Behavioral/Cognitive

Time Course of Motor Preparation during Visual Search with Flexible Stimulus–Response Association

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Whether allocation of visuospatial attention can be divorced from saccade preparation has been the subject of intense research efforts. A variant of the visual search paradigm, in which a feature singleton indicates that the correct saccade should be directed to it (prosaccade) or to the opposite distractor (antisaccade), has been influential in addressing this core topic. We performed a causal assessment of this controversy by delivering an air puff to one eye to invoke the trigeminal blink reflex as monkeys performed this visual search task. Blinks effectively remove saccadic inhibition and prematurely trigger impending saccades in reaction time tasks, thus providing a behavioral readout of the premotor plan. We found that saccades accompanied blinks during the initial allocation of attention epoch and that these movements were directed to the singleton for both prosaccade and antisaccade trials. Blinks evoked at later times were accompanied with saccades to the correct end point location: the singleton on prosaccade trials and the opposite distractor on antisaccade trials. These results provide support for concurrent encoding of visuospatial attention and saccade preparation during visual search behavior.

Introduction

Visual search paradigms serve to enhance selective processing of a stimulus embedded among distractors. Attention is driven automatically by exogenous cues like saliency and voluntarily by endogenous signals set by internal goals (Posner, 1980; Treisman and Gelade, 1980; Desimone and Duncan, 1995; Egeth and Yantis, 1997; Kastner and Ungerleider, 2000; Corbetta and Shulman, 2002; Bisley and Goldberg, 2010). Typically, a saccade is then directed to the selected stimulus, although the ability to cancel the movement or look elsewhere is also valuable. An active research topic has been to determine whether neural processes that mediate visuospatial attention also encode saccade preparation (Awh et al., 2006; Mazer, 2011; Smith and Schenk, 2012). The premotor theory of attention (PMTA) posits that neural modulation associated with attention is also the premotor command for preparing, but not necessarily executing, a saccade to that location (Rizzolatti et al., 1987). To generate a different saccade, the default movement plan has to be canceled and a new motor command programmed. The alternative view claims that the two processes are discrete and sequential because saccade preparation

begins only after target selection is complete (Sternberg, 2001; Woodman et al., 2008; Schall et al., 2011; Purcell et al., 2012).

A flexible stimulus–response association implemented within visual search offers the potential to dissociate spatial attention and saccade preparation. For example, the color or orientation of the singleton can indicate whether the correct saccade should be directed to it (prosaccade) or the opposite distractor (antisaccade). Frontal eye field (FEF) activity has been interpreted in favor of the discrete processes hypothesis, with visually responsive neurons reflecting target selection and motor neurons, which come online later, encoding saccade preparation (Sato and Schall, 2003; Purcell et al., 2010, 2012). Suprathreshold microstimulation of the FEF in primates performing this task also failed to reveal a motor preparation component signal during the target selection epoch (Juan et al., 2004). However, other studies using antisaccades (Everling et al., 1999; Everling and Munoz, 2000) and different cognitive tasks have supported the PMTA (e.g., Sheliga et al., 1995; McPeek et al., 2003; Ramakrishnan et al., 2012), particularly during exogenous attention (Smith et al., 2012) and spatial shifts of attention (Belopolsky and Theeuwes, 2009, 2012). Thus, the relationship between visuospatial attention and saccade preparation remains unresolved.

We took a novel approach to probe this controversy. Ordinarily, a saccade is generated when underlying activity in the oculomotor circuit is robust enough to inhibit pontine omnipause neurons (OPNs), which gate the saccadic system by firing spikes at a tonic rate during fixation and becoming quiescent during saccades (Keller, 1974). It follows that the activity accompanying attentional modulation across the oculomotor neuraxis could encode a premotor signal but cannot trigger the movement until OPN activity stops. Intriguingly, the tonic activity of OPNs also ceases during blinks evoked by an air puff to the eye (Schultz et al., 2010). Indeed, a blink evoked before the average latency of reac-

tive movements prematurely triggers the saccade, revealing its motor intent (Gandhi and Bonadonna, 2005). We used this technique to test whether visuospatial attention and saccade preparation are encoded concurrently in a comparable visual search paradigm that previously indicated sequential processes.

Materials and Methods

All procedures were approved by the Institutional Animal Care and Use Committee at the University of Pittsburgh and complied with the guidelines of the Public Health Service Policy on Humane Care and Use of Laboratory Animals. Two male rhesus monkeys (*Macaca mulatta*) underwent surgery in a sterile environment and under isoflurane anesthesia. The procedure consisted of placing a Teflon-coated stainless-steel wire (Baird Industries) under the conjunctiva of one eye and securing a head-restraint post to the skull. After each surgery, the monkey was returned to its home cage and allowed to fully recover. Postoperatively, antibiotics and analgesics were administered as indicated in the protocol.

Visual stimuli, behavioral control, and data acquisition were controlled by a custom-built LabView architecture on a real-time National Instruments operating system (Bryant and Gandhi, 2005). Each animal was trained to sit in a primate chair with its head restrained and a sipper tube placed near the mouth for delivery of a liquid reward. The chair was placed inside a magnetic field permitting measurement of eye and eyelid positions using the scleral search coil technique (Robinson, 1963). Eyelid movements were sensed by a small Teflon-coated stainless-steel wire taped to the eyelid of the eye not implanted with the scleral coil. Data were sampled at 1 kHz.

Both animals were trained on a color singleton search array under three oculomotor tasks: gap, step, and delay. Each experimental session, or data set, consisted of only one behavioral condition. Every trial began with directing the line of sight to a fixation point for 300–500 ms. In the step task, the fixation point was extinguished, and simultaneously a search array of four isoeccentric (10°) stimuli, spaced apart by 90°, was presented along the cardinal axes. In the gap task, the fixation point was extinguished and the presentation of the search array came after a 200 ms "gap" interval, during which the animal was required to maintain steady gaze. In the delay task, the fixation point remained illuminated during the presentation of the search array and was not extinguished until after a 500–800 ms "overlap" period. Fixation point offset served as the saccade initiation cue. On each trial, one of the four stimuli could be either red or green in color, indicating the singleton stimulus in the array, while the other three targets were purple. The monkeys were trained to make a saccade to the singleton (prosaccade) if it was green and to the opposite distractor, 180° from the singleton (antisaccade), if red. The trigeminal blink reflex was induced by delivering a puff of air at a random time on 30% of the trials. The puff was timed to induce a blink late during the fixation period, during the reaction time period, or shortly thereafter. The puff was generated by an air reservoir (output pressure, ~20 psi) and a solenoid system located outside the experimental room. The air flowed through a narrow Tygon tube and released the puff ~2 cm from the eye. The reflex-blink procedure was reported in detail in a previous paper (Gandhi and Bonadonna, 2005).

Each trial was digitized and stored for off-line analysis with a combination of in-house software and Matlab. To standardize the alignment of all movements, the singleton was always rotated to (10°, 0°). Horizontal and vertical eye velocities were obtained by differentiating the component eye position signals. Eyelid signals were maintained in arbitrary units and examined to detect blinks, which were easily detectable based on a rapid and transient depression in eyelid position followed by a slower elevation toward baseline (Fig. 1) (Evinger et al., 1991). We considered only trials for which the blink occurred ~25 ms after the air puff reached the eye to gain confidence that the blink was indeed induced by the trigeminal blink reflex (for details, see Gandhi and Bonadonna, 2005). If a blink was evoked during the fixation interval, before the search array was presented, the animal did not produce a saccade with the blink (red trace). The transient eyelid depression is associated with a small loopy movement of the eyes, which return close to their original positions by the end of the blink (Goossens and Van Opstal, 2000b). The
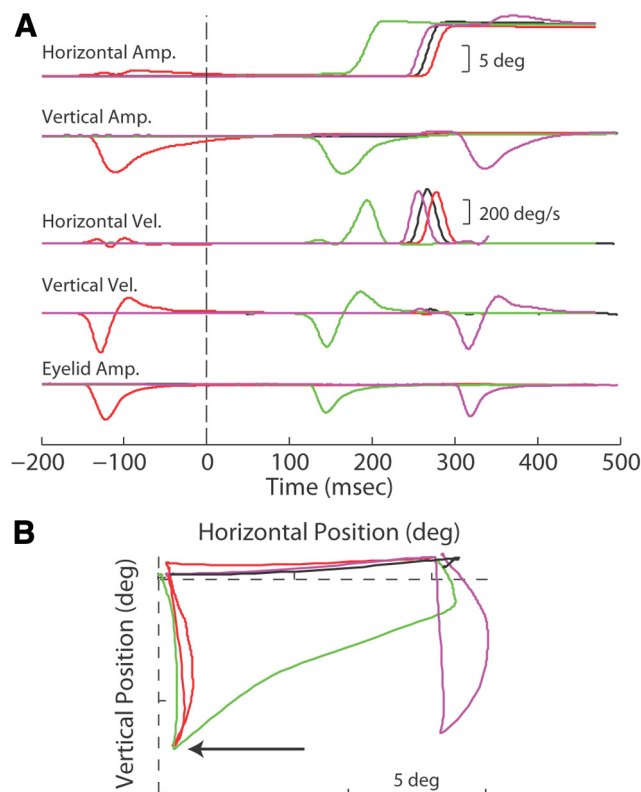

Figure 1. Spatiotemporal illustrations of combined saccade–blink movements. *A*, Horizontal and vertical eye amplitude and velocities (top four rows) and eyelid amplitude (bottom row) are plotted as a function of time. Four representative eye movements are shown. The dashed black line indicates array onset. Red trace denotes an "early blink" trial, in which the blink occurs during the fixation interval. The actual saccade occurs at a regular latency after array onset. Magenta trace represents a trial in which the blink was timed too late; it occurred after the saccade. The green trace identifies a "blink-triggered" movement, in which the saccade accompanies the blink. Such saccades are prematurely triggered, as evidenced by the shorter latency. The black trace indicates a control saccade without a blink. Scale bars: horizontal and vertical eye positions, 5°; horizontal and vertical eye velocities, 200°/s; eyelid position, arbitrary units. *B*, The same movements are represented as spatial trajectories. All traces begin near the origin. The early-blink trial (red trace) shows that the blink-induced eye movement is a loopy perturbation with a small horizontal and a larger vertical component. The eyes return close to their original position well before the rightward eye movement is produced. The magenta trace shows a similar loopy movement after the horizontal saccade is completed. The blink-triggered trial (green trace) starts off as a loopy movement, then deviates from the trajectory in midflight and produces an oblique saccade that reaches the target location. A Euclidean algorithm, which identifies the position and instance the blink-triggered movement deviates from an early-blink template (arrow), was used to detect saccade onset.

saccade is actually produced later in the trial, after the animal processes the search array onset; we refer to such movements as "early blink" trials. In contrast, if the blink is evoked after array onset and after the animal has permission to initiate the eye movement, then the blink is accompanied with a saccade directed to a stimulus. For such "blink-triggered" movements, the blink and saccade overlap temporally (green trace). In some cases, the puff occurred late enough that the blink was induced after the saccade (magenta trace).

Onset and offset of eye movements for which blinks and saccades did not overlap were detected using a standard 30°/s velocity criterion, respectively. Blink-triggered saccades, which encompass both a saccadic and a blink component, could not be consistently analyzed with just a straightforward velocity threshold. Saccade onset and offset were therefore detected using a Euclidean template matching algorithm. The loopy eye movements observed on early blink trials were aligned on movement onset, and the mean of their radial velocity profiles was taken as a template defining the "blink component." Next, we compared the radial velocity profile of each blink-triggered saccade to the template. The time

point when the velocity waveform deviated outside of three SDs of the template and stayed outside for at least 20 ms marked the onset of the "saccadic component" (Fig. 1B, arrow). To detect saccade offset, we first identified the epoch when eye velocity reached zero and then stepped backward in time until a 30°/s threshold was reached. This approach limited the likelihood of false detection due to gross blink-induced perturbations in velocity waveforms.

Results

Two animals performed visual search tasks requiring the generation of either prosaccades or antisaccades based on the color of the singleton (Fig. 2A). The majority of analyses is based on the step task version ($n = 18$ sessions). In control trials in which no air puff was delivered and no blinks were generated, the average latency of correctly performed antisaccades was significantly longer (paired t test, $p < 0.01$) than that of prosaccades (Monkey 1 prosaccade, mean, 244 ms; SD, 24; antisaccade, mean, 271 ms; SD, 28; Monkey 2 prosaccade, mean, 258 ms; SD, 27; antisaccade, mean, 268 ms; SD, 26), consistent with behavior reported previously (Everling et al., 1999; Everling and Munoz, 2000; Sato and Schall, 2003). The effects of air-puff delivery were analyzed across 3442 prosaccade trials and 3435 antisaccade trials.

Published accounts of neural activity waveforms recorded during visual search in the context of a step task can be used to predict the potential outcomes of the blink perturbation, in terms of both the PMTA and when target selection and saccade preparation are discrete and sequential processes. Visually responsive neurons along the oculomotor neuraxis initially respond equally to all stimuli, but exhibit higher selectivity for the singleton stimulus starting ∼100–150 ms after array onset (Schall and Hanes, 1993; McPeek and Keller, 2002; Sato and Schall, 2003; Thomas and Paré, 2007; Balan et al., 2008; Cohen et al., 2009). During prosaccade trials (Fig. 2A, left), this activity remains elevated for the remainder of the trial because the oddball stimulus is also the saccade target (Fig. 2B, left, green trace). In principle, it becomes difficult to determine if the enhancement reflects only spatial attention, which must be directed to the singleton to perform the task correctly, or whether a premotor signal is also encoded in the modulated response. The antisaccade trial (Fig. 2A, right) potentially offers a means to dissociate between the two signals because the eye movement must be directed to the distractor located diametrically opposite to the singleton. Based on FEF activity recorded during this paradigm (Sato and Schall, 2003), visually responsive neurons that respond preferably to the singleton reduce their firing rates (Fig. 2B, right, green trace), and enhancement is observed in neurons that prefer the opposite location (red trace). Notably, there is a brief epoch during which activity associated with the singleton is greater than that for the opposite distractor (Fig. 2B, right, arrow).

According to the PMTA, neural activity such as that schematized in Figure 2B encodes both an attention signal and a motor preparation command, the latter of which should be revealed by a blink. For prosaccade trials, the blink should lead to a reduced latency saccade directed to the singleton (Fig. 2C, left, solid green line), and the shortest saccade latencies should match the time when visually responsive neurons differentiate between the singleton and distractors. During the antisaccade condition, the blink-triggered movement should display a transition in the direction of movements from the singleton at reduced latencies (Fig. 2C, right, solid green line) to the opposite distractor at regular latencies (Fig. 2C, right, solid purple line). According to the discrete stages hypothesis, in contrast, the enhanced activity in visually responsive neurons represents target selection only (Fig.
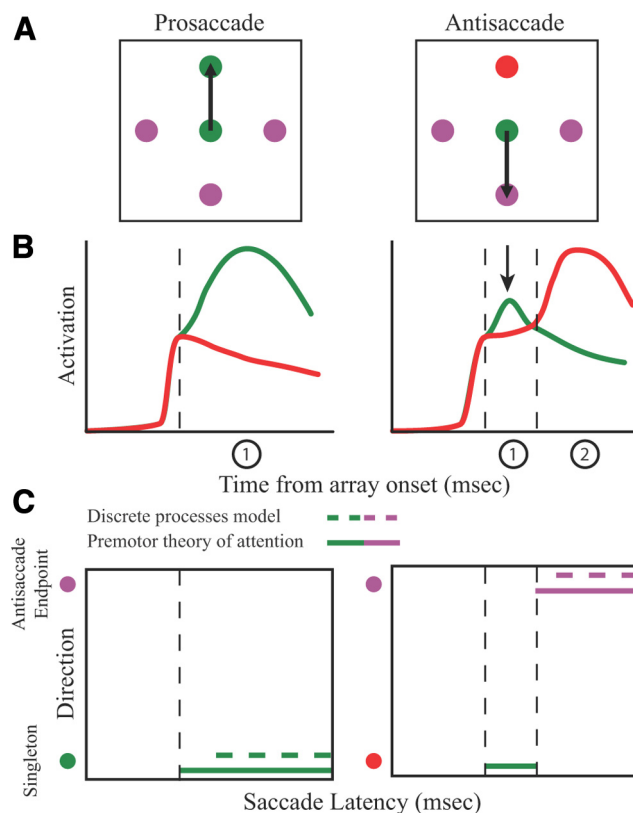

Figure 2. Predictions of blink perturbation on saccade generation for the PMTA and discrete processes hypotheses. *A*, Prosaccade (left) and antisaccade (right) trials were indicated by the color of a singleton among identical distractors in a visual search array. *B*, Schematized activity patterns in visually responsive "singleton neuron" (when the singleton is placed in its receptive field) and an "antineuron" (when the opposite distractor is placed in its receptive field). Green and red traces are schematics of activity patterns of singleton neuron and antineuron, respectively. Waveforms have been adapted from FEF data (compare Sato and Schall, 2003, their Fig. 2A, left column). The initial sensory response is similar in both neurons. For prosaccade trials (left), activity continues to accumulate in the singleton neuron and is suppressed in the antineuron. The vertical dashed line indicates the time when activities in the two neurons become significantly different. For antisaccade trials (right), the enhancement in activity of the singleton neuron is short lived (arrow). It begins to attenuate as activity in the antineuron becomes enhanced, indicating selection of the opposite distractor and, perhaps, the formulation of a new motor plan to produce an antisaccade. As in the prosaccade condition, the first vertical dashed line identifies the time when activities in the two neurons initially become significantly different (singleton neuron shows enhancement). The second vertical line marks the time when activity in the antineuron becomes higher. Epoch 1 refers to the period for which the green trace is greater than the red trace, while Epoch 2 spans the duration for which the red trace resides above the green trace. *C*, Predictions of saccade direction (toward singleton or antisaccade end point) as a function of latency of blink-triggered saccades. For the PMTA, a blink triggers a saccade if activities in the singleton neuron and antineuron are significantly different, and the saccade will be directed to the neuron with higher activity. Thus, on prosaccade trials, the blink is an effective trigger for all time points after the first vertical dashed line (Epoch 1, as in *B*), and all saccades should be directed to the singleton (solid green line). During antisaccade trials, blinks invoked during Epoch 1 (in between the two vertical dashed lines) should produce reduced latency saccades to the singleton (solid green line), while blinks evoked during Epoch 2 should direct saccades to the opposite distractor (solid purple line). For the discrete processes hypothesis, accumulation in motor neurons (data not shown) initiate after target selection is complete. For prosaccades, the effectiveness of the blink to trigger a saccade (dashed green line) will be delayed compared to the PMTA. For antisaccade trials, target selection of the singleton must be suppressed and the opposite distractor target must be selected before motor preparation commences. Thus, a blink evoked during Epoch 1 (in between the two vertical lines) should not trigger a saccade, which is denoted by the absence of a dashed green line in this epoch. Activity in motor neurons will initiate in Epoch 2, but only after target selection is complete. Only after this criterion is fulfilled will a blink become an effective perturbation for triggering a saccade (dashed purple line). Note that the shortest saccade latency is slightly delayed compared to the PMTA prediction. The differential effect predicted for antisaccade trials is the focus of the study. The vertical offset between the saccade direction predictions (horizontal solid and dashed lines) is only for illustration purposes.

2 *B*). Motor preparation occurs only after the target selection process has reached completion (Purcell et al., 2010, 2012; Schall et al., 2011), and there can often be some delay between the two processes (Woodman et al., 2008). Since a blink can only trigger a saccade if premotor activity has accumulated in the oculomotor circuit, the earliest a saccade can be initiated should be later than that expected with the PMTA. This distinction is represented by a later onset of the dashed green trace for prosaccade trials (Fig. 2*C*, left). For antisaccade trials, neural selection of the singleton must be suppressed, and the opposite distractor target must be selected before motor preparation commences. More specifically, since the enhanced activity for the singleton (Fig. 2*B*, right, epoch between the dashed vertical lines) is not associated with motor preparation, a blink should not trigger a saccade in this epoch, which can be noted by the absence of a dashed green line in Figure 2*C* (right). Activity in motor neurons (data not shown) commences only after the opposite distractor is selected, at which point a blink should be able to trigger a saccade to the correct antisaccade end point, although the shortest latency will be longer than that predicted by the PMTA (Fig. 2*C*, right, later onset of dashed purple relative to solid purple trace). Practically, the conceptual differences in onset times of motor preparation may not be easy to evaluate experimentally, due in part to the stochastic nature of neural signals. However, the pivotal test that should differentiate between the two theories comes from antisaccade trials, specifically during the epoch when activity for the singleton is greater than that for the opposite distractor (Fig. 2*B*, right, arrow). Blink-triggered saccades to the singleton would conform to the PMTA and cast strong doubt on the discrete processes framework.

Figure 3 plots saccade latency as a function of blink time relative to saccade cue for prosaccade (left column) and antisaccade (right column) trials in the step condition. Qualitatively, the data can be separated into three groups: (1) When blinks occurred very early before saccade cue (less than −200 ms) or after typical saccade reaction time (>200 ms), saccade latency remained relatively constant and comparable to that observed on control trials (for representative spatial and temporal illustrations, see Fig. 1). Both animals made saccades to the correct end point on >90% of the trials (Monkey 1, 93% prosaccade trials, 90% antisaccade trials; Monkey 2, 96% prosaccade trials, 91% antisaccade trials). (2) As blink timing approached and overlapped with stimulus presentation, saccade latency increased systematically with blink time. This is most likely because the eyes were closed when the array was illuminated, and the visuomotor transformation can only begin after the eyes reopen. For the period beginning 100 ms before array onset and covering the data points for which saccade latency increased, the success rate performance remained consistent (Monkey 1, 90% prosaccade trials, 84% antisaccade trials; Monkey 2, 96% prosaccade trials, 89% antisaccade trials). (3) Most relevant to this study is the subset of trials for which the blink was evoked shortly after array onset but before the typical reaction time of the animal. Almost always, a saccade accompanied the blink, and we refer to these combined blink–saccade movements as blink-triggered saccades (for classification, see Materials and Methods). Such trials can be identified by the cluster of points encompassed by the dotted ellipse (Fig. 3). Performance by both animals on prosaccade trials (Monkey 1, 94%; Monkey 2, 94%) was not significantly different from success rates in other groups (χ^2 test, $p > 0.01$). In contrast, success rates dropped significantly during antisaccade trials in both animals (Monkey 1, 70%; Monkey 2, 80%; χ^2 test, $p < 0.01$).

A closer look at the blink-triggered saccade distributions in Figure 3 reveals that the reduction in saccade latency diminishes
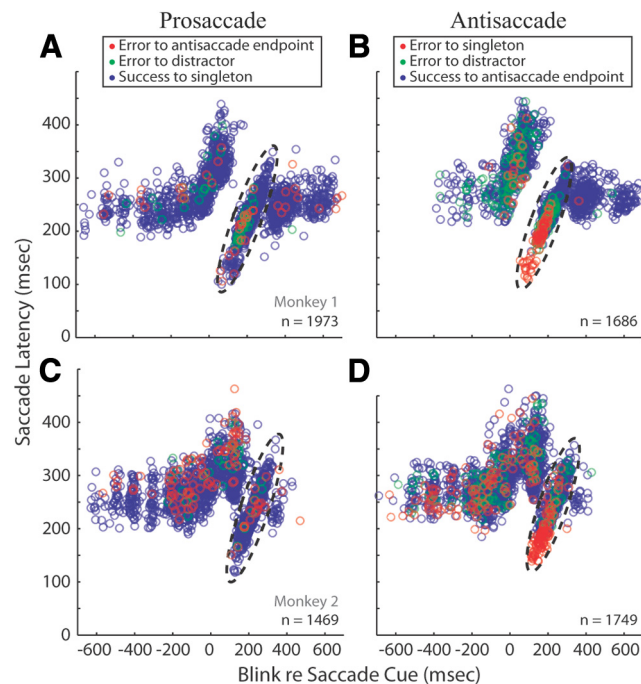

Figure 3. Blink effects on the latency of saccades executed during visual search (step task). *A*, *C*, The latency of saccades evoked during prosaccade trials as a function of the time of blink relative to saccade cue. Each dot represents a puff/blink trial. Every blue point represents a successful saccade to the singleton, red a failure to the antisaccade end point, and green a failure to one of the orthogonal distractors. *B*, *D*, The latency of saccades evoked during antisaccade trials as a function of the occurrence of blink relative to saccade cue. Each blue point represents a successful trial to the antisaccade end point (opposite distractor), red a failure to the singleton, and green a failure to one of the orthogonal distractors. In each panel, the data encircled in the ellipse represent blink-triggered movements (for criterion, see Materials and Methods). Each row illustrates data from one animal.

with later blink times. To better characterize the facilitatory effect of the blink, we isolated the subset of blink-triggered saccades with latencies less than two SDs from the mean of control trials. This subset, on average, constituted 27% of all blink-triggered movements. The mean ± SD reaction times on prosaccade trials were 145 ± 22 ms (Monkey 1, $n = 114$) and 178 ± 19 ms (Monkey 2, $n = 112$). The mean ± SD reaction times on antisaccade trials were 193 ± 23 ms (Monkey 1, $n = 193$) and 185 ± 20 ms (Monkey 2, $n = 115$). The average latency of correct prosaccades remained significantly less than the mean value for correct antisaccades, preserving the cost in reaction time associated with antisaccade generation. Within this subset of data, a saccade was successfully made to the correct end point on >90% of prosaccades trials (Monkey 1, 90%; Monkey 2, 97%), but <50% of antisaccade trials (Monkey 1, 49%; Monkey 2, 27%).

As motivated above (Fig. 2), neural activity differentiates the singleton from distractors shortly after the initial visual response to array presentation (Schall and Hanes, 1993; McPeek and Keller, 2002; Sato and Schall, 2003; Thomas and Paré, 2007; Balan et al., 2008; Cohen et al., 2009). The activity associated with the singleton is transiently higher ~100–150 ms after array onset, even when the correct movement must be directed to another stimulus (Sato and Schall, 2003). We found that a blink perturbation during this putative target selection period consistently triggered a saccade and, on the majority of trials, the movement was directed to the singleton (Monkey 1 prosaccade, 90%; antisaccade, 90%; Monkey 2 prosaccade, 92%; antisaccade, 87%). Therefore, the data demonstrate the existence of premotor activ-
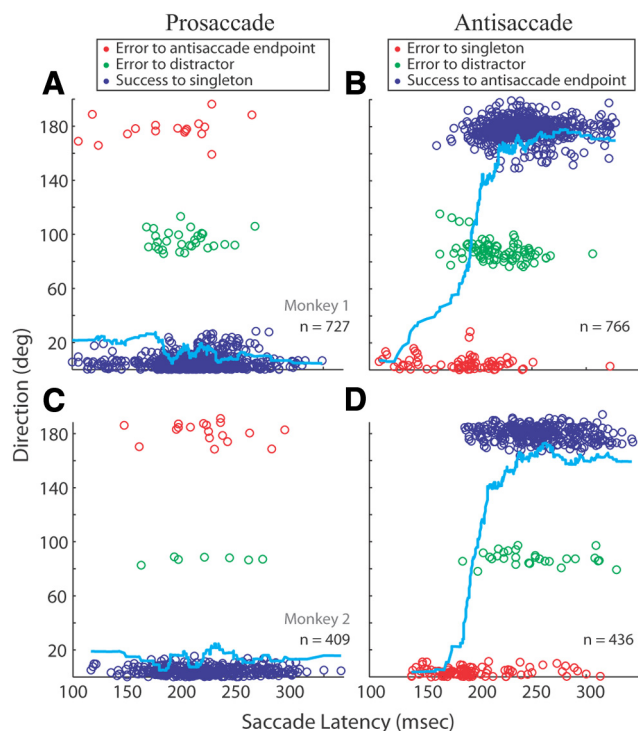
Figure 4. Direction of blink-triggered movements executed during visual search (step task). *A*, *C*, The direction of blink-triggered saccades, those encompassed in the dotted ellipse in Figure 3, evoked during prosaccade trials as a function of saccade latency. Each blue point represents a successful trial to the singleton, red a failure to the antisaccade end point, and green a failure to one of the orthogonal distractors. *B*, *D*, The direction of blink-triggered saccades evoked during antisaccade trials as a function of saccade latency. Each blue point represents a successful trial to the antisaccade end point (opposite distractor), red a failure to the singleton, and green a failure to one of the orthogonal distractors. The cyan line illustrates a moving average across saccade latency. The eye position at the end of the primary saccade relative to the initial eye position (close to origin) was used to calculate the direction metric for each trial. Each row illustrates data from one animal.

ity during allocation of attention, and that the premotor activity is linked to the singleton. This result is better visualized when saccade direction (final eye position relative to the initial eye position) is plotted as a function of latency for all blink-triggered movements (Fig. 4). For prosaccade trials (left column), most movements were directed to the singleton, which is confirmed by the moving average curve (cyan trace) remaining close to the singleton direction across the entire range of saccade latencies. There is a small percentage of trials (<12%) directed to the opposite and orthogonal distractors, but this fraction was not different from the likelihood of errors the animal made during control trials (data not shown). For antisaccade trials (right column), the correct response should be directed 180° away from the singleton. In contrast, the directional plot shows that earliest movements were predominately errors to the singleton, and the transition from the singleton to the correct end point location occurred at longer reaction times. Errors to the orthogonal and opposite distractors were observed; however, the majority of these movements occurred after the time window for target selection and at the same rate made during control trials.

The direction analysis indicates that the saccade is directed toward one of the four targets, but it falls short of revealing whether the end point reaches the stimulus. Figure 5 shows a scatter plot of the end points of the primary saccades associated with blink-triggered movements. For both prosaccade and anti-
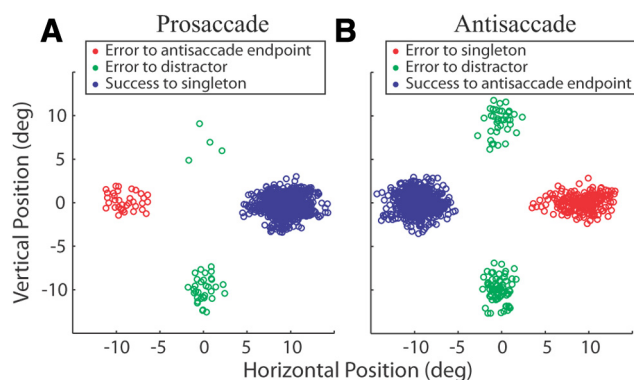

Figure 5. End points of blink-triggered saccades executed during visual search (step task). *A*, The distribution of end points of every blink-triggered movement from both animals is plotted for prosaccade trials. The location of the singleton was always rotated to (10°, 0°) so that all correct movements (blue) are to the right, failures to the opposite distractor (red) are to the left, and failures to the orthogonal distractors (green) are to up or down locations. *B*, The distribution of end points of every blink-triggered movement from both animals is plotted for antisaccade trials. The same location (10°, 0°) is used for the singleton. Thus, correct saccades to the opposite distractor (blue) are to the left, failures to the singleton (red) are to the right, and failures to an orthogonal distractor (green) are to up or down locations.

saccade trials, the end points were closely clustered near one of the four target locations.

The visual search task was also performed in 20 gap and 11 delayed saccade sessions in the same animals (see Materials and Methods). The analyses focus on prosaccade (gap, $n = 4641$; delay, $n = 2189$) and antisaccade (gap, $n = 4642$; delay, $n = 1994$) trials with a puff-induced blink. Figure 6 illustrates data from gap trials in one animal; data from a second animal were comparable. The overall pattern of saccade latency as a function of blink time was similar to the step task and, across all trials, showed the "gap effect" reduction in latency (Saslow, 1967) when compared with step-task data (Monkey 1 prosaccade, mean difference, 6 ms; antisaccade, mean difference, 20 ms; Monkey 2 prosaccade, mean difference, 22 ms; antisaccade, mean difference, 26 ms). However, within the subset of prematurely triggered movements (encircled in ellipse), the latency of movements was not statistically different between the gap and step tasks (t test, $p > 0.05$). Thus, the earliest a saccade can be evoked by the blink perturbation was similar for step and gap tasks, effectively eliminating the gap effect. This result provides a lower limit on how quickly sensory information can be transformed into motor action and that the time course of motor preparation overlaps with attentional allocation. As in the step task, the majority of early blink-triggered saccades was directed to the singleton (Monkey 1 prosaccade, 88%; antisaccade, 86%; Monkey 2 prosaccade, 91%; antisaccade, 90%) (Fig. 6B). With increasing latencies, the blink-triggered saccade transitioned to the opposite distractor in antisaccade trials and remained at the singleton on prosaccade trials, characteristics consistent with the predictions of PMTA (Fig. 2C).

In the delay-task version, the central fixation target remains illuminated when the search array is presented. The animal is required to maintain fixation of the central target until it is extinguished, which serves as the cue to initiate the movement. We predict that the search array is processed and the correct movement is planned during the overlap period. Thus, when a blink is evoked after the saccade initiation cue, all blink-triggered movements should be directed to the correct location. In other words, we did not expect to observe erroneous movements to the singleton during antisaccade trials. Indeed, the distribution of saccade latency as a function of blink time resembled that observed for the
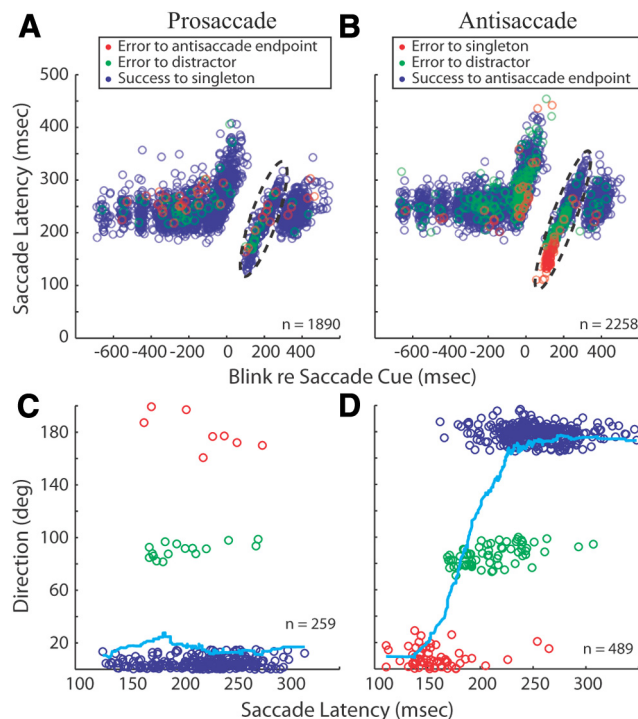
Figure 6. Effects of blinks during visual search in the gap-task. *A*, *B*, Saccade latency is plotted as a function of occurrence of blink relative to saccade cue for prosaccade (*A*) and antisaccade (*B*) trials. Blink-triggered saccades are denoted by points within the dotted ellipses. *C*, *D*, The directions of these blink-triggered saccades are plotted as a function of saccade latency for prosaccade (*C*) and antisaccade (*D*) trials. For prosaccade data (left), each blue point represents a successful trial to the singleton, red a failure to the antisaccade end point, and green a failure to one of the orthogonal distractors. For antisaccade trials (right), each blue dot represents a successful trial to the antisaccade end point, red a failure to the singleton, and green a failure to one of the orthogonal distractors. The cyan line illustrates a moving average across saccade latency (bin size, 30 ms). The eye position at the end of the primary saccade relative to the initial eye position (close to origin) was used to calculate the direction metric for each trial. Data from only one monkey are shown. Data from second animal were similar.

step task (compare Figs. 3, 7*A*,*B*), but nearly every movement was directed to the correct end point target for both prosaccade and antisaccade trials (compare Figs. 4, 7*C*,*D*). The error rate was <2%. [Note that blinks delivered during the overlap period are not effective in triggering saccades in trained animals, even when only one saccade target is illuminated (Gandhi and Bonadonna, 2005) (also see Discussion).]

Discussion

Visual search for a pop-out stimulus embedded among distractors automatically engages visuospatial attention to the singleton, generally followed by directing a saccade to that stimulus. By adopting a flexible stimulus–response mapping, we have the ability to direct the saccade to another location, such as the opposite distractor (antisaccade trials), although it comes at a cost of longer latency. This task variant is well suited to test whether processes defined as visuospatial attention and saccade preparation are dissociated. Invoking the blink reflex at random times within a trial revealed that a motor plan exists well before the typical reaction time and as early as the epoch associated with allocation of attention. For antisaccade trials, the earliest saccades were directed to the singleton, and a transition to the opposite distractor was observed only at longer latencies. For the prosaccade trials, the blink-triggered saccades were directed to the singleton. These findings are most readily consistent with the postulates of PMTA (Riz-
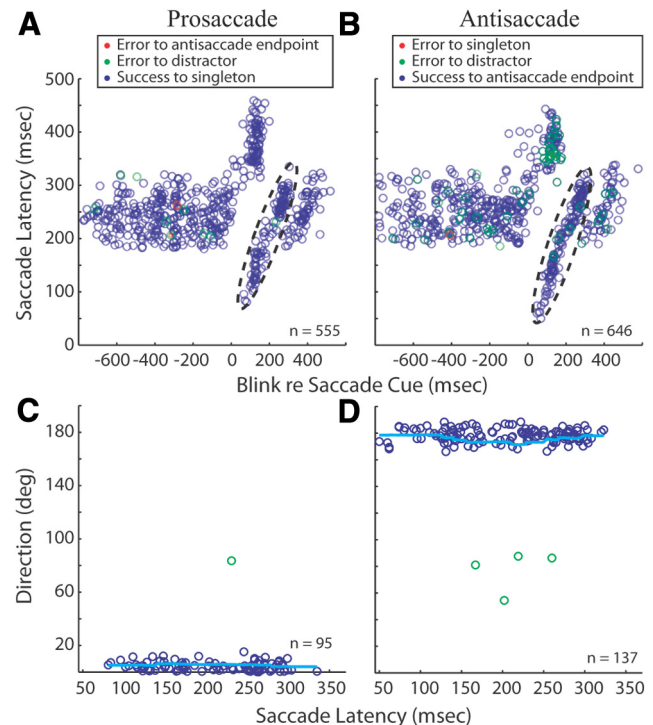
Figure 7. Effects of blinks during visual search in the delay task. Data collected from one animal performing the delayed saccade variant of the search task are shown in exactly the same format as in Figure 6. For prosaccade data (left), each blue point represents a successful trial to the singleton, red a failure to the antisaccade end point, and green a failure to one of the orthogonal distractors. For antisaccade trials (right), each blue dot represents a successful trial to the antisaccade end point, red a failure to the singleton, and green a failure to one of the orthogonal distractors. The cyan line illustrates a moving average across saccade latency. The eye position at the end of the primary saccade relative to the initial eye position (close to origin) was used to calculate the direction metric for each trial. Note the dearth of saccades to the singleton during antisaccade trials. Data from second animal were similar.

zolatti et al., 1987; Hoffman and Subramaniam, 1995; Kowler et al., 1995; Deubel and Schneider, 1996) and argue against a discrete and sequential processes model (Sternberg, 2001; Woodman et al., 2008; Schall et al., 2011; Purcell et al., 2012).

Role of blink perturbation

The saccadic system is potently inhibited by "gates" or neurons that discharge at a tonic rate during fixation and suppress activity during saccades. Examples include the OPNs (Keller, 1974; Evinger et al., 1982; Everling et al., 1998; Gandhi and Keller, 1999), neurons in the substantia nigra (Hikosaka and Wurtz, 1983), the rostral region of the superior colliculus (SC) (Munoz and Wurtz, 1993), lateral intraparietal region (LIP) (Ben Hamed and Duhamel, 2002), and FEF (Hanes et al., 1998; Izawa et al., 2009). When we blink during fixation, the eyes produce a small loopy movement, and the OPNs and rostral SC neurons pause in association with the movement (Schultz et al., 2010; Jagadisan and Gandhi, 2013), while the effects of blinks on gate neurons in the basal ganglia and cortex are not known. Our working hypothesis has been that if the blink is evoked before the average reaction time in oculomotor tasks, the premature inhibition of gates would facilitate the early execution of saccades if the underlying activity in the oculomotor neuraxis encodes a premotor signal. The results presented here conform to this prediction. Interestingly, blinks evoked before the saccade cue do not trigger a movement even when the stimulus location is known (delay task; Fig. 7). A likely interpretation of this result is that motor preparation

signals continue to be encoded in the prelude activity within the oculomotor neuraxis, but that the blink operates only on low-level gates (OPNs, rostral SC) and cannot overcome higher-level gates. That the correct movement is both known to the animal and planned during the overlap period of the delayed saccade task is suggested by the lack of blink-triggered saccades to the singleton in antisaccade trials (Fig. 7B,D).

Concurrent encoding of visuospatial attention and saccade preparation

The ability of blinks to trigger saccades early after array onset indicates that target selection and motor preparation occur concurrently. Of the various types of cells found in oculomotor structures, visuomotor neurons are well suited candidates to encode both processes. The neural activity exhibits selectivity for the singleton in the epoch associated with target selection and also before saccades directed in the movement field. For the majority of neurons in the SC (McPeek and Keller, 2002; Shen et al., 2011) and area LIP (Thomas and Paré, 2007), the selectivity of visuomotor neurons for the singleton varies with reaction time, suggesting a contribution in motor programming. In contrast, the neural discrimination times of most FEF visuomotor neurons are best aligned with array onset, consistent with a role in target selection (Thompson et al., 1996). Additional support for a distinction between the two processes also comes for neural activity recorded during other behavioral tasks (Murthy et al., 2001; Thompson et al., 2005; Ray et al., 2009). Proponents of the discrete processes model have suggested that visuomotor neurons play a crucial role in ascending pathways, sending corollary discharge information from the SC to FEF (Sommer and Wurtz, 2002) and FEF to V4 (Moore and Armstrong, 2003). However, it is difficult to discount their role in motor processing and movement generation since they also project to the brainstem burst generator (Segraves, 1992; Rodgers et al., 2006). Moreover, if one views the circuitry encompassing the FEF, SC, and LIP as an interconnected network void of hierarchical organization (Wurtz et al., 2001), then each class of neurons should perform comparable functions across regions.

Although we favor the conservative interpretation that visuomotor neurons are ideally suited to encode both visuospatial attention and saccade preparation, do the observed behavioral results discount the possibility that the two processes are encoded concurrently but by different populations of neurons? If the visually responsive activities in visual and visuomotor neurons encode target selection, then motor neurons are the candidate cells to reflect saccade preparation. To the best of our knowledge, there is no published account of neural activity of motor neurons in any structure during antisaccade trials in the context of a visual search paradigm. Hence, we can only speculate. It is feasible that low-frequency discharge accumulates in multiple motor neuron ensembles, each preparing a movement to the stimulus in its receptive field. Within an interconnected network, the temporal and spatial distribution of motor activity in each population could be developing concurrently with target selection, all the while being continuously updated by the progression of attention related signals in the visually responsive activity. At a conceptual level, this mechanism is suggestive of a framework not compatible with the PMTA because visuomotor and motor neurons are classified in distinct categories. In reality, however, visuomotor and motor neurons conform to a continuum, which would render the notion compatible with the PMTA.

Despite the suggestion that the blink perturbation unmasks an underlying premotor signal, can the pattern of neural activity linked with a discrete processes model account for the observed behavioral result? Using a stochastic accumulator architecture, which has been influential in simulating dynamic discharge profiles and reaction time distributions among alternative actions (Usher and McClelland, 2001; Wang, 2002), Purcell et al. (2010, 2012) implemented discrete target selection and motor preparation processes by gating or delaying accumulation of activity in motor neurons until competition among visually responsive neurons corresponding to each stimulus was resolved. In light of our results, several assumptions and fast dynamics would be required to rescue the model. The blink perturbation must somehow terminate the ongoing target selection process, perhaps by releasing the gates that delay accumulation in motor neurons, and also initiate and accelerate the movement plan to the current locus of attention, almost instantaneously or within a few milliseconds. The PMTA, in contrast, offers a more conservative and straightforward explanation. Nonetheless, additional studies focusing on the activity patterns in motor neurons during blink perturbations are needed to better differentiate between PMTA and discrete processes constructs. We might discover, for example, that activity in visuomotor neurons may be a better index of motor preparation and generation than motor neurons to account for blink-triggered saccades.

Previous studies of visuospatial attention and motor preparation

Causal approaches have also been used to obtain a behavioral readout of the premotor component, mainly by delivering microstimulation during various oculomotor tasks (Kustov and Robinson, 1996; Gold and Shadlen, 2000; Horwitz et al., 2004; Juan et al., 2004; Schafer and Moore, 2007; Ramakrishnan et al., 2012) or briefly flashing visual targets (distractors) before or during saccades directed to another stimulus (Walker et al., 1997; Godijn and Theeuwes, 2002; McSorley et al., 2004; van Zoest et al., 2008; Viswanathan and Barton, 2013). A drawback of both approaches is that they recruit a population of neurons that mechanistically must integrate or compete with the activity associated with the various stimuli. Such interactions could mask or inhibit processes that occur naturally during the task (Dorris et al., 2007), and therefore could suppress the underlying premotor signal. This mechanism can explain why a premotor signature for the singleton was not observed with suprathreshold FEF microstimulation during visual search antisaccade trials (Juan et al., 2004). The blink perturbation method, in contrast, does not recruit an additional population of neurons that can mask the target-related activity (Goossens and Van Opstal, 2000a), and this approach does reveal a premotor component in the same epoch associated with target selection.

Previous psychological studies (Smith et al., 2004, 2012; Smith and Schenk, 2012), backed by a theoretical basis (Schneider, 1995; Schneider and Deubel, 2002), propose that motor preparation is linked to exogenous, but not endogenous, attention. In the pop-out visual search array, the singleton certainly engages exogenous attention initially, and blink-triggered saccades to the singleton support this idea. However, endogenous attention must be invoked to switch visual selection to the opposite target (Theeuwes, 2010; Markowitz et al., 2011) before the motor preparation process can be initiated. We sampled blink times across the entire timeline of the paradigm and did not encounter any epochs after the attention allocation period during which blinks failed to trigger a saccade. Thus, the results are not entirely consistent with a differential relationship of motor preparation with top-down and bottom-up attention systems. Others have argued against the

dichotomy of exogenous and endogenous attention concepts (Awh et al., 2012) and instead suggested that motor preparation is engaged during spatial shifts of attention, but not when attention is maintained at the same locus (Belopolsky and Theeuwes, 2009, 2012). While the inability of blinks to trigger saccades during the overlap period is consistent with this premise, the lack of blink-triggered saccades immediately after array onset, when attention shifts to the singleton during the overlap period, is not.

Evidence for the PMTA is also available beyond the oculomotor system. Electromyographic activity time locked to target onset has been reported in neck and arm muscles during reactive behaviors (Corneil et al., 2004; Pruszynski et al., 2010) and in neck muscles during shifts in covert orientation (Corneil et al., 2008). Also, cortical mirror neurons that respond to action observation project through the pyramidal tract (Kraskov et al., 2009; Vigneswaran et al., 2013), indicating that they relay premotor information to the spinal cord even when no movement is produced; a suppressive mechanism likely occurs at the level of the spinal cord to prevent muscle recruitment. It is yet another demonstration of a motor command that is prepared but not executed. Thus, both oculomotor and skeletomotor circuits are likely engaged concurrently with visuospatial attention and other cognitive processes.

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