Pop-in: the inversion of pop-out for a feature dimension during visual search in area V4 of the monkey cortex

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Abstract

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

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

Significance statement

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

Introduction

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

In many bottom-up search paradigms, the target pops out, because it has a unique feature. For example, it is the only bright red item among grey distractors, or it is the only circle in the display in which all other elements are squares. There are versions of this paradigm in which subjects do not know beforehand what they will be looking for, but only that it is the unique item. For example, the display might have either one square among circle distractors or one circle among square distractors. The search for items with unique properties is parallel, which means that the time to find an item does not depend strongly on the total number of distractors in a search display (7). Previous studies on the neuronal correlates of pop-out search demonstrated that the responses elicited by pop-out stimuli are stronger in the visual, parietal, and frontal cortex than the responses to stimuli that do not pop-out (8–18). It has been argued that pop-out supports theories of predictive coding (19, 20). According to these theories, higher brain areas send signals to suppress the representations of dominant and more numerous stimuli in lower brain areas, because these lower-level representations are accounted for by the higher-level representations. These suppressive top-down signals are weaker for the pop-out stimulus so that it elicits extra activity, which can be conceived of as a prediction-error.

In top-down search paradigms, the subject looks for a specific item and the target of search is embedded among distractors that are usually so diverse that pop-out does not occur. This form of visual search is often serial, because the time to find the item increases with the number of distractors. The item that the subject looks for needs to be held in working memory and is called a 'search-template' (21, 22). The search template represents a top-down influence on visual selection (1, 23), which needs to be matched to the items in the display until the target has been found. The representations of the items in the display that match the search template are also enhanced in cortical areas. They elicit stronger neuronal responses than non-matching items in areas of the visual, parietal, and frontal cortex (21, 24–30). In serial visual search, the onset of this neuronal response enhancement is delayed if the number of distractors is larger, and it predicts the increase in the subject's response time (31).

Many displays contain salient distractors that interfere with visual search. This is the case in Figure 1 for the green parrot, which attracts attention, making it more difficult to find the keys. These salient stimuli are said to 'capture' attention. Researchers have debated the degree of automaticity of attentional capture, with some researchers arguing that it is mandatory (32) whereas others arguing that it can be prevented by sufficiently strong top-down signals (33). Importantly, conditions exist under which salient display items do not appear to interfere with visual search (34, 35). Recent studies demonstrated that there are even conditions under which salient distractors cause less interference than regular, non-salient distractors (36–39). The signal-suppression hypothesis (38, 39) addresses this weaker interference by proposing that salient distractors are detected but that their representation can be rapidly suppressed.

The suppression of salient distractors is easiest if two conditions are fulfilled. First, the features of the salient distractor are held constant across trials. For example, the salient distractor is always a red circle. Search can become more efficient if the subjects know the features of upcoming distractors (40, 41), so that they can suppress them more efficiently. Indeed, Bichot et al. (42) demonstrated that the representations of stimuli that consistently appear as distractors, across many days, are strongly suppressed in the frontal cortex of monkeys. Second, subjects search for a specific object or feature so that a search template can be established before the search display appears. This is not possible in variants of a pop-out search in which the target properties are not specified. Researchers proposed that such a pop-out search demands a special "singleton detection mode" (34). In this mode, subjects search for any object popping out, which makes them more susceptible for interference by salient distractors.

Two previous studies have examined the neuronal mechanisms for the suppression of salient distractors during visual search. Ipata et al. (43) had monkeys searching for a black target shape among black distractors. They added a salient distractor, which was green and bright, and recorded neurons in the lateral intraparietal area (LIP) in the parietal cortex. As expected, targets elicited stronger neuronal responses than the black distractors, but the activity elicited by the salient green items was even weaker than that elicited by the regular black distractors. Hence, the representation of the salient distractor is efficiently suppressed in the parietal cortex. A later study by Cosman et al. (44) replicated this finding in the frontal eye fields (FEF) in a task where the monkeys searched for a white target letter while the salient distractor was red. Again, the target letter elicited strongest activity, followed by the regular distractors and the salient distractor elicited weakest activity. These results are in accordance with those by Bichot et al. (42) showing the effective suppression of a specific feature that is always distracting in the frontal cortex. Interestingly, the suppression of salient distractors appears to conflict with predictive coding theories. The representation of these salient distractors is suppressed, even though they differ from all other elements, which should cause a prediction error according to predictive coding theories (19, 20). However, it might be argued that the parietal and frontal cortex are too high up in the cortical hierarchy and that the activity elicited by salient distractors is still enhanced in the visual cortex, even after extensive training. The representation of salient distractors in

visual cortex remains to be investigated.

In the present study we tested the generality of the suppression mechanisms by asking three questions: (1) Are salient distractors suppressed in the visual cortex? (2) Is the efficient suppression of a salient distractor stimulus also possible when its features vary across trials? (3) Can salient distractor suppression also occur in singleton detection mode in which the subject searches for a pop-out stimulus on a different feature dimension?

We trained monkeys in a task in which they carried out a pop-out search for a shape while we presented a salient color distractor with a color that varied across trials. They had to select this shape as target for an eye movement to obtain a juice reward. As expected, the target shape singleton elicited stronger V4 activity than the distractors with a different shape. Remarkably, the V4 representation of salient color singleton was only briefly enhanced followed by a period of pronounced suppression below the level of representation of the regular non-pop-out distractors, even though its color was unpredictable. At a behavioral level, the monkeys also selected the salient distractor less often than the regular distractors. We conclude that after extensive training, the neuronal mechanisms for visual search can exploit the presence of a color singleton if it always is a distractor, causing it to ‘pop-in’ instead of popping out.

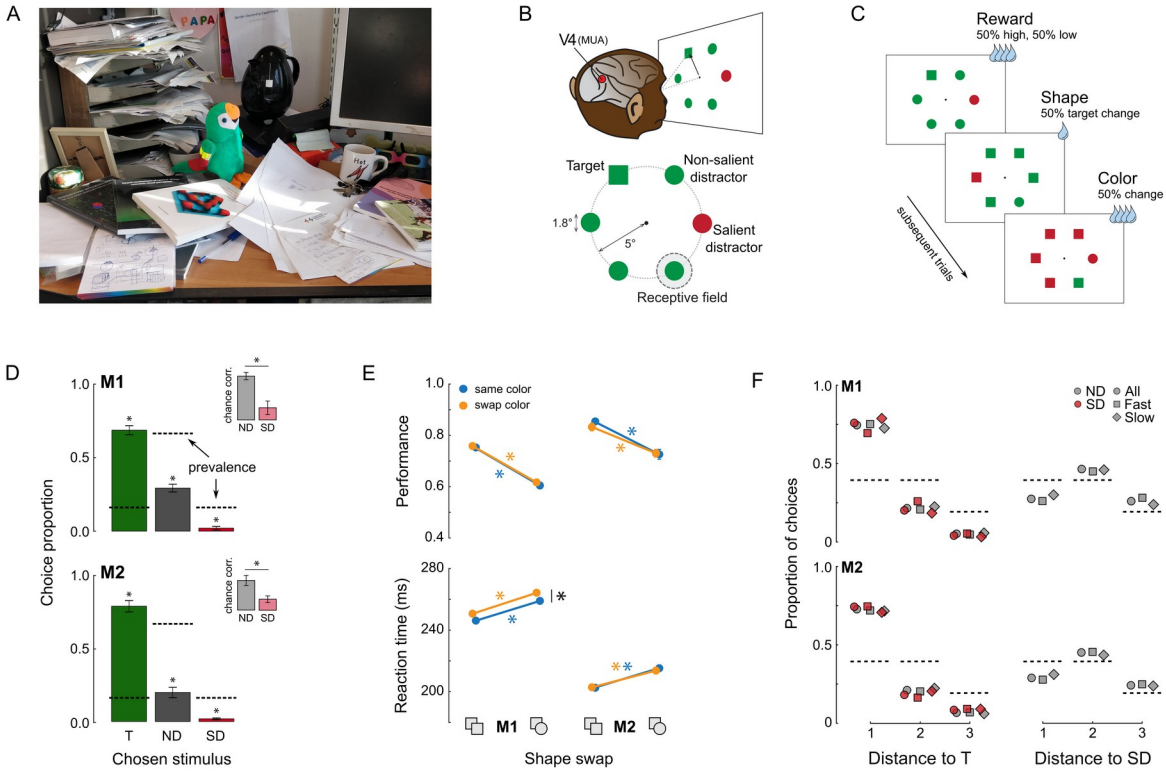

Figure 1. Task description and behavioral results. A) Real-life example of visual search with a salient distractor. When looking for your keys on a crowded desk, you may be looking for small key-shaped objects. Your attention may however be captured by salient objects like the bright green parrot, which might interfere with the process of finding your keys. **B)** We recorded from area V4 while monkeys performed a visual search task in which they selected the odd-shape-out (here a square among circles) with an eye movement. One of the six visual items was in the V4 receptive field. The target was the stimulus that differed from the others by shape. Non-salient distractor stimuli had the same color as the target, while a single salient distractor stimulus popped out because it had a different color. **C)** Example series of three trials. In the second trial the target and distractor shapes swapped with respect to the first trial (this occurred 50% of the time). In the third trial, the target and distractor colors swapped (this also occurred 50% of the time). In addition, the reward magnitude was randomly varied (50% high, 50% low). **D)** Accuracy (green bars) and the proportion of trials on which the monkeys made an error by choosing a non-salient distractor (ND, grey bars) or the salient distractor (SD, red bars). Non-salient distractors are 4 times more prevalent than targets and salient distractors (prevalence indicated with dashed horizontal lines). The insets show the proportion of choices of distractor stimuli corrected for prevalence. Even after this correction, the animals chose the salient distractor less often than the non-salient distractors (* indicate $p < 0.001$ for a one-tailed t-test SD < ND). Error bars indicate the standard deviation over recording sessions. **E)** The effects of color and shape swaps on accuracy (top panel) and reaction time (bottom panel) for both monkeys. Yellow lines indicate trials in which the color scheme swapped relative to the previous trial; blue lines are trials in which the color scheme stayed the same. The horizontal axis indicates whether the target shape changed relative to the previous trial. 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 $p < 0.05$). **F)** Dependence of erroneous choices on the relative locations of the target (T) or salient distractor (SD) stimuli. The proportion of choices on error trials is plotted as function of the distance between the chosen stimulus in the search array (a distance of one indicates the two stimuli were next to each other, a distance of two means there was one stimulus in between, etc.), the identity of the chosen stimulus (grey: ND; red: SD), and the reaction time (30% fastest and slowest response indicated with square and diamond symbols respectively). The dashed lines indicate chance level.

Results

Two monkeys were extensively trained to perform a visual search task (Fig. 1B,C) in which they had to select a single odd-shape-out (target) from an array of six stimuli. On any given trial, the target could either be a circle among squares, or a square among circles. To study whether V4 neurons show suppression of salient distractors, one of the distractor stimuli had a different color than the others (either green among red, or red among green) (Fig. 1B, bottom). The shapes, colors, and locations of the target and salient distractor were randomly assigned on each trial so that the animal could not predict the shape or color of the target and salient distractor. As a result, consecutive trials could have the same shape and colors assigned to the target and distractor, both could change, or one of the feature assignments could stay the same while the other changed. Moreover, to examine a previously reported interaction between stimulus salience and reward in human visual search behavior (45), we randomly rewarded correct responses with either small or large juice rewards (with the large reward being approximately four times the small reward amount). After an initial training phase to learn the task, both monkeys were extensively trained to reach high performance levels (22 training sessions for M1, 56 for M2).

We recorded 34,543 trials in monkey 1 (M1) and 13,815 trials in monkey 2 (M2) in 28 and 16 sessions, respectively. Both monkeys displayed similar eye movement patterns (Fig. 1D), most often choosing the target stimulus (M1: 69%, M2: 78% of choices), followed by non-salient distractors (M1: 29%, M2: 20%), and only rarely choosing the salient distractor stimulus (M1: 2%, M2: 2%). The lower probability of choosing a salient distractor than a non-salient distractor remained when we accounted for the fact that there were four non-salient distractors and only one salient distractor (see Fig. 1D insets, corrected for prevalence). The probability of choosing the target was much higher than chance (one-tailed t-test, M1: $t(26) = 87.4$, $p < 0.001$; M2: $t(15) = 53.5$, $p < 0.001$). On error trials, both animals were significantly less likely to choose the salient distractor than a non-salient distractor (prevalence-corrected, one-tailed paired t-test, M1: $t(26) = -51.6$, $p < 0.001$; M2: $t(15) = -21.6$, $p < 0.001$).

Changing the color scheme on successive trials did not affect accuracy for either animal as indicated by a two-way ANOVA with color-swap and reward quantity as independent variables (all ps > 0.48). It did slow down M1 by a few milliseconds (Fig. 1E; $F(1, 12210) = 38.8$, $p < 0.001$), but had 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 pronounced effect of performance. It decreased the accuracy of both animals and increased the reaction times (Fig. 1E; all $p < 0.001$). There were no interactions between the effects of color and shape changes. These results imply a shape-based priming of pop-out effect across trials (46), but an absence of color-based priming, which is consistent with the animals being in 'shape-searching' mode due to extensive training on the 'odd-shape-out' search task. Unlike previous work in humans (45), we did not observe any main or interaction effects of reward quantity on visual search performance (Supplemental Fig. 1).

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

The signal suppression hypothesis (36) proposes that a salient distractor generates an 'attend-to-me' signal, which is subsequently overwritten by top-down signals causing suppression. This sequence of events should be associated with a brief period of pop-out for the salient distractor when this 'attend-to-me' signal is generated followed by a sustained period of distractor suppression. Because visually guided saccades can occur at very low latencies in both humans and monkeys (47–51), especially after prolonged training (52), we wondered whether the early neuronal pop-out of the salient distractor would result in very rapid saccadic responses to the salient distractor before the distractor suppression could have manifested. To investigate this possibility, we compared the distributions of saccade reaction times (SRTs, Supplemental Fig. 2) for target and salient distractor choices. The probability of eye movements to the salient distractors was highest for the shortest reaction times in both monkeys (Fig. 2A). We calculated the proportion of salient distractor choices ($p_{SD} = n_{SD}/n_{ALL}$) as function of SRTs (Fig. 2B). In both animals, the proportion SD choices was significantly higher for the 12.5% shortest SRTs (first octile) than SRTs in the 2nd-4th octiles (chi-squared test, M1: $X^2(1) = 8.55$, $p < 0.01$; M2: $X^2(1) = 21.41$, $p < 0.001$). The finding that these early saccades are most susceptible to attentional capture by the salient distractor support the signal-suppression theory proposing that salient distractors are detected through a pop-out mechanism before they are suppressed to prevent erroneous choices.

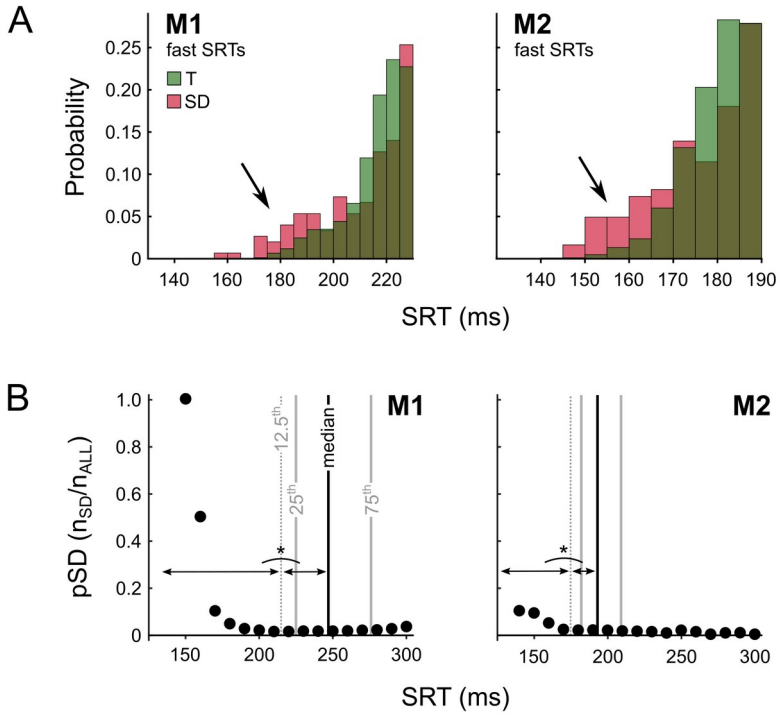

Figure 2. Saccadic reaction times and choices. A) Distributions of shortest saccadic reaction times (SRTs, fastest 25th percentile) for target (T, green) and salient distractor choices (SD, red) in the two monkeys (full SRT distributions in Supplemental Fig. 2). At very fast SRTs, both animals were more likely to select the salient distractor (black arrows) than at later SRTs. **B)** Proportion of salient distractor choices (*pSD*) calculated in a sliding 20 ms window, moving at 10 ms increments. Solid vertical lines are the median, 25th, and 75th percentiles of the full SRT distributions. In both monkeys, the proportion of salient distractor choices is significantly higher for the 12.5% fastest responses (first octile, left of the dashed vertical line) than in the second through fourth octiles (chi-squared test, M1: $X^2(1) = 8.55$, $p < 0.01$; M2: $X^2(1) = 21.41$, $p < 0.001$).

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

We examined the time-course of target enhancement and salient distractor suppression by subtracting V4 activity elicited by the non-salient distractor stimuli from the other two conditions (Fig. 3A, bottom panels). We measured the latency of the enhancement and suppression of targets and salient distractors with a fitting procedure that has been described before (53) (see Methods and Supplemental Fig. 4). The latency of target enhancement was 112 ± 9 ms (averaged across monkeys, standard deviation determined with bootstrapping) and the latency of salient distractors was 158 ± 25 ms. This pattern was also present in individual animals ($M1_T$: 124 ± 20 ms, $M2_T$: 108 ± 15 ms; $M1_{SD}$: 184 ± 14 ms, $M2_{SD}$: 159 ± 11 ms) and the salient distractor suppression was significantly later than the target enhancement (paired t-test, M1: $t(75) = -26.3$, $p < 0.001$; M2: $t(72) = -22.1$, $p < 0.001$; Pooled data: $t(67) = -17.7$, $p < 0.001$). Thus, the pop-in effect was expressed in area V4 as a decreased response to the irrelevant singleton, even though its color was unpredictable.

The brief epoch with an enhanced probability of saccades to the salient distractor suggests that its representation might be briefly enhanced ('attend-to-me' signal; (35, 37, 39)) before it is suppressed. We therefore examined the possibility of an early response enhancement. We observed that the salient distractor (Fig. 3B, red bars) indeed caused a brief epoch of enhanced activity before suppression became evident, in a time-window up to 100 ms after stimulus onset (Fig. 3B shows significant modulation in several 10 ms non-overlapping time bins in both monkeys; t-tests at $p < 0.05$, Bonferroni corrected). This result indicates that the irrelevant color singleton was indeed first detected before it was suppressed.

We also examined a possible influence of the behavioral priming effect, which occurred when the target shape was the same on consecutive trials, on V4 activity. The priming effect did not have a consistent influence on V4 activity (Supplemental Fig. 5), which suggests that it may only manifest in downstream brain regions. Furthermore, V4 activity on error trials was more variable than on correct trials (Supplemental Fig. 3).

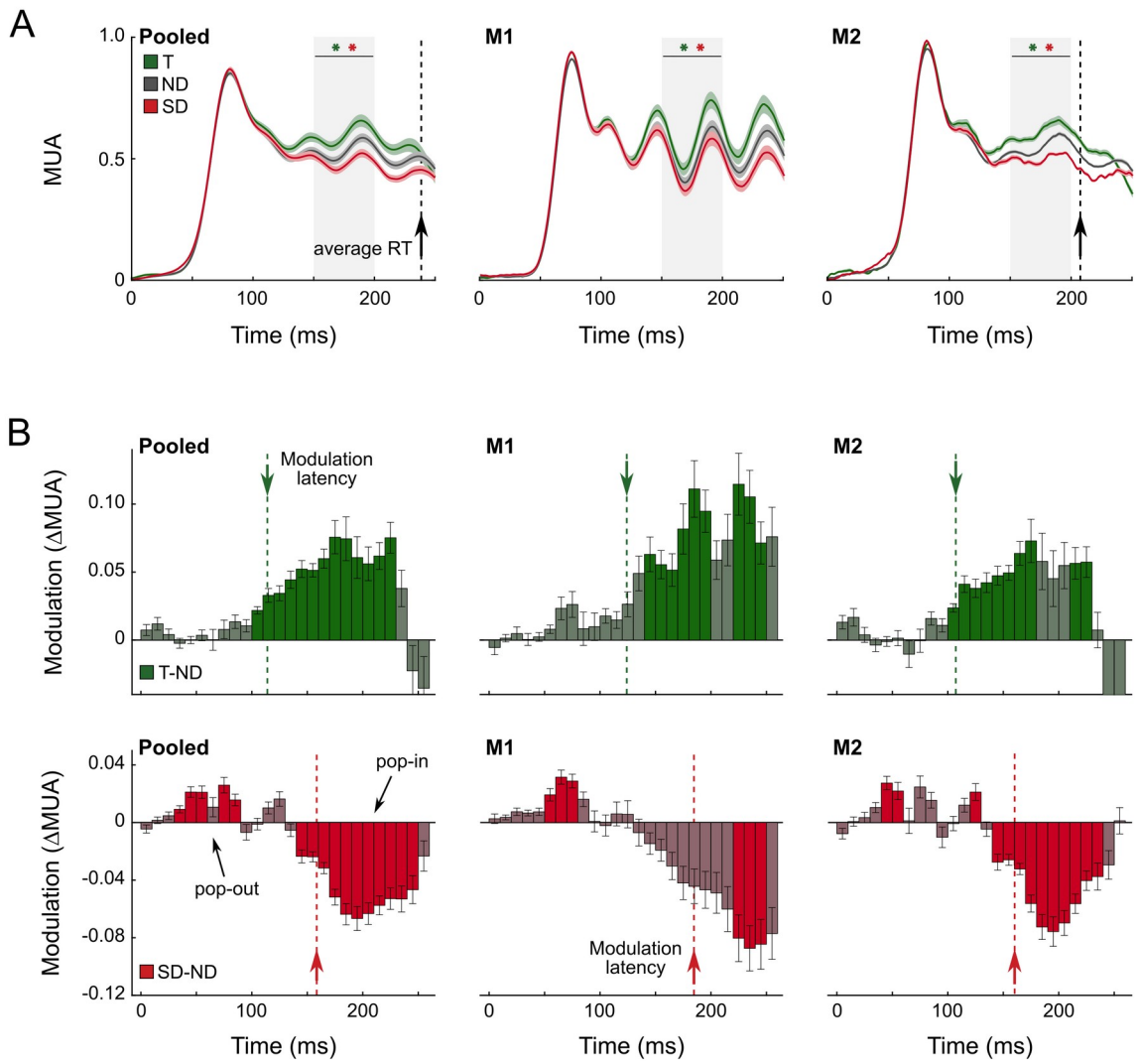

Figure 3. V4 activity during visual search reveals the time-course of pop-out and pop-in. A) Neuronal responses in area V4 responses on correct trials. Average V4 activity elicited by the target (T, green trace), non-salient distractors (ND, gray trace) and the salient distractor (SD, red trace) averaged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

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Discussion

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

The efficiency of visual search depends on bottom-up factors, such as brightness and local feature contrasts causing pop-out, and the top-down search template, the internal representation of the item that the subject is searching for (1, 3, 4, 24). Researchers have hypothesized that stimulus and goal-driven influences on the distribution of attention jointly determine a 'saliency map' of visual space (3–7, 54–56). There are multiple candidate brain regions for such a saliency map, including the LGN (54), pulvinar (57), superior colliculus (58, 59), V1 (60), V4 (61), the parietal (8, 10, 43) and prefrontal cortex (11). Indeed, stimulus-driven pop-out signals have a widespread influence on the neuronal firing rates in early visual cortex (12, 62, 63), parietal cortex (10), frontal cortex (11), and subcortical structures like the superior colliculus (64). Similarly, the top-down influences of the search template on firing rates also occur in most, if not all, of the same brain regions, including V1 (65, 66), V4 (15, 18), the parietal (43) and prefrontal cortex (11, 42, 44). It is conceivable that the relative contributions of the multiple salience maps depends on the task, e.g. on the features that matter and on whether the subject reports the location of the target with an eye or hand movement.

There are many instances in which the representation of visually salient items needs to be suppressed, because task relevant items are less conspicuous, causing a conflict between bottom-up and top-down factors. The signal suppression hypothesis (38, 39) proposed that visually salient stimuli invariably generate a salience signal, which can be overwritten by top-down attentional control to prevent attentional capture (36–39, 44, 67–73). Previous electrophysiological studies in areas LIP and FEF of monkeys revealed that the neuronal activity elicited by a salient distractor with a predictable color is indeed suppressed below the activity elicited by regular distractors (43, 44). The suppression of salient distractors can also be measured as a distractor positivity (Pd) component in the EEG of humans, contralateral to the distractor location (39, 74, 75). The present study went beyond these previous studies by investigating whether such suppressive signals influence spiking activity in the visual cortex of monkeys. Furthermore, we used a new task in which the features of the salient distractor were unpredictable and the monkey was in 'singleton mode', i.e. searching

262 for a pop-out stimulus on a different feature dimension.

263 Unlike the previous studies in parietal and frontal cortex (43, 44), we found that the salient distractor elicited
264 a brief enhancement of V4 activity that later inverted into sustained suppression. This early enhancement
265 was not observed in the previous neurophysiological studies. It seems likely that it occurred in the present
266 study because the distractor color was unpredictable so that it first needed to be registered before it could be
267 suppressed. We also observed a behavioral consequence of this brief pop-out phase because a proportion of
268 the early saccades landed on the salient distractor whereas it was less likely to be selected than regular
269 distractors at later time points, when pop-out inverted into pop-in. This result provides evidence for what, at
270 a psychological level of description, is known as short-lived attentional capture, followed by rapid attentional
271 disengagement (74).

272 Our results indicate that there are at least two processing steps in the present search task (Fig. 4). Initially,
273 the stimulus generates pop-out for color and shape. Later in the trial, the activity elicited by the shape
274 singleton remains enhanced, whereas activity elicited by the color singleton is suppressed, indicating that V4
275 could contribute to a saliency map with enhanced targets and suppressed distractors (Fig. 4). The source of
276 the suppressive pop-in signal is unknown, but it could rely on feedback projections (76, 77) that might have
277 been strengthened during training. In accordance with this view, microstimulation of FEF interacts with
278 stimulus driven activity in early visual cortex in a topographic matter, with an effect that depends on
279 stimulus strength and the presence of distractors (78). It is remarkable that the neuronal mechanisms
280 responsible for the detection of the salient distractor and its suppression apparently co-exist with the
281 mechanisms for pop-out on another feature dimension. An alternative strategy would have been to suppress
282 the influence of color entirely, but this would not have resulted in extra suppression of salient distractors. In
283 contrast, we found that pop-out and pop-in can occur in parallel.

284 Previous studies demonstrated that there is a profound influence of the recent history of trial types during
285 visual search. Repeatedly searching for the same stimulus features causes priming. It reduces an observer's
286 reaction time, improves accuracy, and increases the difference between the strengths of the neuronal
287 representation of targets and distractors (9, 18, 46, 79–83). We here observed a priming effect of shape.
288 When the shape of the search target remained the same on consecutive trials, the monkeys were faster and
289 more accurate than when it was different. Interestingly, we did not find a behavioral priming effect of color
290 as was observed in previous studies (9, 18, 79), a difference that was presumably related to the pop-in effect.

291 Earlier studies also demonstrated an effect of reward quantity on visual search performance (45, 84–86). A
292 study in human subjects demonstrated that visual search is faster if a preceding trial with the same target and
293 distractor features gave rise to a high as opposed to a low reward (45). We did not replicate this effect in our
294 monkeys, where reward magnitude on the previous trial did not strongly affect performance. One possible
295 explanation is that the animals were highly trained, which may have reduced their sensitivity to reward

outcomes on individual trials. However, other explanations, including species differences, are also conceivable.

Our results are relevant for theories of predictive coding (19, 20) that suggest feedback from higher areas suppresses the lower-level representations of the most common features in the display because they are predicted. According to these theories, the representation of the target item is enhanced, because it is not predicted and it therefore does not receive top-down suppression. However, predictive coding implies pop-out for salient distractors too. The pop-in effect observed here implies that training can invert the suppressive feedback signal, which provides evidence against these predictive coding theories. Our findings imply that the extended training history, during which the salient color never coincided with the target of search, engaged plasticity mechanisms inverting pop-out into pop-in, making the mechanisms of visual search more versatile than might have been anticipated.

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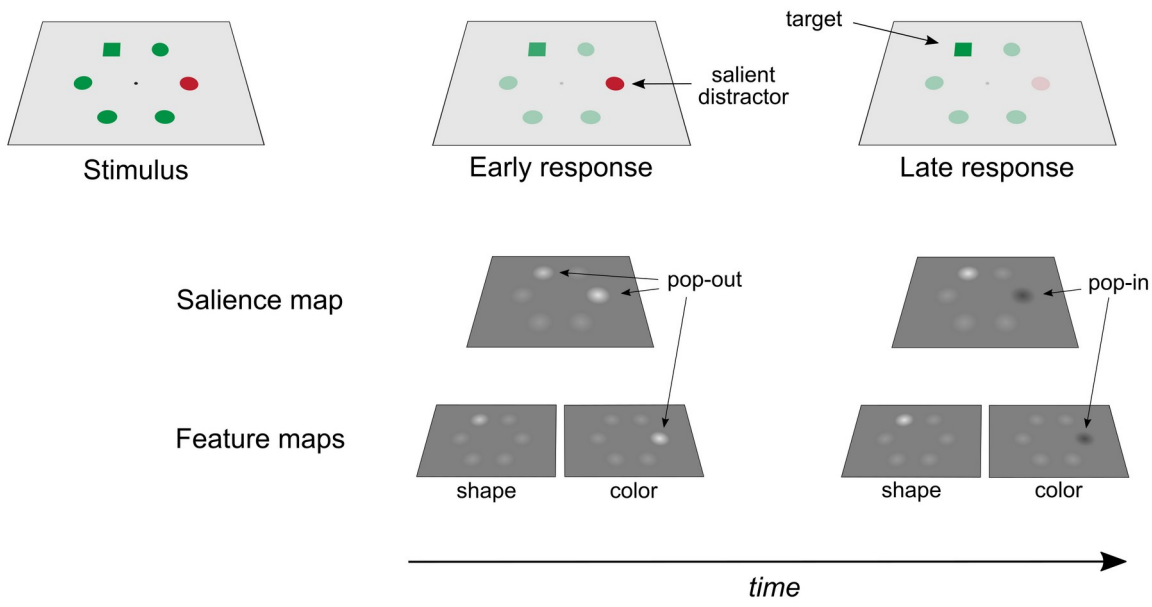

Figure 4. Pop-out and pop-in. During the early phase of the V4 response (middle) to a visual search stimulus (left), activity elicited by the shape and color singletons is enhanced. In a later phase of the response (right), the pop-out of the salient color distractor inverts and becomes pop-in.

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Methods

Subjects

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

Surgical procedures and training

We implanted both monkeys with a titanium head-post (Crist instruments) under aseptic conditions and general anesthesia as reported previously (87–89). The monkeys were first trained to fixate a 0.5 diameter fixation dot and hold their eyes within a small fixation window (1.2 diameter). They then underwent a second operation to implant arrays of 4x4, 4x5 and 5x5 micro-electrodes (Blackrock Microsystems) in V4. The inter-electrode spacing of the arrays was 400 µm. The animals were later extensively trained to perform the visual search task at adequate performance levels (22 training sessions with the final task for M1, 56 sessions for M2). During the early phase of the training the animals were required to make an eye movement from the fixation point to a single target, and in later phases the distractors were introduced at low contrast which over sessions gradually increased to the same contrast as the target.

Electrophysiology

Recordings from the chronically implanted electrode arrays were made with TDT (Tucker Davis Technology) recording equipment using a high-impedance head-stage (RA16AC) and a preamplifier (either RA16SD or PZ2). The signal was referenced to a subdural electrode and digitized at 24.4 kHz. It was band-pass filtered (2nd order Butterworth filter, 500 Hz – 5 kHz) to isolate high-frequency (spiking) activity. This signal was rectified (negative becomes positive) and low-pass filtered (corner frequency = 200 Hz) to produce multi-unit activity (MUA), which is the envelope of the high-frequency activity (90). MUA reflects

the spiking of neurons within 100-150 mm of the electrode and MUA population responses are very similar to those obtained by pooling across single units (89–93). We used a video-camera based eye-tracker (Thomas Recording) to measure the eye position at a sampling frequency of 250 Hz. V4 receptive fields were mapped by presenting white squares (1°, luminance 115 cd/m^2) on a dark background (2 cd/m^2) at different positions of a grid (1° spacing). We defined the RF borders as the locations where activity fell below 50% of the maximum (94).

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

Behavioral task and stimuli

Stimuli were presented on a 21" CRT monitor (Dell Trinitron) with a refresh rate of 85 Hz and a resolution of 1024x768 pixels, viewed at a distance of 87 cm. All stimuli were created using the COGENT graphics toolbox (developed by John Romaya at the LON at the Wellcome Department of Imaging Neuroscience) running in MATLAB (Mathworks Inc.) with custom experimental control software (95). The monkeys were trained to perform a visual search task. A trial started when the monkey 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 within a 1.2° diameter window, 6 stimuli appeared, arranged in a circle around the fixation point, at 5.3° eccentricity. Simultaneously, the fixation dot became green (98.6 cd/m^2) cueing the monkey to make a saccade. The stimuli were visible for 2,000 ms, during which the monkey was required to respond. If the monkey failed to respond in time, the trial was classified as aborted. Each stimulus could be either a square 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 cd/m^2). Stimuli had a size of 1.8° diameter. On each trial, one stimulus had a different shape (the target stimulus), one stimulus had a different color (the salient distractor stimulus), and the 4 remaining stimuli (non-salient distractors) had the same color as the target stimulus and the same shape as the salient distractor. The task of the monkey was to make an eye movement to the target stimulus, while ignoring the salient and non-salient distractors. Choices were detected as the eye-position entering a 4° diameter circular window around one of the stimuli. Upon a correct

response, the monkey received a juice reward. This reward was randomly selected to be either small or large (~4 times the small amount). The trials were ordered in a pseudorandom fashion. We recorded 34,543 trials across 28 sessions in monkey 1 and 13,815 trials across 16 sessions in monkey 2.

Computation of target and salient distractor modulation

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

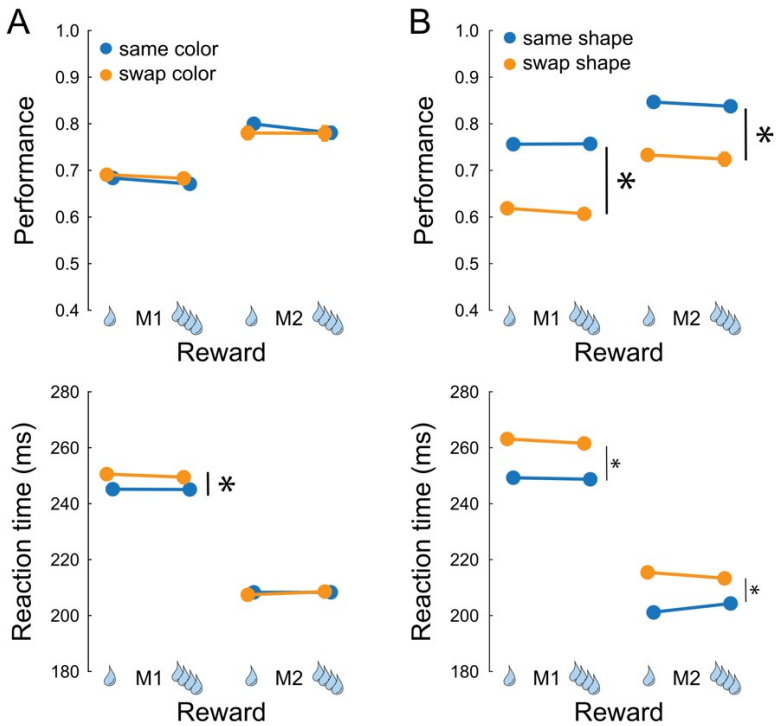
Latency of target selection and distractor suppression

To estimate the latency of the enhancement of the representation of the target and the suppression of the representation of the salient distractor we used a fitting procedure that has been described before (53). Briefly, a cumulative gaussian function was fit to the difference between either the target and the non-salient distractor response (i.e., target modulation) or the non-salient distractor and the salient distractor response (i.e., salient distractor modulation). The latency is estimated as the time point at which the fit reaches 33% of its maximum (Supplemental Fig. 4). The fits were calculated based on the population responses, i.e., after averaging across recording sites. We used a bootstrapping procedure (100 times) with replacement to estimate the mean and standard deviation of these latency estimates and compared latencies of target and salient distractor modulations with paired t-tests.

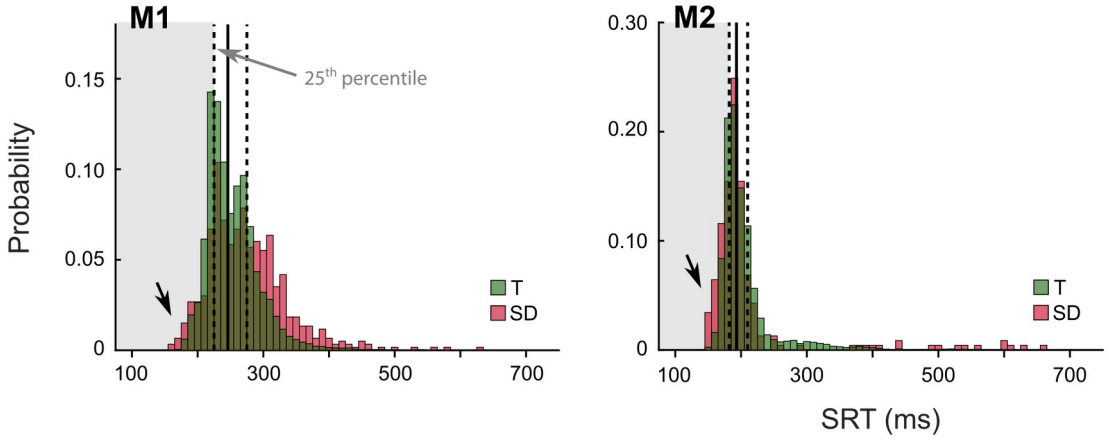
Saccadic reaction times

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

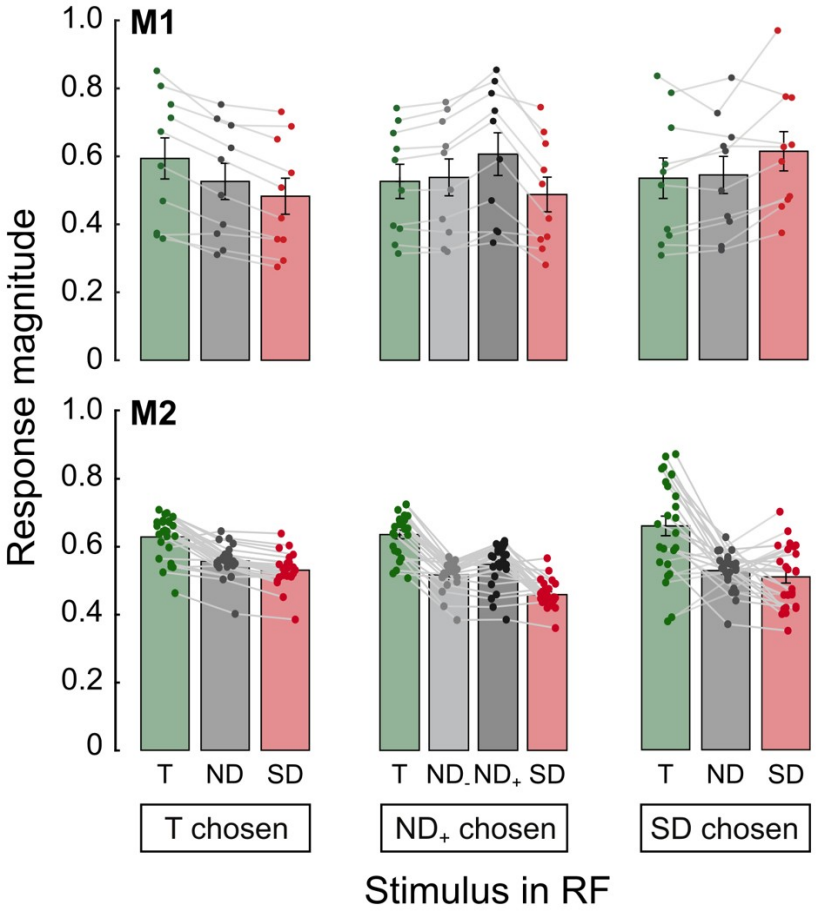
Supplemental figures



Supplemental Figure 1. Influence of previous trial on behavioral performance. A) The effects of preceding reward quantity and color scheme swaps on accuracy (top panel) and reaction time (bottom panel) for both monkeys. Yellow lines indicate trials in which the color scheme swapped relative to the previous trial; blue lines are trials in which the color scheme 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 $p < 0.05$).



Supplemental Figure 2. 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. Solid and dashed vertical lines in the left panels represent the median, 25th and 75th percentiles of the RT distribution.



Supplemental Figure 3. 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.

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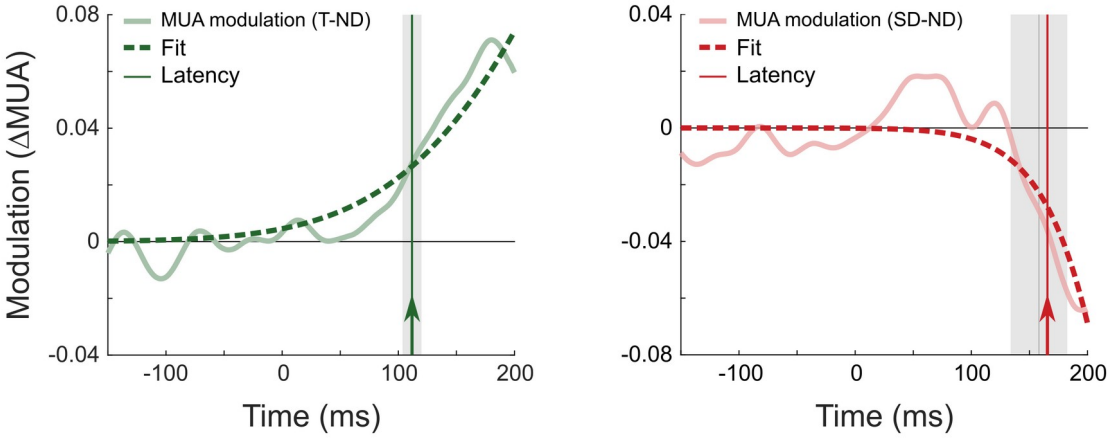
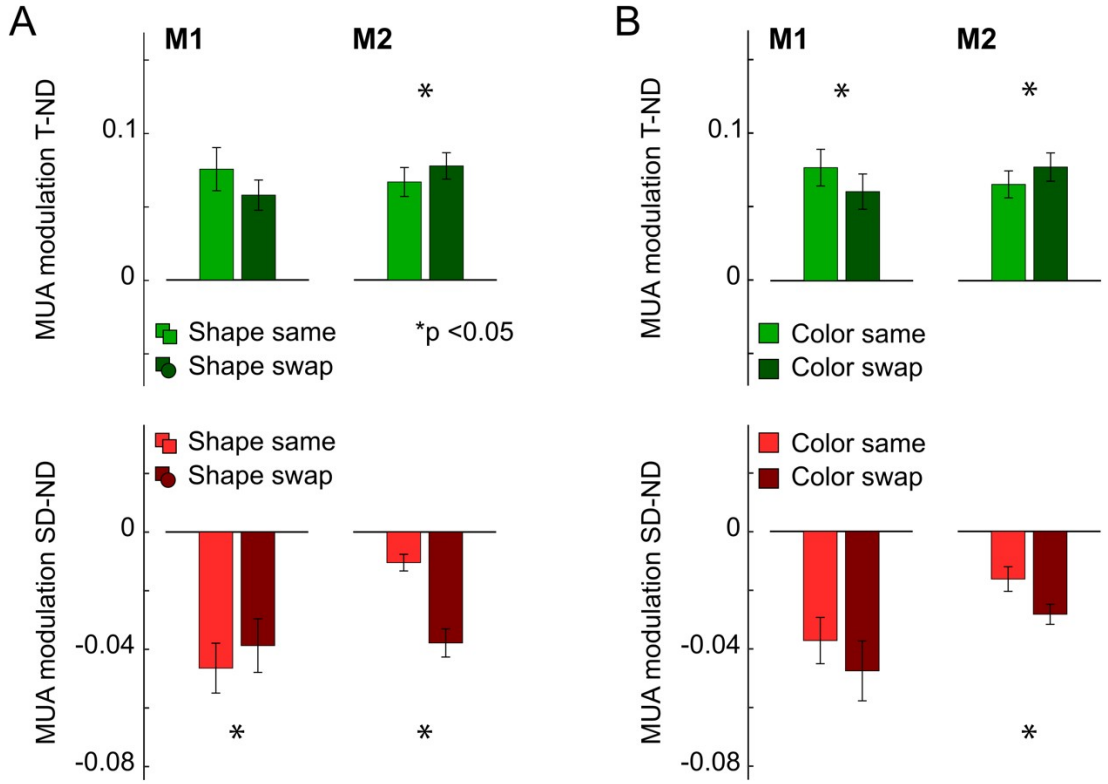


Supplemental Figure 4. Latency analysis of target and salient distractor MUA modulation. Cumulative gaussian functions were fit to the difference between either the average V4 activity elicited by the target and the non-salient distractor (i.e. target modulation, left panel) or the non-salient and salient 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).



Supplemental Figure 5. 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 color scheme 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. Light and dark colors represent trials in which the color assignment stayed the same or changed respectively. Asterisks, significant differences (paired t-test, $p < 0.05$).

Pop-in: the inversion of pop-out for a feature dimension during visual search in area V4 of the monkey cortex

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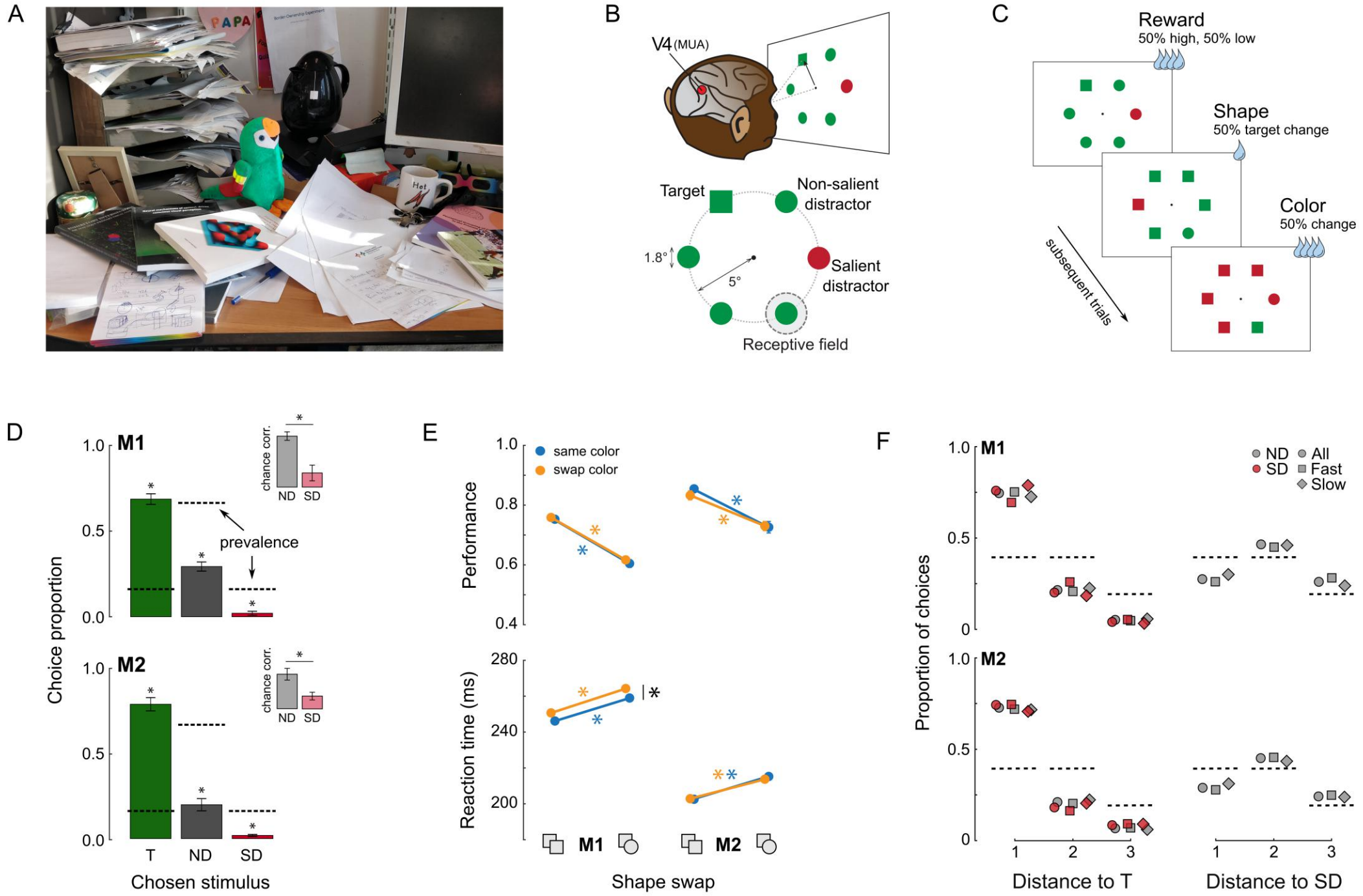

A
B
V4 (MUA)
Target
Non-salient distractor
1.8°
5°
Salient distractor
Receptive field
C
Reward
50% high, 50% low
Shape
50% target change
Color
50% change
subsequent trials
D
M1
M2
Choice proportion
chance corr.
ND
SD
prevalence
T
ND
SD
Chosen stimulus
E
same color
swap color
Performance
Reaction time (ms)
M1
M2
Shape swap
F
ND
SD
All
Fast
Slow
Proportion of choices
Distance to T
Distance to SD

Fig. 1

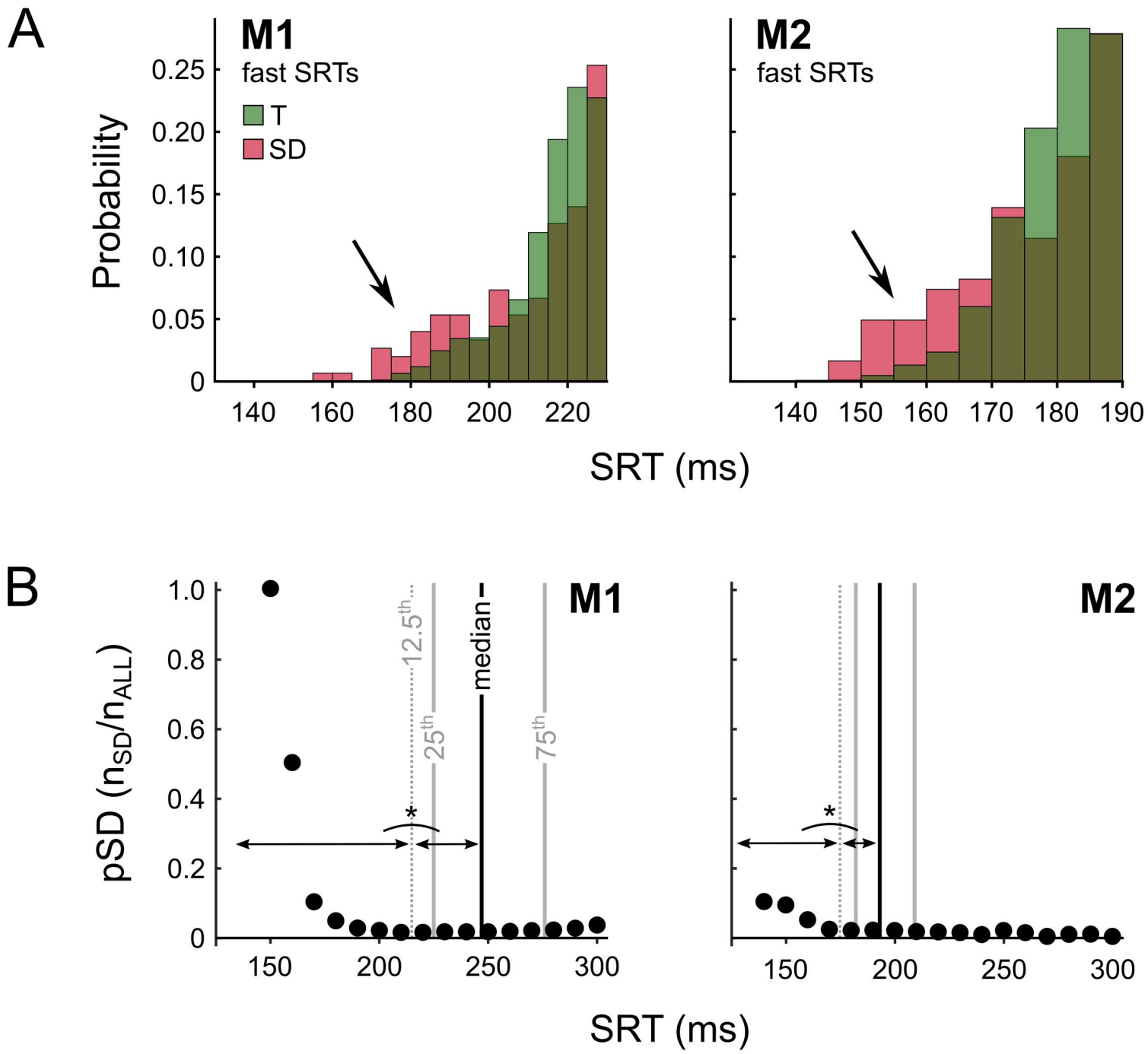

A
M1
fast SRTs
T
SD
Probability
0.25
0.20
0.15
0.10
0.05
0
140
160
180
200
220
M2
fast SRTs
140
150
160
170
180
190
SRT (ms)
B
M1
M2
pSD (n_{SD}/n_{ALL})
1.0
0.8
0.6
0.4
0.2
0
12.5th
25th
median
75th
*
150
200
250
300
SRT (ms)

Fig. 2

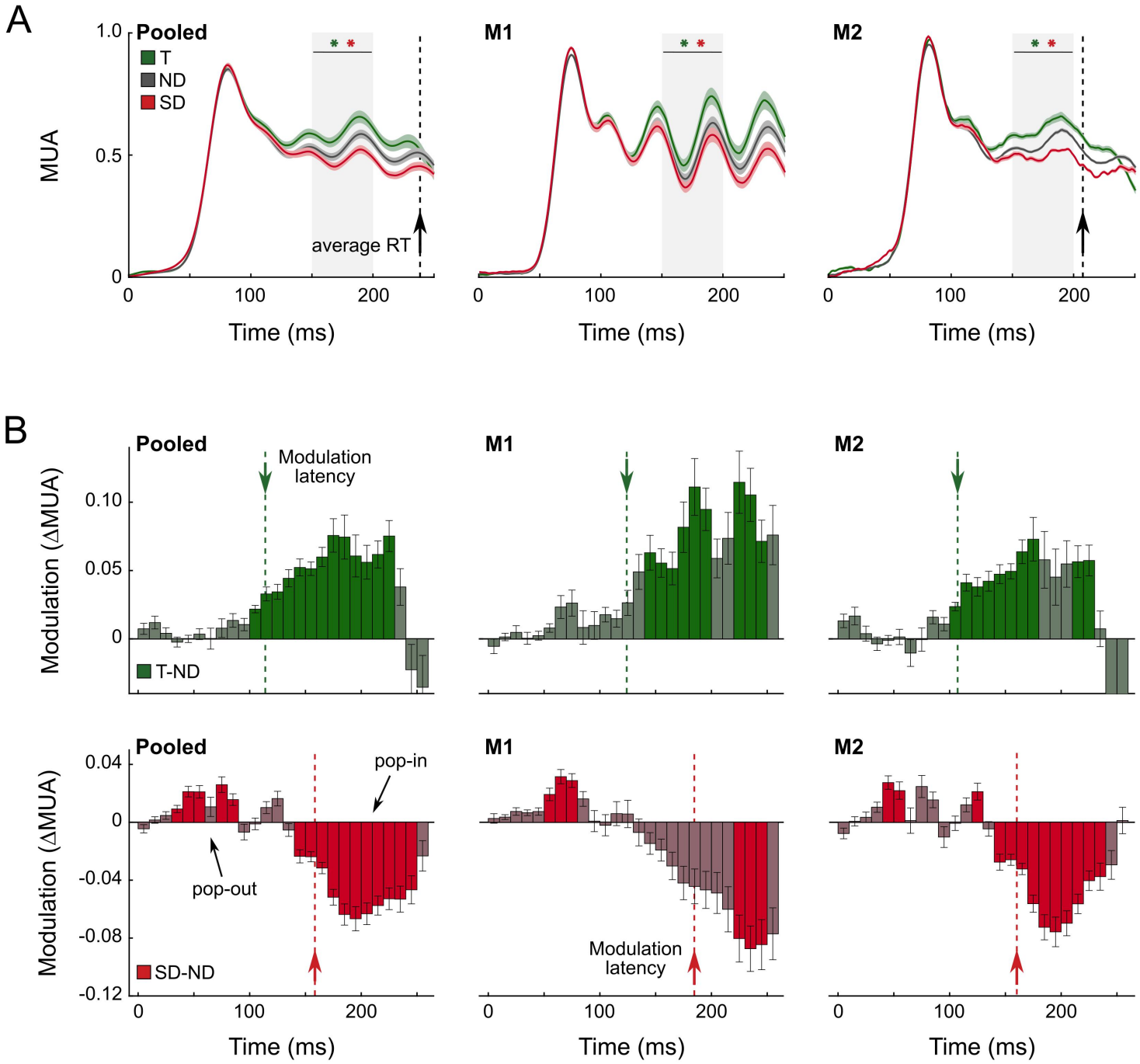

A
Pooled
M1
M2
T
ND
SD
MUA
1.0
0.5
0
average RT
0
100
200
Time (ms)
B
Modulation (ΔMUA)
Modulation latency
0.10
0.05
T-ND
0.04
-0.04
-0.08
-0.12
pop-in
pop-out
SD-ND

Fig. 3

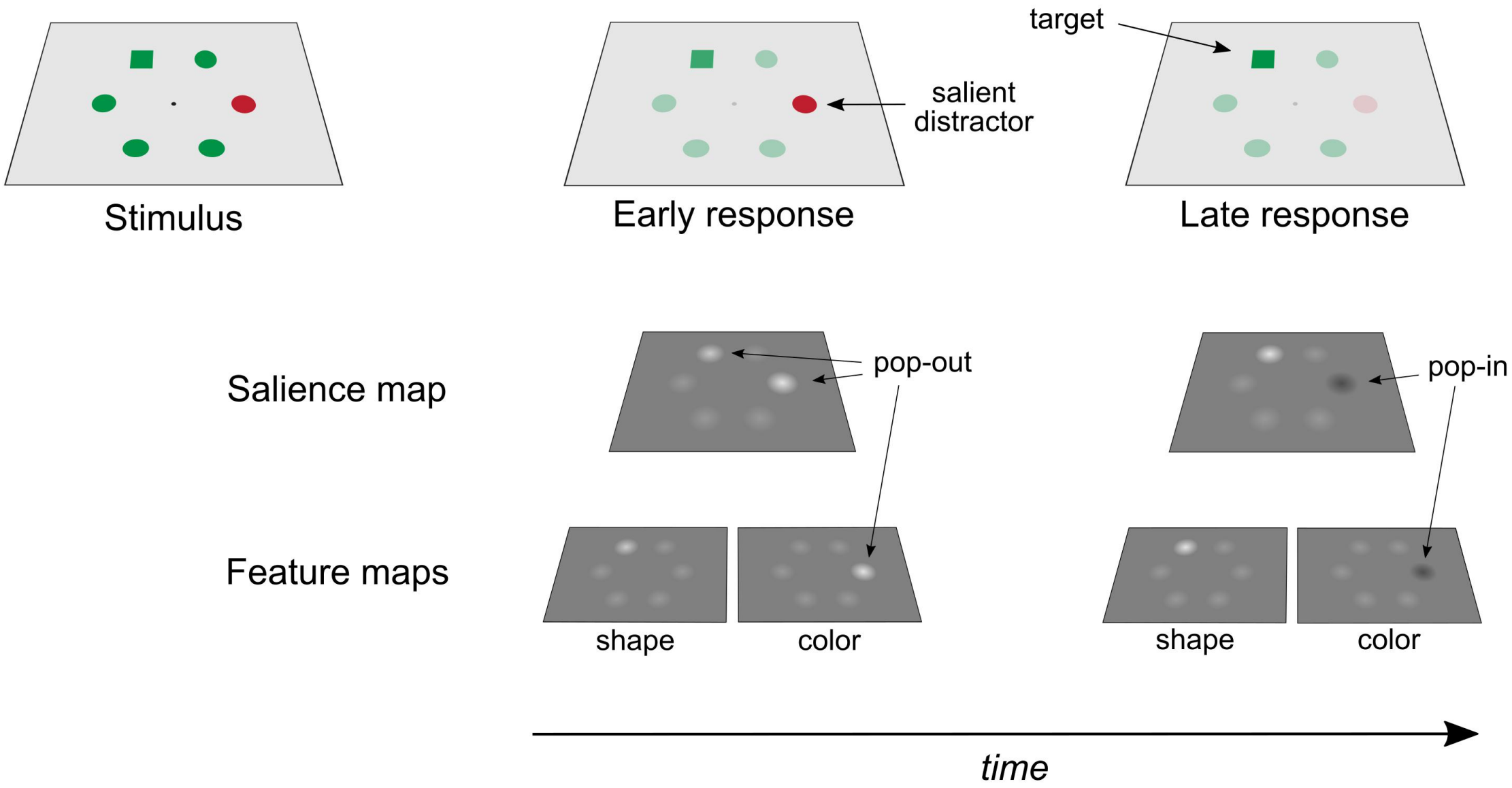
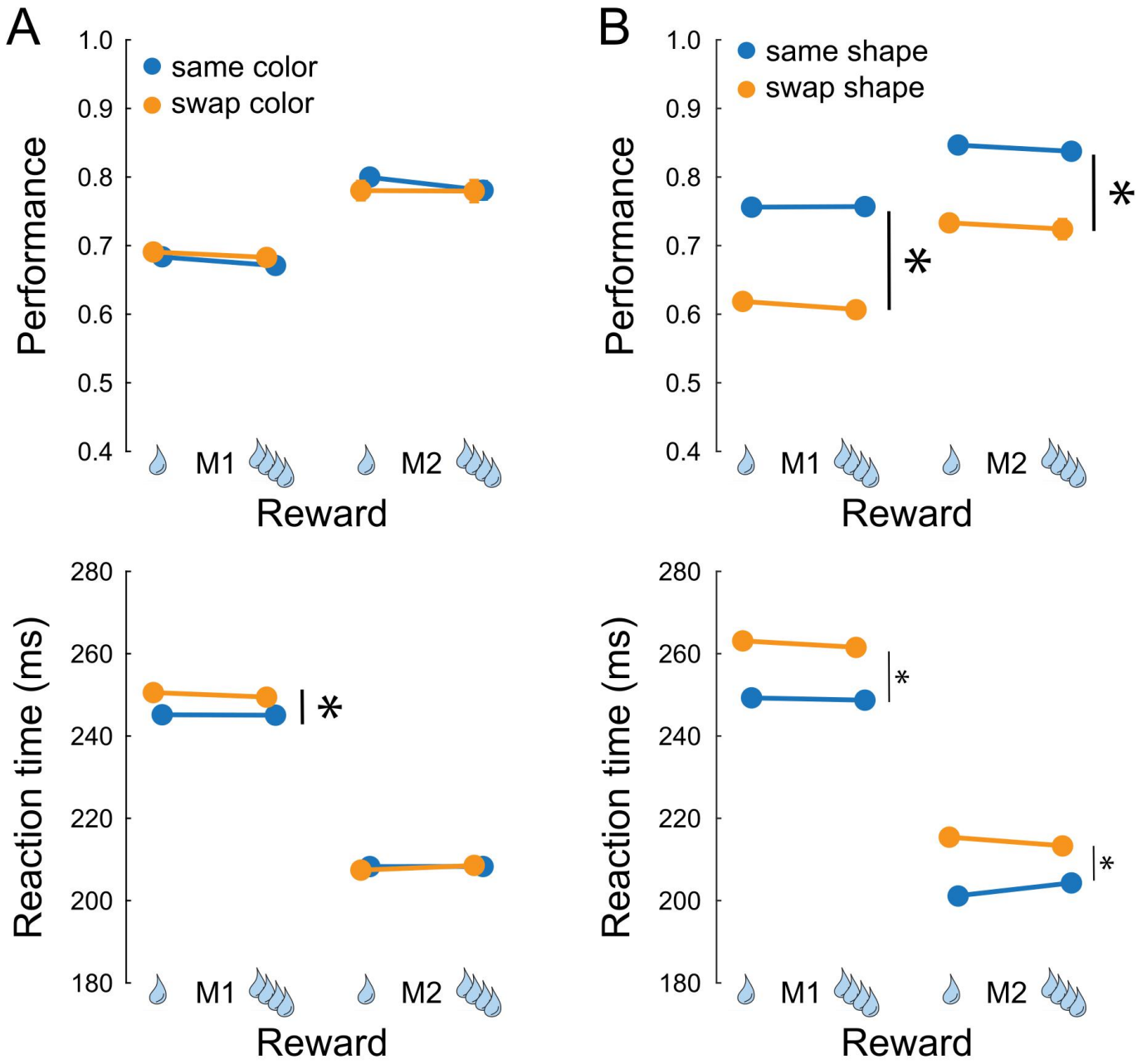
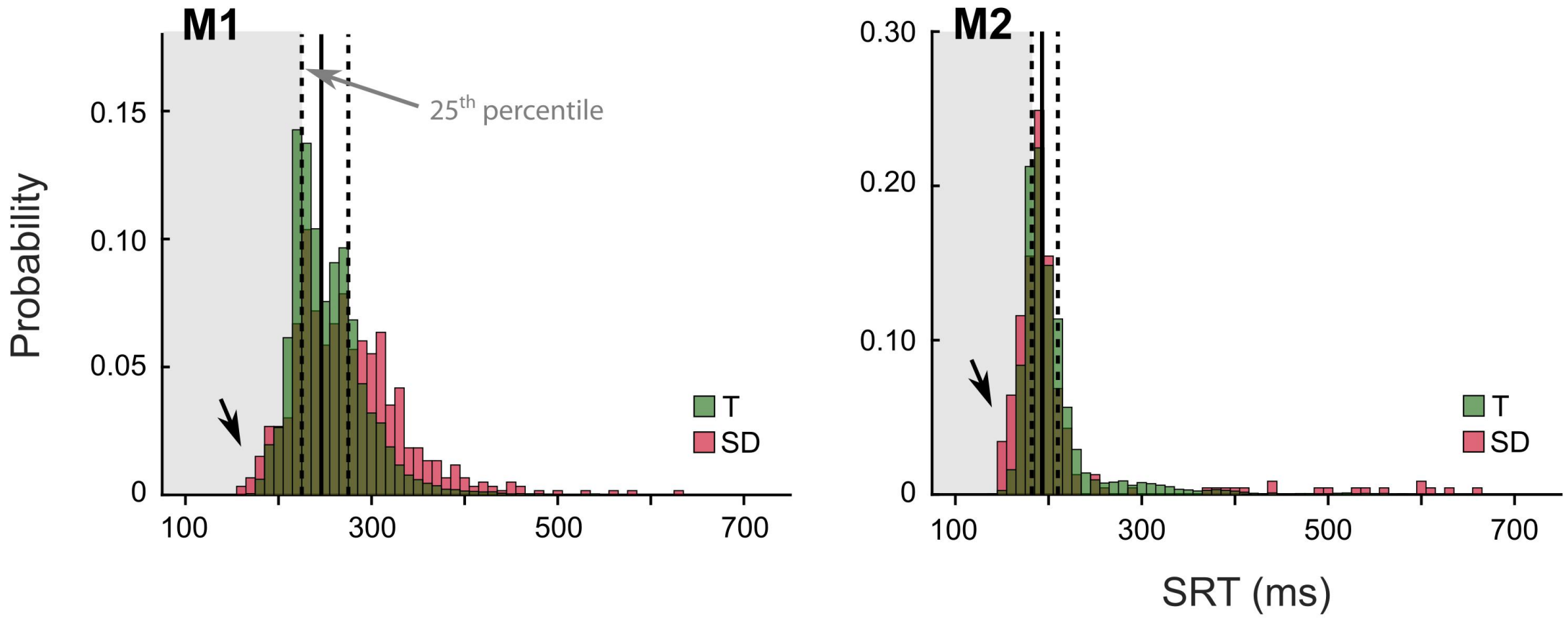

target
salient
distractor
Stimulus
Early response
Late response
Salience map
pop-out
pop-in
Feature maps
shape
color
shape
color
time

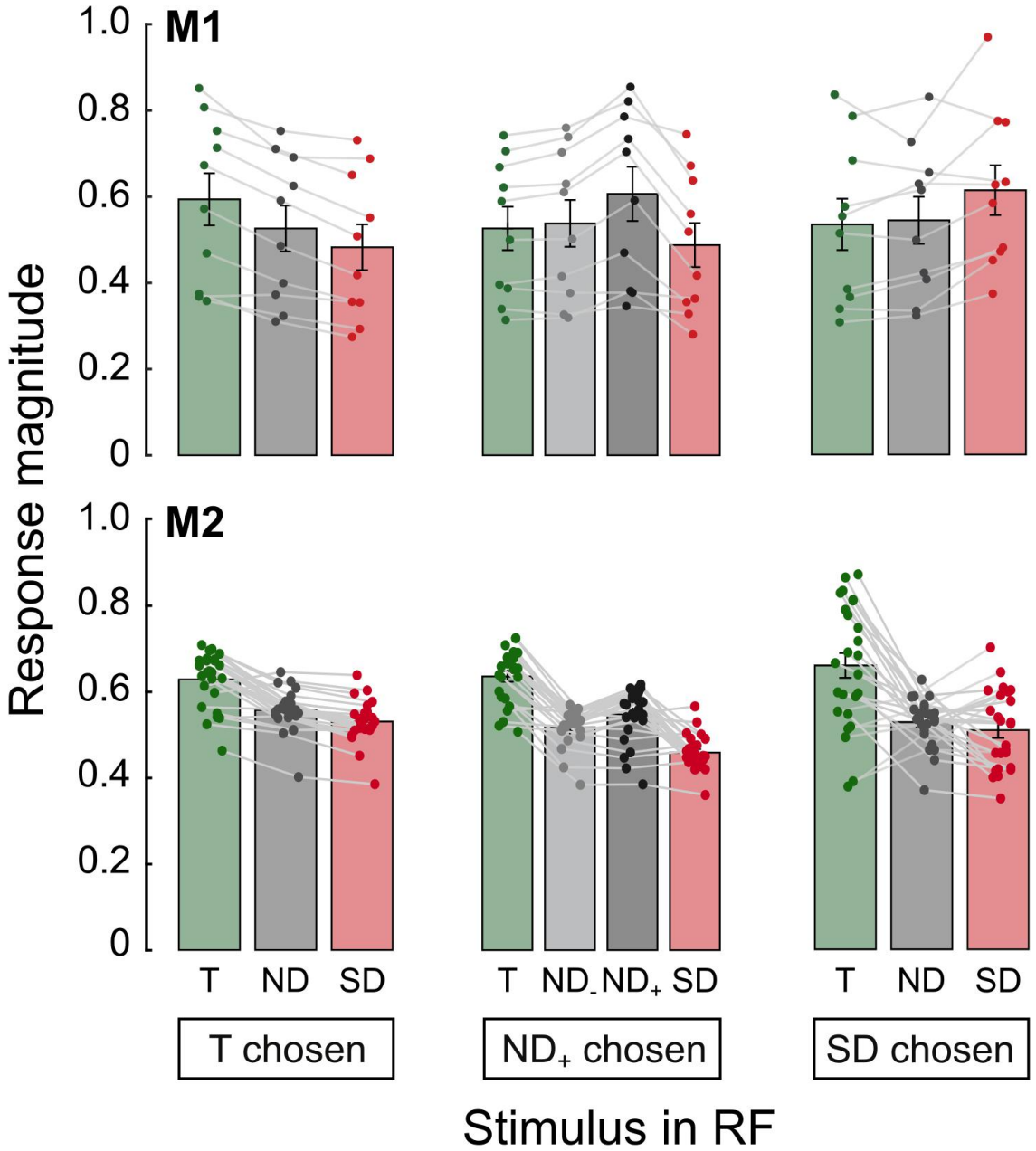
Fig. 4


A
B
same color
swap color
same shape
swap shape
Performance
Reaction time (ms)
1.0
0.9
0.8
0.7
0.6
0.5
0.4
280
260
240
220
200
180
M1
M2
Reward
*

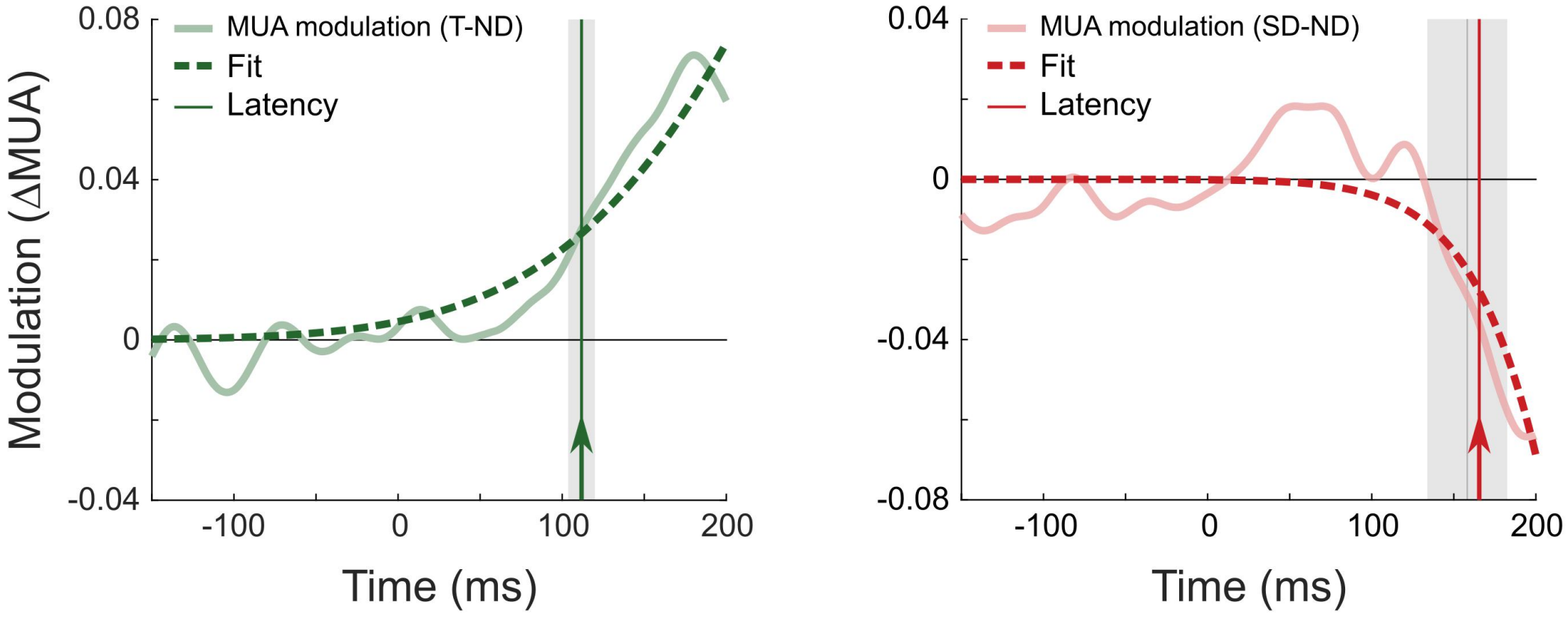
Suppl. Fig. 1


M1
M2
25th percentile
Probability
0.15
0.10
0.05
0
0.30
0.20
0.10
0
100
300
500
700
T
SD
SRT (ms)

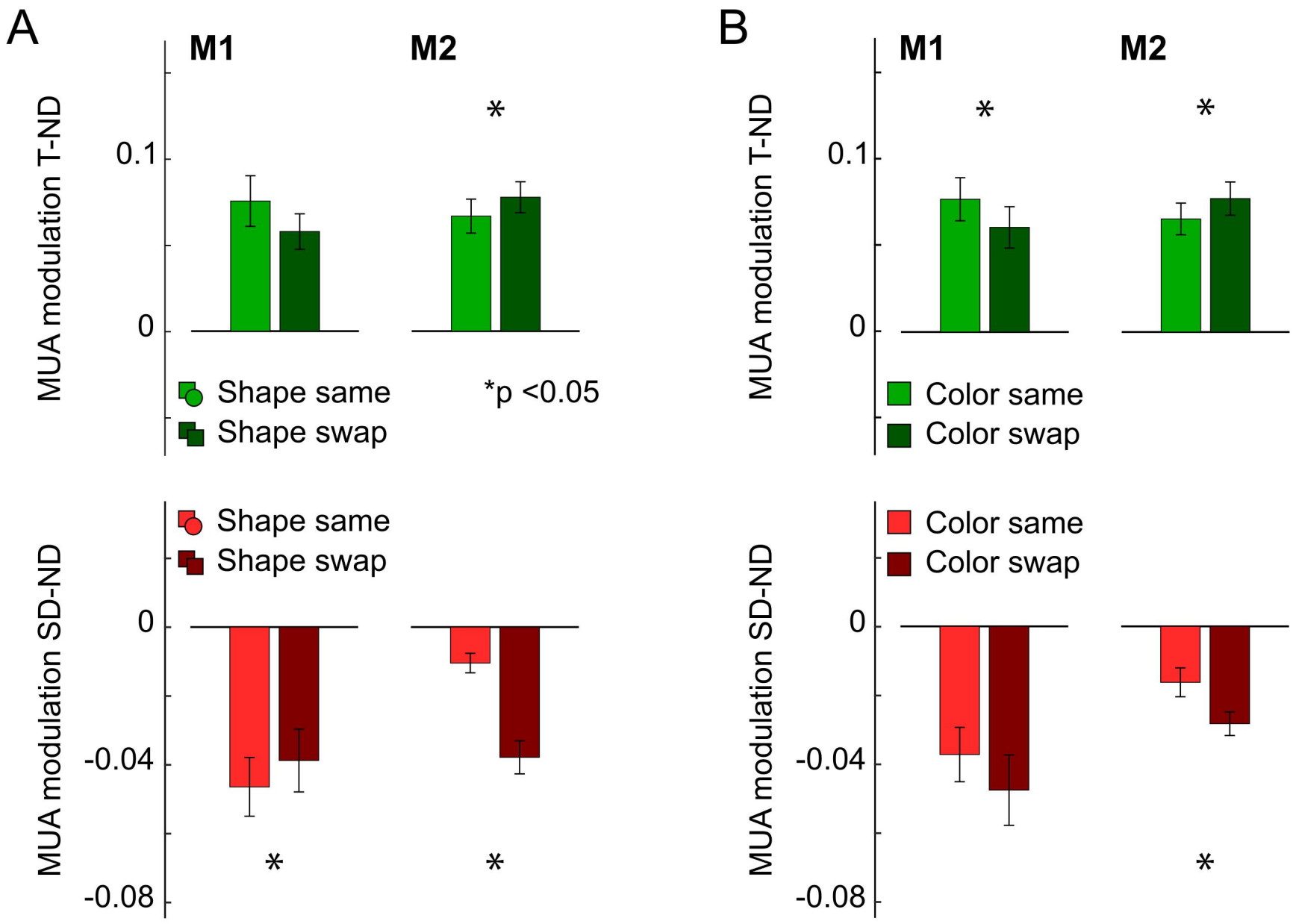
Suppl. Fig. 2


M1
M2
Response magnitude
1.0
0.8
0.6
0.4
0.2
0
T
ND
SD
ND-
ND+
T chosen
ND+ chosen
SD chosen
Stimulus in RF

Suppl. Fig. 3


0.08
0.04
0
-0.04
Modulation (ΔMUA)
MUA modulation (T-ND)
Fit
Latency
-100
0
100
200
Time (ms)
0.04
0
-0.04
-0.08
MUA modulation (SD-ND)
Fit
Latency
-100
0
100
200
Time (ms)

Suppl. Fig. 4


A
M1
M2
MUA modulation T-ND
0.1
0
*
Shape same
Shape swap
*p <0.05
MUA modulation SD-ND
0
-0.04
-0.08
*
*
B
M1
M2
MUA modulation T-ND
0.1
0
*
*
Color same
Color swap
MUA modulation SD-ND
0
-0.04
-0.08
*

Suppl. Fig. 5