

Rapid response learning in amnesia: Delineating associative learning components in repetition priming

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Received 2 December 2004; received in revised form 17 March 2005; accepted 22 March 2005

Available online 11 May 2005

Abstract

Functional brain imaging studies of priming assume that the behavioral facilitation and activity reductions resulting from multiple repetitions reflect the continued tuning of processes engaged during the initial processing of items. Utilizing an object priming paradigm in which participants were asked to make relative size judgments about visually presented common objects, we tested an alternate hypothesis that states that with multiple repetitions participants come to rely on a more efficient response learning mechanism. In experiment 1, the decision cue was inverted such that previous judgments made either once or three times were rendered invalid. Decision inversion resulted in a reduction of all priming, but most critically, led to a reduction of multiple-repetition priming to the level of single-repetition priming. In experiment 2, patients with amnesia failed to show a priming advantage for multiple repetitions, indicating that response learning is dependent on the medial temporal lobes. Taken together, these results suggest that a different process increasingly mediates priming behavior as repetitions increase. With repeated exposure, behavioral facilitation rapidly comes to reflect a more efficient response learning mechanism rather than facilitated access to object knowledge.

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Keywords: Priming; Memory; Learning; Amnesia

1. Introduction

Repetition of a stimulus or presentation of a stimulus closely related to one previously presented results in performance benefits referred to as priming (Scarborough, Cortese, & Scarborough, 1977). A number of theoretical views of priming have postulated that item-specific information is “tuned” with repetition so that it is more readily available on subsequent encounters (Schacter, 1990; Wiggs & Martin, 1998). By this view, stimulus-related neural activity that

was peripheral to the task drops away and only task-relevant activity remains. Because priming effects are often small, experimental examinations of priming have sometimes utilized multiple repetitions of the same item (Jacoby & Dallas, 1981; Logan, 1990). Whether stated explicitly (Gutpa & Cohen, 2002) or implied (Koutstaal et al., 2001), the use of multiple repetitions has reflected the assumption that processing on subsequent trials reflects the continued “tuning” of the same set of cognitive or neural processors that were engaged during the first presentation. This assumption has been particularly pervasive in neural imaging studies of priming (Buckner et al., 1998; Koutstaal et al., 2001; Simons, Koutstaal, Prince, Wagner, & Schacter, 2003). An alternative hypothesis is that repeated processing of a stimulus and its associated response

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results in a form of response learning, whereby some of the task-related processes performed when stimuli are first encountered are bypassed on subsequent encounters in favor of a more efficient and direct associative response mechanism.

In a recent functional imaging study, we examined whether a response learning mechanism could account for neural activity reductions associated with repetition—that were previously assumed to reflect “tuning” of processing subsystems (Dobbins, Schnyer, Verfaellie, & Schacter, 2004). In that study, participants made size judgments about visually presented objects (bigger than a shoebox?). After they were exposed to items either once or three times, the decision cue was inverted (smaller than a shoebox?), a manipulation that should not significantly alter processes associated with item identification or access to item-related size knowledge. The key finding of the study was that inverting the decision cue resulted in a significant reduction of behavioral priming and elimination of repetition-related reductions in the MR signal in prefrontal cortex and fusiform gyrus. While the disruption in neural priming was most evident for items presented three times previously, there was a weaker disruption even when the decision cue was switched after a single presentation. We concluded from this finding that critical item knowledge, previously assumed to be more available after repetition, was in fact no more available with multiple repetitions than it was with a single repetition. Instead, participants appeared to be learning their responses to items and, in doing so, they shifted from a resource-demanding analysis of specific object-size information to a more automatized stimulus–response based strategy (Logan, 1990; Schacter, Dobbins, & Schnyer, 2004). These results stand in contrast to the pervasive assumption of system-wide tuning with multiple repetitions and instead reveal the possibility that major portions of the processing stream may simply be bypassed in favor of a more efficient learning mechanism.

The goal of the present study was to further elucidate the nature of a possible response learning mechanism that underlies priming in multiple-repetition paradigms. Experiment 1 provides a behavioral analogue of the fMRI paradigm in which we address a methodological limitation of the imaging study. This experiment also allows us to evaluate whether the effect of cue inversion depends on the number of items responded to with the original decision cue before decision inversion is undertaken. To determine the neural basis of the response learning mechanism, in experiment 2 we examine whether response learning following multiple repetitions is intact in amnesic patients with damage to medial temporal lobe structures.

2. Experiment 1

The primary goal of this experiment was to replicate the results from the fMRI study (Dobbins et al., 2004), correcting some of the methodological limitations of that study. In the fMRI study, we demonstrated response learning using a three-

block experiment in which the critical manipulation of cue inversion occurred in block 2 and responses in block 2 were compared to those given to the original decision cue in block 1. This temporal difference is potentially problematic for two reasons: First, because of general practice effects or fatigue, the differential time on task may have resulted in between-block differences, that were independent of the introduction of the cue inversion. Second, for repeated items, the critical contrast comparing responses to the same versus inverted decision cue was confounded by the fact that cue inversion always entailed an additional repetition. These confounds were eliminated in the current experiment by comparing the cue inversion condition to the original cue condition within the same temporal block and after the same number of repetitions.

A secondary goal of this experiment was to evaluate whether the effect of cue inversion depends on the extent of time spent responding to the original decision cue. One possibility is that response learning becomes more established and less flexible after a longer period of time, thereby forcing a greater disruption when switching is encountered. Alternatively, response learning may be directly tied to the number of repetitions of a particular stimulus–response pair, regardless of how long a particular response set is maintained. In the latter case, response inversion should have a similar effect, regardless of when in the course of the task it occurs.

2.1. Method

2.1.1. Participants

Fifteen native speakers of English (3 male, 12 female) with normal or corrected to normal vision took part in the experiment. Participants (mean age = 21 years, range 19–24) were recruited through flyers and advertisements at local colleges and universities and received US\$ 10 for their participation. Participants were screened using a short medical questionnaire to ensure that they were free from current psychiatric or neurological disorder, any history of brain injury or excessive drug or alcohol use. Written informed consent was obtained from each participant prior to the experimental session. The Human Subjects Committees of Boston University School of Medicine and the Veterans Affairs Healthcare System approved all procedures.

2.1.2. Stimuli

Stimuli were 408 colored line drawings of simple objects selected from CD-ROM clip-art collections (e.g. Corel Mega Gallery, Corel Corporation, 1997). Pictures represented common animate and inanimate objects in varying orientations and were of varying visual size. They were chosen such that half were larger and half were smaller than a typical shoebox. Experiments were conducted on a Mac Powerbook laptop computer running Psyscope 1.2.5 (Carnegie Mellon University, 1994). Stimuli were presented within a centrally located 8.75 cm × 8.75 cm box. Viewing was approximately 75 cm from the screen.

2.1.3. Procedure

Prior to beginning the task, participants were instructed in the procedures and shown examples of the decision making they would engage in. They were told that they would be asked to make a size judgment by indicating if the real life object depicted in the picture was “bigger than a shoebox” (B). They were to indicate their decision by pushing a “yes” or a “no” key with the index and middle fingers of their right hand respectively. Participants were asked to make their judgments on the whole object as presented, rather than deciding if an object could be folded or crushed to fit within a shoebox. Finally, participants were encouraged to “respond as quickly and accurately as possible” and if they were unsure of an item, then to just “guess”. Pictures were presented at a rate of 1 per 2.5 s, centrally located, and were accompanied at the bottom of the screen by a decision cue that indicated the appropriate decision to be made on that trial. The entire experimental session lasted approximately 45 min.

Each experimental session consisted of four alternating ‘study-test’ cycles.¹ During each study phase, 34 pictures were presented once and 34 pictures were presented three times, for a total of 136 trials. Once-presented items were evenly interspersed throughout the study phase in such a way that one third of the once-presented items were encountered with each full repetition cycle of the thrice-presented items. Following a short pause, participants took part in a test phase consisting of two test blocks. Each test block consisted of 17 pictures presented once during study (low prime), 17 pictures presented thrice during study (high prime) and 17 nonstudied pictures (novel items). None of the pictures were repeated within or between test blocks. The test blocks differed only with regards to the decision made by participants: In one block participants made the same bigger than decision made during the study phase (B; same decision cue), whereas in the other block the decision was inverted to “smaller than a shoebox” (S; inverted decision cue). In two of the cycles, participants made same decisions in the first test block and inverted decisions in the second test block, whereas for the other two cycles the order was switched.

For counterbalancing, pictures were randomly assigned to one of four study-test cycles. Within each cycle, pictures were rotated across the three possible conditions (novel, low prime, high prime). Additionally, to counterbalance the assignment of decision cues to test blocks across the four study-test cycles, two study-test sequences were developed in the following manner: B–B–S, B–B–S, B–S–B, B–S–B or B–S–B, B–S–B, B–B–S, B–B–S. This resulted in a total of six versions of the experiment that ensured that each picture served equally often as a novel, low prime, or high prime item and was tested equally often under same and inverted test cues. A schematic of the two possible experimental runs is presented in Fig. 1.

¹ The study design was modeled after previous fMRI studies using a “study-test” format (Buckner et al., 1998; Buckner, Koutstaal, Schacter, & Rosen, 2000; Koutstaal et al., 2001; Simons et al., 2003).

2.2. Results

Although half of the objects were selected to be bigger and half smaller than a shoebox, participants did not classify items in perfect accordance with our a priori designations. To ensure that the results were not unduly influenced by items that were difficult to judge, only those that were consistently classified by 75% or more of the subjects were included in the analysis. By this criterion, 13% of the items were eliminated. These were all items that had a priori been classified as being smaller than a shoebox and it makes sense that these were less uniformly classified because the range of possible sizes that fit within the box is necessarily more restricted than the range that does not.²

2.2.1. Response latency

Mean response latencies during the test blocks were calculated based on accurate responses only and are presented in Table 1.

2.2.1.1. Cue switching. To evaluate the effect of switching the decision cue, we compared mean RTs of items that were associated with a same versus an inverted decision cue in test block 1 in a 2×3 ANOVA with decision cue (same, inverted) and condition (novel, low prime, high prime) as within-subject factors. As can be seen in Table 1, high primed items were most affected by cue switching. This impression was confirmed by results of the ANOVA, which revealed significant main effects of decision cue ($F(1,14) = 7.27, p < .05$) and condition ($F(2,28) = 49.48, p < .001$), along with a significant decision cue \times condition interaction ($F(2,28) = 17.51, p < .001$). Post hoc testing revealed that reversal of the decision cue did not significantly affect RTs to novel items ($t(14) < 1$), but there was a significant reduction in the magnitude of priming (defined as RT primed—RT novel) for both low primed items ($t(14) = 2.18, p < .05$) and high primed items ($t(14) = 5.41, p < .001$). Most strikingly, the priming advantage of high over low primed items seen in the same cue condition was completely eliminated by inverting the decision cue ($t(14) = 1.03, ns$).

2.2.1.2. Early versus late switch. To directly evaluate whether inverting the decision cue in block 1 or in block 2 had differential effects, a 2×3 ANOVA on responses to inverted cues was performed with test block and condition (novel, low prime, high prime) as factors. There were significant main effects for test block ($F(1,14) = 22.39, p < .001$) and condition ($F(2,28) = 7.67, p < .01$), but no significant interaction ($F(2,28) < 1$). Overall, responding was slower when

² Because elimination of ambiguous responses resulted in an unequal number of “yes” and “no” responses in the analysis, we performed all analyses with response status as an additional variable to evaluate its effect on priming. In neither the latency nor error analysis did response status have any effect on priming. The only effect, apparent in the latency analysis, was that, in general, yes responses were faster than no responses, although this difference was absent when switching occurred in test block 2.

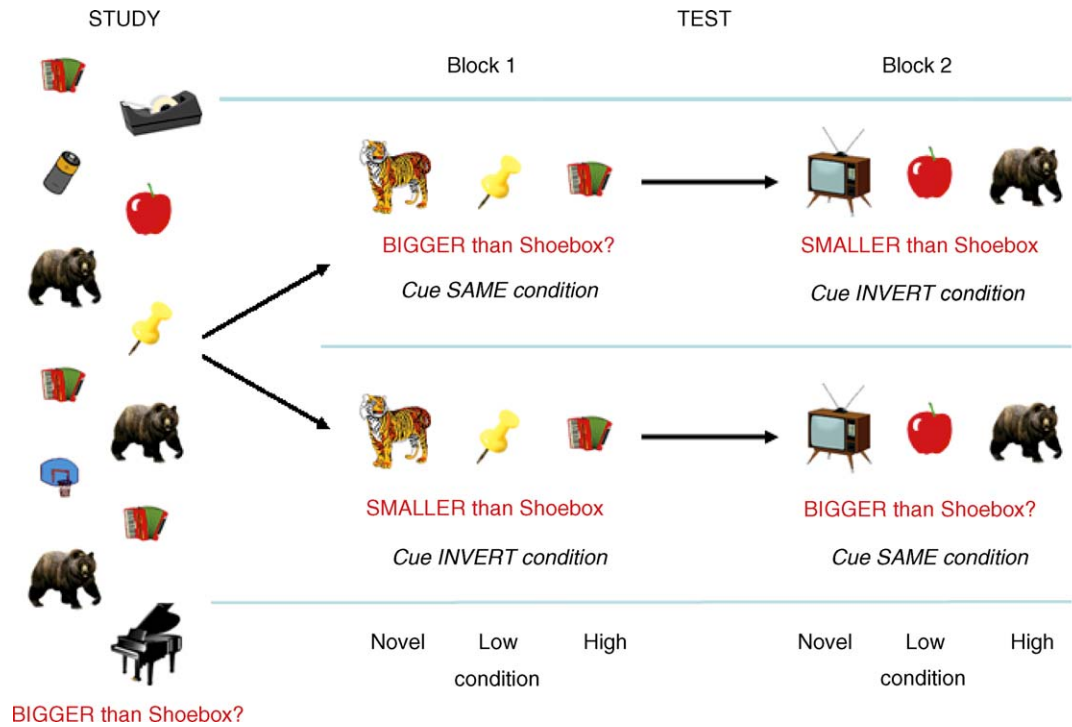


Fig. 1. Schematic of the experimental design. All four runs begin with a study phase in which participants are asked to indicate whether common objects are “bigger than a shoebox”. Items are presented either once or three times. The test phase is divided into two blocks. During the first block, participants make either the same “bigger than a shoebox” decision as during study (two runs) or are asked to invert the decision to “smaller than a shoebox” (two runs). Test block decisions are made for novel objects, objects seen once at study and objects seen three times at study. In test block 2, participants are asked to invert the decision perspective from test block 1 (bigger to smaller, or smaller to bigger) and continue to make decisions on a new set of objects that were novel, seen once at study, or seen three times at study. No objects were repeated within or between test blocks.

decision cue switching occurred in test block 2, following a longer period of responding to the original cue, but equivalent effects of inverting the cue on low and high prime items were present in both test blocks.

2.2.1.3. *Return to the original decision cue.* To evaluate if switching the decision cue disrupted responding to the original decision cue, we examined RTs for same cue responses in block 1 to same cue responses in block 2 (which had been preceded by a block where the cue had been inverted). A 2 × 3 ANOVA with test block and condition (novel, low prime, high prime) as factors revealed a trend towards a main effect of block ($F(1,14) = 3.71, p < .10$), a main effect of condition ($F(2,28) = 65.67, p < .001$) as well as a significant block × condition interaction ($F(2,28) = 14.78, p < .001$). The interaction reflected the fact that responses to novel and low primed items were not affected by interposing a block of trials

with inverted cues (both t 's < 1), whereas responses to high primed items were ($t(14) = 4.86, p < .001$). Put differently, priming for low primed items did not differ between blocks but the priming advantage originally seen for high primed items did not return ($t(14) < 1$).

2.2.2. *Response accuracy*

To evaluate how cue switching affected accuracy, test block 1 errors were analyzed in a 2 × 3 repeated measures ANOVA with decision cue (same, inverted), and condition (novel, low prime, high prime) as factors. There was an increase in errors with inversion of the decision cue (same = 2.5%; inverted = 4.3%), as evidenced by a main effect of cue ($F(1,14) = 5.64, p < .05$) but no other main effects or interactions approached significance.

To evaluate if late switching enhanced errors more than early switching, errors in the inverse cue condition were an-

Table 1
Mean response times and standard errors for experiment 1

Decision cue	Block 1			Block 2		
	Novel	Low	High	Novel	Low	High
Same						
Mean RT (S.E.)	1069 (53)	947 (47)	824 (50)	1075 (51)	962 (55)	944 (53)
Inverted						
Mean RT (S.E.)	1060 (49)	991 (49)	973 (37)	1149 (50)	1106 (55)	1083 (46)

alyzed in 2×3 repeated measures ANOVA with block and condition (novel, low prime, high prime) as factors. This analysis revealed a significant effect of block ($F(1,14) = 41.71$, $p < .001$), indicating that indeed this was the case (block 1 = 4.3%; block 2 = 10.5%).

2.3. Discussion

The results of experiment 1 replicate and extend findings from our fMRI study in demonstrating a role for response learning in a priming paradigm. Inverting the decision cue from “bigger than” to “smaller than” significantly reduced the facilitation resulting from item repetition for both items that had been presented three times in the study phase (high primed items) and those that were presented once (low primed items). Moreover, following cue inversion, latencies for low and high primed items were equivalent. Since the effects of a same versus inverse decision cue were assessed within the same temporal block (test phase 1), the effect of cue inversion could not be ascribed to differential time on task or differential stimulus exposure. Rather, it indicates that a change in decision cue leads to a disruption in the mechanisms that mediate priming. Further, our findings indicate that return to the original decision cue does not fully eliminate the costs associated with cue switching, as high primed items did not regain their advantage over low primed items. The latter finding, however, needs to be interpreted cautiously, as it suffers from a similar temporal confound as that identified in the evaluation of the effect of cue reversal in the fMRI study.

Contrasting with the effects of cue switching in test block 1, inversion of the decision cue in test block 2 resulted in both set-specific and item-specific effects. Delaying the cue inversion led to a general slowing for all item types, and in particular, had an effect on responses to novel items not seen when the cue-inversion occurred in test block 1. This general slowing most likely reflects the implementation of additional cognitive control in order to override a well-established response set. This finding was also evident in the small but significant increase in errors that occurred when switching occurred in test block 2 rather than in test block 1. Despite this general slowing and greater error rate, inverting the decision cue resulted in the same item-specific effects seen after switching in test block 1: high primed items lost their multiple-repetition advantage and displayed an equivalent level of response facilitation as low primed items.

We have postulated (Dobbins et al., 2004) that the selective disruption of priming due to cue inversion reflects previously learned responses being rendered invalid. From this perspective, it makes sense that the extent of disruption depends on the number of times a particular response was made to a stimulus, and thus, was more severe for high primed items than for low primed items. Moreover, once a stimulus–response association was disrupted, the advantage of high primed items was eliminated, and re-instatement of the original decision cue resulted in similar benefits for low and high primed items. Since a suitable control condition was not available for final

test block comparisons, it is possible that the failure to engage response learning is due to a general decay of the response learning mechanism over time. This explanation is unlikely, however, as others have shown robust facilitation effects associated with multiple repetitions, even after considerable amounts of time and intervening items (Logan, 1990). Additionally, in an experiment examining the effects of finger mapping inversion, we found no evidence that response learning decreased in the second test block (Schnyer, Dobbins, Nicholls, Verfaellie, & Schacter, in preparation). More likely then, once response learning has been interrupted by cue reversal, learned responses are no longer retrieved even when the original decision cue has been reinstated.

The response learning evident in the current experiment appears to be a form of “instance learning” (Logan, 1990), whereby an item becomes associated with previous operations performed on it. This type of associative memory allows for the saving of processing resources by redirecting attention from a higher level algorithm to a less resource demanding one (Dobbins et al., 2004; Logan, 1990). An important question is whether this form of learning is dependent on neural structures that have previously been shown to support the rapid acquisition of new associations, such as the medial temporal lobe (MTL; Cohen, Poldrack, & Eichenbaum, 1997). If response learning depends on rapid acquisition of novel associations, it would follow that such learning should be impaired in patients with MTL lesions. Experiment 2 tests this prediction.

3. Experiment 2

3.1. Method

3.1.1. Participants

Ten amnesic participants with radiologically-verified MTL lesions completed the experiment. Results from one patient were excluded, however, because due to a computer error, up to 40% of the responses were lost in two conditions. This left nine patients (mean age = 52.2, range = 20–75; 7 male, 2 female) with amnesia secondary to anoxia ($n = 6$) or encephalitis ($n = 3$, see Table 2 for demographics and neuropsychological performance). Twelve normal individuals (five male, seven female), matched in terms of age ($F < 1$), education ($F < 1$) and verbal IQ ($F < 1$) as measured by the Wechsler Adult Intelligence Scale-III (Wechsler, 1997a), participated as a control group in this experiment. Both amnesic and control participants were native English speakers and had normal or corrected to normal vision. Control subjects were screened using a medical questionnaire and reported being free from current psychiatric or neurological disorder, brain injury or excessive drug or alcohol usage. Written informed consent was obtained from each participant prior to the experimental session and they received US\$ 10 for their participation. The Human Subjects Committees of Boston University School of Medicine and the Veterans Affairs Healthcare System approved all procedures.

Table 2
Patient and control demographics for experiment 2

Patient	Etiology	Age (years)	WAIS-III			WMS-III		
			Ed.	VIQ	GM	AD	VD	WM
1	Encephalitis	74	18	135	45	58	53	141
2	Anoxia	46	14	111	59	72	52	96
3	Encephalitis	47	14	92	45	56	55	85
4	Anoxia	52	12	83	52	56	55	91
5	Anoxia	44	14	90	45	53	52	93
6	Anoxia	20	12	91	45	46	56	79
7	Encephalitis	61	11	106	69	68	77	111
8	Anoxia	75	12	107	59	64	65	83
9	Anoxia	51	17	134	70	67	75	88
Patient mean		52.2	13.8	105.4	54.3	60.0	60.0	96.3
Control mean		55.1	15.1	108.4				

Columns show etiology, demographic and neuropsychological performance values for each of the nine patients and the mean for the 12 controls. *Note:* age and education is in years; WAIS-III, (Wechsler, 1997a), VIQ: verbal IQ; (Wechsler, 1997b), GM: general memory index, AD: auditory delay index, VD: verbal delay index, WM: working memory index.

3.1.2. Stimuli and procedure

Stimuli and procedures were as outlined in experiment 1.

3.2. Results

Responses of control subjects during the study phase were used to evaluate response consensus, in a manner similar to that in experiment 1. Twelve percent of items were ambiguous, and these were again eliminated from further analyses.

3.2.1. Response latency

Mean response latencies during test blocks were calculated based on accurate responses only and are presented in Table 3. Because there was a trend for the responses in the amnesic group (overall mean = 1166 ms) to be slower than those in the control group (overall mean = 1066 ms; $F(1,19) = 3.9$, $p < .07$), analyses were performed on proportional priming scores.

3.2.1.1. Cue switching. Proportional priming scores were entered into a $2 \times 2 \times 2$ ANOVA with group (controls, amnesics) as a between-subjects factor and decision cue (same, inverted) and condition (low prime, high prime) as within-subjects factors. There was a main effect of group ($F(1,19) = 6.46$, $p < .05$), indicating that amnesic participants showed less priming than controls. There was also a main effect of condition ($F(1,19) = 18.61$, $p < .001$) that was modified by a significant group \times condition interaction ($F(1,19) = 8.91$, $p < .01$). This interaction reflected the fact that controls showed more priming for high primed items than for low primed items while there was no difference between high and low primed items in amnesic participants. Priming for both high and low primed items, however, was significantly greater than zero in both groups (t 's > 3.54 ; p 's $< .005$). There was also a significant cue \times condition interaction ($F(1,19) = 7.62$, $p < .05$), which indicated that the high prime advantage disappeared with cue inversion.

Table 3
Mean response times, standard errors and proportional priming scores for experiment 2

Decision cue	Block 1			Block 2		
	Novel	Low	High	Novel	Low	High
Same						
Controls						
Mean RT (S.E.)	1079 (37)	1024 (45)	850 (38)	1155 (35)	1017 (36)	985 (40)
Priming (%)		5.2	21.0		11.8	14.4
Amnesics						
Mean RT (S.E.)	1210 (56)	1146 (38)	1114 (60)	1165 (63)	1144 (58)	1126 (51)
Priming (%)		4.5	7.8		1.4	2.9
Inverted						
Controls						
Mean RT (S.E.)	1192 (34)	1116 (36)	1065 (32)	1146 (41)	1124 (39)	1037 (41)
Priming (%)		6.3	10.6		1.4	9.4
Amnesics						
Mean RT (S.E.)	1197 (48)	1124 (72)	1111 (48)	1250 (53)	1190 (50)	1221 (62)
Priming (%)		6.6	7.1		4.7	2.4

Although the group \times cue \times condition interaction failed to reach significance ($F(1,19)=2.84$, $p < .11$), this pattern was driven by the performance of control subjects. An ANOVA on the control data revealed the expected cue \times condition interaction ($F(1,11)=16.96$, $p < .005$), indicating that the high prime advantage was reduced following cue inversion. There was no evidence for a similar interaction in the amnesic data ($F < 1$). Moreover, in the amnesic group, neither the main effect of cue nor condition was significant (F 's < 1).

3.2.1.2. Early versus late switch. To compare the effect of cue inversion during test block 1 and test block 2, a $2 \times 2 \times 2$ ANOVA was performed with group (controls, amnesics) as a between-subject factor and test block and condition (low prime, high prime) as within-subject factors. There was a main effect of block ($F(1,19)=4.38$, $p < .05$), indicating that there was less priming when switching occurred in block 2 than in block 1. However, the effect of block did not interact with either the effect of condition or group, suggesting that there was no differential effect of late compared to early switching in either group.³ There was a marginal condition effect ($F(1,19)=4.16$, $p < .06$), which was modified by a significant group \times condition interaction ($F(1,19)=7.70$, $p < .05$). The interaction reflected the fact that with cue inversion, normal controls still showed greater priming in the high than in the low prime condition ($t(11)=3.47$, $p < .01$), while there was no difference between high and low priming (mean = 5.7%; $t < 1$) in the amnesic group.

3.2.1.3. Return to the original decision cue. To evaluate if switching the decision cue disrupted responding to the original decision cue, a $2 \times 2 \times 2$ ANOVA was performed with group (controls, amnesics) as a between-subjects factor and block and condition (low prime, high prime) as within-subjects factors. There was a main effect of group ($F(1,19)=12.58$, $p < .005$) and of condition ($F(1,19)=14.30$), both of which were modified by a group \times condition interaction ($F(1,19)=5.02$, $p < .05$). There was also a cue \times condition interaction ($F(1,19)=7.34$, $p < .05$) and a marginally significant group \times block \times condition interaction ($F(1,19)=4.36$, $p < .06$). To evaluate the three-way interaction, separate ANOVA's were performed on the data of the control subjects and the amnesic participants. In the control subjects, the block \times condition interaction was significant ($F(1,11)=17.84$, $p < .005$), indicating that the high prime advantage seen before switching was not present when returning to the original decision cue after switching. In the amnesic

participants, by contrast, there was no block \times condition interaction ($F < 1$).

3.2.2. Response accuracy

To examine how cue switching affected accuracy, test block 1 errors were analyzed in a $2 \times 2 \times 3$ ANOVA with group (controls, amnesics) as a between-subjects factor and decision cue (same, inverted) and condition (novel, low prime, high prime) as within-subjects factors. This analysis revealed a main effect of group, indicating that amnesic participants (mean = 10.8%) made more errors than controls (mean = 5.9%; $F(1,19)=10.36$, $p < .01$). This effect was modified by a marginal group \times cue interaction ($F(1,19)=3.96$, $p < .07$) which reflected the fact that for controls, errors increased with cue inversion (from 4.6 to 7.2%), but this was not true for amnesic participants (same cue = 11.5%; inverse cue = 10.2%). There was also a significant effect of condition ($F(2,38)=5.80$, $p < .01$), reflecting the fact that error rates to novel items (mean = 10.5%) were higher than those to low primed (mean = 8.0%; $t(11)=2.49$, $p < .08$) and high primed (6.7%; $t(11)=3.80$, $p < .001$) items. The latter two did not differ from each other ($t(11)=1.31$).

To evaluate if late switching affected accuracy differently than early switching, we performed a $2 \times 2 \times 3$ ANOVA with group (controls, amnesics) as a between-subjects factor and block and condition (novel, low prime, high prime) as within-subjects factors. No effects were significant.

3.3. Discussion

In contrast to nonamnesic participants, amnesic individuals failed to show reliable response learning, which we operationalized as the difference in priming between high and low primed items. Nonamnesic individuals demonstrated a robust high prime advantage in the first test block as long as the decision cue remained the same as during study, but amnesic participants showed equivalent priming for high and low primed items. Moreover, when the decision cue was switched in test block 1, there was a loss of the multiple-repetition advantage associated with high primed items for nonamnesic participants, similar to what was seen in young participants in Experiment 1. By contrast, for amnesic participants, there was no change in the pattern of priming for either high or low primed items as a result of cue inversion and priming in these conditions did not differ, irrespective of decision cue. These results suggest that the response learning previously seen in experiment 1 and in our fMRI study (Dobbins et al., 2004) is critically dependent on intact MTL structures.

The fact that priming in amnesic participants was spared for low primed items, and was significant for high primed items, albeit impaired, indicates that a component of priming is not MTL dependent. This finding is not new, as an extensive literature has revealed intact priming in amnesia for familiar items following a single presentation (Schacter, Chiu, & Ochsner, 1993). In the present task, such priming likely reflects facilitated access to the object knowledge that

³ Although block did not interact with any other effect, it appears that for control subjects, priming for low prime items was reduced following cue switch in block 2, a finding not present in block 1. Given the absence of an appropriate control for cue inversion in test block 2, this finding is of questionable significance. Also, for amnesic participants, priming for low prime items in block 2 was numerically, albeit nonsignificantly, lower than in block 1, but this appears to reflect a general reduction in priming for amnesic participants in test block 2, whether switching occurs or not.

precedes size deliberations. The dissociation between intact object priming and disrupted response learning adds to the evidence that priming does not reflect a unitary mechanism, but rather, that different processes interact to support behavioral facilitation.

The failure to obtain robust response learning in MTL patients is consistent with the notion that this form of learning is dependent on an associative learning mechanism whereby participants learn to associate a particular response to a stimulus (Cohen et al., 1997; Logan, 1990). Further evidence for this possibility comes from a comparison of the control subjects in this experiment with the young participants in experiment 1. In contrast to young participants, older control subjects did not reveal a significant reduction in single repetition priming with cue inversion. This may reflect differential encoding abilities between the groups, with older controls requiring more than a single presentation in order to reliably bind together an item and its associated response—a pattern that is in keeping with the known deficits in associative memory that occur with aging (Naveh-Benjamin, 2000).

While the current experiment has demonstrated that the facilitation associated with multiple repetitions is associative in nature, it should not be assumed that this is necessarily the case for all forms of multiple-repetition priming. For example, Seger, Rabin, Zarella, and Gabrieli (1997) found that amnesic participants show normal, increasing levels of facilitation in generating verbs to repeated nouns—another example of multiple-repetition priming. However, the facilitation in that paradigm was not specific to a given stimulus cue, as it transferred to novel nouns. Therefore, priming in verb generation, in contrast to the response learning observed here, is likely to be nonassociative in nature and would be expected to be preserved in amnesia.

4. General discussion

The human brain operates in such a way as to continuously look for ways to more efficiently respond to environmental demands. This drive towards efficiency or conservation of resources is the fundamental basis of learning and has also been tied to the phenomenon of repetition priming (Gutpa & Cohen, 2002; Logan, 1988). Sensitivity views of repetition priming, which were originally formulated to account for the facilitation associated with a single previous exposure, propose that stimulus-related knowledge is more readily accessible with repetition, resulting in more efficient processing on a subsequent presentation (Graf & Ryan, 1990; Jacoby, 1991; Schacter, 1990). A number of functional imaging studies have used multiple-repetition paradigms under the assumption that the enhanced priming across multiple repetitions reflects quantitative increases within the same set of “tuned” processes (Buckner et al., 1998; Koutstaal et al., 2001; Simons et al., 2003). The results of the experiments presented here, however, do not support such an account. If priming following multiple repetitions reflects facilitated ac-

cess to size information, then a change in decision cue should not affect the magnitude of priming, yet priming was significantly decreased in control participants. Moreover, since amnesic patients have preserved access to size information (as evidenced by intact single-repetition priming), this view would predict that they should show greater priming following multiple repetitions than following a single repetition, but this was not the case. The present findings, instead, argue that for normal individuals, the neural systems originally used in evaluating the size properties of the stimuli were bypassed in favor of a more efficient, MTL dependent, response learning mechanism. While such response learning is most clearly evident following multiple repetitions, it appears that some degree of response learning may occur even with a single repetition, at least in young participants (see also Dobbins et al., 2004).

A possible alternative explanation that might be offered for the priming disruptions that occur after decision cue inversion would be to argue that the nature of the information accessed to make size decisions differs depending on the nature of the decision cue. By such a view, different features of an item may provide clues as to whether an item is larger or smaller than the target. This is inconsistent with the currently prevailing notion that relative size judgments are inferred from retrieval of absolute size information (Banks, 1977; Shoben & Wilson, 1998). Yet, even allowing for the possibility that inversion of a relative size judgment would require access to separate features, an interpretation of priming in terms of access to size information does not adequately account for our findings. In particular, we found that after the experience of decision switching the learned response appears to be suppressed, even when the original (valid) decision cue has been restored. Such a finding would not be expected if attention is simply shifted to an alternative set of features, since returning to the original decision cue should have reinstated the facilitated processing.

The notion that repeated processing of the same item leads to a shift from processing task-relevant information to reliance on a direct association between an item and the required response raises a question as to the nature of the association that is established. One possibility is that response learning reflects establishment of a direct association between an item and a specific motor output. Consistent with this possibility, in our previous fMRI study (Dobbins et al., 2004), we found disruption of behavioral priming not only when the decision cue was reversed, but also, and to the same extent, when the finger mapping was reversed. However, two other studies did not find disruption of response facilitation with changes in motor mapping (Dennis & Schmidt, 2003; Logan, 1990). More importantly, in a recent behavioral study using the same design and procedure as the experiments reported here, we found no evidence for a disruption in response learning when finger mapping was inverted (Schnyer et al., in preparation), suggesting that the observed response learning is not at the level of a particular motor output.

A more likely possibility, therefore, is that an item becomes associated with a particular decision. Such a view

is consistent with previous work examining instance learning (Dennis & Schmidt, 2003; Logan, 1988, 1990), which has suggested that learned instances reflect mapping at the “stimulus-interpretation level”. In the current paradigm, such mapping could be either to the appropriate response (“yes” versus “no”), or to the relative size decision (“bigger than” versus “smaller than”). One way to differentiate between these two possibilities comes from the pattern of errors associated with switching. If a stimulus has been bound to its yes/no response, switching should lead to a greater likelihood that the incorrect answer will be retrieved, and this should be evident in an increase in errors in the primed conditions – especially in the high primed condition – compared to the novel condition. By contrast, if an item has been bound to a relative size category then retrieval of the category should be readily interpretable in the context of either decision cue. Although the translation from “bigger than” to “smaller than” may slow responding, this should not increase the likelihood of errors for primed compared to novel items. The error data are consistent with mapping at the level of a relative size decision, as there was no disproportionate effect of cue inversion on primed items. Given this finding, it may be more appropriate to refer to the form of learning examined here as “decision learning”. However, until we reach a better understanding of the conditions that give rise to mapping at various levels, we prefer to use the term response learning as a more general term that can encompass a broader set of findings.

The failure to observe response learning in amnesic patients provides compelling evidence that this type of learning is dependent on MTL structures, and is consistent with a growing body of evidence that the medial temporal lobes are particularly important in associative memory (Davachi & Wagner, 2001; Eichenbaum, 2001; Giovanello, Schnyer, & Verfaellie, 2004; Jackson & Schacter, 2004). It leaves open the question, however, whether the establishment and expression of an association between an item and its response reflects a form of explicit or implicit memory. On the one hand, the MTL memory system is critically involved in explicit memory and it has been argued that this system is only engaged when information is consciously apprehended (Clark & Squire, 1998; Moscovitch, 2000). From this perspective, it could be postulated that response learning similarly requires explicit awareness of the learned associations. While the finding of MTL dependence is consistent with explicit learning, recent studies have revealed that some forms of associative learning depend on the MTL but nonetheless reflect an implicit form of memory (Chun & Phelps, 1999; Manns & Squire, 2001). Response learning in the current study may fall in the latter category. Future studies will be needed to distinguish between these two possibilities.

More generally, our findings suggest that there are at least two mechanisms contributing to repetition priming. Repetition of a stimulus leads to tuning of the original processes that allow access to stimulus knowledge. At the same time, it leads to the emergence of a new, more efficient mechanism—response learning. Output behavior reflects ei-

ther, one of these simultaneously engaged pathways reaching the processing goal first (Logan, 1988) or the more deliberative pathway being abandoned entirely. With a single learning experience, response learning was less robust than following multiple presentations, suggesting that changes in the representational structure dominate the reaction time output early on in learning. However, after multiple presentations, when response learning becomes more established, it provides the most efficient way to reach the processing goal and thereby dominates the output. In any given situation, then, behavioral expression primarily reflects the process that produces the maximum level of facilitation. It remains an open question to what extent such a model can account for other observed specificity effects in repetition priming (see Schacter et al., 2004). At the very least, it appears that tasks in which the response demands remain constant across the first and subsequent presentations of a stimulus encourage the use of MTL-dependent response learning that comes to dominate the behavioral output.

Acknowledgements

This work was supported by K23MH64004 and P50 NS26985 to Boston University and by the Medical Research Service of the Department of Veterans Affairs.

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