

Eye position effects in saccadic adaptation in macaque monkeys

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Wulff S, Bosco A, Havermann K, Placenti G, Fattori P, Lappe M. Eye position effects in saccadic adaptation in macaque monkeys. *J Neurophysiol* 108: 2819–2826, 2012. First published August 29, 2012; doi:10.1152/jn.00212.2012.—The saccadic amplitude of humans and monkeys can be adapted using intrasaccadic target steps in the McLaughlin paradigm. It is generally believed that, as a result of a purely retinal reference frame, after adaptation of a saccade of a certain amplitude and direction, saccades of the same amplitude and direction are all adapted to the same extent, independently from the initial eye position. However, recent studies in humans have put the pure retinal coding in doubt by revealing that the initial eye position has an effect on the transfer of adaptation to saccades of different starting points. Since humans and monkeys show some species differences in adaptation, we tested the eye position dependence in monkeys. Two trained *Macaca fascicularis* performed reactive rightward saccades from five equally horizontally distributed starting positions. All saccades were made to targets with the same retinotopic motor vector. In each session, the saccades that started at one particular initial eye position, the adaptation position, were adapted to shorter amplitude, and the adaptation of the saccades starting at the other four positions was measured. The results show that saccades that started at the other positions were less adapted than saccades that started at the adaptation position. With increasing distance between the starting position of the test saccade and the adaptation position, the amplitude change of the test saccades decreased with a Gaussian profile. We conclude that gain-decreasing saccadic adaptation in macaques is specific to the initial eye position at which the adaptation has been induced.

eye position signal; motor learning; oculomotor control; saccadic adaptation

FOR AN ACTIVE EXPLORATION of the ambient scene, primates make rapid eye movements (saccades) that shift the direction of gaze from one target of interest to another. Saccades are so brief that no visual feedback is available during the saccade because latencies in the visual system are so high that feedback can be processed only after the saccade is finished. Therefore, the saccadic motor command has to be prepared in advance to accurately aim the fovea at a new target. Since the mechanical properties of the oculomotor plant can change due to growth, injury, or muscle fatigue, a fixed motor command could lead to saccadic targeting errors. For this reason, the saccadic amplitude is continuously adjusted to current requirements such that the amplitude becomes shorter if the saccade consistently overshoots the target and longer if the saccade consistently undershoots the target. This plasticity mechanism is called saccadic adaptation. It can be mimicked in the laboratory using

the McLaughlin adaptation paradigm (McLaughlin 1967) in which the saccade target is systematically displaced during execution of the saccade. Over several trials the amplitude becomes shorter in the case that the target is stepped backward and longer if the target is stepped forward along the direction of the saccade. In humans, saccadic adaptation is achieved in a few tens of trials (Albano 1996; Deubel 1987; Frens and Van Opstal 1994) whereas in monkeys a few hundred trials are needed (Deubel 1987; Straube et al. 1997). This indicates that the adaptive mechanisms differ between humans and monkeys.

Our study is concerned with the reference frame of saccadic adaptation. If adaptation takes place in an oculocentric reference frame (retina referenced), it should be specific to the retinocentric coordinates of the target and thus to the motor vector (i.e., direction and amplitude) of the adapted saccade. Indeed, many studies found that the transfer of adaptation from adapted saccades of a certain vector to saccades with different vectors is incomplete, both in humans (Albano 1996; Deubel 1987; Frens and Van Opstal 1994; Miller et al. 1981; Semmlow et al. 1989) and in monkeys (Deubel 1987; Noto et al. 1999; Straube et al. 1997).

On the other hand, if saccadic adaptation takes place in an orbito-centric reference frame (head referenced), it would be specific to the starting position of the saccade in head-centric coordinates. In other words, the initial eye position of the saccade, i.e., the eye position in the orbit, would influence the adaptation state. Early studies that investigated the impact of the initial eye position on the transfer of adaptation indicated nearly complete transfer of adaptation from an adapted saccade to saccades with the same vector but different starting position in humans (Albano 1996; Frens and Van Opstal 1994; Semmlow et al. 1989) and in monkeys (Noto et al. 1999). Thus adaptation was considered to be unspecific to the initial eye position. In consequence, the plastic modulations to the visuo-motor system were assumed to be coded in a purely retinal reference frame.

More recent studies, however, have demonstrated that interleaved amplitude adaptation in opposite directions at different positions in space, called differential adaptation, is possible in humans (Alahyane and Pelisson 2004; Shelhamer and Clendaniel 2002) and monkeys (Tian and Zee 2010). This suggests that eye position information, i.e., a signal representing the position of the eye in the orbit is available to the saccadic adaptation mechanism. To explain this discrepancy, some authors have suggested that the default of the adaptation system is to generalize the adaptation to the complete saccadic operating range (i.e., all starting positions) but that in situations that demand independent control at different starting positions

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(like in differential adaptation) the eye position information is used (Hopp and Fuchs 2004; Pelisson et al. 2010). Hence, the adaptation would only be specific to the initial eye position if at least two conflicting modifications are applied simultaneously and the eye position signal would remain unused in the normal case. However, if saccadic adaptation, for example, is needed to compensate for position-dependent dysmetria produced by a single paretic eye muscle, the grade of required change of amplitude depends on the orbital eye position and the adaptation would need to be eye position specific.

In fact, there have been recent studies revealing eye position specificity of saccadic adaptation in humans without the differential adaptation paradigm (Havermann et al. 2011; Zimmermann and Lappe 2011; Zimmermann et al. 2011). For example, in the study of Havermann et al. (2011) subjects performed reactive saccades started at five equally horizontally distributed starting positions along the horizontal median. From these different initial positions, saccades of a fixed vector were made. Thus the targets all had the same retinocentric coordinates when the subject was fixating the corresponding fixation point. In each session, the saccades starting from one selected initial eye position were adapted using the McLaughlin adaptation paradigm and then the adaptation of the saccades starting at the other four positions was measured. The adaptation magnitude in the test saccades was found to be a linear function of the distance between the start position of the test saccades and the start position of the adapted saccades. Thus the induced adaptation was not uniformly transferred to all starting position.

In the current study, we perform a similar experiment with macaque monkeys. In each session, the saccades starting in one initial eye position were adapted and the adaptation of the saccades starting at four other positions was measured. We found that the adaptation state was reduced at positions that are different from the adapted initial eye position. Additionally, the adaptation at different test positions followed a Gaussian function of the distance to the adaptation position. With these findings, we confirm that an eye position signal is employed in saccadic adaptation and we demonstrate that adaptation of reactive saccades in monkeys is not simply generalized over the complete saccadic operating range to all initial eye positions but that it is eye position specific.

MATERIALS AND METHODS

Experiments were approved by the Bioethical Committee of the University of Bologna and were performed in accordance with national laws on care and use of laboratory animals and with the European Communities Council Directive of 24th November 1986 (86/609/EEC), recently revised by the Council of Europe guidelines (Appendix A of Convention ETS 123). The head-restraint system on the head of the trained *Macaca fascicularis* was surgically implanted in asepsis and while the animals were under general anesthesia (sodium thiopental, 8 mg·kg⁻¹·h⁻¹ iv) following the procedures reported in Galletti et al. (1995). Adequate measures were taken to minimize pain or discomfort. A full program of postoperative analgesia (ketorolac trometazyn, 1 mg/kg im immediately after surgery, and 1.6 mg/kg im on the following days) and antibiotic care [Ritardomicina (benzatinic benzylpenicillin plus dihydrostreptomycin plus streptomycin) 1–1.5 ml/10 kg every 5–6 days] followed the surgery.

Recording of eye movements and stimulus presentation. During the recording sessions, signals from both eyes were recorded simultaneously with an infrared oculometer (ISCAN) at a sampling rate of 100 Hz. Before each experimental session, the monkey was required to perform a calibration task that allowed us to calibrate the signals from each eye separately. In this task, the monkey fixated sequentially 10 light emitting diodes (LEDs) that were mounted on a frontoparallel panel at a distance of 15 cm from the eyes. In front of each eye, there were five LEDs in a cross arrangement with the central one being aligned with the eye's primary position. The four peripheral LEDs were located $\pm 15^\circ$ left and right and below and above of the central one. Calibration factors for each eye were extracted from the eye traces recorded in the calibration task.

During a recording session, the monkey sat in a primate chair with its head restrained and it faced a 17-inch monitor (Acer, AL 1716 As) with a visible display size of 33,5 × 26,8 cm. The viewing distance of 32 cm from the animal's eyes to the screen resulted in a visual field of 55.3° × 45.4°. The display had a resolution of 1,280 × 1,024 pixels and a frame rate of 60 Hz. For stimuli presentation and data analysis, we used MATLAB with the psychtoolbox extension (Brainard 1997). The stimuli were green and red dots with a radius of 0.18°.

Behavioral task. In Fig. 1, the procedure of saccadic adaptation of reactive saccades is explained. The sketches in Fig. 1, A–E, show the layout of a trial in the adaptation phase of the session. During the execution of the saccade in those adaptation trials, the target is shifted to another location and thus an error signal is induced at the end of the saccade due to the misplaced saccadic landing position. Preadaptation trials to define a baseline of the saccadic amplitude and test trials to measure the amount of adaptation in each position will be explained later in detail.

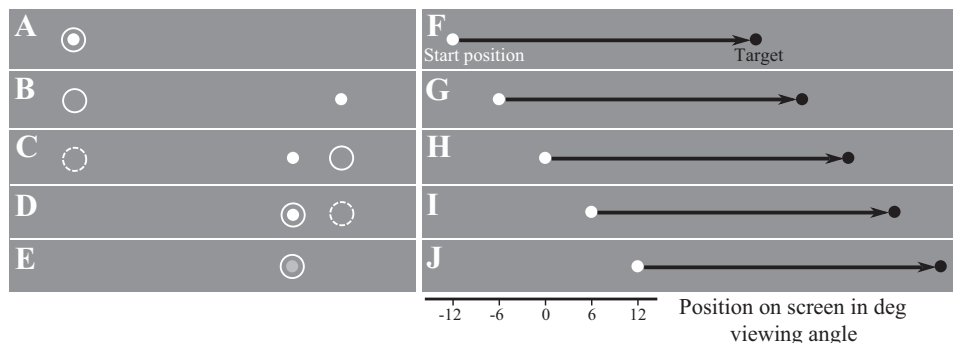


Fig. 1. Experimental procedure for adaptation of reactive saccades. *A*: at the beginning of the trial the green fixation point was presented and the monkey's gaze (circle) was directed towards it. *B*: after a randomized time the fixation point was switched off and the green target appeared. *C*: as soon as the onset of the saccade was detected, the target was shifted to the left. In consequence of the target back step, the saccade overshoot the target and thus a visual error was induced. *D*: monkey made a second saccade to land on the target. *E*: after a randomized time the target became red and the monkey released the button to get its reward. *F–J*: after the monkey pressed the button the fixation point could appear at five different positions. From all these starting positions, saccades of the same vector were initiated.

To start a new trial, the monkey had to press a button near its chest, out of his visual field, when the screen was all black. The button presses/releases were recorded by LABVIEW with 1-ms resolution. After the button press, a green fixation point was placed at one of five possible starting positions at -12° , -6° , 0° , $+6^\circ$, or $+12^\circ$ horizontal gaze direction (Fig. 1, *F–J*). All stimuli were presented along the screen horizontal line at the animal's eye level, that is with 0° vertical gaze direction. The monkey had to establish and maintain fixation at this point. The monkey's eye position was monitored online by the tracker system such that the direction of gaze had to enter and stay in a window of $4^\circ \times 4^\circ$ centered around the fixation point. After a randomized time between 1,000 and 1,500 ms the fixation point was switched off. Simultaneously, a green target appeared rightwards to the fixation point. The monkeys were trained to make a saccade towards the target as quickly as possible and to establish fixation at the green target. During the adaptation phase in every trial, the target stepped back as soon as the monkey left the window centered around the fixation point. We employed slightly different experimental layouts for the two monkeys because *monkey B* did not adapt well if a target step of 5° was presented, which we used in the sessions of *monkey A*. Thus, for *monkey A*, the target was presented 22° rightwards from the fixation point and during the saccade the target stepped back 5° . For *monkey B*, a saccade of 24° amplitude and a target back step of 2° were applied. It should be kept in mind that different target step sizes lead to different maximal achievable adaptation states in the two monkeys. However, the adaptation in relation to the applied step size is expected to be of comparable size. In the initial trials of the adaptation phase, the saccades of the monkeys landed close to the position of the first target. Due to the inward shift of the target during the saccade, a visual error was induced at the end of the saccade. This led to saccadic adaptation and thus to a decreased amplitude of the following saccades. The shifted target turned red after a randomized time between 600 and 1,000 ms. This was the signal for the monkey to release the button. If the monkey released the button within a maximum time of 1,000 ms, he was rewarded with a defined amount of water. In the case that the monkey released the button before the turning red of the target, i.e., already during the trial, or too late after the turning red, the trial was aborted, the monkey did not get any reward, and the screen turned black so that a new trial could be started by the monkey pressing the button. Trials that were aborted were discarded from the analysis.

Every session consisted of 850 completed trials. The first part of each session consisted of 100 so called preadaptation trials that did not contain a target step. The preadaptation trials were used to measure the baseline of the saccadic amplitude in every possible saccade position. Hence there were 5 blocks of 20 preadaptation trials each, 1 block at each of the 5 positions. The saccadic endpoint was determined in the offline analyses when the velocity of the saccade dropped under the threshold of one-tenth of the maximal reached velocity in that saccade.

Afterwards the adaptation phase started, in which 350 adaptation trials were performed by the monkey. During the adaptation phase, all saccades were started at the same starting point and all trials contained an inward target step that led to a decreased amplitude. A comparison between the saccade made in the first trial and the saccade made in the last trial of the adaptation phase is shown in Fig. 2, *left*. After the adaptation phase, the monkey usually had achieved a maximal amount of adaptation at the adaptation position and the amplitude of the saccades did not decrease any further but stayed constant.

After the adaptation phase ended the test phase began. It consisted of at least 20 test saccades at each of the four test positions and at the adaptation position in a randomized sequence. The test trials were used to measure the postadaptation gain (see Fig. 2, *right*) and to calculate the gain change compared with the preadaptation trials. In a test trial, the target was not stepped back when the onset of the saccade had been detected but instead it was switched off for 300 ms and then switched on again at the same initial target position. Subse-

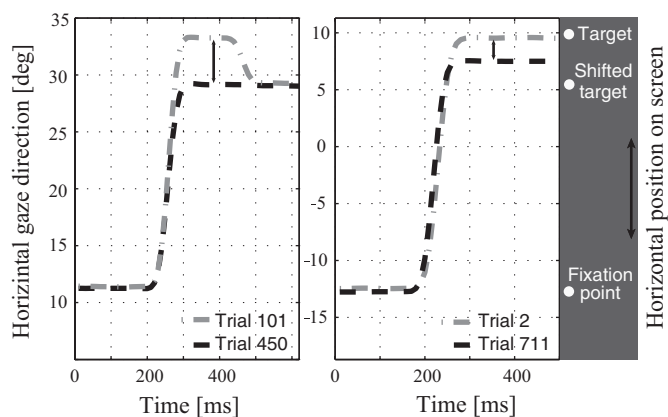


Fig. 2. Horizontal eye position during different trials in the session of *monkey A* with adaptation position $+12^\circ$. In the beginning of each trial, the monkey is fixating the presented fixation point. *Left*: shown are the trajectories of the first and the last trial of the adaptation phase. In the first trial (101), a saccade to the first target is initiated and a corrective saccade is needed to foveate the new target due to the inward target shift made during the saccade. In the last trial of the adaptation phase (450), the saccadic amplitude has been adapted and the saccade ends closely to the new target. *Right*: comparison between two trajectories which both started at test position -12° in the same session. Trial 2 is a preadaptation trial, and trial 711 is a test trial performed after the adaptation of the saccades started $+12^\circ$. Amplitude is also shortened but to a lesser extent than the saccade at the adaptation position.

quently to the reappearance of the target, it turned red after a randomized time so that the monkey could fulfill its task successfully and got rewarded. The target was switched off during the saccade to avoid that the monkey could see the target at the end of the saccade. Hence, no visual error signal was induced in the test trials. This way we tried to maintain the monkey's adaptation as complete as possible. However, to enable the monkey to accomplish the trial and to earn its reward, we needed to switch the target on after 300 ms. Subsequently to the reappearance of the target, it turned red like in the adaptation trials. The monkey then could complete the trial successfully by releasing the button. Shafer et al. (2000) showed for macaque monkeys that compared with the conventional adaptation paradigm the achieved adaptation decreases significantly if the shifted target is switched on 112 or 208 ms after the saccade end. Nevertheless, the authors pointed out that visual errors occurring even >300 ms after the saccade still can have an effect on saccadic gain adaptation (Shafer et al. 2000). Thus, to reinforce the monkey's adaptation during the test phase, the test trials were interspersed with adaptation trials at the adaptation position. Every test trial was followed by two adaptation trials. The last block of the session consisted of 100 deadadaptation trials to extinguish the monkey's adaptation.

The whole experiment consisted of five experimental sessions, which all were completed by both monkeys. Since every session consisted of 850 successful trials, each monkey ran a minimum of 4,250 trials. This led to a total number of 8,500 recorded successful trials. The analysis was based on the 2,000 recorded successful preadaptation and test trials. Experimental sessions were separated in time by at least 24 h between two sessions to be sure that no more adaptation remained from the last session in the monkeys saccadic system. In every session, the saccadic amplitude was adapted at one out of the five saccade positions and afterwards the amount of adaptation was tested at all five positions.

RESULTS

Figure 3 shows the saccadic end points that were recorded in one session of *monkey A*. The first phase of the session consists of the preadaptation trials at all five positions. These trials did not contain a target step and were used to determine the baseline

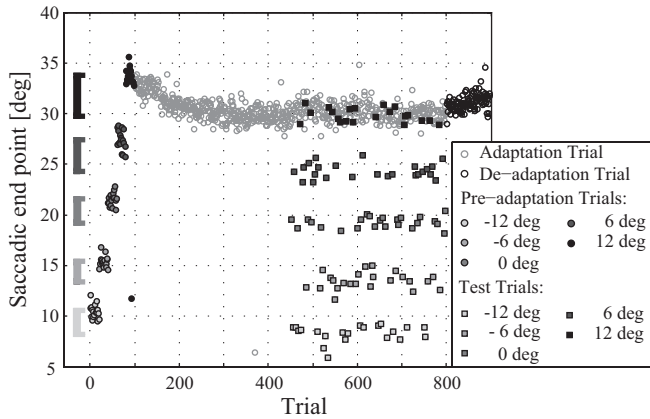


Fig. 3. Example session. Landing points of the saccades during the +12° adaptation session of *monkey A*. Saccades started at the same fixation point are presented in the same shade, and the unfilled circles represent adaptation and deadaptation trials at the position +12°. Brackets at *left* denote the change of amplitude at the 5 test positions, namely the difference of the mean preadaptation amplitude and mean postadaptation amplitude.

saccadic gain. During the following adaptation phase in this session, all adaptation saccades started at +12° and the target was stepped against the saccadic direction by 5°. After the shortening of the amplitude saturated at the end of the adaptation phase, the test phase started with *trial 451*. Test trials, to measure the postadaptation amplitude at all five positions, were interspersed with adaptation trials that were started at the adaptation of this session at +12°. In the end of each session, 100 deadaptation trials in which the target was not stepped but kept its position were performed by the monkey.

For every single session, we compared the adaptation induced at the adaptation position to the adaptation transferred to the other positions. For that purpose, the preadaptation trials were used to calculate an averaged baseline amplitude at each test position in one session including the adaptation position. The preadaptation trials, like the test trials, had five different starting positions, but the target was always presented at the same retinocentric coordinates. Thus the saccadic amplitude in the preadaptation trials did not depend on the start position. Analogously, the test trials were used to calculate the amplitude, i.e., the postadaptation gain, at each of the five positions after the adaptation.

The amount of adaptation δA_j measured in a single test trial j is given as:

$$\delta A_j = A_{pre,m} - A_{post,j}$$

with $A_{pre,m}$ being the mean preadaptation amplitude at that position and $A_{post,j}$ the postadaptation amplitude measured in one test trial. Then, the gain change achieved in one test position is given by:

$$gain\ change = (A_{post,m}) / (A_{pre,m})$$

$A_{post,m}$ is the mean of all δA_j at this position, i.e., the achieved amount of adaptation in one test position. Saccades that were shorter than 20% of the preadaptation amplitude were discarded from the analysis. This concerned <2% of all completed trials.

Figure 4 shows the adaptation of the two participating monkeys in all five sessions. The five panels correspond to the five experimental sessions. Each panel shows the adaptation of

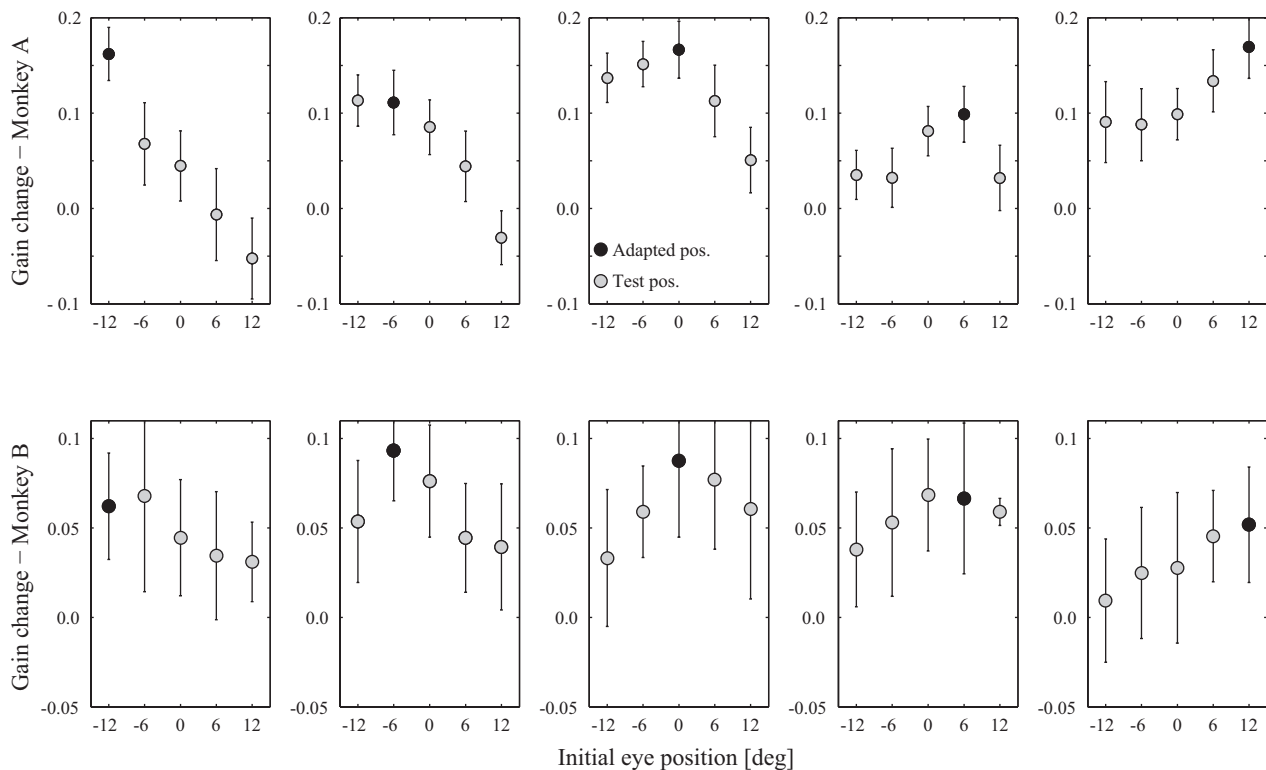


Fig. 4. Individual adaptation patterns of both monkeys of all five experimental sessions. Each panel shows the gain change and its standard deviation of all five test positions of one session in the spatial order of their appearance on the screen from -12° to +12° in steps of 6°. In each session, the adaptation was obtained for a different starting position, this adaptation position is indicated by the filled circles. Total adaptation states of *monkey A* and *monkey B* differ because of the different target step sizes of 5° and 2°, respectively.

all five test positions of one session. The position on the x -axis in every panel corresponds to the initial eye position of the test saccade in the session. The outermost circle on the left in every panel depicts the adaptation of the saccades starting at -12° , and the circle on the right depicts the adaptation of the saccades starting at $+12^\circ$. The adaptation position of the displayed session is indicated by the filled black circle.

The adaptation patterns show that the amplitude of the saccades in the test positions are adapted but to a lesser extent than in the saccades at the adaptation position. In addition, the adaptation decreased with increasing distance of the test position to the adaptation position. A two-factor repeated-measures ANOVA on the adaptation ΔA data measured in all test trials with both monkeys showed a significant interaction of the two factors adaptation position and test position at a significance level of $P < 0.05$ [$F(16,16) = 3.18$; $P = 0.01$]. This confirmed the existence of an eye position effect in the adaptation of reactive saccades.

The averaged results of both monkeys are presented in Fig. 5. For each monkey, the gain change in every test position was normalized to the gain change that was achieved at the adaptation position in the corresponding session. Thus the data points corresponding to the four test positions now directly indicate the loss of adaptation at one test position compared with the adaptation that was achieved at the adaptation position. The resulting adaptation patterns were fit with Gaussian functions, which are also presented in the charts. The Gaussian shape of the transfer profile indicates that the transferred adaptation is a symmetric function of the distance between the initial eye positions of the adaptation saccade and the test saccade, no matter if the centrality of the test position in the visual field increases or decreases with respect to the adaptation position.

We thus conclude that for reactive saccades in monkeys the amount of adaptation, which is transferred from an adapted saccade with a constant retinal vector and a fixed starting position to a saccade of the same retinal vector but with a different starting position, is a function of the distance of the starting points of the two saccades. Thus the initial eye position of a reactive saccade affects the attained adaptation at other spatial positions. Saccadic adaptation is specific to the initial eye position.

DISCUSSION

Our study is the first study in monkeys that systematically adapted saccadic amplitude at one single starting position and tested the degree to which the adaptation was transferred to other starting positions. In the only other study that included transfer between eye positions, monkeys adapted saccades from various intermixed starting positions in one hemifield and afterwards performed saccades from similarly intermixed starting positions in the other hemifield. The authors found almost complete transfer of adaptation to the unadapted hemifield (Noto et al. 1999, Fig. 8). Tian and Zee (2010), on the other hand, showed that eye position can be employed as a context cue in saccadic adaptation in monkeys if differential adaptation is exerted. The seemingly opposite findings of these two studies can be reconciled if one assumes that simultaneous adaptation from different starting position leads to a generalization to other starting positions while differential adaptation at different starting positions leads to specificity of adaptation to the respective starting position (Hopp and Fuchs 2004; Pelisson et al. 2010).

In our study, the monkeys adapted at only one starting position. This is a neutral experimental setting that neither favors generalization nor differentiation. The results show clearly that the eye position signal is part of the adaptation process.

Comparison with studies in humans. In humans, early studies saw no eye position influence (Albano 1996; Frens and Van Opstal 1994; Semmlow et al. 1989), but later studies found eye position specificity in the differential adaptation paradigm (Alahyane and Pelisson 2004; Shelhamer and Clendaniel 2002). More recently, a dependence of adaptation transfer on initial eye position was described. (Havermann et al. 2011; Zimmermann and Lappe 2011; Zimmermann et al. 2011).

The results of Havermann et al. (2011) revealed a possible explanation for the complete transfer of adaptation between several different initial eye positions that was found in earlier studies (Albano 1996; Frens and Van Opstal 1994; Semmlow et al. 1989). The initial eye position influenced the transfer of adaptation strongly if the initial eye position of the adapted saccade was placed in the peripheral visual field. In the case of adaptation at initial eye positions in the central visual field (which the earlier studies had tested), the gain change was transferred completely to peripheral, initial eye positions.

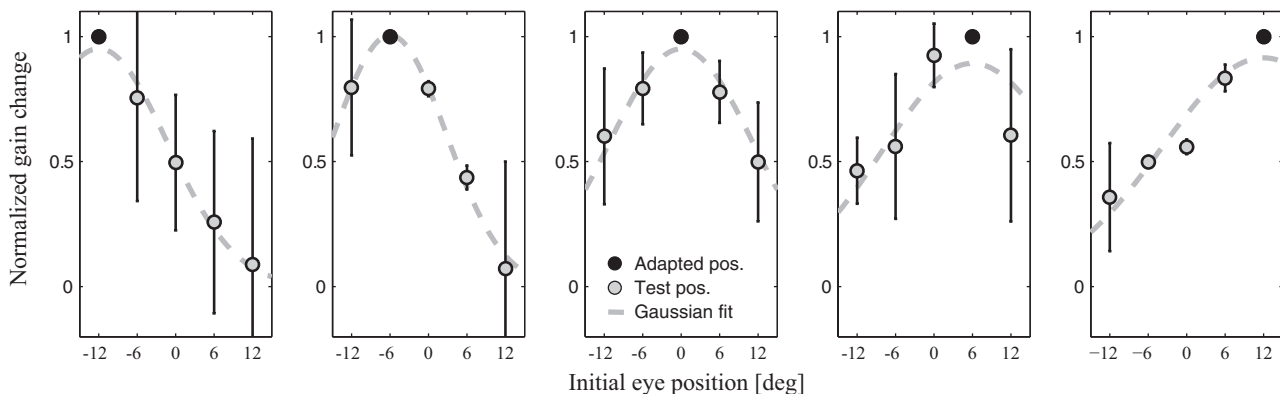


Fig. 5. Averaged results of *monkey A* and *monkey B*. Circles show the mean normalized gain change in each test position of every session together with SD. Adaptation position of the displayed session is again indicated by the filled circle. Data have been fitted with a Gaussian function. Width of the Gaussian fits: $\sigma_{-12^\circ} = 10.7^\circ$, $\sigma_{-6^\circ} = 8.9^\circ$, $\sigma_{0^\circ} = 11.8^\circ$, $\sigma_{6^\circ} = 14.3^\circ$, $\sigma_{12^\circ} = 15.9^\circ$.

However, in our data, even adaptation at the central eye position transferred only partially to other eye positions. Moreover, the observed transfer profile in monkeys differs from that in humans. In humans, the transfer profile was linear for all adaptation positions with a slope close to zero for central adaptation positions and steeper slopes for more peripheral adaptation positions. In contrast, our data show a Gaussian shaped transfer profile with a peak at the respective adaptation position for all five adaptation positions.

Since the adaptation performance in humans and monkeys also differs in other aspects, it is likely that the adaptation circuitries in the two species is not identical. Havermann et al. (2011) have proposed an explanation for their data in terms of eye position gain fields. With modifications, this explanation may also work for monkeys, as detailed below.

A possible neural mechanism for different eye position dependencies of adaptation in humans and monkeys. In many areas of the oculomotor pathways, such as the superior colliculus (SC), the frontal eye field, or the lateral intraparietal area neurons discharge in association with a certain range of saccadic vectors, i.e., encode target information in a retinocentric reference frame. However, their discharge rate is modulated by eye position gain fields (Andersen and Mountcastle 1983; Zipser and Andersen 1988; Campos et al. 2006; Van Opstal et al. 1995; Cassanello and Ferrera 2007). This means that the activity of cells that fire before an upcoming saccade is modulated by the position of the eye in the orbit. The modulation varies monotonically with the initial eye position. Pouget and Sejnowski (1997) approximated the response of such a neuron by the product of a Gaussian function of retinal location and a sigmoid function of eye position. They proposed to use the receptive fields of such neurons as a set of nonlinear basis functions for a sensorimotor transformation. Accordingly, a combination of retinocentric encoding with eye position modulation can form a population code that creates a head-centric representation. Moreover, the same population can support both retinocentric and head-centric representations depending on the readout (Pouget and Sejnowski 1997).

An eye position modulation of the cell response has also been described for some single neurons in the fastigial nucleus (Fuchs et al. 1993), the NRTP (Crandall and Keller 1985), area V3A (Galletti and Battaglini 1989), and area V6A (Galletti et al. 1995). Although such eye position modulations have not been described in the cerebellum, which plays a prominent role in adaptation (Catz et al. 2008; Golla et al. 2008; Inaba et al. 2003; Optican and Robinson 1980), the input, which is projected to the cerebellum, originates from parts of the saccadic circuitry, that commonly show eye position modulation. For example, saccades evoked by microstimulation in the SC are modulated by the initial eye position (Groh 2011). Hence, the signal representing the initial eye position affects also directly the readout of the SC and, consequently, the input to the cerebellum.

Figure 6A shows the input composition to the adaptive circuitry in the cerebellum proposed by Havermann et al. (2011) to account for the linear transfer of adaptation to other eye positions in humans. Layer I symbolizes a population of neurons with different retinocentric receptive fields and eye position gain fields. All cells of this population directly project to the adaptive circuitry. At each retinocentric receptive field position, neuronal subpopulations exist that fire more strongly

for starting positions on the left than on the right and vice versa as a result of the gain field modulation. The subpopulation that shows a strong response for saccades starting on the right side contributes strongly to the saccadic drive if the initial eye position is on the right. The model then assumes that neurons with a strong response induce strong adaptation. Hence, if saccades starting from the right are adapted, only the inputs from the right preferring subpopulation will be adapted and saccades starting from the left will remain unadapted. Figure 6B shows how the linear transfer profile in humans may arise from a retinocentric reference frame with such an eye-position-dependent modulation.

Figure 6D shows a different composition of the input to the cerebellum. The additional layer II constructs a head-centric target representation from the collective responses of layer I (Pouget and Sejnowski 1997). Thus, for every head-centric target location there is one subpopulation in layer II, which shows a peaked response for this target location (Fig. 6, E and F). If adaptational modification is only applied for active inputs into the adaptive circuitry, the adaptation state would decrease with decreasing firing rate of the adapted subpopulation. Therefore, the head-centric target representation in layer II explains the Gaussian shape of the adaptation transfer profile that is observed in the monkey data.

In Fig. 6D, the head-centric encoding is represented by a specialized layer II of head-centric neurons. Such head-centric neurons have been found in the parietal cortex of monkeys (Galletti et al. 1993; Bremmer et al. 1998). However, following the basis function model of Pouget and Sejnowski (1997) such an explicit representation is not always necessary. Instead, the appropriate input combination might be directly fed into the adaptive circuitry, circumventing a specialized head-centric layer.

Trade-off between head-centric and retinocentric encoding for combined eye-head movements. The basis function representation contains the target information in multiple reference frames simultaneously. Thus the target information could be provided to the adaptive circuitry in different encodings at the same time. Hence, there might also be units in layer II that react similarly to the neurons in layer I and thus might lead to a linear transfer profile. This would allow the system to use either reference frame depending on the size of the saccade.

In our study, the monkeys performed saccades with an amplitude of 22°, whereas in the study of Havermann et al. (2011) amplitudes of 7° were used. Gaze shifts are usually a combination of movements of the head and the eyes (Guitton 1992; Freedman and Sparks 1997; Stahl 1999). The head movement amplitude in such an eye-head saccade is related to the deflection angle of the eye that would result if the head was not participating in the movement. Gaze shifts ending in a central region of the visual field do not involve any head movements. Hence, it is sufficient and economical that these shifts are coded retinocentrically with an additional considered eye position signal instead of a head centered encoding. In the case of larger gaze shifts, the participation of the head movement in the shift requires the coding of the gaze movement in a head-centric reference frame. Since our setup employs larger amplitudes than the setup of Havermann et al. (2011), higher deflection angles of the eye would occur in the case of pure eye saccades that lead to a larger contribution of the head to the total gaze shift. Therefore,

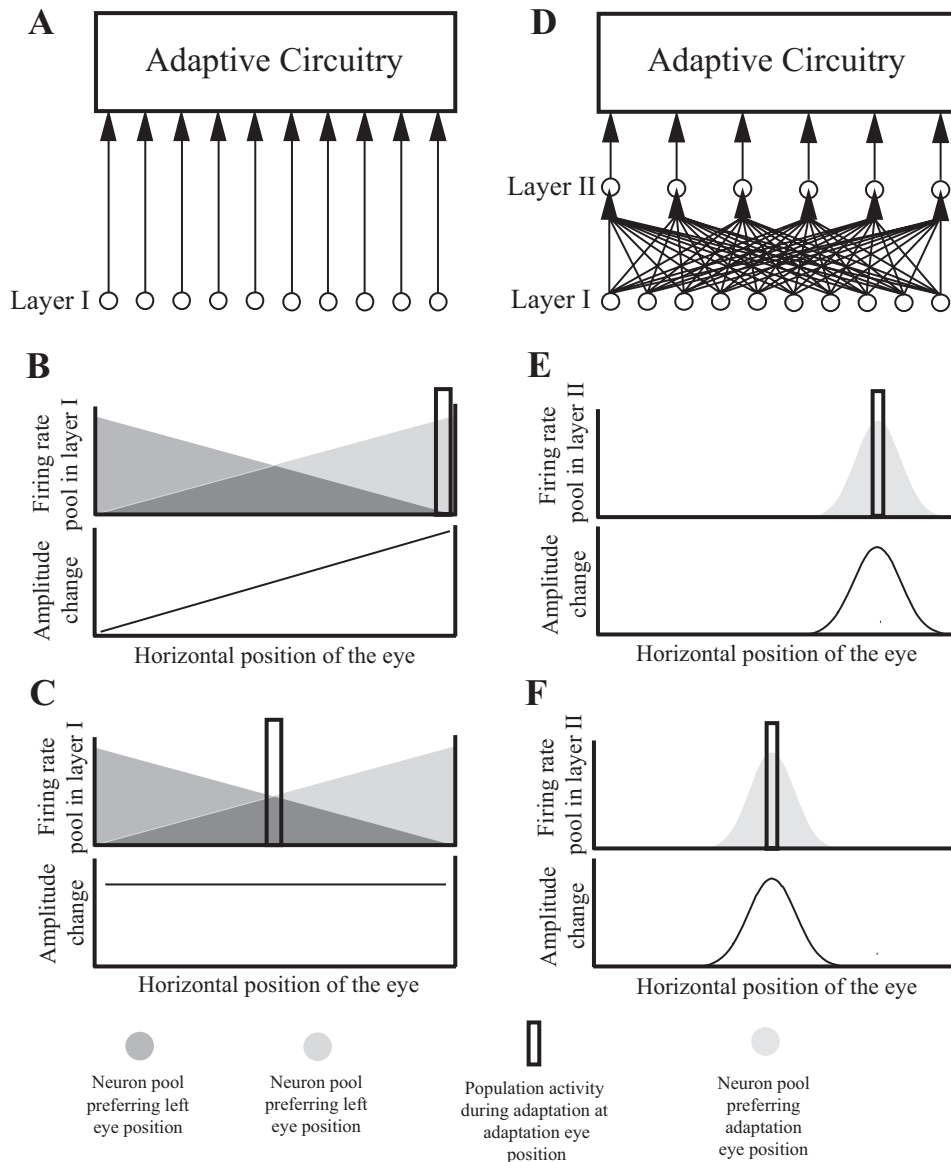


Fig. 6. Possible neural mechanism of the eye position specificity in saccadic adaptation in humans and monkeys showing how the eye position specificity of adaptation might be rooted in the composition of the input to the adaptive circuitry. *A–C*: based on Havermann et al. (2011): In this model, the linear transfer of adaptation to different initial eye positions in humans arises from gain field modulation. *A*: layer I consists of neurons with different retinocentric receptive fields and eye position specific gain modulation. *B*: at each receptive field position subpopulation exist with different gain field preferences (e.g., left vs. right eye positions). The subpopulation that prefers the current initial eye position provides the main part of the input to the circuitry and thus, drives the adaptation. After successful adaptation, a shift of the initial eye position to the side, which is preferred by this neuron pool, leads to a higher firing rate of this pool and thus leads to an increased amplitude modulation. In contrast, a shift of the eye position to the other direction leads to a decreased firing rate of that pool and thus to a decreased amplitude change. *C*: if the adapted saccade is started at a central position, two subpopulations, one preferring right and one preferring left initial eye positions, contribute to the amplitude modulation. For test saccades with initial eye positions deviating from the adapted one, the increase and decrease in firing rates of the 2 subpopulations compensate each other. This leads to the complete transfer of adaptation after adaptation at central eye positions that is found in human data. *D–F*: sketch of an extended model of the eye position specificity of saccadic adaptation to account for the Gaussian shaped transfer function. *D*: layer I consists of the same neurons described in *A*. Retinocentric receptive fields with an eye position specific gain modulation form a set of nonlinear basis functions (Pouget and Sejnowski 1997). Units in the additional layer II use this set to constitute receptive fields that code the target information in head-centric space. *E*: during adaptation at one position, one subpopulation provides the main input to the adaptive circuitry and other subpopulations are silent. *F*: if the initial eye position is changed now to either of the two directions, the firing rate of the subpopulation that has driven the adaptation falls and another (nonadapted) subpopulation drives the saccade.

the gaze shift needs to be expressed in head-centric coordinates. The input provided by units with a head-centric receptive field to the adaptive circuitry could gain a higher weight than the input from units with retinocentric receptive fields. A peaked adaptation transfer profile would be the consequence, like the Gaussian shaped profile that we found in the monkey data. In contrast, the amplitude size employed

by Havermann et al. (2011) does not demand a head centered coding since only eye movements are expected to take part in the gaze shift. Therefore, a higher weight would be given to the input provided by units with retinocentric receptive fields and eye position modulation. In agreement with the results of their human studies, this leads to the flat adaptation transfer profiles across different initial eye positions.

To conclude, we have shown that saccadic adaptation in monkeys is eye position specific. The specificity can be explained by employing cells with retinocentric receptive fields and an eye position modulation. The peaked adaptation transfer profile differs from the previously found linear transfer profile in humans. This difference might be due to differences in the adaptive circuitry between the species or it can be caused by amplitude dependent selection of one of several simultaneously provided representations of the target position in different reference frames.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: S.W., K.H., P.F., and M.L. conception and design of research; S.W., A.B., and G.P. performed experiments; S.W., A.B., and G.P. analyzed data; S.W., A.B., P.F., and M.L. interpreted results of experiments; S.W. prepared figures; S.W. drafted manuscript; S.W., A.B., P.F., and M.L. edited and revised manuscript; S.W., A.B., P.F., and M.L. approved final version of manuscript.

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