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1 **Inversion of pop-out for a distracting feature dimension in monkey visual cortex**

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23 Project Administration, Funding Acquisition; R.R.M. Teeuwen: Formal Analysis, Data Curation, Writing – Original
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29 **Abstract**

30 During visual search, it is important to reduce the interference of distracting objects in the scene. The
31 neuronal responses elicited by the search target stimulus are typically enhanced. However, it is equally
32 important to suppress the representations of distracting stimuli, especially if they are salient and capture
33 attention. We trained monkeys to make an eye movement to a unique ‘pop-out’ shape stimulus among an
34 array of distracting stimuli. One of these distractors had a salient color that varied across trials and differed
35 from the color of the other stimuli, causing it to also pop-out. The monkeys were able to select the pop-out
36 shape target with high accuracy and actively avoided the pop-out color distractor. This behavioral pattern
37 was reflected in the activity of neurons in area V4. Responses to the shape targets were enhanced, while the
38 activity evoked by the pop-out color distractor was only briefly enhanced, directly followed by a sustained
39 period of pronounced suppression. These behavioral and neuronal results demonstrate a cortical selection
40 mechanism that rapidly inverts a pop-out signal to ‘pop-in’ for an entire feature dimension thereby
41 facilitating goal-directed visual search in the presence of salient distractors.

42 **Keywords:** Visual search, V4, monkey, suppression, enhancement.

43

44 **Significance statement**

45 Goal-directed behaviors like visual search involve both the selection of behaviorally relevant targets and the
46 suppression of task-irrelevant distractors. This is especially important if distractors are salient and capture
47 attention. Here we demonstrate that non-human primates suppress a salient color distractor while searching
48 for a target that is defined by shape, i.e. another feature dimension. The neuronal activity of V4 neurons
49 revealed the temporal evolution of target selection and distractor suppression. The neuronal responses
50 elicited by the pop-out target stimuli were enhanced whereas responses elicited by salient pop-out color
51 distractors were suppressed, after an initial brief phase of response enhancement. Our results reveal a ‘pop-
52 in’ mechanism by which the visual cortex inverts an attentional capture signal into suppression to facilitate
53 visual search.

54 **Introduction**

55 Humans and animals usually need to select one of several stimuli for action. This selection process relies on
56 priority signals in the brain such as the salience of stimuli and the subject's goals (1–7). In the visual domain,
57 for example, one could be faced with the task of locating a target object among distractor objects, e.g., trying
58 to find one's keys on a cluttered desk (Fig. 1A). A combination of bottom-up and top-down processes often
59 solves this problem (3). If the keys have a high saliency because they are bright red, for example, they 'pop
60 out' from the background, which would be considered a bottom-up contribution. However, top-down factors
61 also play an important role. You may, for example, imagine the shape of your keychain or try to remember
62 where the keys most likely are. Visual search is therefore a very useful experimental paradigm to study the
63 role of bottom-up and top-down factors in visual selection.

64 In many bottom-up search paradigms, the target pops out, because it has a unique feature. For example, it is
65 the only bright red item among grey distractors, or it is the only circle in the display in which all other
66 elements are squares. There are versions of this paradigm in which subjects do not know beforehand what
67 they will be looking for, but only that it is the unique item. For example, the display might have either one
68 square among circle distractors or one circle among square distractors. The search for items with unique
69 properties is usually parallel, which means that the time to find an item does not depend strongly on the total
70 number of distractors in a search display (7). Previous studies on the neuronal correlates of pop-out search
71 demonstrated that the responses elicited by pop-out stimuli are stronger in the visual, parietal, and frontal
72 cortex than the responses to stimuli that do not pop-out (8–18). In top-down search paradigms, the subject
73 looks for a specific item known as 'search-template' (21, 22). The search template represents a top-down
74 influence on visual selection (1, 23) and the representations of the items in the display that match the search
75 template are also enhanced in areas of the visual, parietal, and frontal cortex (19, 22–29).

76 Many displays contain salient distractors that interfere with visual search. This is the case in Figure 1 for the
77 green parrot, which captures attention, making it more difficult to find the keys. Researchers have debated
78 the degree of automaticity of attentional capture, with some researchers arguing that it is mandatory (30)
79 whereas others arguing that it can be prevented by sufficiently strong top-down signals (31). Importantly,
80 conditions exist under which salient display items do not appear to interfere with visual search (32, 33) or
81 cause even less interference than regular, non-salient distractors (34–37).

82 The mechanism by which salient distractors can be suppressed is not yet fully understood and there are
83 contrasting views (38). One possibility is that salient distractors initially capture attention, but that it is
84 rapidly curtailed by top-down suppression mechanisms (39). Support for such reactive suppression comes
85 from human EEG studies employing markers of distractor selection and suppression (40–43). The signal
86 suppression hypothesis (35–37) proposed another account, in which a top-down influence prevents the
87 capture of attention by salient distractors so that there is no need for disengagement. This viewpoint received

88 support from behavioral studies (34, 35, 44) and other human EEG studies (34, 36, 37, 45, 46). We note,
89 however, that the relation between this putative suppressive signal and its EEG signatures is under dispute
90 (43, 47).

91 The degree to which salient distractors attract attention and, hence the need for disengagement, depends on
92 how predictable they are. Salient distractors are more efficiently suppressed if their features are predictable,
93 for example, because they are the same across trials or are known in advance (48, 49). Bichot et al. (50)
94 demonstrated that the representations of stimuli that consistently appear as distractors, across many days, are
95 strongly suppressed in the frontal cortex of monkeys. Like distractor predictability, foreknowledge about the
96 target also decreases the influence of salient distractors. If the subject knows the target, a search template can
97 be established before the display appears and the influence of salient distractors is weaker than in pop-out
98 search in which the target properties are not specified. Researchers proposed that pop-out search demands a
99 special ‘singleton detection mode’ (32). If subjects search for a salient target with unknown features, they are
100 more susceptible for interference by salient distractors. The degree of interference by the distractor depends
101 on the relation between the features of the target and the distractor (35, 36, 38, 51, 52). Interference is strong
102 if the target and salient distractor are defined on the same feature dimension, e.g., if they both have an
103 orientation that differs from that of all other distractors. Interference is weaker if they are defined on a
104 different feature dimension, e.g., the target differs in orientation from the other items whereas the salient
105 distractor differs in color. In this situation, the features can be weighted. The target dimension receives a
106 higher weight than the salient distractor so that the degree of distraction can be diminished (40, 52–54).

107 Two previous studies have examined the neuronal mechanisms for the suppression of salient distractors
108 during visual search. Ipata et al. (55) had monkeys searching for a black target shape among black
109 distractors. They added a salient distractor, which was green and bright, and recorded neurons in the lateral
110 intraparietal area (LIP) of the parietal cortex. As expected, targets elicited stronger neuronal responses than
111 the black distractors, but the activity elicited by the salient green items was even weaker than that elicited by
112 the regular black distractors. Hence, the representation of the salient distractor is efficiently suppressed in the
113 parietal cortex. A later study by Cosman et al. (56) replicated this finding in the frontal eye fields (FEF) in a
114 task where the monkeys searched for a white target letter while the salient distractor was colored. Again, the
115 target letter elicited strongest activity, followed by the regular distractors and the salient distractor elicited
116 weakest activity. These results are in accordance with those of Bichot et al. (50) showing the effective
117 suppression of a specific feature that is always distracting in the frontal cortex. (57, 58). However, parietal
118 and frontal cortex are relatively high up in the cortical processing hierarchy and activity elicited by salient
119 distractors might still be enhanced in the visual cortex, even after extensive training. The representation of
120 salient distractors in visual cortex remains to be investigated.

121 In the present study we tested the generality of the suppression mechanisms by asking three questions: (1)
122 Are salient distractors suppressed in the visual cortex? (2) Is the efficient suppression of a salient distractor

123 stimulus also possible when its features vary across trials? (3) Can salient distractor suppression occur when
124 the subject searches for a pop-out stimulus on a different feature dimension?

125 We trained monkeys in a task in which they carried out a pop-out search for a shape while we presented a
126 salient color distractor with a color that varied across trials. They had to select the shape singleton as target
127 for an eye movement to obtain a juice reward. As expected, the shape singleton elicited stronger V4 activity
128 than the distractors with a different shape. Remarkably, the V4 representation of salient color singleton was
129 briefly enhanced followed by a period of pronounced suppression below the level of representation of the
130 regular non-pop-out distractors, even though its color was unpredictable. At a behavioral level, the monkeys
131 also selected the salient distractor less often than the regular distractors, indicating active avoidance. We
132 conclude that after extensive training, the neuronal mechanisms for visual search can exploit the presence of
133 a color singleton if it is always a distractor, and rapidly cause it to ‘pop-in’ instead of pop-out, thus avoiding
134 capture and promoting efficient goal-directed behavior.

135 **Results**

136 Two monkeys were extensively trained to perform a visual search task (Fig. 1B,C) in which they had to
137 select a single odd-shape-out (target) from an array of six stimuli. On any given trial, the target could either
138 be a circle among squares, or a square among circles. To study whether V4 neurons show suppression of
139 salient distractors, one of the distractor stimuli had a different color than the others (either green among red,
140 or red among green) (Fig. 1B, bottom). The shapes, colors, and locations of the target and salient distractor
141 were randomly assigned on each trial so that the animal could not predict the shape or color of the target and
142 salient distractor. As a result, consecutive trials could have the same shape and colors assigned to the target
143 and distractor, both could change, or one of the feature assignments could stay the same while the other
144 changed. Moreover, to examine a previously reported interaction between stimulus salience and reward in
145 human visual search behavior (59), we randomly rewarded correct responses with either small or large juice
146 rewards (with the large reward being approximately four times the small reward amount). After an initial
147 training phase to learn the task, both monkeys were extensively trained to reach high performance levels (22
148 training sessions for M1, 56 for M2).

149 We recorded 34,543 trials in monkey 1 (M1) and 13,815 trials in monkey 2 (M2) in 28 and 16 sessions,
150 respectively. Both monkeys displayed similar eye movement patterns (Fig. 1D), most often choosing the
151 target stimulus (M1: 69%, M2: 78% of choices), followed by non-salient distractors (M1: 29%, M2: 20%),
152 and only rarely choosing the salient distractor stimulus (M1: 2%, M2: 2%). The lower probability of
153 choosing a salient distractor than a non-salient distractor remained when we accounted for the fact that there
154 were four non-salient distractors and only one salient distractor (see Fig. 1D insets, corrected for prevalence).
155 The probability of choosing the target was much higher than chance (one-tailed t-test, M1: $t(26) = 87.4$, $p <$
156 0.001 ; M2: $t(15) = 53.5$, $p < 0.001$). On error trials, both animals were significantly less likely to choose the
157 salient distractor than a non-salient distractor (prevalence-corrected, one-tailed paired t-test, M1: $t(26) = -$

158 51.6, $p < 0.001$; M2: $t(15) = -21.6$, $p < 0.001$).

159 Swapping the colors of the target and salient distractor on successive trials did not affect accuracy for either
160 animal as indicated by a two-way ANOVA with color-swap and reward quantity as independent variables
161 (all p s > 0.48). It did slow down M1 by a few milliseconds (Fig. 1E; $F(1, 12210) = 38.8$, $p < 0.001$), but had
162 no effect on M2's reaction time ($F(1, 7484) = 1.59$, $p = 0.83$). A change of the target shape had a much more
163 pronounced effect of performance. It decreased the accuracy of both animals and increased the reaction times
164 (Fig. 1E; all $p < 0.001$). There were no interactions between the effects of color and shape changes. These
165 results imply a shape-based priming of pop-out effect across trials (60), but an absence of color-based
166 priming, which is consistent with the animals being in 'shape-searching' mode due to extensive training on
167 the 'odd-shape-out' search task. Unlike previous work in humans (59), we did not observe any main or
168 interaction effects of reward quantity on visual search performance (SI Appendix, Fig. S1).

169 What happened when the monkeys made an error? They predominantly selected the distractor stimulus that
170 was adjacent to the target in the search array (Fig. 1F), a pattern that was neither influenced by the location
171 of the salient distractor, nor by the saccadic reaction time (comparing the 30% fastest and 30% slowest
172 saccades) (squares and diamonds in Fig. 1F). The distribution of erroneous saccades relative to the target
173 position was the same for salient and non-salient distractors (red and grey symbols in Fig. 1F), which
174 indicates that the probability of choosing the salient distractors was decreased uniformly (Fig. 1D) with little
175 influence of the target location.

176 Whereas the signal suppression hypothesis (34) proposes that a salient distractor can be proactively
177 suppressed to avoid attentional capture, the stimulus-driven rapid-disengagement account suggests that
178 capture does temporarily occur but that it is then quickly suppressed. The latter scenario should be associated
179 with a brief period of pop-out for the salient distractor followed by a sustained period of distractor
180 suppression. Because visually guided saccades can occur at very low latencies in both humans and monkeys
181 (61–65), especially after prolonged training (66), and fast saccades tend to be more strongly influenced by
182 stimulus salience (67–69), we wondered whether an early neuronal pop-out of the salient distractor would
183 result in very rapid saccadic responses to the salient distractor before the distractor suppression could have
184 manifested. To investigate this possibility, we compared the distributions of saccade reaction times (SRTs;
185 SI Appendix, Fig. S2) for target and salient distractor choices. A larger proportion of the salient distractor
186 choices than the target choices occurred at the shortest reaction times in both monkeys (Fig. 2A). We
187 calculated the proportion of salient distractor choices ($p_{SD} = n_{SD}/n_{ALL}$) as function of SRT (Fig. 2B). In both
188 animals, the proportion SD choices was significantly higher for the 12.5% shortest SRTs (first octile) than
189 for SRTs in the 2nd-4th octiles (chi-squared test, M1: $X^2(1) = 8.55$, $p < 0.01$; M2: $X^2(1) = 21.41$, $p < 0.001$). In
190 M1 there was even a brief epoch in which the salient distractor was chosen more often than the target, but
191 saccades to the salient distractor were strongly suppressed for longer SRTs. Also, in M2 the salient distractor
192 choices decreased for longer SRTs, but the target was always chosen with the highest probability (SI

193 Appendix, Fig. S2). This result indicates that the distractor pops out in an early interval after stimulus
194 presentation, but that the pop-out signal is rapidly suppressed to prevent erroneous choices.

195 Next, we compared the neuronal responses in V4 elicited by target stimuli, non-salient distractor stimuli and
196 salient distractor stimuli on correct trials (Fig. 3A, top panels). We pooled the data across animals (Fig. 3,
197 left panels) because the results were similar for M1 and M2 (Fig. 3, middle and right panels). The late V4
198 response elicited by target stimuli was stronger than that elicited by non-salient distractor stimuli (time
199 window 150-200 ms after stimulus onset, $t(34) = 8.9$, $p < 0.001$; M1: $t(9) = 5.6$, $p < 0.001$; M2: $t(24) = 7.0$, p
200 < 0.001). The response elicited by the salient distractor stimulus was weaker than that elicited by the target
201 stimulus and, importantly, also weaker than that elicited by the non-salient distractor stimulus ($t(34) = -9.9$, p
202 < 0.001 ; M1: $t(9) = -5.4$, $p < 0.001$; M2: $t(24) = -9.1$, $p < 0.001$). This ordering of response strength was very
203 consistent among recording sites (SI Appendix, Fig. S3).

204 We examined the time-course of target enhancement and salient distractor suppression by subtracting V4
205 activity elicited by the non-salient distractor stimuli from the other two conditions (Fig. 3B). We measured
206 the latency of the enhancement and suppression of targets and salient distractors with a fitting procedure that
207 has been described before (70) (see Material and Methods and SI Appendix, Fig. S4). The latency of target
208 enhancement was 112 ± 9 ms (averaged across monkeys, standard deviation determined with bootstrapping)
209 and the latency of suppression of salient distractors was 158 ± 25 ms. This pattern was also present in
210 individual animals (M1_T: 124 ± 20 ms, M2_T: 108 ± 15 ms; M1_{SD}: 184 ± 14 ms, M2_{SD}: 159 ± 11 ms) and the
211 salient distractor suppression was significantly later than the target enhancement (paired t-test, M1: $t(75) = -$
212 26.3 , $p < 0.001$; M2: $t(72) = -22.1$, $p < 0.001$; Pooled data: $t(67) = -17.7$, $p < 0.001$). Thus, the pop-in effect
213 was expressed in area V4 as a decreased response to the irrelevant singleton, even though its color was
214 unpredictable.

215 The brief early epoch with an enhanced probability of saccades to the salient distractor suggests that the
216 distractor representation might be briefly enhanced in V4 (33, 35, 37) before it is suppressed. We therefore
217 examined the possibility of an early response enhancement. We observed that the salient distractor (Fig. 3B,
218 red bars) indeed caused a brief epoch of enhanced activity before suppression became evident, in a time-
219 window up to 100 ms after stimulus onset (Fig. 3B shows significant modulation in several 10 ms non-
220 overlapping time bins in both monkeys; t-tests at $p < 0.05$, Bonferroni corrected).

221 We also examined a possible influence of the behavioral priming effect, which occurred when the target
222 shape was the same on consecutive trials, on V4 activity. The priming effect did not have a consistent
223 influence on V4 activity (SI Appendix, Fig. S5), which suggests that the increase in SRT may originate in
224 downstream brain regions, as a post-selective process (54). Furthermore, V4 activity on error trials was more
225 variable than on correct trials (SI Appendix, Fig. S3).

226 **Discussion**

227 Goal-directed behaviors require a selection process that highlights relevant stimuli and suppresses
228 distractors. Here, we used a visual search paradigm to investigate the representations of relevant and
229 irrelevant pop-out stimuli (7) in area V4 of the monkey visual cortex. We presented a salient pop-out color
230 distractor with an unpredictable color while the monkeys searched for a singleton shape. Our results
231 demonstrate that the visual brain can suppress the representation of pop-out stimuli on an irrelevant feature
232 dimension while enhancing the representation of pop-out stimuli on a relevant feature dimension. A brief
233 neuronal activity enhancement preceded the suppression of distractor representations (Fig. 4), suggesting that
234 an initial pop-out process is required before it can invert into pop-in. To our knowledge, this is the first
235 demonstration of ‘pop-in’ for an irrelevant feature dimension, which presumably emerged during the
236 monkeys’ considerable training.

237 The efficiency of visual search depends on bottom-up factors that determine the salience of stimuli, such as
238 brightness and local feature contrasts causing pop-out, and the top-down search template, the internal
239 representation of the item that the subject is searching for (1, 3, 4, 22). Researchers have hypothesized that
240 stimulus salience and goal-driven influences on the distribution of attention jointly determine a ‘priority
241 map’ of visual space (3–7, 71–73). There are multiple candidate brain regions for such a priority map,
242 including the LGN (71), pulvinar (74), superior colliculus (75, 76), V1 (77), V4 (66), the parietal (8, 10, 55)
243 and prefrontal cortex (11). Indeed, stimulus-driven pop-out signals have a widespread influence on the
244 neuronal firing rates in early visual cortex (12, 78, 79), parietal cortex (10), frontal cortex (11), and
245 subcortical structures like the superior colliculus (80). Similarly, the top-down influences of the search
246 template on firing rates also occur in most, if not all, of the same brain regions, including V1 (81, 82), V4
247 (15, 18), the parietal (55) and prefrontal cortex (11, 50, 56). It is conceivable that the relative contributions of
248 the multiple priority maps depend on the task, e.g., on the features that matter and on whether the subject
249 reports the location of the target with an eye or hand movement.

250 There are many instances in which the representation of visually salient items needs to be suppressed,
251 because task relevant items are less conspicuous, causing a conflict between bottom-up and top-down
252 factors. The signal suppression hypothesis (36, 37) proposed that top-down suppression signals can prevent
253 attentional capture by salient distractors if their features are known in advance (34–37, 44–46, 51, 56, 83–
254 85). An alternative possibility is that salient distractors attract attention, but that it is rapidly disengaged (39).
255 Previous electrophysiological studies in areas LIP and FEF of monkeys revealed that the neuronal activity
256 elicited by a salient distractor with a predictable color can indeed be suppressed below the activity elicited by
257 regular distractors (55, 56). The suppression of salient distractors has also been measured as a distractor
258 positivity (Pd) component in the EEG of humans (37, 38, 86) but a recent study using the steady-state
259 visually evoked potential (SSVEP) did not find evidence for suppression below the activity elicited by
260 regular distractors (47). This SSVEP study used displays with only few items, however, and it has been

261 suggested that such displays do not emphasize pop out but require other search processes ('clump scanning')
262 (41, 52, 87). The present study went beyond these previous studies by investigating whether suppressive
263 signals influence spiking activity in the visual cortex of monkeys. Furthermore, we used a new task in which
264 the features of the salient distractor were unpredictable, and the monkey was searching for a pop-out
265 stimulus on a different feature dimension.

266 Unlike the previous studies (55, 56), we found that the salient distractor elicited a brief enhancement of V4
267 activity that later inverted into sustained suppression. It seems likely that the early response enhancement
268 occurred because the color of the salient distractor was unpredictable so that it first needed to be registered
269 before it could be suppressed. We also observed a behavioral consequence of this brief pop-out phase
270 because a proportion of the early saccades landed on the salient distractor whereas it was less likely to be
271 selected than regular distractors at later time points, when pop-out has inverted into pop-in. This result
272 provides evidence for short-lived attentional capture, followed by rapid attentional disengagement (38, 39)
273 and goes against the proactive top-down suppression of attentional capture proposed by the signal
274 suppression theory.

275 In a previous study on the role of area V4 during visual search Ogawa and Komatsu (15) trained monkeys to
276 search for either shape or color singletons in displays that also included a singleton in the other dimension, as
277 a salient distractor. Unlike in the present study, however, the monkeys searched for shape and color
278 singletons in alternating blocks of trials. When they made an error, they selected the salient distractor more
279 often than regular distractors, which is also different from the current results. Accordingly, V4 activity
280 elicited by the target of search was strongest, V4 activity elicited by salient distractors was intermediate and
281 stronger than that elicited by regular distractors (15). In other words, in the previous study both the singleton
282 target and the singleton distractor popped out, while in the present study, the color singleton was never
283 relevant and its V4 representation was suppressed below the activity elicited by regular distractors.

284 Our results indicate that there are at least two processing steps in the present search task (Fig. 4). Initially,
285 there is pop-out in two feature dimensions: color and shape. Later in the trial, the activity elicited by the
286 shape singleton remains enhanced, whereas activity elicited by the color singleton is suppressed, indicating
287 that V4 could contribute to a priority map with enhanced target and suppressed distractor representations
288 (Fig. 4). The source of the suppressive pop-in signal is unknown, but it could rely on feedback projections
289 (88, 89) that might have been strengthened during training. In accordance with this view, microstimulation of
290 FEF interacts with stimulus driven activity in early visual cortex in a topographic manner, with an effect that
291 depends on stimulus strength and the presence of distractors (90). It is remarkable that the neuronal
292 mechanisms for the registration of the salient distractor and its later suppression can co-exist with the
293 mechanisms for pop-out on another feature dimension. Previous studies anticipated that the degree to which
294 different feature dimensions cause pop-out can be weighted (52–54). However, to our knowledge, these
295 theories did not anticipate that dimension weights could become negative, causing attentional repulsion of

296 singletons on a specific feature dimension. A limitation of our results is that we do not know whether the
297 activity elicited by the regular distractors, which we used as a reference to compute target modulation and
298 salient distractor modulation, changed during training (91, 92). Future studies could address this question by
299 including neutral distractors with a third color, which is always irrelevant for the task.

300 Previous studies demonstrated a profound influence of the recent history of trial types during visual search.
301 Repeatedly searching for the same stimulus features causes priming. It reduces an observer's reaction time,
302 improves accuracy, and increases the difference between the strengths of the neuronal representation of
303 targets and distractors (9, 18, 60, 93–97). We here observed a priming effect of shape. When the shape of the
304 search target remained the same on consecutive trials, the monkeys were faster and more accurate than when
305 it was different. Interestingly, we did not find a behavioral priming effect of color as was observed in
306 previous studies (9, 18, 93), in which the search target was a color singleton. It therefore seems likely that
307 priming only occurs for the feature dimension that defines the search goal.

308 Earlier studies also demonstrated an effect of reward quantity on visual search performance (59, 98–100). A
309 study in human subjects demonstrated that visual search is faster if a preceding trial with the same target and
310 distractor features gave rise to high, as opposed to low, reward (59). We did not replicate this effect in our
311 monkeys, where reward magnitude on the previous trial did not strongly affect performance. One possible
312 explanation is that the animals were highly trained, which may have reduced their sensitivity to reward
313 outcomes on individual trials. However, other explanations, including species differences, are also
314 conceivable.

315 In conclusion, our work shows parallel mechanisms of target enhancement and salient distractor suppression
316 during visual search in V4 that rapidly develop and manifest behaviorally as efficient distractor avoidance
317 and goal-directed target selection. It seems likely that the conversion of initial distractor enhancement into
318 functional and profound suppression that occurs round 150 ms after stimulus onset reflects a top-down
319 dynamic adjustment of the weights of individual feature dimensions. The extended training history, during
320 which the salient color never coincided with the search target, must have engaged plasticity mechanisms
321 inverting pop-out into pop-in, making the mechanisms of visual search more versatile than might have been
322 anticipated.

323 **Materials and Methods**

324 **Subjects.** All animal procedures complied with the NIH Guide for Care and Use of Laboratory Animals, and
325 were approved by the institutional animal care and use committee of the Royal Netherlands Academy of Arts
326 and Sciences. Two male macaque monkeys participated in the experiment. They were 5 (M1) and 8 (M2)
327 years old at the start of the experiments and weighted between 7-8 (M1) and 8-9 (M2) kg over the course of
328 the recordings. The monkeys were socially housed in pairs in a specialized primate facility with natural
329 daylight, controlled humidity and temperature. The home-cage was a large floor-to-ceiling cage that allowed
330 natural climbing and swinging behavior. The cage had a solid floor, covered with sawdust, and was enriched
331 with toys and foraging items. The diet consisted of monkey chow supplemented with fresh fruit. The access
332 to fluid was controlled, according to a carefully designed regime for fluid uptake. During weekdays the
333 animals received diluted fruit juice in the experimental set-up upon correctly performed trials. We ensured
334 that the animals drank sufficient fluid in the set-up and supplemented extra fluid after the recording session if
335 the monkeys did not drink enough. In the weekend the animals received at least 700 ml of water in the home-
336 cage supplied in a drinking bottle. The animals were regularly checked by veterinary staff and animal
337 caretakers and their weight and general appearance were recorded in an electronic logbook daily during
338 fluid-control periods.

339 **Surgical procedures and training.** We implanted both monkeys with a titanium head-post (Crist
340 instruments) under aseptic conditions and general anesthesia as reported previously (101–103). The monkeys
341 were first trained to fixate a 0.5 diameter fixation dot and hold their eyes within a small fixation window (1.2
342 diameter). They then underwent a second operation to implant arrays of 4x4, 4x5 and 5x5 micro-electrodes
343 (Blackrock Microsystems) in V4. The inter-electrode spacing of the arrays was 400 μm . The animals were
344 later extensively trained to perform the visual search task at adequate performance levels (22 training
345 sessions with the final task for M1, 56 sessions for M2). During the early phase of the training the animals
346 were required to make an eye movement from the fixation point to a single target, and in later phases the
347 distractors were introduced at low contrast which over sessions gradually increased to the same contrast as
348 the target.

349 **Electrophysiology.** Recordings from the chronically implanted electrode arrays were made with TDT
350 (Tucker Davis Technology) recording equipment using a high-impedance head-stage (RA16AC) and a
351 preamplifier (either RA16SD or PZ2). The signal was referenced to a subdural electrode and digitized at 24.4
352 kHz. It was band-pass filtered (2nd order Butterworth filter, 500 Hz – 5 kHz) to isolate high-frequency
353 (spiking) activity. This signal was rectified (negative becomes positive) and low-pass filtered (corner
354 frequency = 200 Hz) to produce multi-unit activity (MUA), which is the envelope of the high-frequency
355 activity (104). MUA reflects the spiking of neurons within 100-150 μm of the electrode and MUA
356 population responses are very similar to those obtained by pooling across single units (103–107). We used a
357 video-camera based eye-tracker (Thomas Recording) to measure the eye position at a sampling frequency of

358 250 Hz. V4 receptive fields were mapped by presenting white squares (1° , luminance 115 cd/m^2) on a dark
359 background (2 cd/m^2) at different positions of a grid (1° spacing). We defined the RF borders as the locations
360 where activity fell below 50% of the maximum (108).

361 We removed trials with artifacts first by calculating the time-average for each trial and removing trials with
362 extreme average MUA responses. We used an iterative z-scoring procedure (values higher than 3 were
363 removed). If z-scores higher than 20 remained in the cleaned collection of trials, the process was repeated,
364 leading to the removal of less than 2% of all the trials. We also removed trials that included any samples
365 (without averaging) that had a z-score higher than 10. To normalize MUA, we subtracted the spontaneous
366 activity level in a 100 ms time window prior to the onset of the stimulus and divided by the peak response
367 after LOWESS smoothing (26 ms window). We only included recording sites with a signal-to-noise (SNR)
368 higher than 2.5. SNR was computed for individual recording sessions by dividing the peak of the smoothed
369 response by the standard deviation of the spontaneous activity level across trials. We excluded recording
370 sites with fewer than 3 recording sessions that met the SNR criterion. For the other recording sites, we
371 averaged the activity per recording site across sessions so that every recording site contributed only once to
372 the statistics.

373 **Behavioral task and stimuli.** Stimuli were presented on a 21" CRT monitor (Dell Trinitron) with a refresh
374 rate of 85 Hz and a resolution of 1024×768 pixels, viewed at a distance of 87 cm. All stimuli were created
375 using the COGENT graphics toolbox (developed by John Romaya at the LON at the Wellcome Department
376 of Imaging Neuroscience) running in MATLAB (Mathworks Inc.) with custom experimental control
377 software (109). The monkeys were trained to perform a visual search task. A trial started when the monkey
378 acquired fixation on a 0.3° red (26.2 cd/m^2) fixation dot in the center of the screen. After 200 ms of fixation
379 within a 1.2° diameter window, 6 stimuli appeared, arranged in a circle around the fixation point, at 5.3°
380 eccentricity. Simultaneously, the fixation dot became green (98.6 cd/m^2) cueing the monkey to make a
381 saccade. The stimuli were visible for 2,000 ms, during which the monkey was required to respond. If the
382 monkey failed to respond in time, the trial was classified as aborted. Each stimulus could be either a square
383 or a circle and was either red (76.0 cd/m^2) or green (114.1 cd/m^2), presented on a gray background (54.2
384 cd/m^2). Stimuli had a size of 1.8° diameter. On each trial, one stimulus had a different shape (the target
385 stimulus), one stimulus had a different color (the salient distractor stimulus), and the 4 remaining stimuli
386 (non-salient distractors) had the same color as the target stimulus and the same shape as the salient distractor.
387 The task of the monkey was to make an eye movement to the target stimulus, while ignoring the salient and
388 non-salient distractors. Choices were detected as the eye-position entering a 4° diameter circular window
389 around one of the stimuli. Upon a correct response, the monkey received a juice reward. This reward was
390 randomly selected to be either small or large (~ 4 times the small amount). The trials were ordered in a
391 pseudorandom fashion. We recorded 34,543 trials across 28 sessions in monkey 1 and 13,815 trials across 16
392 sessions in monkey 2.

393 **Computation of target and salient distractor modulation.** Average MUA responses for target, non-salient
394 distractor, and salient distractor stimuli were calculated for individual monkeys and the pooled data. To
395 compute target and salient distractor modulation we subtracted the response to non-salient distractors from
396 the response to targets and salient distractors, respectively, for each recording site in a 150-200 ms time
397 window after stimulus onset. As statistical test we used paired t-tests over recording sites. The time-courses
398 of target and salient distractor modulation were furthermore evaluated by recalculating the modulation in 10
399 ms non-overlapping bins and statistically tested with a series of t-tests, using Bonferroni correction for
400 multiple comparisons.

401 **Latency of target selection and distractor suppression.** To estimate the latency of the enhancement of the
402 representation of the target and the suppression of the representation of the salient distractor we used a fitting
403 procedure that has been described before (70). Briefly, a cumulative gaussian function was fit to the
404 difference between either the target and the non-salient distractor response (i.e., target modulation) or the
405 non-salient distractor and the salient distractor response (i.e., salient distractor modulation). The latency is
406 estimated as the time point at which the fit reaches 33% of its maximum (SI Appendix, Fig. S4). The fits
407 were calculated based on the population responses, i.e., after averaging across recording sites. We used a
408 bootstrapping procedure (100 times) with replacement to estimate the mean and standard deviation of these
409 latency estimates and compared latencies of target and salient distractor modulations with paired t-tests.

410 **Saccadic reaction times.** We investigated the susceptibility to attentional capture by the salient distractor as
411 a function of saccadic reaction time (SRT). We removed SRTs that were faster than 75 ms because we
412 deemed such responses to be too fast to be visually guided based on previous reports . This resulted in the
413 removal of 6 target (M1: 2, M2: 4) and 9 salient distractor responses (M1: 7, M2: 2). For the remaining
414 responses we calculated the 25th percentile SRT per animal and classified all faster responses as ‘fast SRTs’.
415 The values of these fast SRTs for target and salient distractor choices were compared with Wilcoxon rank
416 sum tests. We also used the full range of SRTs to calculate a proportion of salient distractor choices ($p_{SD} =$
417 N_{SD}/N_{ALL}) within a 20 ms sliding window moving through the range of SRTs with 10 ms increments.

418 **Data, Materials, and Software availability.** All Data & Analysis Code reported in this paper are available
419 on GIN (<https://doi.org/10.1101/2022.06.23.497353>).

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655 **Figure Legends**

656 **Figure 1. Task description and behavioral results.** **A)** Real-life example of visual search with a salient
657 distractor. When looking for your keys on a crowded desk, you may be looking for small key-shaped objects.
658 Your attention may however be captured by salient objects like the bright green parrot, which might interfere
659 with the process of finding your keys. **B)** We recorded from area V4 while monkeys performed a visual
660 search task in which they selected the odd-shape-out (here a square among circles) with an eye movement.
661 One of the six visual items was in the V4 receptive field. The target was the stimulus that differed from the
662 others by shape. Non-salient distractor stimuli had the same color as the target, while a single salient
663 distractor stimulus popped out because it had a different color. **C)** Example series of three trials. In the
664 second trial the target and distractor shapes swapped with respect to the first trial (this occurred 50% of the
665 time). In the third trial, the target and distractor colors swapped (this also occurred 50% of the time). In
666 addition, the reward magnitude was randomly varied (50% high, 50% low). **D)** Accuracy (green bars) and
667 the proportion of trials on which the monkeys made an error by choosing a non-salient distractor (ND, grey
668 bars) or the salient distractor (SD, red bars). Non-salient distractors are 4 times more prevalent than targets
669 and salient distractors (prevalence indicated with dashed horizontal lines). The insets show the proportion of
670 choices of distractor stimuli corrected for prevalence. Even after this correction, the animals chose the salient
671 distractor less often than the non-salient distractors (* indicates $p < 0.001$ for a one-tailed t-test $SD < ND$).
672 Error bars indicate the standard deviation over recording sessions. **E)** The effects of color and shape swaps
673 on accuracy (top panel) and reaction time (bottom panel) for both monkeys. Yellow lines indicate trials in
674 which the target and salient distractor colors swapped relative to the previous trial; blue lines are trials in
675 which those colors stayed the same. The horizontal axis indicates whether the target shape changed relative
676 to the previous trial. Error bars (often smaller than the data points) indicate S.E.M., asterisks denote $p <$
677 0.001 for main effects as indicated by two-way ANOVAs (no interaction effects were significant at $p <$
678 0.05). **F)** Dependence of erroneous choices on the relative locations of the target (T) or salient distractor
679 (SD) stimuli. The proportion of SD or ND choices on error trials is plotted as function of the distance
680 between the chosen stimulus in the search array (a distance of one indicates the two stimuli were next to each
681 other, a distance of two means there was one stimulus in between, etc.), the identity of the chosen stimulus
682 (grey: ND; red: SD), and the reaction time (30% fastest and slowest response indicated with square and
683 diamond symbols respectively). The dashed lines indicate chance level.

684

685 **Figure 2. Saccadic reaction times and choices.** **A)** Distributions of shortest saccadic reaction times (SRTs,
686 fastest 25th percentile) for target (T, green) and salient distractor choices (SD, red) in the two monkeys. The
687 distributions were normalized such that both the red and green bars sum up to 100% (see SI Appendix, Fig.
688 S2 for the full SRT distributions, normalized within choice type (as here) and also by the total number of
689 saccades). The dark colors indicate overlap between the red and green distributions. The probability of
690 choosing the salient distractor was increased at short SRTs (black arrows). **B)** Proportion of salient distractor
691 choices (p_{SD}) calculated in a sliding 20 ms window, moving at 10 ms increments. Solid vertical lines are the
692 median, 25th, and 75th percentiles of the full SRT distributions. In both monkeys, the proportion of salient
693 distractor choices is significantly higher for the 12.5% fastest responses (first octile, left of the dashed
694 vertical line) than in the second through fourth octiles (chi-squared test, M1: $X^2(1) = 8.55$, $p < 0.01$; M2:
695 $X^2(1) = 21.41$, $p < 0.001$).

696

697

698 **Figure 3. V4 activity during visual search reveals the time-course of pop-out and pop-in.** **A)** Neuronal
699 responses in area V4 responses on correct trials. Average V4 activity elicited by the target (T, green trace),
700 non-salient distractors (ND, gray trace) and the salient distractor (SD, red trace) averaged across animals (left
701 panel) and for individual monkeys (M1: middle panel; M2: right panel). Shaded area corresponds to S.E.M.
702 across recording sites. Black arrows indicate the average reaction time (for M1 this was later than 250 ms
703 and is not depicted). The light grey areas indicate the time window used for statistical testing of the response
704 modulation, with * indicating $p < 0.001$ with a paired t-test (green: T-ND; red: SD-ND). **B)** Time-course of
705 neuronal target and salient distractor modulation. Top row, difference in activity elicited by the target and
706 non-salient distractor (T-ND; non-overlapping 10 ms time bins) pooled across monkeys (left) and individual
707 animals (middle and right panels). Green bars indicate significant epochs at $p < 0.05$ (t-test with Bonferroni
708 correction for multiple comparisons). Bottom row, difference in activity elicited by the salient distractor and
709 non-salient distractor (SD-ND) with the red bars indicating $p < 0.05$ (t-test, Bonferroni correction). In both
710 animals, there is an initial epoch of salient distractor enhancement, followed by suppression, later than 150
711 ms. Colored arrows indicate the latency of target enhancement (green) and salient distractor suppression
712 (red).

713

714 **Figure 4. Pop-out and pop-in.** During the early phase of the V4 response (middle) to a visual search
715 stimulus (left), both the shape and color singletons pop-out. In a later phase of the response (right), top-down
716 influences invert the pop-out of the salient color distractor into pop-in.

Figure 1

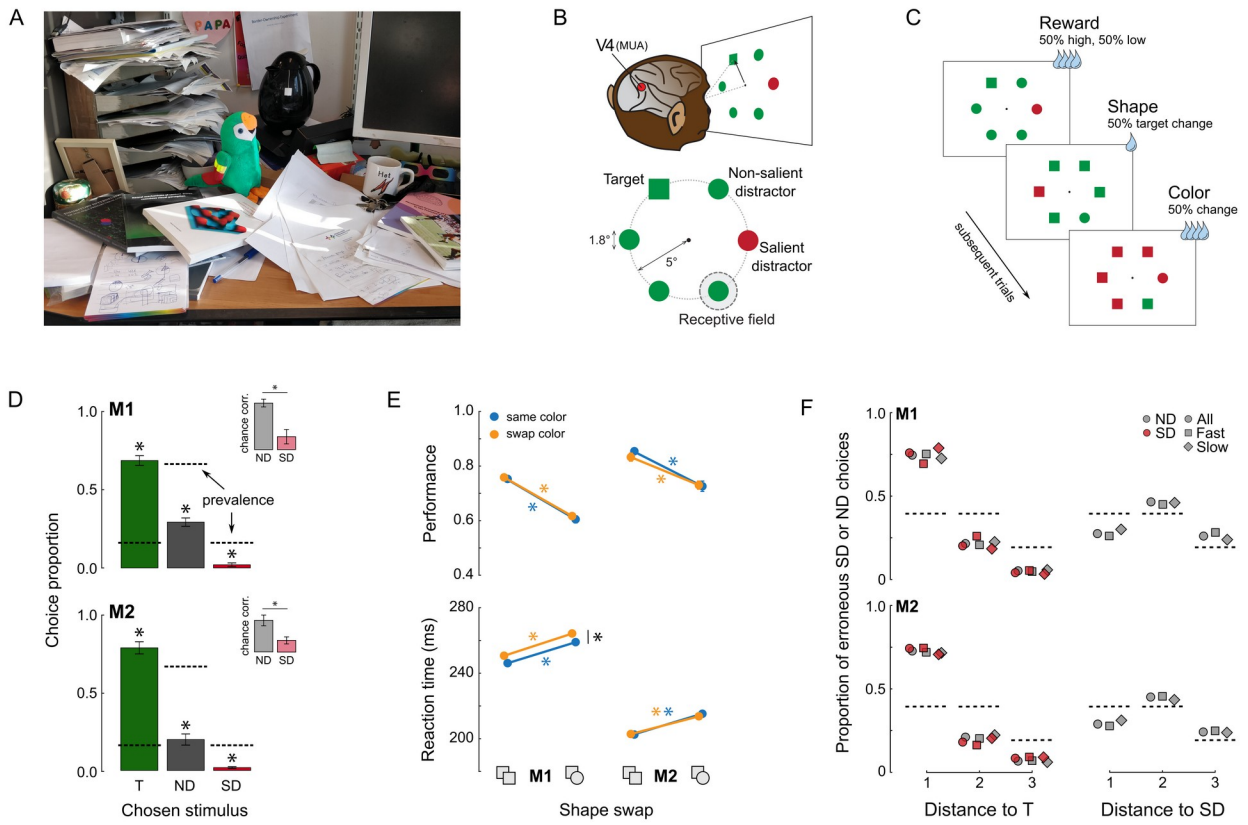


Figure 2

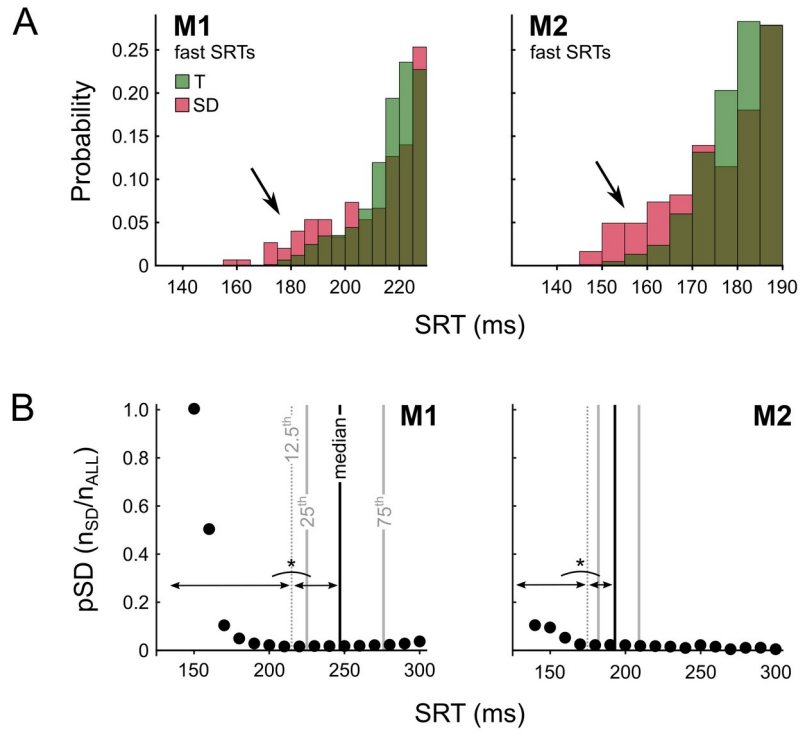


Figure 3

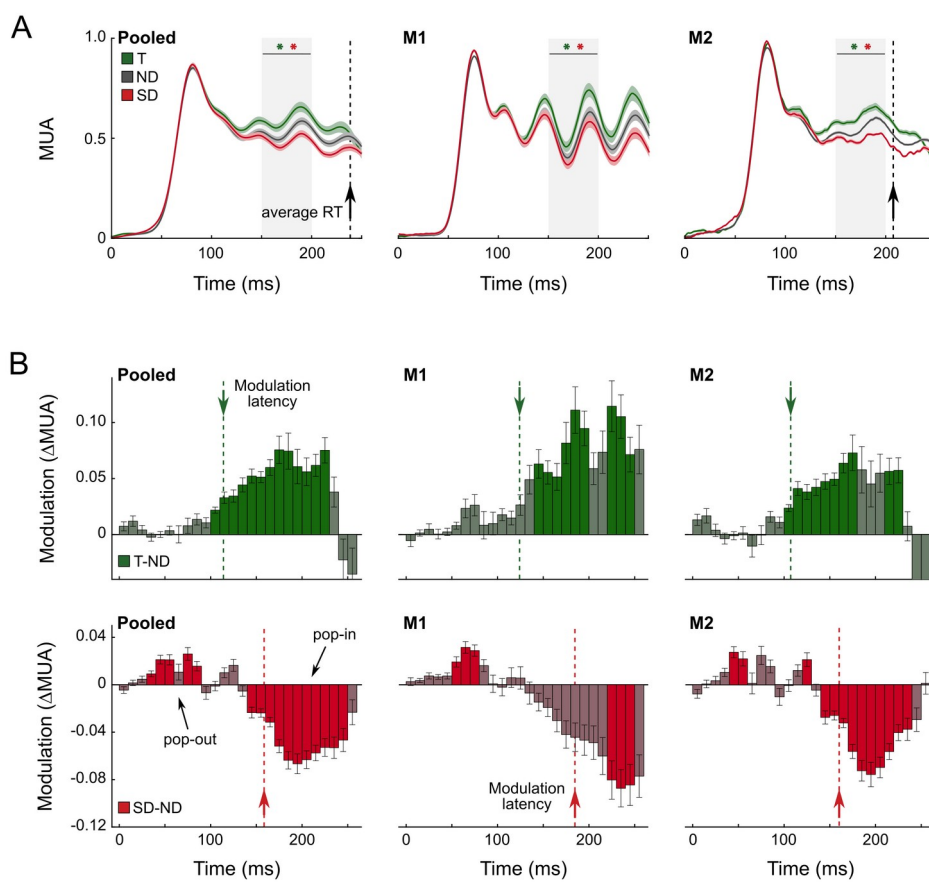
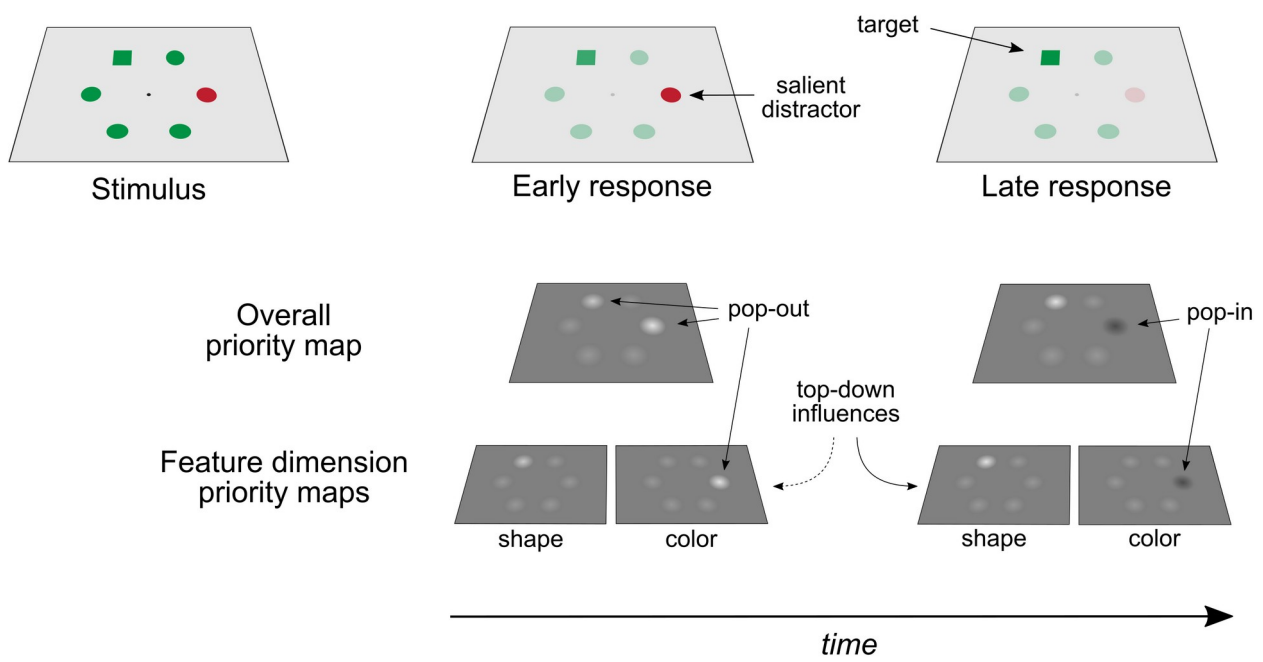


Figure 4



Supporting Information for

Inversion of pop-out for a distracting feature dimension in monkey visual cortex

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This PDF file includes

Supplemental Figures S1-S5

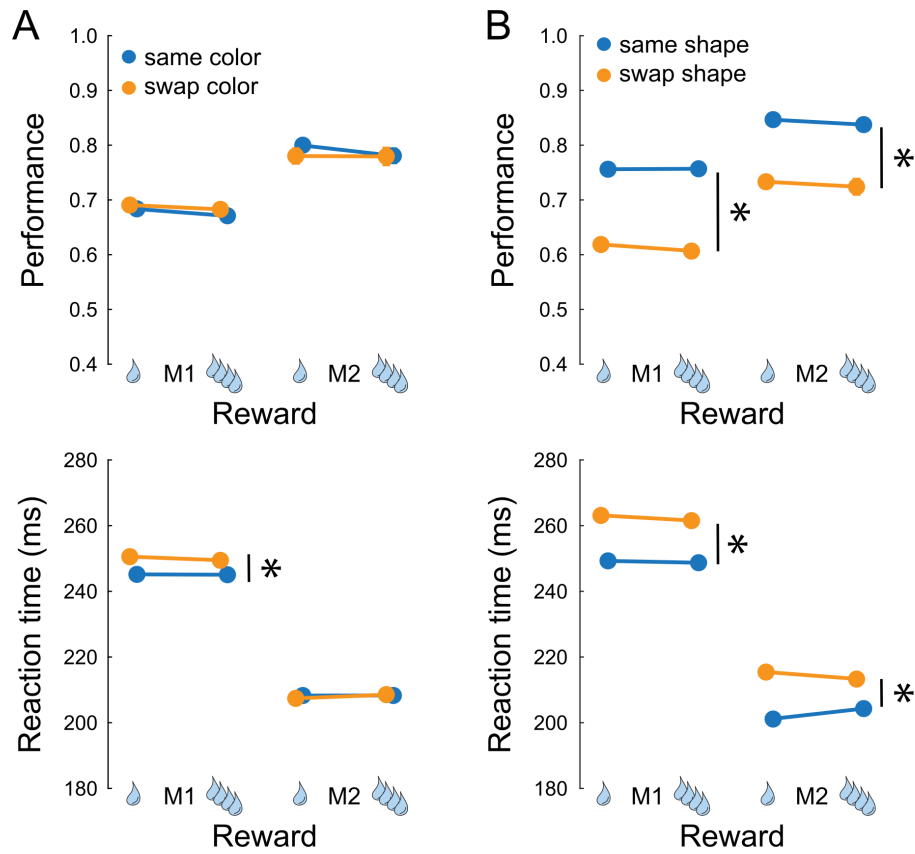


Figure S1. Influence of previous trial on behavioral performance. A) The effects of preceding reward quantity and the swapping of target and salient distractor colors (top panel) and reaction time (bottom panel) for both monkeys. Yellow lines indicate trials in which the target and distractor colors swapped relative to the previous trial; blue lines are trials in which the colors of the target and salient distractor stayed the same. Reward quantity is indicated on the horizontal axis (large rewards were four times larger than small rewards). **B)** The effects of preceding reward quantity and shape swaps on accuracy (top panel) and reaction time (bottom panel) for both monkeys. Yellow lines indicate trials in which the target and distractor shapes swapped relative to the previous trial; blue lines are trials in which the shape assignment stayed the same. Error bars (often smaller than the data points) indicate S.E.M., asterisks denote $p < 0.001$ for main effects as indicated by two-way ANOVAs (no interaction effects were significant at $p < 0.05$).

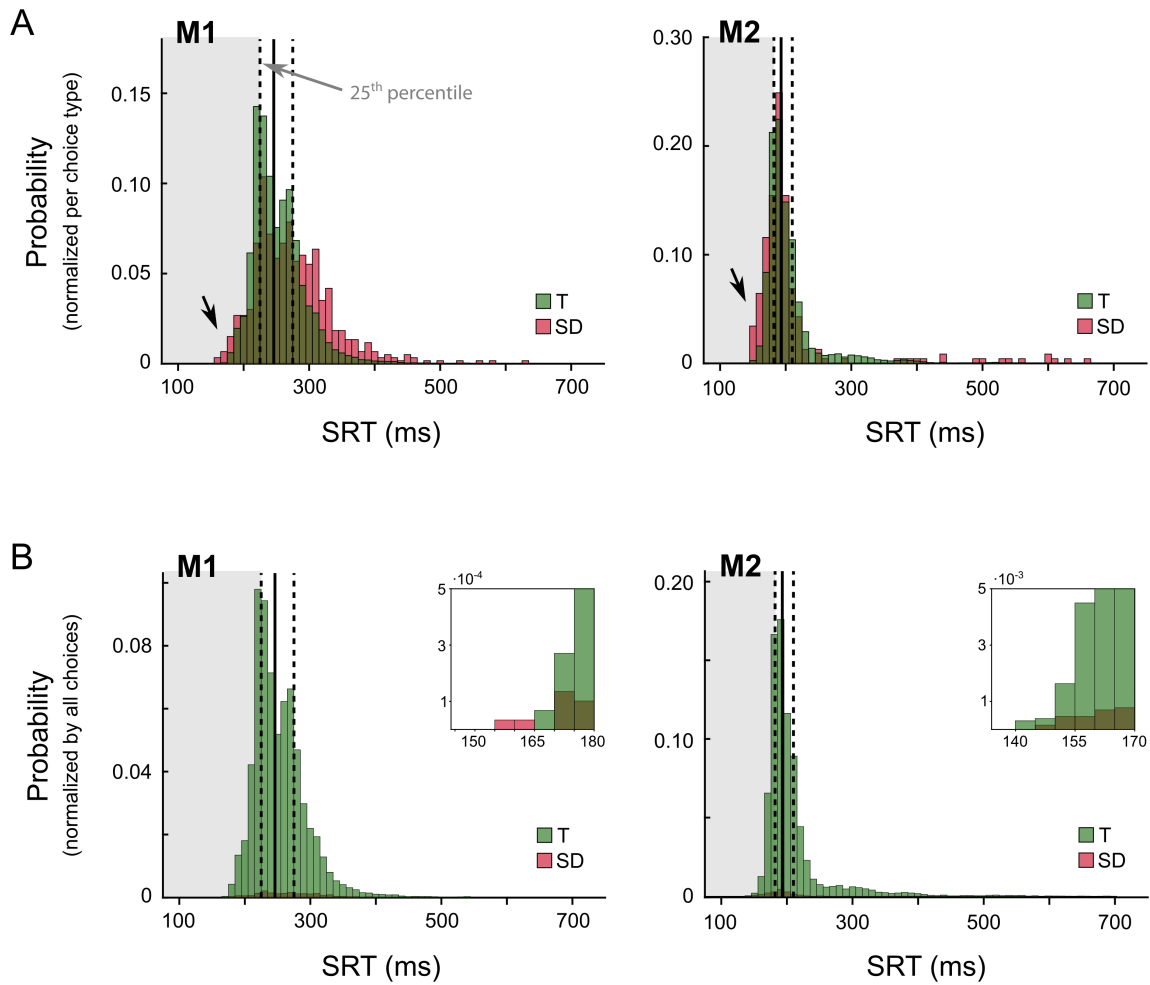


Figure S2. Saccadic reaction times and choices. Distributions of saccade reaction times (SRTs) for target (T, green) and salient distractor choices (SD, red) of the two monkeys (M1, M2). Solid and dashed vertical lines represent the median, 25th and 75th percentiles of the RT distribution. Histograms in **A**) show the distributions normalized per choice type (T or SD) as in Figure 2A, while histograms in **B**) show the distributions normalized to the total number of responses (T, SD, and ND combined). Insets in panel **B**) zoom in on the fast tail of the distributions.

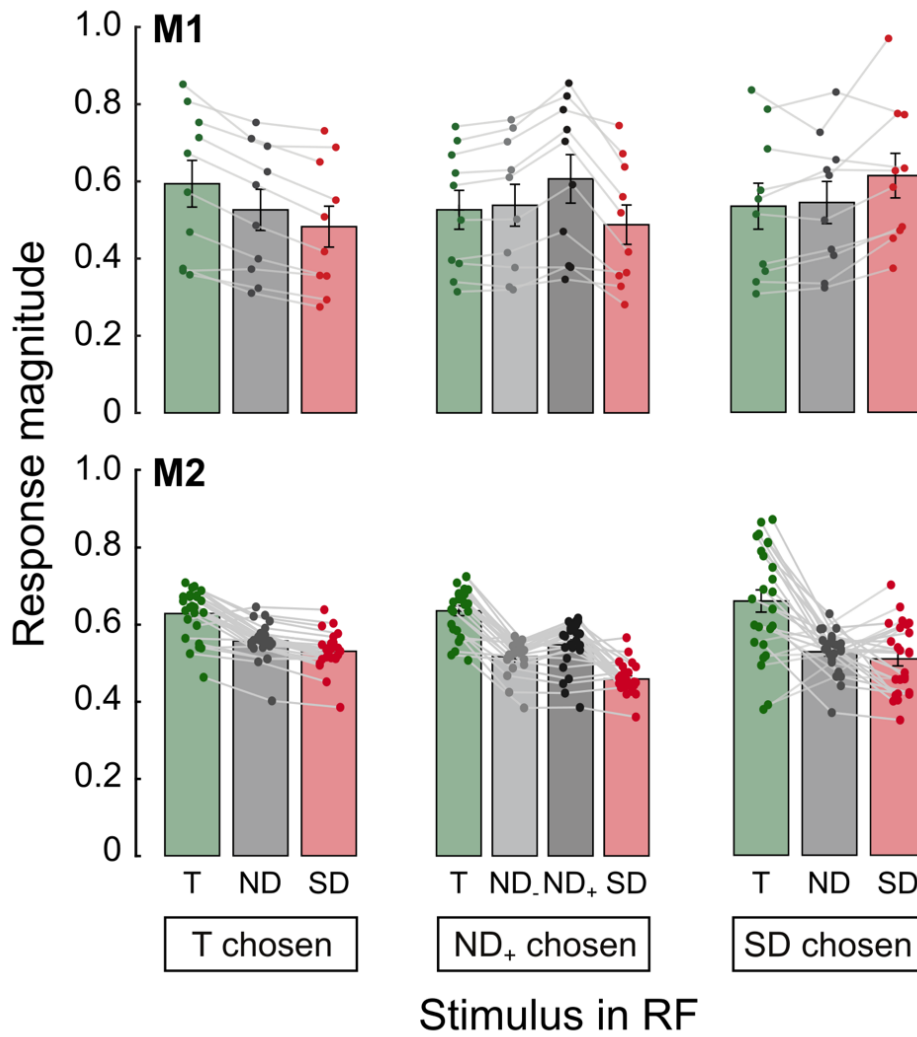


Figure S3. V4 activity and its dependence on choice. Average activity of V4 neurons at individual recording sites, 150-200 ms after stimulus onset. Left, correct responses to the target in M1 (top row) and M2 (bottom). Middle, erroneous responses in which the animals selected one of the non-salient distractors (ND+). ND-, response elicited by non-salient distractors that were not chosen. Right, erroneous responses in which the salient distractor was chosen. Bar colors represent the stimulus in the RF (green: target, light gray: non-salient distractor, red: salient distractor). Dark grey bars show the response elicited by the chosen non-salient distractors (ND+). Light grey bars show the response elicited by ND-. The data of individual recording sites are shown as colored data points, connected by gray lines. Error bars represent S.E.M. across recording sites.

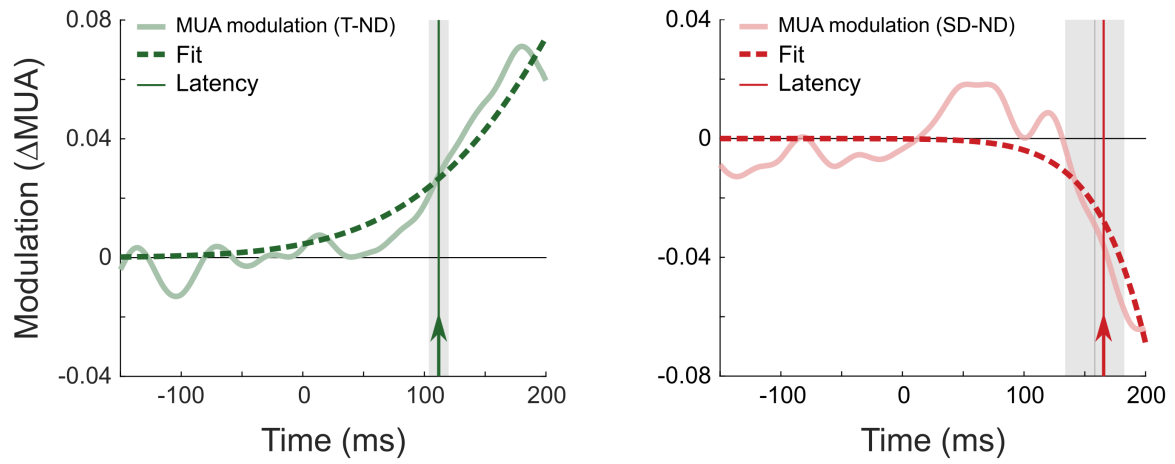


Figure S4. Latency analysis of target and salient distractor MUA modulation. Cumulative Gaussian functions were fit to the difference between either the average V4 activity elicited by the target and the non-salient distractor (i.e. target modulation, left panel) or the non-salient and salient distractors (i.e., salient distractor modulation, right panel). The latency (vertical line and arrow) is estimated as the time point at which the fit (dashed line) reaches 33% of its maximum. The grey area and grey vertical line indicate the mean latency and standard deviation of a bootstrap analysis (100 samples with replacement).

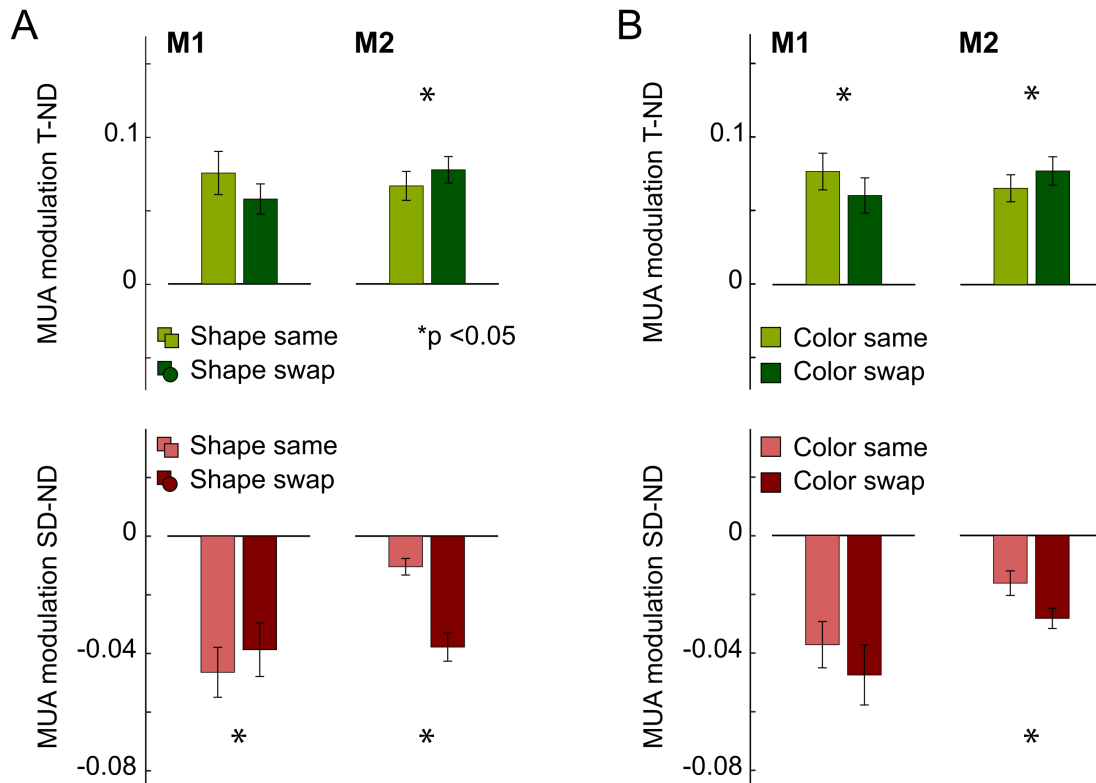


Figure S5. Influence of the previous trial on V4 activity. **A)** The effect of shape assignment changes on consecutive trials on the modulation of V4 activity by the target (T-ND; top row) and salient distractor (SD-ND; bottom row) in the 150-200 ms time window after stimulus onset. Bars are the mean across recording sites and error bars denote S.E.M. Light and dark colors represent trials in which the shape assignment stayed the same or changed, respectively. **B)** The effect of target and salient distractor color swapping on consecutive trials on the modulation of V4 activity by the target (T-ND; top row) and salient distractor (SD-ND; bottom row) in the 150-200 ms time window after stimulus onset. Light and dark colors represent trials in which the color assignment stayed the same or were swapped, respectively. Asterisks, significant differences (paired t-test, $p < 0.05$).