Repetition Suppression Accompanying Behavioral Priming

in Macaque Inferotemporal Cortex

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ABSTRACT

In tasks requiring judgments about visual stimuli, humans exhibit repetition priming, as evidenced by responding more rapidly to the second presentation of a stimulus. It has been suggested that repetition priming is related to repetition suppression, a phenomenon first discovered in monkey inferotemporal cortex in which the strength of the population neuronal response to a visual stimulus is reduced upon repetition of the stimulus. According to the sharpening hypothesis, repetition suppression gives rise to repetition priming by selectively attenuating the activity of neurons weakly responsive to the repeated stimulus while leaving unaltered the activity of neurons strongly responsive to it and thus sharpening its cortical representation. To test this hypothesis, we monitored neuronal activity in monkeys performing a symmetry decision task. We found (a) that monkeys exhibit repetition priming and (b) that neurons in IT simultaneously exhibit repetition suppression but (c) that repetition suppression is greater for stimuli that elicit stronger responses. Thus repetition suppression, although it accompanies repetition priming, does not mediate repetition priming as postulated by the sharpening hypothesis.
In humans, prior experience with a visual stimulus results in faster perceptual processing of that stimulus upon subsequent exposure, a form of implicit memory known as repetition priming (1-2). It has been suggested that repetition priming depends on repetition suppression, a decline in the strength of the response to a repeated stimulus in single neurons of monkey inferotemporal cortex (IT) (3-6). A comparable signal reduction has been observed at the level of BOLD (blood oxygenation dependent) responses in human temporal-lobe visual cortex (7-10), although under rare circumstances signal enhancement may occur instead (10-12). Furthermore, BOLD signal reductions in visual cortex accompany behavioral priming in humans (9, 13-17), as expected if repetition suppression were to mediate priming (18). The idea that repetition suppression (a reduction in response strength) might cause repetition priming (an improvement in perceptual processing) seems paradoxical. However, the two phenomena have been reconciled under the sharpening hypothesis, which posits that repetition suppression enhances stimulus selectivity in IT by exerting a proportionally greater effect on weak visual responses than on strong responses (20-23). Evaluating the sharpening hypothesis requires testing whether repetition suppression occurs under conditions that elicit repetition priming, and if so whether suppression results in sharper neuronal tuning for primed stimuli.

Repetition priming has not previously been demonstrated in the monkey (24). To elicit it, we trained two rhesus macaques (m1 and m2) on a symmetry decision task (Fig. 1A). Within each session, the monkey had to indicate with an eye movement whether each of 120 visual stimuli was laterally symmetric or asymmetric. Each stimulus was presented twice, for a total of 240 trials per session. The sequence was arranged so that the lag between the first and second presentations of a stimulus (the number of intervening trials involving other stimuli) was either
0, 1, 2, 4, 8 or 16 (Fig. 1B). The monkeys completed a total of 118 sessions (67 and 51 in m1 and m2), across which the average percent correct score was 82.5% (84.3% and 80.2% in m1 and m2) \( (30) \). Across all pairs of trials in which the monkey responded correctly to both the first and second presentations (1434-1500 pairs at each lag, mean = 1461), the mean reaction time (RT) was 315 ms (311 and 321 ms in m1 and m2). Critically, in these trials, there was a robust effect of repetition, in that the RT in response to the second presentation of the stimulus was shorter on average in both monkeys (Fig. 2A). This effect was highly significant at all lags \( (p < 5 \cdot 10^{-3}, \text{one-sided Wilcoxin signed-rank test}) \) and especially at lag 0 \( (p = 1 \cdot 10^{-24}) \). The reduction of RT could in principle have been due to repetition either of the stimulus or of the response, because repeating the same stimulus required repeating the same response. However, a memory kernel analysis assessing the influence of response direction (same vs. different) on trials when the stimuli were different \( (26) \) revealed that prior execution of a given response actually resulted in an increase of the RT \( (31) \). This effect, which was significant only at lags of 0 and 1 (rank-sum tests, with Bonferroni correction), may have arisen from a location-based inhibition of return for saccades to previously fixated locations \( (27) \). We conclude that processing the stimulus, as distinct from generating the response, was enhanced upon repetition of the stimulus, and thus that the monkeys exhibited repetition priming.

We proceeded to evaluate whether repetition priming is accompanied by repetition suppression among IT neurons. We monitored the activity of 152 IT neurons (85 and 67 in m1 and m2) over the course of 118 behavioral sessions, which yielded 1537-1641 paired neuronal responses at each lag \( (\text{mean} = 1581) \) \( (30) \). The visual response was suppressed on the second presentation of the stimulus in both monkeys (Fig. 2B-C). Suppression occurred for both symmetric and asymmetric stimuli. The effect was highly significant at lags of 0 and 1 \( (p = 1 \cdot 10^{-24}) \).
and \( p = 8 \times 10^{-4} \) respectively, one-sided Wilcoxon signed-rank test) and decreased monotonically as a function of lag, with suppression becoming marginal at lag 8 (\( p = 0.04 \)) and insignificant at lag 16 (\( p = 0.34 \)). The population response to the second presentation began at the same latency as to the first presentation (80 ms; bootstrap test; \( p > 0.05 \)). However, at a marked delay after the onset of the response (67 ms for repetition at lag 0), a significant suppression developed during the second presentation (\( p < 0.05 \), t-test within a 40 ms sliding boxcar window). These observations on timing are concordant with previous results obtained outside the priming paradigm (3, 32). The fact that the strength of the earliest phase of the response was identical on first and second presentations allows us to reject the accumulator model, according to which the earliest phase of the response to the second presentation is stronger and net suppression arises only because the response terminates earlier (11, 20). The fact that suppression developed well after the onset of the response suggests that repetition-induced changes occur in feedback or lateral, rather than in feed-forward pathways.

Having established that repetition priming and repetition suppression occur under the same circumstances, we next assessed whether the strength of one was correlated with the strength of the other across trials. Across all pairs of trials in which the monkey responded correctly to both presentations of a stimulus, we conducted an analysis of the correlation between normalized measures of priming and suppression (33). The two measures were not correlated (Pearson correlation test, \( p = 0.75, r = 0.0032, n = 9486 \)). This result is consonant with the failure in several human imaging studies to detect a consistent positive cross-subject correlation between behavioral priming and BOLD signal reductions in visual cortex (14-17). The finding that these measures of suppression and priming are uncorrelated does not rule out the existence of a causal relation between the two, because cross-trial variance in the two measures could have derived
from independent sources of variability outside the processes of suppression and priming themselves. However, it certainly provides no support for the idea that suppression contributes to priming.

Finally, we assessed whether repetition suppression took the form predicted by the sharpening hypothesis. According to this hypothesis (20-23), the degree of suppression is proportionally greater for stimuli than elicit a weak response from a given neuron than for stimuli that elicit a strong response, with the consequence that stimulus selectivity is enhanced upon repetition (Fig 3A). In contrast, according to the scaling hypothesis (20, 34) the degree of suppression is a constant proportion of the initial response regardless of stimulus efficacy, with the consequence that selectivity is unaffected (Fig. 3B). To determine which model better accounted for the data, we assessed the relation between response strength and the magnitude of repetition suppression (Fig. 4A). In agreement with the prediction of the scaling model and contrary to the prediction of the sharpening model, there was a highly significant positive linear correlation between the strength of suppression and the strength of the response (9486 stimulus pairs, $p = 3.3\cdot10^{-6}$, $R^2 = 0.0023$). Stimulus repetition had the effect of reducing the strength of the original response by 4.5% on average (2.6% - 6.4%, upper and lower 95% confidence intervals) (35). In order to visualize directly the effect of repetition suppression on stimulus selectivity in IT, we constructed a selectivity profile for each neuron representing response strength as a function of stimulus rank (from the least effective to the most effective stimulus) for first and second presentations (36). Then, averaging across neurons, we constructed population selectivity profiles. The first and second presentation profiles appear closely similar in shape (Fig. 4B) and in fact were not significantly different when normalized to eliminate the overall reduction in firing rate resulting from response suppression ($p = 1.0$, Kolmogorov-Smirnov test).
Thus, upon repetition, the sharpness of neuronal tuning for images in the stimulus set was unaltered.

We conclude that repetition suppression in monkey IT cortex is not obviously related to repetition priming and that, if it does contribute to priming, it must do so by some mechanism other than sharpening (37). To discover a direct neuronal correlate of behavioral priming may require extending the approach described in this study from temporal areas that process visual stimuli to frontal areas that mediate stimulus-response associations and control behavioral output (9, 15, 17).

FIGURE CAPTIONS

Fig. 1. (A) Sequence of events in the symmetry decision task. The monkey initiated each trial by fixating on a white dot in the center of the screen. After 200 ms, a central stimulus and an upper and lower saccade target appeared. M1 was rewarded for making an upward saccade in response to a symmetric stimulus, or a downward saccade in response to an asymmetric stimulus. M2 learned the opposite association. (B) Sample stimulus presentation sequence with examples of repeats at lags of 0, 1, and 4 intervening trials. A new set of stimuli was generated for each session so as to avoid over-training on particular stimuli (Supporting Online Materials, Section I C).

Fig. 2. (A) Repetition priming, a behavioral measure, averaged across all sessions. Priming was assessed as RT_1-RT_2, the difference between first-presentation and second-presentation reaction times (triangles: m1; squares: m2; circles: both monkeys). (B) Repetition suppression, a neurophysiological measure, averaged across all neurons. Suppression was assessed as FR_1-FR_2,
the difference between first and second presentations of firing rate over the interval of 80-280 ms following stimulus onset (symbolic conventions as in A). (C) Population histograms of neural responses, aligned on stimulus onset. Black line: first presentation; thick, medium and thin red lines: second presentations at lag 0, 1, and 2. Black arrow: latency of visual response. White arrow: latency of suppression effect at lag 0.

**Fig. 3.** Alternative models of repetition suppression. Each graph represents response strength vs. stimulus identity for a hypothetical neuron. Black (and red) curves represent responses to the first (and second) presentations of the stimuli. The pattern of response suppression (difference between black and red curves) shown here would result from priming with the full set of stimuli and then probing with the full set.

**Fig. 4.** (A) Magnitude of repetition suppression (FR₁-FR₂) as a function of mean response strength [(FR₁+FR₂)/2] for all pairs of first and second stimulus presentations. Mean response strength was constrained to be a multiple of 2.5 Hz because FR₁ and FR₂ were measured over intervals of 200 ms. The area of each circle is proportional to the square root of the number of cases in which the firing rate assumed a given value (indicated by the location of the center of the circle relative to the horizontal axis). The average value of repetition suppression across these cases is indicated by the location of the circle relative to the vertical axis. Solid line: linear regression fit; dotted lines: 95% confidence intervals. (B) Population tuning curves representing the mean across all neurons of response strength plotted as a function of stimulus rank for presentation 1 (FR₁: red curve) and presentation 2 (FR₂: red curve). For each neuron, stimuli were ranked on the basis of response strength, (FR₁+FR₂)/2. Then data were pooled across
neurons by sorting the stimuli into 40 bins by rank. Coarse binning was necessary in order to accommodate differences among neurons in the number of stimulus pairs eliciting responses.
REFERENCES AND NOTES


18. The relation of BOLD signal reduction to repetition suppression in neurons is unclear because the BOLD signal may reflect pre-synaptic events as distinct from spiking activity (19).


24. Repetition priming (1-2), in which perceptual judgment of a stimulus improves upon repetition, is distinct from several other experience-induced behavioral effects that have been demonstrated in the monkey, notably (a) response priming, in which the selection of a given response direction is enhanced upon repetition (25-26), and (b) priming of popout, in which the selection of a singleton target stimulus embedded within an array of dissimilar distracters is facilitated by repetition of the identity or location of the singleton (26-27) and (c) expertise effects, in which explicit and prolonged training results in accurate discrimination (28-29).


30. Behavioral priming and neuronal suppression effects were restricted to stimuli to which the monkeys responded correctly to both first and second presentations. For neuronal analysis, stimuli that failed to evoke any spikes on both presentations were also excluded. Because there was a tendency towards a transient, non-stimulus-specific decrease in both and RT firing rate very early in a session, we excluded the first 12 trials of each session from subsequent analysis in order to restrict our focus to data collected under stationary conditions (Supporting Online Material, Section II A). Both monkeys exhibited a significant behavioral bias toward classifying stimuli as symmetric (Supporting Online Material, Section II B). The population neuronal response to symmetric stimuli was significantly stronger than to asymmetric stimuli (Supporting Online Material, Section II C). However, behavioral priming and neuronal suppression occurred regardless of stimulus type (Supporting Online Material, Section II D).

31. For details of analysis, see Supporting Online Material, Section II E.

32. For details of analysis, see Supporting Online Material, Section II F.

33. For the correlation analysis, behavioral priming and neuronal suppression were normalized as \((RT_1-RT_2)/(RT_1+RT_2)\), and \((FR_1-FR_2)/(FR_1+FR_2)\) respectively. Correlation analyses were also performed separately for each of 24 data sets consisting of the intersections of two monkeys, two stimulus types, and six lags (Supporting Online Material, Section III H).

35. This correlation analysis was based on data pooled across all six lags. The effect remained significant in data sets consisting of trials at lag 0 \((N = 1,537, \ p = 2.4 \cdot 10^{-9}, R^2 = 0.023)\) and lag 1 \((N = 1,555, \ p = 7.1 \cdot 10^{-4}, R^2 = 0.0074)\).

36. To detect repetition-induced changes in selectivity requires (a) that neurons be responsive to a reasonable percentage of the stimuli and (b) that the responses be selective. These criteria were met (Supporting Online Material, Section II G).

37. Response suppression could potentially give rise to behavioral priming by an effect other than sharpening. It has been demonstrated in a modeling study that suppression is accompanied under some circumstances by an increase in synchronous spiking \((20, 38)\). Increased synchrony at the level of IT could result in enhanced post-synaptic efficacy and stronger firing in areas in frontal cortex receiving projections from IT. Consistent with this hypothesis, one repetition priming study has demonstrated that BOLD signal decreases in extra-striate visual cortex are accompanied by BOLD signal increases in frontal cortex \((9)\).


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A

1. Fixation
2. Symm. stimulus
3. Saccade up

B

Lag 0
Lag 1
Lag 4

1. Fixation
2. Asym. stimulus
3. Saccade down

figure 1
figure 3

A

Sharpening model

B

Scaling model

Firing rate

worst best worst

Stimulus
Figure 4

A

Suppression (Hz)

Response strength (Hz)

N Observations

1000 100 10

B

Firing rate (Hz)

Stimulus rank