) regions enable subjects to associate previous decision outcomes with pre-semantic lexical identifiers of objects or words. This frees PFC resources (**b**) and enables a direct mapping from object identification to response output, without semantic or conceptual analysis (instance-based responding). Activation reductions occur because the conceptual stage of processing is bypassed and because deliberate classification is no longer required. Further reductions in activity might also occur because attending to lower-level representations might be less demanding than focusing on conceptual attributes that are processed less automatically.

whether, and, if so, in what sense, specificity effects depend on MTL structures. This issue typically arises when patients with amnesia who have MTL damage do not show a particular type of specificity, leaving open the question of whether specificity in control subjects is a manifestation of explicit retrieval, or reflects an unconscious or implicit process that is impaired in amnesia. When there is evidence that rules out a contribution from explicit retrieval, we can infer that the MTL is involved in an unconscious form of memory<sup>99</sup>. However, evidence from neuroimaging studies or behavioural investigations of patients with well-characterized focal lesions<sup>101</sup> is needed to define which MTL structures may be crucial.

A third important issue concerns the types of theoretical account that can illuminate the nature of stimulus, associative and response specificity. A comprehensive review of the main theoretical accounts of priming is beyond the scope of this article (for discussion, see REFS 6,18,102–104), but we note a few relevant points. There is a long history in priming research of competing claims made by ‘abstractionist’ views, which hold that priming reflects the influence of pre-existing lexical or object representations, and ‘exemplar’ or ‘instance’ views, which hold that priming reflects the influence of newly established memory traces (for review, see REFS 18,20).

As stated previously, the evidence provides some support for both views of priming, but we believe that some of the ideas associated with exemplar- or instance-based

views are going to be necessary to account for specificity effects. To help stimulate thinking along these lines, we suggest a theoretical approach based on three key assumptions relating to task demands, stimulus factors and response mapping.

The first assumption is that priming effects at a given level of neural representation require that subjects attended to that, or a ‘higher’ level, during initial processing and, to a large extent, that the levels, or stages, that are engaged during processing are a function of a subject’s processing goals<sup>105</sup>. In terms of functional anatomy, we assume that regions of the PFC are crucial for directing attention to particular levels of analysis of the presented materials, and also for making decisions. This assumption means that researchers need to pay special attention to the attention and decision demands of tasks, because these factors have a crucial impact on which regions will subsequently demonstrate priming-related changes.

Second, we assume that the solutions, or ‘instances’, that result from a previous encounter serve as valuable input for future encounters, are stimulus/probe-specific, and, in some cases, might require the participation of MTL structures. In addition to evidence from contextual cuing<sup>99</sup> and response cue-reversal effects<sup>97</sup>, this assumption also receives some support from selective-looking protocols in adults. For example, control subjects fixate altered regions of previously viewed pictures more often than pictures that remained intact<sup>106</sup>. This differential viewing time remains even with stimuli for which subjects cannot explicitly report the change, but such effects are absent in patients with amnesia.

The third assumption is that with increasing exposure or repetitions, subjects come to rely on retrieval of previous solutions or instances, and avoid controlled higher-level processing of the stimuli (automaticity develops with repetition). Within this framework, we assume that the effective use of response learning obviates the need for higher-level processing of stimuli because identification of the stimulus triggers retrieval of the previous response or decision. FIGURE 3 presents and explains a preliminary model based on these assumptions.

Last, we suggest that the widespread existence of specificity effects across several domains of priming implies that specificity is a functional or adaptive feature of priming. Although little is known about the adaptive value of priming, observations of priming-related activity reductions in neuroimaging studies indicate that priming might be associated with some type of resource conservation. In line with this idea, we have argued that response specificity is adaptive because it reduces the need to recover stored representations of object knowledge and therefore helps to conserve valuable limited-capacity executive functions<sup>97</sup>. Stimulus and associative specificity might be conceptualized as a consequence of increasingly automatic retrieval that reduces demands on executive functions. Future studies that focus on function could complement approaches that focus on the structures and mechanisms of priming.



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**Competing interests statement**

The authors declare no competing financial interests.

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**Schacter's homepage:** <http://www.wjh.harvard.edu/~dsweb/Home.html>

**Dobbins' homepage:** <http://www.pbs.duke.edu/faculty/idobbins/idobbins.html>

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