Context Cue Dependent Saccadic Adaptation in Rhesus Macaques Cannot Be Elicited Using Color

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Abstract

When the head does not move, rapid movements of the eyes called saccades are used to redirect the line of sight. Saccades are defined by a series of metrical and kinematic (evolution of a movement as a function of time) relationships. For example, the amplitude of a saccade made from one visual target to another is roughly 90% of the distance between the initial fixation point ($T_0$) and the peripheral target ($T_1$). However, this stereotypical relationship between saccade amplitude and initial retinal error ($T_1-T_0$) may be altered, either increased or decreased, by surreptitiously displacing a visual target during an ongoing saccade. This form of motor learning (called saccadic adaptation) has been described in both humans and monkeys. Recent experiments in humans and monkeys have suggested that internal (proprioceptive) and external (target shape, color, and/or motion) cues may be used to produce context dependent adaptation. We tested the hypothesis that an external contextual cue (target color) could be used to evoke differential gain (actual saccade/initial retinal error) states in rhesus monkeys. We did not observe differential gain states correlated with target color regardless of whether targets were displaced along the same vector as the primary saccade or perpendicular to it. Furthermore, this observation held true regardless of whether adaptation trials using various colors and intrasaccade target displacements were randomly intermixed or presented in short or long blocks of trials. These results are consistent with hypotheses that state that color cannot be used as a contextual cue and are interpreted in light of previous studies of saccadic adaptation in both humans and monkeys.

Introduction

Saccades have been frequently studied in an attempt to uncover the neural mechanisms underlying the maintenance of movement accuracy and precision. Furthermore, saccades have been frequently used to study the ability of primates to pair arbitrary sensory stimuli (e.g. a visual object’s color, shape, orientation, and/or motion properties) with a specific motoric response (for reviews see: Hopp & Fuchs, 2004; Iwamoto & Kaku, 2010; Pélisson, Alahyane, Panouillères, Tilikete, 2010; Herman, Blangero, Madelain, Khan, Harwood, 2013; Liversedge, Gilchrist, & Everling, 2011; Gold & Shadlen, 2007; Shadlen & Kiani, 2013). Saccades are rapid, conjugate eye movements that may be used to reorient the line of sight such that the high-resolution region of the retina (the fovea) can be aligned with objects of interest (Leigh & Zee, 1999). Primate saccades are defined by a series of stereotypical metrical relationships between amplitude, peak velocity, and duration (Bahill, Clark, & Stark, 1975; Baloh, Sills, Kumley & Honrubia, 1975; vanGisbergen, Van Opstal, & Ottes, 1984) and primary saccade gain (movement amplitude/initial retinal error) is approximately 0.90-0.95 (Hyde, 1959; Becker & Fuchs, 1969; Becker, 1972; Henson, 1978, 1979; Prablanc, Masse, and Echallier, 1978; Kowler & Blaser, 1995). Modifications to these relationships may result from neuromuscular disease (Leigh & Zee, 1999) or, in the case of saccade gain, by experimental manipulations.

Under laboratory conditions, motor learning in the saccadic system (“saccadic adaptation”) has mostly been studied by surreptitiously introducing a visual error at the
end of a saccade that was aimed at a target located at a particular vector (magnitude and direction) relative to where the subject was fixating (Albano, 1996; McLaughlin, 1967; Deubel, 1987, 1991; Deubel, Wolff, & Hauske, 1986; Miller, Anstis, & Templeton, 1981; Noto, Watanabe, Fuchs, 1999; Robinson, Noto, & Bevans, 2003; Scudder, Batournia, & Tunder, 1998; Semmelow, Gauthier, & Vercher, 1987; Straube, Fuchs, Usher, Robinson, 1997). Under these circumstances: 1) changes in primary saccade amplitude follow a roughly exponential time course with “rate constants” around 30–60 saccades in humans (Albano, 1996; Deubel et al, 1986; Deubel, 1987) and 100-800 saccades in monkeys (Straube et al, 1997); 2) the change in primary saccade gain is appropriate to reduce the visual error induced at the end of the movement, but is rarely large enough to consistently place the fovea on the location of the target after it was displaced during the saccade; 3) the magnitude of backward adaptation is larger than forward adaptation in response to the same post-saccadic visual error (Straube et al, 1997); 4) adaptation effects transfer to saccades with vectors similar to those initially adapted (“adaptation fields”; Noto et al, 1999); and 5) a corrective movement is not necessary for learning to progress (Wallman & Fuchs, 1998), which indicates that a visual error signal is sufficient enough to drive this form of motor learning.

There has recently been a great deal of interest in “context dependent” saccadic adaptation (see Péllisson et al, 2010, Herman et al, 2013 for reviews). In this type of experiment a cue, either internal (e.g. proprioceptive feedback of eye position) or external (e.g. visual target properties), is used during and after the learning process to elicit different gain states. For example, Alahyane & Péllisson (2004) have shown that human horizontal saccade amplitude can be simultaneously reduced and increased to the same initial target displacement ($T_1$-$T_0$) depending upon the vertical orbital eye position (either 12.5° up or 25° down) at which a subject initiates the primary saccade. On the other hand, differential changes in saccade gain based on eye position have proven difficult to elicit in rhesus monkeys under similar conditions (Figures 2 & 8 in Tian & Zee, 2010).

The use of external visual cues to drive different gain states during saccadic adaptation has led to a mixture of results in human subjects. Deubel (1995), in a few human subjects, was unable to elicit distinct gain states during horizontal adaptation using colored, static targets (red crosses and green circles) that were displaced by a few degrees of visual angle along the same axis as the primary saccade. Subsequent investigations of human saccadic adaptation were also unable to elicit context dependent adaptation using either static shapes (diamonds versus squares; Bahcall & Kowler, 2000) or moving visual targets with different shapes and colors (Azadi & Harwood, 2014). However, other explorations of saccadic adaptation have shown that visual cues such as flickering versus non-flickering targets (Herman et al., 2009), yellow squares versus green circles (Madelain et al., 2010), and other properties of moving targets (speed and direction) (Azadi & Harwood, 2014) can be used to elicit different gain states.

Given the different behaviors of human subjects in context cue adaptation experiments using different visual stimuli, and the potential for monkeys to have different behavior to the same stimuli that elicited context dependent adaptation behavior in humans, we designed the current study to test the hypothesis that color can be used as a contextual cue in a saccade adaptation task. Although our results concur
with those observations made by Deubel (1995) and Azadi & Harwood (2014), our experiments provide a more extensive data set to support the assertion that the saccadic adaptive control system does not differentiate between color targets of the same shape. These data are interpreted in the light of previous context dependent adaptation studies.

Materials and Methods

All procedures were approved by the Institutional Animal Care and Use Committee of the University of Pittsburgh and were in compliance with the guidelines set forth in the United States Public Health Service Guide for the Care and Use of Laboratory Animals. Three male rhesus monkeys (BB, BU, & WE) weighing 7.0 -13.0 kg served as subjects. Each monkey had a small head-restraint device secured to the skull during an aseptic surgery. In an additional aseptic surgery, monkeys BB and BU had a scleral coil implanted for monitoring gaze position (Judge et al. 1980). After full recovery, each animal was trained to sit in a primate chair with their head restrained and a sipper tube was placed near the mouth for reward delivery. Subjects were subsequently trained to make gaze shifts to visual targets, but were not used for adaptation studies prior to their participation in the current series of experiments.

For monkeys BB and BU, visual stimuli, behavioral control, and data acquisition were controlled by a custom-built program that uses LabVIEW architecture on a real-time operating system supported by National Instruments (Austin, TX) (Bryant and Gandhi 2005). These animals sat inside a frame containing two alternating magnetic fields that induced voltages in the eye coil and thus permitted measurement of horizontal and vertical eye positions (Robinson 1963). Visual targets were displayed on a 55 inch, 120 Hz resolution LED monitor. For monkey WE, eye movements were monitored using an eye tracker (Eye Link 1000, SR Research Ltd, Mississauga, Ontario, Canada) and visual targets were presented on a 21 inch, 100 Hz resolution CRT monitor.

General Chronology of Experimental Sessions, Trial Types, and Reward Criterion

Every adaptation session had at least three phases that occurred in the following chronological order: 1) a “pre-adaptation phase” in which only probe trials were presented; 2) an “adaptation phase in which only adaptation trials were presented; and 3) a “post-adaptation phase” in which only probe trials were presented. Both probe and adaptation trials (Figure 1A, B) began with the illumination of an initial fixation target \(T_0\). Subjects were required to look at and maintain fixation of \(T_0\) for a variable duration (500-1000ms, 50 or 100ms increments). Trials were aborted if the line of sight deviated beyond a computer-defined window (3° radius) surrounding \(T_0\). However, if fixation was maintained, a peripheral target \(T_1\) was illuminated. \(T_0\) and \(T_1\) overlapped between 0 to 750ms in 250ms increments. If the subject continued to maintain fixation of \(T_0\) for the duration of this overlap period, then \(T_0\) was extinguished, cuing the animal to make a saccade to \(T_1\). To this point both probe and adaptation trial types were identical. During “probe” trials (Figure 1A), \(T_1\) remained illuminated until the position of the line of sight exited the computer window centered on the location of the no longer visible \(T_0\). \(T_1\) was
turned off after the line of sight crossed this position criterion during probe trials; therefore, no visual feedback was available on these trials. “Adaptation” trials (Figure 1B) were similar to probe trials except that after $T_1$ was extinguished, a target ($T_2$) was immediately illuminated in a new spatial location. The new location could be further away from (forward adaptation) or closer to (backward adaptation) $T_0$ along the horizontal meridian during trials attempting to elicit adaptation of the horizontal component of the primary saccade vector (Figure 1C). In experiments attempting to elicit changes in the vertical component of the primary saccade vector, targets could be displaced above (upward adaptation) or below (downward adaptation) the horizontal meridian (Figure 1D). The latter experiments are hereafter referred to as “orthogonal adaptation” experiments. Lastly, note that the horizontal direction (left or right) of the primary saccade during adaptation trials was pseudorandomly alternated between sessions.

During the preadaptation phase, the locations of $T_1$ always included the $T_1$ used during adaptation trials and typically the $T_2$ locations and a target location that would evoke a primary saccade in the direction opposite that produced during adaptation trials (for specific examples of targets, see Hypotheses, Predictions, and Experimental Session Subtypes below). Subjects were rewarded for entering a window surrounding $T_1$ that had a radius of $6^\circ$ and remaining in the window for a minimum of 250ms. During the adaptation phase, the reward window associated with $T_1$ was elliptical, centered on a location between $T_1$ and $T_2$, and enlarged such that it encompassed and extended beyond these targets by $\sim 5^\circ$. The reward window associated with the $T_1$ used during adaptation trials remained enlarged during the post-adaptation probe phase and subjects needed to maintain fixation within this window for a minimum of 250ms in order to be rewarded. The reward criterion for other $T_1$ locations during the post-adaptation phase was the same as that used during the pre-adaptation phase.

In each of our color cue experiments, the targets ($T_0$, $T_1$, $T_2$) were red, green, or yellow dots subtending $\sim 1^\circ$ of visual angle. Target color remained constant within a given trial and trials using a particular color were randomly intermixed throughout all phases of the experiment. Therefore, during adaptation trials, the fixation point color could indicate forward (green) or backward (red) adaptation. Target locations during probe and adaptation trials remained fixed within a data collection session.

The exact number of probe trials during the pre- and post-adaptation epochs varied depending upon the number of colors used in a given experiment (one versus three), the type of experiment and thereby the number of potential $T_1$ and $T_2$ locations used during adaptation trials, and the willingness of the subject to sustain effort for long periods during the post-adaptation phase. Furthermore, we attempted to keep the length of the adaptation phase relatively constant across experimental sessions such that the subject experienced 450 or more adaptation trials per condition (900+ adaptation trials total per session). Hence, the duration of the adaptation phase was relatively constant across sessions within a subject.

Data Acquisition and Analysis
For both animals, each trial was digitized and stored on the computer’s hard disk for offline analysis in MATLAB (R2013b; Natick, Massachusetts, U.S.A). Horizontal and vertical eye positions were stored with a resolution of 1ms. Component velocities were obtained by differentiating the eye position signals. The onset and offset of saccades were identified using a velocity criterion of 40°/second. Saccade amplitude was defined as the change in eye position from the beginning to end of the eye movement based on this velocity criterion. All of the data reported here are the result of measuring the first (“primary”) saccade made towards T1 that was associated with the adaptation trials for a particular session. This has traditionally been used to assess the subject’s motoric state at various time points during adaptation experiments (see Hopp & Fuchs (2004) for review). The primary saccade needed to occur within 500ms after the offset of T0 and have a horizontal amplitude greater than 5° in order to be considered for further analysis.

Saccade gain was defined by the following formula:

\[
\text{Saccade Gain} = \frac{\text{Saccade Amplitude}}{T1-\text{Initial Eye Position}}
\]

By definition a saccade with a gain that is less than 1.0 is hypometric whereas a saccade with a gain greater than 1.0 is hypermetric. During color context cue experiments, trials were then parsed based on whether the target color within a trial was red, green, or yellow. For each color, the average gain or amplitude of saccades made during all pre-adaptation phase probe trials using the T1 that was used during adaptation trials (“pre-probe trials”) was compared with average of an equal number of probe trials presented after a particular adaptation segment (“post-probe” trials). Across all color cue experiments, the mean (±SD) number of pre- and post-adaptation trials used for comparison was 22.9 ± 6.0 (range = 12:42) and was not different across colors (green = 22.9±6.1; yellow = 23.2±6.2; red = 22.1± 5.6; p = .8106 Kruskal-Wallis test). The difference between pre- and post-adaptation means for a given color within an experimental session was compared using a Wilcoxon rank sum test. A Kruskal-Wallis test was used to assess the effect of color on gain across multiple sessions. All tests were done in the MATLAB Statistical Toolbox; significance was determined using a Bonferroni corrected p-value (p < 0.0167) in the case where three means were compared.

**Hypotheses, Predictions, and Experimental Session Subtypes**

During saccadic adaptation, a sensory signal can be considered a contextual cue if at least two different gain states are elicited based on that cue (Alahyane & Pelisson, 2004; Herman et al, 2009; Tian & Zee, 2010). Experiments detailed in the current report were designed to test the hypothesis that a target’s color could act as a contextual cue. This hypothesis predicts that saccade gain changes between the pre- and post-adaptation phases within experimental sessions will be dependent upon the retinal error associated with adaptation trials that use different colored targets. During the adaptation phase of our horizontal adaptation experiments, red targets were associated with retinal errors that typically elicit gain-decreases and green targets were
associated with retinal errors that typically elicit gain-increases. The aforementioned hypothesis would be supported by results showing that gain of post-adaptation probe trials relative to pre-adaptation probe trials are consistently smaller for saccades to red targets and larger for saccades to green targets. Furthermore, probe trials using colors not associated with persistent retinal errors during the adaptation phase (e.g. yellow) should elicit similar gain states between the pre- and post-adaptation phases. The null hypothesis in our study states that any change in gain between the pre- and post-adaptation phases of a given experiment will not be dependent upon target color. We tested these predictions using the following types of experiments and describe the specific outcomes based the aforementioned general hypotheses in each case:

1) Horizontal Intermixed Color Experiments

During horizontal intermixed color experiments, the fixation target ($T_0$) was fixed at (-10º, 0º) in some sessions and at (10º, 0º) in other sessions. As illustrated in Figure 1C, if a subject began horizontal adaptation trials by fixating a $T_0$ located at (-10º, 0º), then $T_1$ during these trials was always located at (8º, 0º). $T_2$ could be located at (-1º, 0º) or (17º, 0º) during horizontal backward (red targets) and forward (green targets) adaptation trials, respectively. The difference between $T_1$ and $T_2$ was always 9º during horizontal adaptation experiments. The mirror images (as reflected through the ordinate) of these targets were used during adaptation trials that began at (10º, 0º). For simplicity, we will describe the remaining experiments and portray data in our figures as if all trials began with the $T_0$ located at (-10, 0). During horizontal intermixed color experiments, if color can be used as a contextual cue, then saccade gain during post-adaptation probe trials should be significantly smaller for trials using red targets and larger for trials using green targets relative to matched color probe trials in the pre-adaptation phase. However, if gain does not change between the pre- and post-adaptation phases or a significant gain change occurs in same direction regardless of target color, then color does not act as a contextual cue.

2) Backward-Null Color Intermixed

Backward- null adaptation sessions used the same $T_0$ and $T_1$ as horizontal color intermixed experiments and the $T_2$ during red trials (backward) was also located at (-1º, 0º). However, during green “adaptation” trials, the target remained lit at the $T_1$ for the duration of the trial. As with the horizontal intermixed color experiments, trials using a particular color were randomly intermixed throughout all phases of the experiment. During these experiments, if color can be used as a contextual cue, then saccade gain during post-adaptation probe trials should be significantly smaller for trials using red targets and remain constant for trials using green targets relative to matched color probe trials in the pre-adaptation phase. However, if gain does not change between the pre- and post-adaptation phases or a significant gain change occurs in same direction regardless of target color, then color does not act as a contextual cue.
3) **Orthogonal Color Intermixed**

Orthogonal adaptation sessions used the same \( T_0 \) and \( T_1 \) as horizontal experiments. However, during these sessions \( T_2 \) was located either 9° above (green targets) or below (red targets) \( T_1 \) during upward and downward adaptation trials, respectively (Figure 1D). As with the horizontal intermixed experiments, trials using a particular color were randomly intermixed throughout all phases of the experiment. During these experiments, if color can be used as a contextual cue, then the vertical component of saccades during post-adaptation probe trials should be deviated significantly downward for trials using red targets and upward for trials using green targets relative to matched color probe trials in the pre-adaptation phase. However, if the vertical component does not change between the pre- and post-adaptation phases or a significant change in the vertical component occurs in the same direction regardless of target color, then color does not act as a contextual cue.

4) **Backward-Upward Color Intermixed Experiments**

Backward-upward color intermixed sessions used the same \( T_0 \) and \( T_1 \) as horizontal experiments. However, during these sessions \( T_2 \) was located either 9° above [(8, 9), green targets] or closer to the initial fixation point [(-1,0), red targets]. As with the horizontal intermixed experiments, trials using a particular color were randomly intermixed throughout all phases of the experiment. During these experiments, if color can be used as a contextual cue, then the vertical component of saccades during post-adaptation probe trials should be significantly deviated upward for trials using green targets and the horizontal component should be significantly smaller relative to matched color probe trials in the pre-adaptation phase. However, if there is not a change in these components between the pre- and post-adaptation phases or a significant change in the vertical and horizontal components occur in same direction regardless of target color, then color does not act as a contextual cue.

5) **Horizontal Short and Long Block Color Experiments**

Previous context cue adaptation experiments (e.g. Herman et al, 2009; Tian & Zee, 2010) have suggested that presenting short, alternating blocks of trials with each cue can aid the progression of context dependent adaptation. The target locations (\( T_0 \), \( T_1 \), \( T_2 \)), pre- and post-adaptation phases during our block color experiments were identical to those used during the horizontal intermixed color experiments described above. However, during the adaptation phase of short block experiments, red (backward) and green (forward) adaptation trials were presented in alternating blocks of approximately thirty trials. In long block (or sequential) experiments, a “red adaptation only” phase consisting of approximately 600 trials was followed by a “green adaptation only” phase of approximately the same length. Note also that a brief (~30 trials) “red only probe” phase occurred between these two adaptation epochs in the sequential
experiments. The predictions of our hypotheses for these block experiments were identical to those of the horizontal intermixed color experiments.

6) **White Target Experiments**

Horizontal and backward-null intermixed experiments using white targets subtending ~1° of visual angle were used to assess our subjects’ motoric output without the potential for color as a contextual cue. The target locations, trial types, and epoch sequence were the same as the horizontal intermixed and backward-null color experiments mentioned above. Note that if a differential gain state can be elicited using color and these changes are color dependent, then we should observe no differential gain states in the white target experiments. Furthermore, if color cannot be used as a contextual cue in the color experiments, then we should observe the same change in gain as we observed in the color cue experiments.

7) **Initial Eye Position Short Block Experiments**

Initial eye position (IEP) context cue experiments were patterned off of those previous reported by Tian & Zee (2010). The same targets used during white target experiments were used during our IEP experiments, which means the only contextual cue available to the subject was the eye position at saccade onset. Similar to the aforementioned color and white target experiments, the primary saccade direction could be leftward or rightward in any given experiment; however, all data are portrayed as if saccades were rightward. Furthermore, backward or forward adaptation could occur in a given session from either of the vertical eye positions (±10°); however, all data are portrayed and hypotheses are discussed as if backward adaptation trials always occurred when saccades were initiated from the downward eye position and all forward adaptation trials occurred when saccades were initiated from the upward eye position. Lastly, the horizontal distance between the T0, T1, and T2 locations during IEP experiments was the same as that used during the aforementioned horizontal color cue and white target control experiments (T1-T0 = 18°; T2-T1 = ± 9°).

During the pre-adaptation phase of IEP experiments, subjects performed only probe trials whose T0 locations, and therefore IEP, varied randomly. The adaptation phase consisted of alternating blocks of ~30 adaptation trials. All trials within a block were initiated from a single T0 position, which meant that vertical eye position was kept roughly constant within a given block. The post-adaptation phase consisted of two blocks of ~30 probe trials in which IEP was held constant. In line previous reports (Alahyane & Pélisson, 2004; Tian & Zee, 2010), if IEP can be used as a contextual cue under these circumstances, then post-adaptation probe trials relative to pre-adaptation probe trials should have a smaller horizontal gain when initiated from the downward IEP and larger horizontal gain when saccades initiated from the upward IEP. If IEP is not a robust contextual cue, then horizontal should not change or change in the same direction from both eye positions.
Results

Horizontal Intermixed Color Experiments

Figure 2A portrays data from a horizontal intermixed color experiment (BBHI3). During the pre-adaptation phase of this experiment the mean (± SD) gain of primary saccades made to T₁ was similar regardless of color (green = 0.92 ± 0.03; red = 0.90 ± 0.05; yellow = 0.91 ± 0.03). Qualitatively, saccade gain during red (backward) and green (forward) adaptation trials did not change during the adaptation phase and saccade gain during probe trials executed in the post-adaptation phase was similar to the pre-adaptation phase (post-probe green = 0.90 ± 0.04; red = 0.88 ± 0.05; yellow = 0.89 ± 0.04). In fact, saccade gain did not change significantly for any of the colors between the pre- and post-adaptation phases (p<0.016, Bonferroni corrected Wilcoxon rank sum test).

Figure 2B portrays data from another horizontal intermixed color experiment (WEHI4). During the pre-adaptation phase of this experiment the mean (± SD) gain of primary saccades made to T₁ was similar regardless of color (green = 0.93 ± 0.03; red = 0.94 ± 0.04; yellow = 0.93 ± 0.03). In contrast to the previous example (Figure 2A), saccade gain during red (backward) and green (forward) adaptation trials increased during the adaptation phase resulting in post-adaptation probe trials that were larger than those in the pre-adaptation phase (post-probe green = 0.99 ± 0.03; red = 1.01 ± 0.04; yellow = 1.01 ± 0.05; p<0.0001, Bonferroni corrected Wilcoxon rank sum test).

The histogram in Figure 2C provides the mean (± SD) change in gain between pre- and post-adaptation probe trials for each color across all 12 experimental sessions (Monkey BB: n= 5, WE: n= 5, BU: n= 2). In 5/12 experiments (42%) saccade gain did not change between pre- and post-adaptation epochs for any of the colors. In 5 of the remaining experiments, gain values for at least two colors changed significantly; however, note that gain changes were always in the same direction in these experiments. Lastly, the histogram plot in Figure 2D summarizes the change in saccade gain between pre- and post-adaptation probe trials for each color across all 12 horizontal intermixed color experiments. In brief, the change in saccade gain was not different between colors (p = 0.7527, Kruskal-Wallis test) nor were any of the changes in gain different than zero (green p-value = 0.2334; yellow p = 0.0522; red p = 0.2744; Wilcoxon signed rank test).

Horizontal Intermixed White Target Experiments

Figure 3A portrays data from a horizontal intermixed white target experiment (BBWTHI1). During the pre-adaptation phase of this experiment the mean (± SD) gain of primary saccades made to T₁ was 0.96 ± 0.04. Qualitatively, saccade gain during backward (black triangles) and forward (gray triangles) adaptation trials did not change during the adaptation phase and saccade gain during probe trials executed in the post-adaptation phase was similar to the pre-adaptation phase (post-probe gain = 0.95 ± 0.05; p = 0.3711, Bonferroni corrected Wilcoxon rank sum test).
In contrast, Figure 3B portrays data from another horizontal intermixed white target experiment (BBWTHI3) in which saccade gain changes between the pre- and post-adaptation phases. During the pre-adaptation phase of this experiment the mean (± SD) gain of primary saccades made to $T_1$ was $0.92 ± 0.06$. Qualitatively, saccade gain during backward (black triangles) and forward (gray triangles) adaptation trials increased slightly during the adaptation phase resulting in a post-probe saccade gain that was larger than the pre-adaptation phase (post-probe gain = $0.97 ± 0.06$; $p = 0.0029$, Bonferroni corrected Wilcoxon rank sum test).

The histogram in Figure 3C provides the mean (± SD) change in gain between pre- and post-adaptation probe trials across all 11 experimental sessions (Monkey BB: $n= 3$, WE: $n= 5$, BU: $n= 3$). In 5/11 experiments (45%) saccade gain changed between pre- and post-adaptation epochs and this change tended to be an increase (4/5 experiments). However, as with the horizontal intermixed color experiments described above, the change in gain across all 11 experiments (Figure 3D) was not different from zero ($p = 0.1748$, Wilcoxon signed rank test).

**Backward-Null Intermixed Color Experiments**

Figure 4A portrays data from a horizontal backward-null intermixed color experiment (BBNS2). During the pre-adaptation phase of this experiment the mean (± SD) gain of primary saccades made to $T_1$ was similar regardless of color (green = $0.96 ± 0.04$; red = $0.94 ± 0.05$; yellow = $0.94 ± 0.05$). Qualitatively, saccade gain during red (backward) and green (forward) adaptation trials decreased during the adaptation phase resulting in post-adaptation gains for every color that were significantly smaller than the pre-adaptation phase (post-probe green = $0.88 ± 0.04$; red = $0.87 ± 0.05$; yellow = $0.88 ± 0.03$; $p< 0.000001$, Bonferroni corrected Wilcoxon rank sum test).

Figure 4B portrays data from another horizontal backward-null intermixed color experiment (BBSN4). During the pre-adaptation phase of this experiment the mean (± SD) gain of primary saccades made to $T_1$ was similar regardless of color (green = $0.90 ± 0.03$; red = $0.89 ± 0.04$; yellow = $0.90 ± 0.04$). In contrast to the previous example (Figure 4A), saccade gain during red (backward) and green (forward) adaptation trials remained relatively constant during the adaptation phase. In post-adaptation phase, saccades made during probe trials were either not different than (post-probe green = $0.92 ± 0.05$; red = $0.90 ± 0.04$; $p > 0.016$, Bonferroni corrected Wilcoxon rank sum test) or slightly larger than those in the pre-adaptation phase (yellow = $0.92 ± 0.04$, $p = 0.0099$).

The histogram in Figure 4C provides the mean (± SD) change in gain between pre- and post-adaptation probe trials for each color across all 10 experimental sessions (Monkey BB: $n= 5$, WE: $n= 5$, BU: $n= 2$). In 6/10 (60%) experiments, saccade gain significantly decreased between pre- and post-adaptation epochs for all three colors. The histogram plot in Figure 4D summarizes the change in saccade gain between pre- and post-adaptation probe trials for each color across all 10 horizontal backward-null color experiments. In summary, the change in saccade gain was not different between colors
(p = 0.7217, Kruskal-Wallis test) and the change in gain was different than zero for each color (p< 0.05, Wilcoxon signed rank test).

**Backward-Null White Target Intermixed Experiments**

Figure 5A portrays data from a horizontal-null white target intermixed experiment (BBWTNI1). During the pre-adaptation phase of this experiment the mean (± SD) gain of primary saccades made to T$_1$ was 0.94 ± 0.04. Qualitatively, saccade gain during backward (black triangles) and forward (gray triangles) adaptation trials did not change during the adaptation phase and saccade gain during probe trials executed in the post-adaptation phase was similar to the pre-adaptation phase (post-probe gain = 0.94 ± 0.07; p = 0.7958, Bonferroni corrected Wilcoxon rank sum test).

In contrast, Figure 5B portrays data from another horizontal intermixed white target experiment (BUWTNI2) in which saccade gain changes between the pre- and post-adaptation phases. During the pre-adaptation phase of this experiment the mean (± SD) gain of primary saccades made to T$_1$ was 0.99 ± 0.02. Qualitatively, saccade gain during backward (black triangles) and forward (gray triangles) adaptation trials increased slightly during the adaptation phase resulting in a post-probe saccade gain that was larger than the pre-adaptation phase (post-probe gain = 0.95 ± 0.03; p < 0.0001, Bonferroni corrected Wilcoxon rank sum test).

The histogram in Figure 5C provides the mean (± SD) change in gain between pre- and post-adaptation probe trials across all 8 experimental sessions (Monkey BB: n= 2, WE: n= 3, BU: n= 3). In 6/8 experiments (75%) saccade gain changed between pre- and post-adaptation epochs and this change tended to be a decrease (5/8 experiments). Although there was a trend towards a decrease in saccade gain across all 8 experiments, this change was not different from zero (Figure 5D; p = 0.1094, Wilcoxon signed rank test).

**Orthogonal Intermixed Color Experiments**

Figures 6A (BBUDC4) and 6B (WEUDC4) portray data from two orthogonal intermixed color experiments in which vertical saccade amplitude significantly increased between the pre- and post-adaptation epochs for all three colors. The histogram in Figure 6C provides the mean (± SD) change in gain between pre- and post-adaptation probe trials for each color across all 9 experimental sessions (Monkey BB: n = 4, WE: n = 5). In 5/9 (56%) experiments saccade gain increased significantly between pre- and post-adaptation epochs for all three colors. Lastly, the histogram plot in Figure 6D summarizes the change in saccade gain between pre- and post-adaptation probe trials for each color across all 9 orthogonal intermixed color experiments. In brief, the change in saccade gain was not different between colors (p = 0.9569, Kruskal-Wallis test) nor were any of the changes in gain different than zero (green p-value = 0.0742; yellow p = 0.0769; red p = 0.0547; Wilcoxon signed rank test).
Horizontal (Short) Block Color Experiments

Figure 7A portrays data from a horizontal block color experiment (BBHB2). During the pre-adaptation phase of this experiment the mean (± SD) gain of primary saccades made to T₁ was similar regardless of color (green = 0.95 ± 0.05; red = 0.95 ± 0.05; yellow = 0.94 ± 0.04). Qualitatively, saccade gain during red (backward) and green (forward) adaptation trials did not change during the adaptation phase in which adaptation trials were presented in alternating blocks of ~30 trials. Furthermore, saccade gain during probe trials executed in the post-adaptation phase was not different than those in the pre-adaptation phase (post-probe green = 0.94 ± 0.04; red = 0.95 ± 0.04; yellow = 0.92 ± 0.05; p<0.016, Bonferroni corrected Wilcoxon rank sum test).

Figure 7B portrays data from another horizontal block color experiment (BUHB2). During the pre-adaptation phase of this experiment the mean (± SD) gain of primary saccades made to T₁ was similar regardless of color (green = 0.95 ± 0.02; red = 0.94 ± 0.03; yellow = 0.94 ± 0.03). In contrast to the previous example (Figure 7A), saccade gain during red (backward) and green (forward) adaptation trials increased during the adaptation phase resulting in post-adaptation probe trials that were larger than those in the pre-adaptation phase (post-probe green = 0.99 ± 0.03; red = 0.99 ± 0.03; yellow = 0.99 ± 0.04; p<0.00001, Bonferroni corrected Wilcoxon rank sum test).

The histogram in Figure 7C provides the mean (± SD) change in gain between pre- and post-adaptation probe trials for each color across all 9 experimental sessions (Monkey BB: n= 2, WE: n= 4, BU: n= 3). In 3/12 experiments (25%) saccade gain changed between pre- and post-adaptation epochs for all three colors and, as with previous examples, the change in gain was always in the same direction. Lastly, the histogram plot in Figure 7D summarizes the change in saccade gain between pre- and post-adaptation probe trials for each color across all 9 horizontal block color experiments. In brief, the change in saccade gain was not different between colors (p = 0.7662, Kruskal-Wallis test) nor were any of the changes in gain different than zero (green p-value = 0.3008; yellow p = 0.3008; red p = 0.5703; Wilcoxon signed rank test).

Horizontal Sequential (long block) Color Experiments

Figure 8A portrays data from an exemplar horizontal sequential experiment (BBHS3). The gains of saccades made to T₁ were similar regardless of color in the pre-adaptation phase of this experiment (green = 0.94 ± 0.06; red = 0.94 ± 0.05; yellow 0.92 ± 0.04). During the first adaptation block (red trials, backward adaptation), the gain of the primary saccades gradually declined such that the gain of the red probe trials that immediately followed this adaptation block was significantly smaller than the red probe trials from the pre-adaptation phase (post probe mean ± SD = 0.80 ± 0.05; p <0.0001, Bonferroni corrected Wilcoxon rank sum test). During the ensuing green (forward) adaptation block, the gain of saccades produced gradually increased such that the gain of the last 15 green adaptation trials at of this segment was qualitatively similar to that of
the pre-adaptation green probe trials (mean ± SD 1.00 ± 0.03). In fact, the gain of the
pre-adaptation probe trials for green, red, and yellow targets were not different than the
post-adaptation probe trials of that same color (post probe green = 0.95 ± 0.06, red =
0.95 ± 06, yellow = 0.96 ± 0.05; two-tailed t-test, p > 0.05, Bonferroni corrected
Wilcoxon rank sum test).

The histogram in Figure 8B provides the mean (± SD) change in gain between
pre- and post-adaptation probe trials for each color across all 8 experimental sessions
(Monkey BB: n= 3, WE: n= 5). In the majority of cases (5/8), two or more of the colors
did not change significantly between the pre- and post-adaptation phases. In the
remaining three cases (BBHS2, WEHS2, WEHS4), post-adaptation probe trials were
significantly smaller than pre-adaptation probe trials for all three colors; this is most
likely the result of incomplete recovery from the gain reduction that occurred during the
red adaptation segment. Regardless, it should be noted that the change in gain in these
three cases is in the same direction. Lastly, the histogram plot in Figure 8D summarizes
the change in saccade gain between pre- and post-adaptation probe trials for each color
across all 8 horizontal sequential experiments. In brief, the change in saccade gain was
not different between colors (p = 0.9614, Kruskal-Wallis test) nor were any of the
changes in gain different than zero (green p-value = 0.4609; yellow p = 0.5469; red p =
0.3828; Wilcoxon signed rank test).

Unlike the outcome of horizontal intermixed and blocked sessions, changes in
saccade gain were observed during the red-only and green-only adaptation phases in
sequential blocks which illustrates that each of our subjects were able to modify
saccade gain in response to large intra-saccade target displacements within the time
frame of our experiments. Figure 7D illustrates this point by plotting the gain across the
different epochs. Each session was divided into six epochs. Mean (± SD) gain during
“Pre-Adapt Probe”, “Red Probe Only”, and “Post-Adapt Probe” epochs was assessed by
averaging all probe trials within these segments regardless of color. Mean gain during
the adaptation epochs was assessed by averaging 15 adaptation trials at the end of a
particular adaptation segment. In this figure, each session is represented by a different
color and each monkey by a different symbol (BB = ●; WE = ▲). Lastly, the mean (±
SD) across all sessions for a particular epoch is represented by a grey square and
dotted line. Generally, the changes in gain observed across phases in the exemplar
session (Figure 8A) were present across all experimental sessions (Figure 8D). On
average, saccade gain: 1) decreased significantly between Pre-Adapt Probe and End
Red Adapt (p = 0.0016, Kruskal-Wallis test) epochs; 2) was maintained at this new,
however gain state throughout the Red Probe Only phase (p = 0.0021, Kruskal-Wallis
test) and; 3) returned to baseline levels by the last 15 trials of the green adaptation
phase (End Green Adapt; p = 0.1348, Kruskal-Wallis test).

**Backward- Up Intermixed Color Experiments**

The results from each of the aforementioned experiments suggest that the
adaptive control system does not use color as a contextual cue. If this is true, then error
signals provided on adaptation trials using one color should transfer to both adaptation
and probe trials that use other colors. We tested this prediction by concurrently
intermixing backward (red) and upward (green) adaptation trials during the adaptation phase of our concurrent experiments. Figure 9B shows the horizontal amplitude versus trial plots for one of these experiments in subject BB (BBBUC1). As with the previously described experiments, the horizontal amplitude of saccades during the preadaptation phase was similar between probe trials using different colors. During the adaptation phase, the horizontal amplitude of saccades decreased during adaptation trials using both red and green targets even though target displacement in the horizontal direction only occurred during red adaptation trials. This reduction in horizontal amplitude was also observed in the post-probe phase such that probe trials using red, green, and yellow targets were significantly smaller than that of comparable trials in the preadaptation phase. Finally, the percent transfer (green or yellow change in gain/red change in gain) from red to green probe trials was 92% whereas the transfer between red and yellow probe trials was 103% for this experiment.

Significant changes in horizontal saccade amplitude were seen for all three colors in all four experiments (Figure 9C). The percent transfer from red to green probe trials was 85% whereas the transfer between red to yellow probe trials was 80% across all experiments.

Figure 9B shows the vertical amplitude versus trial plots for the same experiment as Figure 9A. The vertical amplitude was similar between probe trials using different colors in the preadaptation phase. During the adaptation phase, the vertical amplitude of saccades increased (was deviated upwards) during adaptation trials using both red and green targets even though target displacement in the vertical direction only occurred during green adaptation trials. This increase in vertical amplitude was also observed in the post-probe phase such that probe trials using red, green, and yellow targets were significantly larger than that of comparable trials in the preadaptation phase. Finally, the percent transfer (red or yellow change in gain/green change in gain) from green to red probe trials was 87% whereas the transfer between green and yellow probe trials was 94% for this experiment.

Significant changes in vertical amplitude were seen in all three colors in 3 of 4 experiments (Figure 9D). The percent transfer from green to red probe trials was 79% whereas the transfer between green to yellow probe trials was 80% across all experiments.

**Initial Eye Position (Short) Block Experiments**

Previously, Tian & Zee (2010) were able to show that initial eye position (IEP) could be used to elicit differential gain states as long as backward and forward trials were presented in alternating blocks during the adaptation phase. We attempted to repeat this experiment in order to compare the magnitude of gain modifications using an external (target color) with an internal (proprioceptive) cue. Figure 10 portrays data from two exemplar IEP experiments in monkey WE (A: WEIEPB3; B: WEIEPB4). In Figure 10A, the mean (± SD) gain of primary saccades made to T1 and initiated from the up IEP (gray circles) during the pre-adaptation phase was smaller than those initiated from the down IEP (black circles; p<0.00001, Wilcoxon rank sum test). Qualitatively, gain for those saccades initiated from the up IEP (forward adaptation trials, gray triangles) increased slightly whereas saccades initiated from the down IEP (backward adaptation,
black triangles) decreased slightly. Post-adaptation probe trials were run in blocks of
~30 trials (Tian & Zee, 2010). Saccade gain during down IEP post-adaptation probe
trials were smaller than those in the pre-adaptation phase (p< 0.0001, Wilcoxon rank
sum test). Saccade gain during up IEP post-adaptation probe trials were larger than
those in the pre-adaptation phase (p< 0.0001, Wilcoxon rank sum test). This pattern
occurred in 3/9 of our experiments (Figure 10C).

In the remaining six experiments saccade gain either changed in the same
direction regardless of IEP (e.g. Figure 10B; Figure 10C, 2/9 experiments) or saccade
gain changed significantly for saccades initiated from only one of the two IEPs (Figure
10C, 4/9 experiments). The histogram in Figure 10D provides the mean (± SD) change
in gain between pre- and post-adaptation probe trials across all nine experimental
sessions (Monkey BB: n= 3, WE: n= 5, BU: n= 1). The change in gain was not different
from zero for backward adaptation (p = 0.3008, Wilcoxon signed rank test), but was
different from zero for forward adaptation contexts (asterisk, p = 0.0195, Wilcoxon
signed rank test). This type of variability within and between subjects was also reported
by Tian & Zee (2010) (see Discussion).

Discussion

Major Observations

The experiments reported here were designed to test the hypothesis that distinct
saccade gain states could be elicited using static, colored targets as the contextual cue.
In our experiments the intra-saccade target displacement during adaptation trials was
large (9° or ~50% of primary saccade amplitude) and was either along the same axis as
(Figures 2, 4, 7, 8), or orthogonal (Figure 6) to, our subjects’ primary saccades. Under
these conditions, subjects were unable to elicit distinct adaptation states based on color
regardless of whether the color cues were presented in randomly intermixed trials
(Figures 2, 6), in short (Figure 7) or long blocks (Figure 8), or when only one (red) of the
three possible color cues had an intra-saccade target displacement (Figure 4).

Furthermore, we observed near complete transfer between trials meant to reduce
horizontal amplitude (using red targets) and those trials that were meant to increase the
vertical component of the primary movement (using green targets; Figure 9). Lastly, the
behavior of our subjects during control trials using white targets (Figures 3, 5) was
qualitatively similar to that observed during color cue experiments. These observations
are consistent with those hypotheses that state that color cannot be used as a visual
cue for adaptation and are in line with prior observations made in humans (Deubel,
1995; Azadi & Harwood, 2014; Benjamin et al, in press).

A rather simple and parsimonious explanation can readily account for our
findings: adaptation is driven by the average error (visual or motor) across numerous
trials. During horizontal randomly intermixed trials (Figures 2, 3), the average error is
zero and, hence, no change in saccade gain was observed. This was true for color
context trials and white target trials. During “backward-null” trials, the target either
stepped closer to the original fixation point or remained illuminated at the original
location. The average error across trials for this condition is therefore larger than the
error during the horizontal intermixed experiments and in a direction that would normally
elicit backward adaptation. Accordingly, the saccade gain decreased (Figures 4, 5) relative to the slight (but not significant) increase in the former condition (Figures 2, 3).

For the sequential adaptation experiment (Figure 8), the target steps in the same direction on every trial. Thus, the average error is greatest in this condition, as is the change in saccade gain. Finally, Figure 9 provides a test of the simple hypothesis. When the target location is displaced either horizontally or vertically in randomly intermixed trials, the average error across trials contains a combination of both components. As predicted, saccades adapted in both dimensions.

Context Dependent Adaptation: Comparison to Previous Observations

Attempts to elicit context dependent saccadic adaptation have primarily been made using human subjects (for reviews see Pélisson et al, 2010; Herman et al, 2013, but note Tian & Zee, 2010). To the best of our knowledge, the experiments discussed in the current report were the first attempt to elicit context dependent saccade adaptation in the rhesus monkey using a visual cue of any type. Furthermore, our report improves and extends the human experiments performed by both Deubel (1995) and Azadi & Harwood (2014) in several ways: 1) Deubel made his observations in two human subjects with very few trials and only two experiments. Our dataset therefore represents a much more powerful assessment of Deubel’s preliminary observations using colored, static targets; 2) we used large intra-saccade target displacements (50% of target eccentricity) which have been successful at eliciting large gain changes in head-restrained monkey subjects (Figure 11 from Cecala & Freedman, 2009). This should have increased the likelihood of observing even a small, color dependent change in saccade gain; 3) both Deubel (1995) and Azadi & Harwood (2014) attempted to simultaneously increase and decrease saccade gain within the same axis of the primary saccade, which is much like the “horizontal intermixed” experiments in the current report (Figure 2). Our “horizontal short block” (Figure 7), “horizontal sequential” (Figure 8), “backward-null” (Figure 4), “orthogonal intermixed” (Figure 6), and “backward-up intermixed” (Figure 9) experiments represent novel tests of the stated hypotheses (see Methods) and therefore help to clarify our understanding of the adaptive mechanism underlying primate adaptation. What remains unclear is why the saccadic adaptive control system would take into account some internal and external cues (initial eye position: Alahyane & Pélisson, 2004; target flicker: Herman et al., 2009; target shape, color: Madelain et al, 2010; moving target direction and/or speed: Azadi & Harwood, 2014), but not others (target shape, color: Deubel, 1995; Bahcall & Kowler, 2000; Azadi & Harwood, 2014)?

Previous work in both humans (Alahyane & Pélisson, 2004) and monkeys (Tian & Zee, 2010) has shown that differential modifications to saccade gain can occur if different post-saccade visual errors are provided to saccades that were initiated from markedly different orbital eye positions. We were able to replicate this, albeit noisy, phenomenon using methods similar to that of Tian & Zee (2010) as a control for our color cue experiments (Figure 10). Additional studies of eye position effects in monkeys and
humans have shown that gain modifications at one eye position only partially transfer to
saccades generated from other orbital eye positions and that the amount of transfer
debut in a roughly Gaussian fashion (Haverman et al., 2011; Zimmermann & Lappe,
2011; Wulff et al., 2012). Wulff and colleagues (2012) have hypothesized that the
differential gain states observed in the aforementioned experiments could result from
eye position modulation of the adaptive control mechanism’s afferents during saccade
production. The adaptive control mechanism would thereby recognize each of these
inputs as a unique motor command to be assigned a unique gain state.

The medioposterior cerebellum (MPC), composed of the caudal fastigial nucleus and
the oculomotor vermis, has been implicated in the adaptive control of saccadic eye
movements (for reviews see Robinson & Fuchs, 2001; Iwamoto & Kaku, 2010; Prsa &
Thier, 2011). Saccade related information from the deeper layers of the superior
colliculus (dSC) is believed to be relayed to the MPC via the nucleus reticularis tegmenti
pons (NRTP). Single unit recordings from the dSC suggest that the motor command
produced in this structure: 1) specifies the amplitude and direction of a saccade (see
Gandhi & Katnani, 2011 for review); 2) is modulated by orbital eye position (van Opstal
et al., 1995; Krauzlis et al. 2000; Pare & Munoz, 2001; Campos et al., 2006) and; 3)
specifies a movement to the location of the first peripheral target (T₁), not the subject’s
actual movement, during the McLaughlin task (Quessy et al., 2010; Frens and Van
Opstal, 1997; but see Takeichi et al., 2007). Therefore, an eye position modulated
motor command meant to generate a saccade towards T₁ during the McLaughlin task
could be sent from the dSC to the cerebellar adaptive control mechanism and paired
with a particular saccade gain state (Wulff et al, 2012). This hypothesized mechanism
could account for eye position effects on gain adaptation observed in primate subjects.

Why then might some external (in this case visual) cues be able to drive context
dependent learning and not others? In our experiments, the use of chromatic cues (red,
green, or yellow visual targets) was unable to drive contextual adaptation. Chromatic
modulation of sensory activity has been observed in the dSC (White et al. 2009; White
& Munoz, 2011) and is most likely the result of inputs to these layers from V4 (Fries,
1984; Lock et al., 2003) and/or the frontal eye fields (FEF; Schall et al., 1995). However,
the chromatic visual responses of neurons in the SC show “strong sensitivity, but only
moderate selectivity, for color” (White et al., 2009) and the motor responses of
visuomotor cells may not be significantly different under the conditions used in our, and
previous, context cue experiments using color (White et al. 2009; White & Munoz, 2011;
Deubel, 1995; Azadi & Harwood, 2014). Based on these physiological observations,
and the assumption that an efference copy of the color invariant SC motor command is
provided to the cerebellar adaptive control mechanism, we would not expect target color
would be able to drive context dependent adaptation because there is not a gain field
for color in the dSC like there is for eye position.

Using human subjects, Herman and colleagues (2009) were able to elicit context
dependent adaptation using flickering (a square wave at a rate of 5 Hz) versus non-
flickering visual targets. To our knowledge no one has contrasted the effects of this
exact stimulus on the motor activity produced by single units in the deeper layers of the
SC. However, neuronal adaptation in the visual response has been observed in the superficial and deep layers of the SC to sequentially presented stimuli at time intervals similar to that used by Herman and colleagues (e.g. 1.25-59Hz, Mayo & Sommer, 2008; 0.8-20Hz, Fecteau and Munoz, 2005). Therefore, it is possible that flickering and non-flickering stimuli are represented differently within the SC and that the motor commands associated with these stimuli can be differentiated by the cerebellar adaptive control mechanism. This hypothesis can account for the context dependent learning observed in human adaptation experiments using flickering cues and can be addressed empirically with neuronal recordings in the deep layers of the SC of monkeys.

Azadi & Harwood (2014) were able to use the speed and direction (clockwise or counter-clockwise) of circularly moving targets as a contextual cue in humans. Keller et al. (1996) compared the movement fields of deep layer SC neurons of monkeys when they produced saccades to stationary targets versus when they made interceptive saccades to targets moving at either 45 or 60°/sec away from the fixation point. While their dataset was not exhaustive, these authors observed a systematic shift in the center of the movement field in the direction of target motion and a reduction in the firing rate for the optimal vector. If the SC population activity is different during motions at different speeds and directions, then the cerebellar adaptive control system could use this information to recognize two distinct “contexts” and pair these contexts with specific gains. Again, this hypothesis can be addressed empirically with single unit neuronal recordings.

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Figure 1. Delayed Probe and backward adaptation trial types and target locations. Probe (A) and adaptation (B) trials begin in the same fashion. Subjects are initially required to fixate a target ($T_0$) for a variable duration within a computer-defined window. A peripheral target ($T_1$) is then presented and the subject must maintain fixation of $T_0$ for a variable “delay period” during which $T_0$ and $T_1$ overlap. If the subject maintains fixation to the end of the delay period, then $T_0$ is extinguished, cuing the subject to produce a saccade to $T_1$. When the subject produces a saccade towards $T_1$ they will leave the computer defined window and trigger the offset of $T_1$. In probe trials, this target is never illuminated again. In backward adaptation trials, another target ($T_2$) is presented at a location between $T_0$ and $T_1$. During a forward adaptation experiment $T_2$ would be presented at a more eccentric location. Although not shown here, note that the color of the target remains constant within a trial. However, the target color may be red, green, or yellow between trials. Panels C and D illustrate the location of targets during horizontal and vertical adaptation experiments, as well as the location of the reward windows during adaptation trials. Colors correspond to those used during adaptation trials in the adaptation phase (See Materials and Methods for further details).

Figure 2. Horizontal Intermixed Color Experiments. Horizontal, primary saccade gain during the preadaptation, adaptation, and post-probe segments of experiments BBHI5 (A) and WEHI4 (B). Each symbol (circle or triangle) represents data from a single trial. Circles represent probe trials; triangles represent adaptation trials; symbol colors represent the color of the targets within a given trial. Inset portrays the direction of the primary saccade (black arrow) and the direction of the intrasaccade target displacement during red (red arrow) and green (green arrow) adaptation trials. (C) Each bar represents the change in gain between pre- and post-adaptation probe trials of a particular color (green, yellow, or red) for each of the 12 horizontal intermixed experimental sessions. Asterisk indicates a significant change in gain ($p < 0.016$, Bonferroni corrected Wilcoxon rank sum test). (D) The average change in gain ($\pm$ SD) for each color across all 12 experimental sessions. The change in gain was not different between colors ($p = 0.7527$, Kruskal-Wallis test).

Figure 3. Horizontal Intermixed White Target Experiments. Horizontal, primary saccade gain during the preadaptation, adaptation, and post-probe segments of experiments BBWTHI1 (A) and BBWTHI3 (B). Each symbol (circle or triangle) represents data from a single trial. Circles represent probe trials; triangles represent adaptation trials; during the adaptation phase, black triangles represent backward adaptation trials, whereas gray symbols represent forward adaptation trials. Inset
portrays the direction of the primary saccade (black arrow pointed to the right) and the
direction of the intrasaccade target displacement during backward (black arrow pointed
to the left) and forward (gray arrow) adaptation trials. (C) The change in gain between
pre- and post-adaptation probe trials is plotted for each of the 11 white target horizontal
intermixed experimental sessions. Asterisk indicates a significant change in gain (p<
0.016, Bonferroni corrected Wilcoxon rank sum test). (D) The average change in gain (±
SD) across all 11 experimental sessions. The change in gain was not different from zero
(p = 0.1748, Wilcoxon signed rank test).

Figure 4. Backward-Null Color Experiments. Horizontal, primary saccade gain during
the preadaptation, adaptation, and post-probe segments of experiment BBNS2 (A) and
BBSN4 (B). Symbols, colors, and inset are the same as described for figure 2. (C) Each
bar represents the change in gain between pre- and post-adaptation probe trials of a
particular color (green, yellow, or red) for each of the 10 backward-null experimental
sessions. Note: a very small positive change in gain did occur for the green and red
trials in experiment BUNS2. Asterisk indicates a significant change in gain (p< 0.016,
Bonferroni corrected Wilcoxon rank sum test). (D) The average change in gain (± SD)
for each color across all 10 experimental sessions. The change in gain was not different
between colors (p = 0.7217, Kruskal-Wallis test).

Figure 5. White Target Backward-Null Experiments. Horizontal, primary saccade
gain during the preadaptation, adaptation, and post-probe segments of experiments
BBWTN1 (A) and BUWTN2 (B). Each symbol (circle or triangle) represents data from a
single trial. Circles represent probe trials; triangles represent adaptation trials; during
the adaptation phase, black triangles represent backward adaptation trials, whereas
gray symbols represent null trials. Inset portrays the direction of the primary saccade
(black arrow pointed to the right) and the direction of the intrasaccade target
displacement during backward adaptation (black arrow pointed to the left) and null (gray
X) trials. (C) The change in gain between pre- and post-adaptation probe trials is plotted
for each of the 8 white target horizontal backward-null experimental sessions. Asterisk
indicates a significant change in gain (p< 0.016, Bonferroni corrected Wilcoxon rank
sum test). Note, the change in BBWTN1 between pre- and post-adaptation probe trials
was zero. (D) The average change in gain (± SD) across all 8 experimental sessions.
The change in gain was not different from zero (p = 0.1094, Wilcoxon signed rank test).

Figure 6. Orthogonal Intermixed Experiments. Vertical, primary saccade amplitude
during the preadaptation, adaptation, and post-probe segments of experiment BBUDC2
(A) and WEUDC4 (B). Symbols, colors, and inset are the same as described for figures
2 and 4. (C) Each bar represents the change in vertical amplitude between pre- and
post-adaptation probe trials of a particular color (green, yellow, or red) for each of the 9
backward-null experimental sessions. Asterisk indicates a significant change in
amplitude (p< 0.016, Bonferroni corrected Wilcoxon rank sum test). (D) The average
change in amplitude (± SD) for each color across all 9 experimental sessions. The
change in amplitude was not different between colors (p = 0.9569, Kruskal-Wallis test).
Figure 7. Horizontal Color Block Experiments. Horizontal, primary saccade gain during the preadaptation, adaptation, and post-probe segments of experiment BBHB2 (A) and BUHB2 (B). Symbols, colors, and inset are the same as described for figures 2, 4, 6. (C) Each bar represents the change in gain between pre- and post-adaptation probe trials of a particular color (green, yellow, or red) for each of the 9 horizontal color block experimental sessions. Asterisk indicates a significant change in gain (p< 0.016, Bonferroni corrected Wilcoxon rank sum test). Note, the change in gain between pre- and post-adaptation green probe trials in experiment WEHB3 was nearly zero. (D) The average change in gain (± SD) for each color across all 9 experimental sessions. The change in gain was not different between colors (p = 0.7662, Kruskal-Wallis test).

Figure 8. Horizontal Sequential Experiments. (A) Horizontal, primary saccade gain during the preadaptation, red and green adaptation, red probe only, and post-probe segments of experiment BBHS3. Symbols, colors, and inset are the same as described for figures 2,4,6,7. (B) Each bar represents the change in gain between pre- and post-adaptation probe trials of a particular color (green, yellow, or red) for each of the 8 horizontal color sequential experimental sessions. Asterisk indicates a significant change in gain (p< 0.016, Bonferroni corrected Wilcoxon rank sum test). Note, the change in gain between pre- and post-adaptation yellow probe trials in experiment WEHS3 was nearly zero. (C) The average change in gain (± SD) for each color across all 8 experimental sessions. The change in gain was not different between colors (p = 0.9614, Kruskal-Wallis test). (D) Saccade gain as a function of session epoch (Pre-Adapt, End Red Adapt, Red Probe Only, End Green Adapt, and Post-Probe) during all Horizontal Sequential Experiments. Circles and triangles represent data from monkeys BB and WE, respectively. Pre-, Red Only, and Post-Probe mean gain was taken from all trials in that epoch regardless of color. Gains from the adaptation phases were calculated using either the last 15 (End Red Adapt and End Green Adapt epochs) or the first 15 (Begin Green Adapt epoch) adaptation trials. Grey squares represent the grand mean (±SD) across all sessions for that epoch. Asterisk denotes a significant change in the grand mean between an epoch and the pre-adaptation phase (p< 0.01, Kruskal-Wallis test).

Figure 9. Backward-Up Intermixed Experiments. Horizontal (A) and vertical (B) primary saccade amplitude during the preadaptation, adaptation, and post-probe segments of experiment BBBUC1. A circle or triangle represents data from a single trial. Solid colored circles represent probe trials; open colored triangles represent adaptation trials; black triangles with colored borders represent recovery trials. Symbol/outline colors (red, green, or yellow) represent the color of the targets within a given trial. Inset portrays the direction of the primary saccade (black arrow), the direction of the intrasaccade target displacement during red (red arrow) and green (green arrow) adaptation trials. (C, D) Each bar represents the change in vertical (C) or horizontal (D) gain between pre- and post-adaptation probe trials for the 4 backward-up experiments. Asterisk indicates a significant change in gain (p< 0.016, Bonferroni corrected Wilcoxon rank sum test).
Figure 10. Initial Eye Position (IEP) Context Cue Experiments. Horizontal, primary saccade gain during the preadaptation, adaptation, and two post-probe segments of experiments WEIEPB3 (A) and WEIEPB4 (B). Circles represent probe trials; triangles represent adaptation trials; during the adaptation phase, black triangles represent backward adaptation trials, whereas gray triangles represent forward adaptation trials. Inset portrays the direction of the primary saccade (longer black or gray arrow pointed to the right) as well as the direction of the intra-saccade target displacement when the eyes were deviated 10 degrees downward (black, backward adaptation) or upward (gray, forward adaptation). (C) The change in gain between pre- and post-adaptation probe trials is plotted for each of the 9 IEP experimental sessions. Asterisk indicates a significant change in gain ($p < 0.016$, Bonferroni corrected Wilcoxon rank sum test). (D) The average change in gain ($\pm$ SD) across all 9 experimental sessions. The change in gain was not different from zero for backward adaptation ($p = 0.3008$, Wilcoxon signed rank test), but was different from zero for forward adaptation contexts (asterisk, $p = 0.0195$, Wilcoxon signed rank test).
A. Delayed Probe Trial

B. Delayed Adaptation Trial

C. Example Horizontal Targets

D. Example Vertical Targets
A C

Pre-Adaptation

BBH13 Adaptation Only Post-Adaptation

0 200 400 600 800 1000 1200 1400 1600

Gain

B

WEHI4

0 200 400 600 800 1000 1200 1400

Saccade Number

D

Experimental Session

BBH1 BBH2 BBH3 BBH4 BBH5 WEHI1 WEHI2 WEHI3 WEHI4 WEHI5 BUIH1 BUIH2

Change in Gain

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Change in Gain

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